
# Review of the National Ambient Air Quality Standards for Ozone:

## Policy Assessment of Scientific and Technical Information

## OAQPS Staff Paper – Second Draft

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Office of Air Quality Planning and Standards
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**DISCLAIMER**

This document has been reviewed by the Office of Air Quality Planning and Standards (OAQPS), U.S. Environmental Protection Agency (EPA), and approved for publication. This second draft OAQPS Staff Paper contains the initial conclusions of the staff of the OAQPS and does not necessarily represent those of the EPA. Mention of trade names or commercial products is not intended to constitute endorsement or recommendation for use.

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# 1. INTRODUCTION

## 1.1 PURPOSE

This second draft Staff Paper, prepared by staff in the U.S. Environmental Protection Agency's (EPA) Office of Air Quality Planning and Standards (OAQPS), evaluates the policy implications of the key studies and scientific information contained in the final document, *Air Quality Criteria for Ozone and Related Photochemical Oxidants* (USEPA, 2006; henceforth referred to as the CD), prepared by EPA's National Center for Environmental Assessment (NCEA). This second draft Staff Paper also presents and interprets results from several analyses (e.g., air quality analyses, human exposure analyses, and human health risk assessments) and discusses an environmental assessment of vegetation-related impacts. We believe that these analyses should be considered in EPA's current review of the national ambient air quality standards (NAAQS) for ozone ($O_3$). This second draft Staff Paper presents conclusions and identifies options that the we believe are appropriate for the Administrator to consider concerning whether, and if so how, to revise the primary (health-based) and secondary (welfare-based) $O_3$ NAAQS.

The policy assessment to be presented in the final version of this draft Staff Paper is intended to help "bridge the gap" between the scientific assessment contained in the CD and the judgments required of the EPA Administrator in determining whether it is appropriate to revise the NAAQS for $O_3$. Emphasis will be placed on identifying those conclusions and uncertainties in the available scientific literature that the staff believes should be considered in selecting an indicator, averaging times, forms[1], and levels for the primary (health-based) and secondary (welfare-based) standards, which must be considered collectively in evaluating the health and welfare protection afforded by $O_3$ standards. The final Staff Paper will evaluate the policy implications of the key studies and scientific information contained in the CD, identify the critical elements that EPA believes should be considered in the current review of the NAAQS for $O_3$, and present factors relevant to the evaluation of current primary and secondary $O_3$ NAAQS, as well as conclusions and identification of options for the Administrator to consider.

This second draft Staff Paper is being provided to CASAC and the public for review at a meeting planned for August 24-25, 2006. Following that meeting, we will complete revision of the human exposure analyses, health risk assessment and environmental assessment of

[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.

vegetation-related impacts. Taking into account these revised analyses and CASAC and public comments, we will prepare a final Staff Paper, based on the CD, and will make that final document available to CASAC and the public in early Fall 2006.

While this draft Staff Paper should be of use to all parties interested in the $O_3$ NAAQS review, it is written with an expectation that the reader has some familiarity with the technical discussions contained in the CD.

## 1.2 BACKGROUND

### 1.2.1 Legislative Requirements

Two sections of the Clean Air Act (Act) govern the establishment and revision of the NAAQS. Section 108 (42 U.S.C. 7408) directs the Administrator to identify and list "air pollutants" that "in his judgment, may reasonably be anticipated to endanger public health and welfare" and whose "presence . . . in the ambient air results from numerous or diverse mobile or stationary sources" and, if listed, to issue air quality criteria for them. These air quality criteria are intended to "accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health or welfare which may be expected from the presence of [a] pollutant in ambient air . . . ."

Section 109 (42 U.S.C. 7409) directs the Administrator to propose and promulgate "primary" and "secondary" NAAQS for pollutants identified under section 108. Section 109(b)(1) defines a primary standard as one "the attainment and maintenance of which in the judgment of the Administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health."[2] A secondary standard, as defined in Section 109(b)(2), must "specify a level of air quality the attainment and maintenance of which, in the judgment of the Administrator, based on such criteria, is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of [the] pollutant in the ambient air."[3]

In setting standards that are "requisite" to protect public health and welfare, as provided in section 109(b), EPA's task is to establish standards that are neither more nor less stringent

[2] The legislative history of section 109 indicates that a primary standard is to be set at "the maximum permissible ambient air level . . . which will protect the health of any [sensitive] group of the population," and that for this purpose "reference should be made to a representative sample of persons comprising the sensitive group rather than to a single person in such a group". [S. Rep. No. 91-1196, 91st Cong., 2d Sess. 10 (1970)].

[3] Welfare effects as defined in section 302(h) [42 U.S.C. 7602(h)] include, but are not limited to, "effects on soils, water, crops, vegetation, man-made materials, animals, wildlife, weather, visibility and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and on personal comfort and well-being."

than necessary for these purposes. In so doing, EPA may not consider the costs of implementing the standards. See generally *Whitman v. American Trucking Associations*, 531 U.S. 457, 464, 475-76 (2001).

The requirement that primary standards include an adequate margin of safety was intended to address uncertainties associated with inconclusive scientific and technical information available at the time of standard setting. It was also intended to provide a reasonable degree of protection against hazards that research has not yet identified. *Lead Industries Association v. EPA*, 647 F.2d 1130, 1154 (D.C. Cir 1980), cert. denied, 101 S. Ct. 621 (1980); *American Petroleum Institute v. Costle*, 665 F.2d 1176, 1186 (D.C. Cir. 1981), cert. denied, 102 S.Ct. 1737 (1982). Both kinds of uncertainties are components of the risk associated with pollution at levels below those at which human health effects can be said to occur with reasonable scientific certainty. Thus, in selecting primary standards that include an adequate margin of safety, the Administrator is seeking not only to prevent pollution levels that have been demonstrated to be harmful but also to prevent lower pollutant levels that may pose an unacceptable risk of harm, even if the risk is not precisely identified as to nature or degree.

In selecting a margin of safety, the EPA considers such factors as the nature and severity of the health effects, the size of the sensitive population(s) at risk, and the kind and degree of the uncertainties that must be addressed. The selection of any particular approach to providing an adequate margin of safety is a policy choice left specifically to the Administrator's judgment. *Lead Industries Association v. EPA*, supra, 647 F.2d at 1161-62.

Section 109(d)(1) of the Act requires that "not later than December 31, 1980, and at 5-year intervals thereafter, the Administrator shall complete a thorough review of the criteria published under section 108 and the national ambient air quality standards . . . and shall make such revisions in such criteria and standards and promulgate such new standards as may be appropriate . . . ." Section 109(d)(2) requires that an independent scientific review committee "shall complete a review of the criteria . . . and the national primary and secondary ambient air quality standards . . . and shall recommend to the Administrator any new . . . standards and revisions of existing criteria and standards as may be appropriate . . . ." Since the early 1980's, this independent review function has been performed by the Clean Air Scientific Advisory Committee (CASAC), a standing committee of EPA's Science Advisory Board.

### 1.2.2 History of Ozone NAAQS Reviews

Tropospheric (ground-level) $O_3$ is formed from biogenic precursor emissions and as a result of anthropogenic precursor emissions. Naturally occurring $O_3$ in the troposphere can result from biogenic organic precursors reacting with naturally occurring nitrogen oxides ($NO_x$) and by stratospheric $O_3$ intrusion into the troposphere. Anthropogenic precursors of $O_3$, specifically

$NO_x$ and volatile organic compounds (VOC), originate from a wide variety of stationary and mobile sources. Ambient $O_3$ concentrations produced by these emissions are directly affected by temperature, solar radiation, wind speed and other meteorological factors.

The EPA initially established primary and secondary NAAQS for photochemical oxidants on April 30, 1971 (36 FR 8186). Both primary and secondary standards were set at an hourly average of 0.08 parts per million (ppm), total photochemical oxidants, not to be exceeded more than one hour per year.

On February 8, 1979, EPA completed its first periodic review of the criteria and standards for $O_3$ and other photochemical oxidants (44 FR 8202). In that action, EPA made significant revisions to the original standard: the level of the primary and secondary NAAQS was changed to 0.12 ppm; the indicator was changed to $O_3$; and the form of the standards was changed to be based on the expected number of days per calendar year with a maximum hourly average concentration above 0.12 ppm (i.e., attainment of the standard occurs when that number is equal to or less than one).

On March 9, 1993, EPA concluded its second periodic review of the criteria and standards for $O_3$ by deciding that revisions to the $O_3$ NAAQS were not warranted at that time (58 FR 13008). The timing of this decision was required by a court order issued to resolve a lawsuit filed to compel EPA to complete its review of the criteria and standards for $O_3$ in accordance with the Act. This decision reflected EPA's review of relevant scientific and other information assembled since the last review, as contained in the 1986 $O_3$ CD (USEPA, 1986), its Supplement (USEPA, 1992) and the 1989 $O_3$ Staff Paper (USEPA, 1989), although it did not take into consideration a large number of studies on the health and welfare effects of $O_3$ published since the literature was last assessed in the $O_3$ Supplement. The final decision emphasized the Administrator's intention to proceed as rapidly as possible with the next periodic review of the air quality criteria and standards to consider the more recent information.

Under a court-ordered schedule and a highly accelerated review process, EPA completed its third review of the $O_3$ NAAQS on July 18, 1997, based on the 1996 $O_3$ CD (USEPA, 1996a) and 1996 $O_3$ Staff Paper (USEPA, 1996b). EPA revised the primary and secondary $O_3$ standards on the basis of the then latest scientific evidence linking exposures to ambient $O_3$ to adverse health and welfare effects at levels allowed by the 1-hr average standards (62 FR 38856). The $O_3$ standards were revised by replacing the existing primary 1-hr average standard with an 8-hr average $O_3$ standard set at a level of 0.08 ppm. The form of the primary standard was changed to the annual fourth-highest daily maximum 8-hr average concentration, averaged over three years. The secondary $O_3$ standard was changed by making it identical in all respects to the revised primary standard.

### 1.2.3 Litigation Related to the 1997 Ozone Standards

Following promulgation of the revised $O_3$ NAAQS, petitions for review were filed addressing a broad range of issues. On May 14, 1999, in response to those challenges, the U.S. Court of Appeals for the District of Columbia Circuit (D.C. Circuit) remanded the $O_3$ NAAQS to EPA, finding that section 109 of the Act, as interpreted by EPA, effected an unconstitutional delegation of legislative authority.[5] In addition, the D.C. Circuit Court directed that EPA should consider the potential beneficial health effects of $O_3$ pollution in shielding the public from the effects of solar ultraviolet (UV) radiation, as well as the adverse health effects.

EPA petitioned the U.S. Supreme Court for certiorari on the constitutional issue but did not request review of the D.C. Circuit ruling regarding its obligation to consider the potential beneficial health effects of $O_3$. On February 27, 2001, the U.S. Supreme Court unanimously reversed the judgment of the D.C. Circuit on the constitutional issue, holding that section 109 of the CAA does not delegate legislative power to the EPA in contravention of the Constitution, and remanded the case to the D.C. Circuit Court to consider those challenges to the $O_3$ NAAQS that had not been addressed by that Court's earlier decisions.[6] On March 26, 2002, the D.C. Circuit Court issued its final decision, finding the 1997 $O_3$ NAAQS to be "neither arbitrary nor capricious," and denying the remaining petitions for review.[7]

In response to the D.C. Circuit's remand to consider the potential beneficial health effects of $O_3$ pollution in shielding the public from the effects of solar (UV) radiation, On November 14, 2001, EPA proposed to leave the 1997 8-hr NAAQS unchanged (66 FR 52768). After considering public comment on the proposed decision, EPA reaffirmed the 8-hr $O_3$ NAAQS set in 1997 (68 FR 614). Finally, on April 30, 2004, EPA announced the decision to make the 1-hr $O_3$ NAAQS no longer applicable to areas one year after the effective date of the designation of those areas for the 8-hr NAAQS (69 FR 23966). For most areas the date that the 1-hr NAAQS no longer applied was June 15, 2005. (See 40 CFR 50.9 for details.)

### 1.2.4 Current Ozone NAAQS Review

EPA initiated the current NAAQS review in September 2000 with a call for information (65 FR 57810). A project work plan (USEPA, 2002) for the preparation of the CD was released in November 2002 for CASAC and public review. EPA held a series of workshops in mid-2003 on several draft chapters of the CD to obtain broad input from the relevant scientific

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[5] *American Trucking Associations v. EPA*, 175 F.3d 1027 (D.C. Cir., 1999)

[6] *Whitman v. American Trucking Associations*, 531 U.S. 457 (2001)

[7] *American Trucking Associations v. EPA*, 283 F.3d 355, (D.C. Cir. 2002)

communities. These workshops helped to inform the preparation of the first draft CD (EPA, 2005a), which was released for CASAC and public review on January 31, 2005.

During the process of preparing the first draft CD, NCEA revised the planned format of the CD described in the 2002 work plan. These revisions were made as part of a collaborative effort with OAQPS staff to modify the review process so as to enhance the Agency's ability to meet this and future NAAQS review schedules. As described in Chapter 1 of the first draft CD, emphasis is placed on interpretative evaluation and integration of evidence in the main body of the document, with more detailed descriptions of individual studies being provided in a series of accompanying annexes. This change is intended to streamline the document so as to facilitate timely CASAC and public review and to focus more clearly on issues most relevant to the policy decisions to be made by the Administrator. The modified review process envisions that key policy-relevant issues will be identified earlier in the review process through enhanced collaboration between NCEA and OAQPS, leading to a more efficient linkage between the CD and the Staff Paper. At the CASAC meeting held on May 4-5, 2005, to review the first draft CD, this new format for the CD was met with general approval of CASAC and the public. A second draft CD (EPA, 2005b) was released for CASAC and public review on August 31, 2005, and the final CD was released in March 2006. In a June 8, 2006 letter to the Administrator, CASAC offered additional advice to the Agency concerning Chapter 8 of the final CD (Integrative Synthesis) to help inform this second draft Staff Paper (Henderson, 2006).

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The schedule for completion of this review is governed by a consent decree resolving a lawsuit filed in March 2003 by a group of plaintiffs representing national environmental organizations, alleging that EPA had failed to complete the current review within the period provided by statute. *American Lung Association v. Whitman* (No. 1:03CV00778, D.D.C. 2003). The modified consent decree that now governs this review, entered by the court on December 16, 2004, provides that EPA will sign for publication notices of proposed and final rulemaking concerning its review of the $O_3$ NAAQS no later than March 28, 2007 and December 19, 2007, respectively. A series of interim target dates are designed to ensure that these deadlines will be met, including release of a second draft Staff Paper by July 2006, followed by CASAC and public review by August 2006, with completion of a final Staff Paper by early Fall 2006.

## 1.3 GENERAL APPROACH AND ORGANIZATION OF THE DOCUMENT

The policy assessment in this second draft Staff Paper is based on staff's evaluation of the policy implications of the scientific evidence contained in the CD and results of quantitative analyses based on that evidence. Taken together, this information informs conclusions and identification of options on certain elements of the $O_3$ standards under review. While the CD

focuses on new scientific information available since the last review, it appropriately integrates that information with scientific criteria from previous reviews. The quantitative analyses presented in this second draft Staff Paper (and described in more detail in technical support documents) are based on the most recently available air quality information, so as to provide current characterizations of $O_3$ air quality patterns and estimated health and environmental risks related to exposure to ambient $O_3$ concentrations.

Following this introductory chapter, this draft Staff Paper is organized into three main parts: the characterization of ambient $O_3$ air quality data; $O_3$-related health effects and primary $O_3$ NAAQS; and $O_3$-related welfare effects and secondary $O_3$ NAAQS. The content of these parts is discussed more fully below.

The characterization of ambient $O_3$ and related photochemical oxidants is presented in Chapter 2 and includes information on $O_3$ properties, current $O_3$ air quality patterns, historic trends, and background levels. This chapter provides a frame of reference for subsequent discussion of current and alternative $O_3$ NAAQS and alternative forms of $O_3$ standards.

Chapters 3 through 6 comprise the second main part of this draft Staff Paper dealing with human health and primary standards. Chapter 3 presents an overview of key policy-relevant health effects evidence, major health-related conclusions from the CD, and an examination of issues related to the quantitative assessment of evidence from controlled human exposure and epidemiological studies. Chapters 4 and 5 describe the scope and methods used in conducting human exposure and health risk assessments and present results from those assessments. Chapter 6 includes a discussion of the adequacy of the current primary standard and identifies alternative primary standards that we believe are appropriate for the Administrator to consider.

Chapters 7 and 8 comprise the third main part of this draft Staff Paper. Chapter 7 presents a policy-relevant assessment of $O_3$ welfare effects evidence and discusses the scope and methods that we have used in conducting vegetation-related exposure and risk assessments. Chapter 8 includes a discussion of the adequacy of the current secondary standard and identifies alternative secondary standards that we believe are appropriate for the Administrator to consider.

The conclusions and identification of options presented in this second draft Staff Paper are informed by comments received from CASAC and the public in their reviews of the first draft Staff Paper as well as CASAC's additional advice concerning the final CD. The final Staff Paper will be informed by further comments received from CASAC and the public in their review of this second draft Staff Paper. The final Staff Paper will take into account the scientific evidence reviewed in the final CD and will include: 1) the results of comparative air quality analyses, human exposure and health risk assessments, and vegetation-related environmental assessments; 2) the overall evaluation of the adequacy of the current primary and secondary NAAQS; and 3) conclusions and identification of options that we believe are appropriate for the

Administrator to consider concerning whether and if so how to revise the $O_3$ NAAQS to address public health and welfare effects associated with exposure to $O_3$ and related photochemical oxidants.

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# 2. AIR QUALITY CHARACTERIZATION

## 2.1 INTRODUCTION

This chapter generally characterizes ambient ozone ($O_3$) and related photochemical oxidants in terms of measurement methods, recent concentrations and trends, relationships between different air quality indicators, and estimates of policy-relevant background. This information is useful for interpreting the available exposure, health, and welfare effects information, and for evaluating the adequacy of the current primary and secondary standards for $O_3$ and developing options for alternative standards. The information presented in this chapter was drawn from the Criteria Document (CD) and additional analyses of data from various $O_3$ monitoring networks.

This chapter particularly focuses on 1-hr, 8-hr, and 24-hr average concentrations metrics in characterizing urban $O_3$ air quality because these are the metrics most frequently used in the health effect studies discussed in the CD and Chapter 3 of this Staff Paper. For the vegetation exposure and risk assessment discussed in Chapter 7 of this Staff Paper, both the current secondary standard 8-hr. metric and the cumulative, concentration-weighted metric, SUM06, are used.

## 2.2 CHEMICAL AND PHYSICAL PROPERTIES, FORMATION, AND TRANSPORT

### 2.2.1 Chemical and Physical Properties

Ozone and other oxidants form mainly by chemical reactions in the atmosphere involving two classes of precursor pollutants, volatile organic compounds or VOCs and nitrogen oxides ($NO_x$) in the presence of sunlight. Ozone is, therefore, a secondary pollutant. Carbon monoxide (CO) can have a limited impact on $O_3$ formation in urban areas. The formation of $O_3$, other oxidants, and oxidation products from these precursors is a complex process involving many factors: the intensity and spectral distribution of sunlight; atmospheric mixing and processing on cloud and aerosol particles; the concentrations of the precursors in ambient air; and the rates of chemical reactions of the precursors. A more detailed discussion of these processes can be found in Chapter 2 of Volume 1 of Air Quality Criteria for Ozone and Related Photochemical Oxidants (CD, pp.2-1 – 29).

The effects of sunlight on $O_3$ formation, aside from the role of solar radiation in meteorological processes, depend on its intensity and its spectral distribution. Intensity varies diurnally, seasonally, and with latitude, but the effect of latitude is strongest in the winter. Ultraviolet radiation from the sun plays a key role in initiating the photochemical processes leading to $O_3$ formation and affects individual photolytic reaction steps. However, there is little

empirical evidence in the literature, directly linking day-to-day variations in observed surface UV radiation levels with variations in tropospheric $O_3$ levels (CD, p.AX2-90).

### 2.2.2 Formation

The chemical formation of $O_3$ in the troposphere results from the oxidation of nitric oxide (NO) to nitrogen dioxide ($NO_2$) by organic ($RO_2$) or hydro-peroxy ($HO_2$) radicals. Photolysis (the chemical process of breaking down molecules into smaller units through the absorption of light) of $NO_2$ yields NO and a ground-state oxygen atom, $O(^3P)$, which then reacts with molecular oxygen to form ozone (CD, p.2-2).

In urban areas, both biogenic and anthropogenic VOCs are important for $O_3$ formation. In non-urban, vegetated areas, biogenic VOCs emitted from vegetation tend to be the most important. In the remote troposphere, $CH_4$ and CO are the main carbon-containing precursors to $O_3$ formation. In coastal environments and other selected environments, atomic Cl and Br radicals can also initiate the oxidation of VOCs (CD, p.2-2 and 2-3).

Oxidized nitrogen compounds are emitted to the atmosphere mainly as NO which is oxidized to $NO_2$ which subsequently can be reduced back to NO. Consequently, NO and $NO_2$ are often grouped together into their own family called $NO_x$ (CD, p.2-3). $NO_x$ is considered a good surrogate for $NO_y$ and, thus, is commonly monitored and reported (see Table 2-1). Oxidized nitrogen containing compounds are essential to the formation of $O_3$ in the air. There are a large number of oxidized nitrogen containing compounds in the atmosphere including NO, $NO_2$, $NO_3$, $HNO_2$, $HNO_3$, $N_2O_5$, $HNO_4$, PAN and its homologues, other organic nitrates and particulate nitrate. Collectively these species are referred to as $NO_y$.

### 2.2.3 Transport

The transport of $O_3$ and other secondary pollutants is determined by meteorological and chemical processes extending typically over spatial scales of several hundred kilometers (e.g., Civerolo et al., 2003; Rao et al., 2003). An analysis of the output of regional model studies conducted by Kasibhatla and Chameides (2000) suggests that $O_3$ can be transported over a few thousand kilometers in the upper boundary layer of the eastern half of the United States during specific $O_3$ episodes. Convection is capable of transporting $O_3$ and its precursors vertically through the troposphere as shown in Annex AX2.3.2 of the CD. Nocturnal low-level jets (LLJs) can also transport pollutants hundreds of kilometers over the mid-Atlantic region, the central U.S. and California (Zhang et al., 2001). Turbulence associated with LLJs can bring these pollutants to the surface and result in secondary $O_3$ maxima in the early morning in many locations. However, the presence of mountain barriers can limit both horizontal and vertical

**Table 2-1. NOx Emission Sources, 1970-2004**

| | Nitrogen Oxides (NOx) National Emissions Totals (thousands of tons) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Source Category** | **1970** | **1975** | **1980** | **1985** | **1990** | **1991** | **1992** | **1993** | **1994** |
| FUEL COMB. ELEC. UTIL. | 4,900 | 5,694 | 7,024 | 6,127 | 6,663 | 6,519 | 6,504 | 6,651 | 6,565 |
| FUEL COMB. INDUSTRIAL | 4,325 | 4,007 | 3,555 | 3,209 | 3,035 | 2,979 | 3,071 | 3,151 | 3,147 |
| FUEL COMB. OTHER | 836 | 785 | 741 | 712 | 1,196 | 1,281 | 1,353 | 1,308 | 1,303 |
| CHEMICAL & ALLIED PRODUCT MFG | 271 | 221 | 213 | 262 | 168 | 165 | 163 | 155 | 160 |
| METALS PROCESSING | 77 | 73 | 65 | 87 | 97 | 76 | 81 | 83 | 91 |
| PETROLEUM & RELATED INDUSTRIES | 240 | 63 | 72 | 124 | 153 | 121 | 148 | 123 | 117 |
| OTHER INDUSTRIAL PROCESSES | 187 | 182 | 205 | 327 | 378 | 352 | 361 | 370 | 389 |
| SOLVENT UTILIZATION | 0 | 0 | 0 | 2 | 1 | 2 | 3 | 3 | 3 |
| STORAGE & TRANSPORT | 0 | 0 | 0 | 2 | 3 | 6 | 5 | 5 | 5 |
| WASTE DISPOSAL & RECYCLING | 440 | 159 | 111 | 87 | 91 | 95 | 96 | 123 | 114 |
| HIGHWAY VEHICLES | 12,624 | 12,061 | 11,493 | 10,932 | 9,592 | 9,449 | 9,306 | 9,162 | 9,019 |
| OFF-HIGHWAY | 2,652 | 2,968 | 3,353 | 3,576 | 3,781 | 3,849 | 3,915 | 3,981 | 4,047 |
| MISCELLANEOUS | 330 | 165 | 248 | 310 | 369 | 286 | 255 | 241 | 390 |
| MISCELLANEOUS | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| TOTAL | 26,883 | 26,377 | 27,079 | 25,757 | 25,529 | 25,179 | 25,260 | 25,357 | 25,349 |
| FIRES | NA | NA | NA | NA | 362 | 247 | 234 | 234 | 382 |
| Total without FIRES | 26,883 | 26,377 | 27,079 | 25,757 | 25,167 | 24,932 | 25,026 | 25,123 | 24,967 |

**Table 2-1. NOx Emission Sources, 1970-2004 (cont'd)**

**Nitrogen Oxides (Nox)**
**National Emissions Totals (thousands of tons)**

| Source Category | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 |
|---|---|---|---|---|---|---|---|---|---|---|
| FUEL COMB. ELEC. UTIL. | 6,384 | 6164 | 6276 | 6232 | 5721 | 5330 | 4917 | 4699 | 4270 | 3740 |
| FUEL COMB. INDUSTRIAL | 3,144 | 3151 | 3101 | 3050 | 2709 | 2723 | 2757 | 2870 | 2870 | 2870 |
| FUEL COMB. OTHER | 1,298 | 1197 | 1177 | 1101 | 768 | 766 | 779 | 725 | 725 | 725 |
| CHEMICAL & ALLIED PRODUCT MFG | 158 | 125 | 127 | 129 | 102 | 105 | 107 | 105 | 105 | 105 |
| METALS PROCESSING | 98 | 83 | 89 | 89 | 86 | 89 | 94 | 84 | 84 | 84 |
| PETROLEUM & RELATED INDUSTRIES | 110 | 139 | 143 | 143 | 120 | 122 | 124 | 149 | 149 | 149 |
| OTHER INDUSTRIAL PROCESSES | 399 | 433 | 460 | 467 | 451 | 479 | 504 | 487 | 487 | 487 |
| SOLVENT UTILIZATION | 3 | 2 | 3 | 3 | 4 | 4 | 4 | 8 | 8 | 8 |
| STORAGE & TRANSPORT | 6 | 15 | 16 | 16 | 14 | 15 | 16 | 16 | 16 | 16 |
| WASTE DISPOSAL & RECYCLING | 99 | 153 | 157 | 163 | 162 | 129 | 130 | 152 | 152 | 152 |
| HIGHWAY VEHICLES | 8,876 | 8733 | 8792 | 8619 | 8371 | 8394 | 7774 | 7365 | 7365 | 7365 |
| OFF-HIGHWAY | 4,113 | 4179 | 4178 | 4156 | 4084 | 4167 | 4156 | 4086 | 4086 | 4086 |
| MISCELLANEOUS | 267 | 412 | 187 | 179 | 251 | 276 | 184 | 356 | 356 | 356 |
| MISCELLANEOUS | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TOTAL | 24,956 | 24787 | 24705 | 24348 | 22845 | 22598 | 21549 | 21102 | 20672 | 20142 |
| FIRES | 258 | 405 | 179 | 172 | 236 | 263 | 171 | 341 | 341 | 341 |
| Total without FIRES | 24,698 | 24,382 | 24,526 | 24,176 | 22,609 | 22,335 | 21,378 | 20,761 | 20,331 | 19,801 |

dispersion such as observed in Los Angeles and Mexico City and will resulting in a greater frequency and duration of days with high $O_3$ concentrations (CD, p.2-10).

### 2.2.4 Precursors, Sources and Emissions

Although there are direct sources of $O_3$ (electrical discharges, lightning), ambient $O_3$ pollution problems are generally acknowledged to result from the secondary formation of $O_3$ via the processes described in section 2.2.1.

Table 2-2 (see http://www.epa.gov/airtrends/econ-emissions.html) lists the main sources of VOC emissions from 1970-2004. The categories in the table are self explanatory with the exception of the fires and miscellaneous categories. The fires category includes both wild fires and prescribed burns. The miscellaneous category includes mainly structural fires and sources from agricultural activities. One category not in either table is biogenic emissions. Biogenic emissions are an important factor on warm to hot days in heavily vegetated areas. As can be seen in the table, highway vehicles have been the single largest source of VOC emissions over the years ranging from about 49% of total emissions in 1970 to about 27% of total emissions in 2004. Starting in 2001, solvent use and highway vehicles were the two main sources of VOCs with roughly equal contributions to the total emissions.

Table 2-1 contains the same emission information but for $NO_X$ emissions. Again, highway vehicles are the single largest source of $NO_X$ emissions over the years ranging from about 47% of total emissions in 1970 to about 37% of total emissions in 2004.

### 2.2.5 Tropospheric vs. Stratospheric Ozone

The atmosphere can be divided into several distinct vertical layers, based primarily on the major mechanisms by which they are heated and cooled. The lowest major layer is the troposphere, which extends from the earth's surface to about 8 km above the surface in polar regions and to about 16 km above the surface in tropical regions. The planetary boundary layer (PBL) is the lower sub-layer of the troposphere, extending from the surface to about 1 or 2 km, and is most strongly affected by surface conditions. The stratosphere extends from the top of the troposphere, to about 50 km in altitude. The emphasis in this chapter is placed on concentrations of $O_3$ occurring in the lower troposphere, in particular in the PBL (CD, p.2-1).

In urban environments, the rate of $O_3$ formation is sensitive to the rate of photolysis of several species including $H_2CO$, $H_2O_2$, $O_3$, and especially $NO_2$. Monte Carlo calculations suggest that model simulations of photochemical $O_3$ production are most sensitive to uncertainty in the photolysis rate coefficient for $NO_2$ (CD, p.AX2-90).

**Table 2-2. VOC Emission Sources, 1970-2004**

**Volatile Organic Compounds (VOC)**
**National Totals (thousands of tons)**

| Source Category | 1970 | 1975 | 1980 | 1985 | 1990 | 1991 | 1992 | 1993 | 1994 |
|---|---|---|---|---|---|---|---|---|---|
| FUEL COMB. ELEC. UTIL. | 30 | 40 | 45 | 32 | 47 | 44 | 44 | 45 | 45 |
| FUEL COMB. INDUSTRIAL | 150 | 150 | 157 | 134 | 182 | 196 | 187 | 186 | 196 |
| FUEL COMB. OTHER | 541 | 470 | 848 | 1,403 | 776 | 835 | 884 | 762 | 748 |
| CHEMICAL & ALLIED PRODUCT MFG | 1,341 | 1,351 | 1,595 | 881 | 634 | 710 | 715 | 701 | 691 |
| METALS PROCESSING | 394 | 336 | 273 | 76 | 122 | 123 | 124 | 124 | 126 |
| PETROLEUM & RELATED INDUSTRIES | 1,194 | 1,342 | 1,440 | 703 | 611 | 640 | 632 | 649 | 647 |
| OTHER INDUSTRIAL PROCESSES | 270 | 235 | 237 | 390 | 401 | 391 | 414 | 442 | 438 |
| SOLVENT UTILIZATION | 7,174 | 5,651 | 6,584 | 5,699 | 5,750 | 5,782 | 5,901 | 6,016 | 6,162 |
| STORAGE & TRANSPORT | 1,954 | 2,181 | 1,975 | 1,747 | 1,490 | 1,532 | 1,583 | 1,600 | 1,629 |
| WASTE DISPOSAL & RECYCLING | 1,984 | 984 | 758 | 979 | 986 | 999 | 1,010 | 1,046 | 1,046 |
| HIGHWAY VEHICLES | 16,910 | 15,392 | 13,869 | 12,354 | 9,388 | 8,860 | 8,332 | 7,804 | 7,277 |
| OFF-HIGHWAY | 1,616 | 1,917 | 2,192 | 2,439 | 2,662 | 2,709 | 2,754 | 2,799 | 2,845 |
| MISCELLANEOUS | 1,101 | 716 | 1,134 | 566 | 1,059 | 756 | 486 | 556 | 720 |
| | | | | | | | | | |
| TOTAL | 34,659 | 30,765 | 31,106 | 27,404 | 24,108 | 23,577 | 23,066 | 22,730 | 22,569 |
| FIRES | 917 | 587 | 1,024 | 465 | 983 | 678 | 407 | 478 | 638 |
| Total without FIRES | 33,742 | 30,178 | 30,082 | 26,939 | 23,125 | 22,899 | 22,659 | 22,252 | 21,931 |

**Table 2-2. VOC Emission Sources, 1970-2004 (cont'd)**

**Volatile Organic Compounds (VOC)**
**National Totals (thousands of tons)**

| Source Category | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 |
|---|---|---|---|---|---|---|---|---|---|---|
| FUEL COMB. ELEC. UTIL. | 44 | 50 | 52 | 56 | 54 | 62 | 61 | 52 | 52 | 52 |
| FUEL COMB. INDUSTRIAL | 206 | 179 | 175 | 174 | 172 | 173 | 176 | 170 | 170 | 170 |
| FUEL COMB. OTHER | 823 | 893 | 893 | 889 | 919 | 949 | 950 | 790 | 790 | 790 |
| CHEMICAL & ALLIED PRODUCT MFG | 660 | 388 | 388 | 394 | 251 | 254 | 262 | 214 | 214 | 214 |
| METALS PROCESSING | 125 | 73 | 78 | 78 | 66 | 67 | 71 | 69 | 69 | 69 |
| PETROLEUM & RELATED INDUSTRIES | 642 | 477 | 487 | 485 | 457 | 428 | 441 | 375 | 375 | 375 |
| OTHER INDUSTRIAL PROCESSES | 450 | 435 | 438 | 443 | 438 | 454 | 420 | 406 | 406 | 406 |
| SOLVENT UTILIZATION | 6,183 | 5477 | 5621 | 5149 | 5036 | 4831 | 5012 | 4692 | 4692 | 4692 |
| STORAGE & TRANSPORT | 1,652 | 1294 | 1328 | 1327 | 1237 | 1176 | 1192 | 1205 | 1205 | 1205 |
| WASTE DISPOSAL & RECYCLING | 1,067 | 509 | 518 | 535 | 487 | 415 | 420 | 457 | 457 | 457 |
| HIGHWAY VEHICLES | 6,749 | 6221 | 5985 | 5859 | 5681 | 5325 | 4952 | 4543 | 4543 | 4543 |
| OFF-HIGHWAY | 2,890 | 2935 | 2752 | 2673 | 2682 | 2644 | 2622 | 2688 | 2688 | 2688 |
| MISCELLANEOUS | 551 | 1940 | 816 | 718 | 791 | 733 | 532 | 883 | 883 | 883 |
| | | | | | | | | | | |
| TOTAL | 22,041 | 20871 | 19530 | 18782 | 18270 | 17512 | 17111 | 16544 | 16544 | 16544 |
| FIRES | 464 | 1870 | 744 | 645 | 667 | 615 | 412 | 785 | 785 | 785 |
| Total without FIRES | 21,577 | 19001 | 18786 | 18136 | 17603 | 16898 | 16699 | 15759 | 15759 | 15759 |

### 2.2.6 Relationship of Ozone to Photochemical Oxidants

Photochemical oxidants are strongly oxidizing compounds, which are the primary constituents of photochemical smog. The photochemical oxidants found in ambient air in the highest concentrations are $O_3$ and nitrogen dioxide ($NO_2$). Other oxidants, such as hydrogen peroxide ($H_2O_2$) and peroxyacylnitrates (PANs) are produced in much smaller quantities than $O_3$. In 1971, EPA promulgated NAAQS to protect the public health and welfare from adverse effects of photochemical oxidants, at that time, defined on the basis of commercially available measurement methodology. After 1971, however, $O_3$-specific commercial analytical methods became available, as did information on the concentrations and effects of the related non-$O_3$ photochemical oxidants. As a result, the indicator or chemical designation of the standards was changed in 1979 from photochemical oxidants to $O_3$. As discussed in Chapter 3, use of $O_3$ for this NAAQS has served as a surrogate or indicator for the health effects associated with the overall photochemical oxidant mix, including $O_3$-related effects. However, it is virtually impossible to quantify in a practical manner the aggregate effects of photochemical oxidants that generally exist in concentrations not measurable with routine technologies, and are fundamentally intertwined with $O_3$ atmospheric chemistry. Ambient $O_3$ can be measured reliably and has been associated independently with health outcomes, and therefore has the attributes of being both a reasonable and practical indicator of the ambient mix of photochemical oxidants.

## 2.3 DATA SOURCES

Two main sources of monitoring data were used for this assessment, the state-supplied data from various types of monitors housed in the Air Quality System (AQS) data base (which includes National Park Service monitors) and the Clean Air Status and Trends Network (CASTNET). The vegetation exposure analysis also uses an enhanced Veroni Neighborhood Average (eVNA) spatial interpolation technique to combine 2001 monitor data from both AQS and CASTNET with 2001 modeled data from the Community Multi-scale Air Quality (CMAQ) model. This interpolated surface is used to fill in the gaps left by a sparse rural monitoring network in the western United States.

Air quality models are often used to simulate the formation, transport, and decay of air pollution. The CMAQ modeling system is a comprehensive three-dimensional grid-based Eulerian air quality model designed to estimate $O_3$ and particulate concentrations and deposition over large spatial scales (Dennis et al., 1996; Byun and Ching, 1999). The CMAQ model is a publicly available, widely-used, peer-reviewed, state-of-the-science model consisting of a number of science attributes that are critical for simulating the oxidant precursors and nonlinear

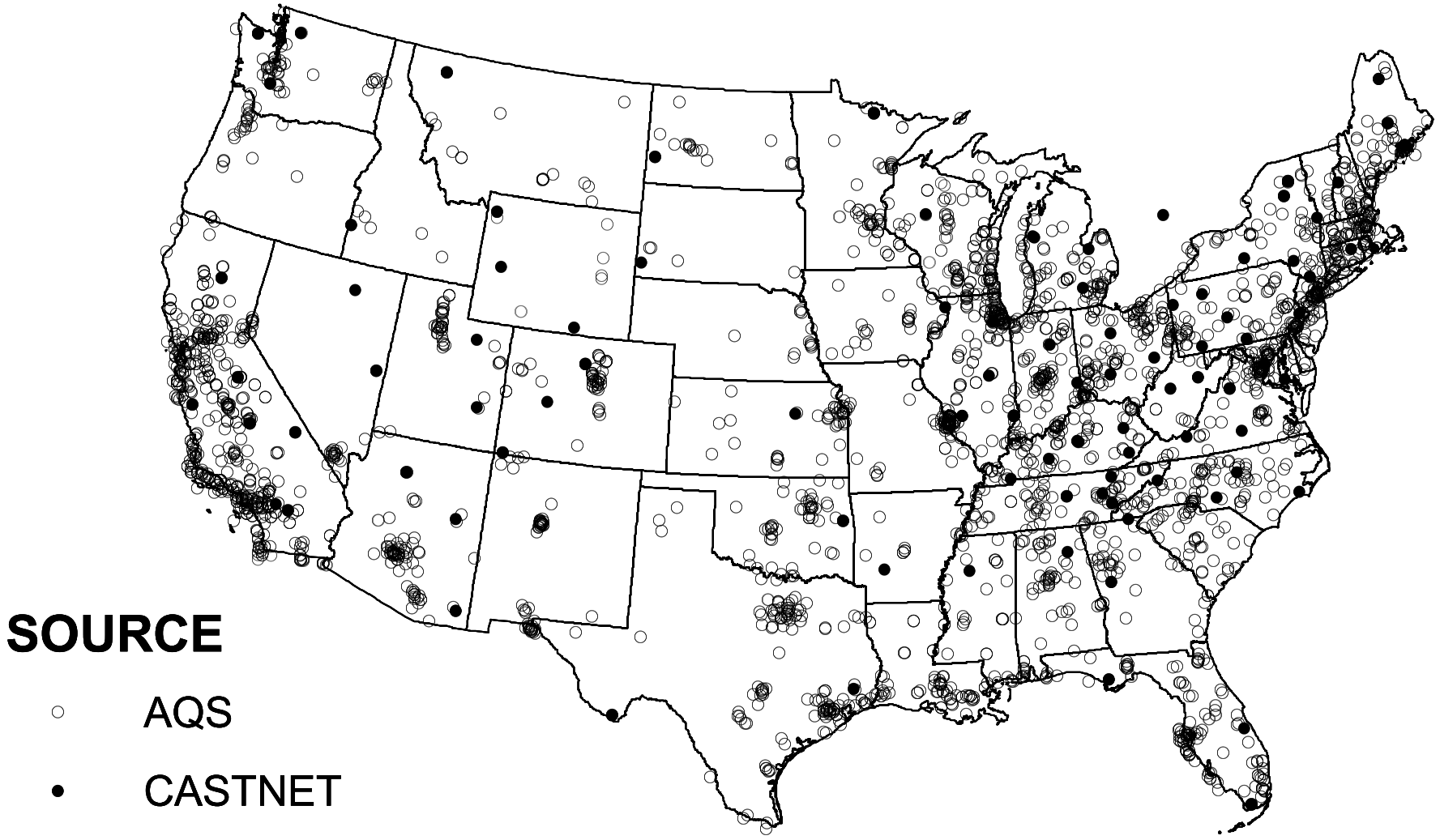


**Figure 2-1. Locations of Ozone Monitors from AQS and CASTNET**

organic and inorganic chemical relationships associated with the formation of $O_3$, as well as sulfate, nitrate, and organic aerosols.

For this Staff Paper, the three most recent years of reported and certified data available in AQS was 2002-2004. The 2005 data would not be certified until July 1, 2006.

### 2.3.1 Air Quality System (AQS)

EPA's ambient air quality surveillance regulations are found at 40 CFR Part 58. Section 58.20 requires States to provide for the establishment of air quality surveillance systems in their State Implementation Plans (SIP). The air quality surveillance system consists of a network of monitoring stations designated as State and Local Air Monitoring Stations (SLAMS), which measure ambient concentrations of those pollutants for which standards have been established in 40 CFR Part 50. SLAMS, National Air Monitoring Stations (NAMS), which are a subset of SLAMS, and Photochemical Assessment Monitoring Stations (PAMS) must meet the requirements of 40 CFR Part 58, Appendices A (Quality Assurance Requirements), C (Ambient Air Quality Monitoring Methodology), D (Network Design Criteria), and E (Probe and Path Siting Criteria).

The Air Quality System (AQS) is EPA's repository of ambient air quality data. AQS stores data from over 10,000 monitors; 5000 of which are currently active. Of these, over 3000 measure and report $O_3$ concentration data (See Figure 2-1). These monitors make up the SLAMS, PAMS, NAMS, and other special purpose monitors used and operated by the States. AQS also contains meteorological data, descriptive information about each monitoring station (including its geographic location and its operator), and data quality assurance/quality control information. The Office of Air Quality Planning and Standards (OAQPS) and other AQS users rely upon the data system to assess air quality, assist in Attainment/Non-Attainment designations, evaluate State Implementation Plans for Non-Attainment Areas, perform modeling for permit review analysis, and other air quality management functions. AQS information is also used to prepare reports for Congress as mandated by the Clean Air Act (see http://www.epa.gov/ttn/airs/airsaqs/sysoverview.htm).

The NAMS/PAMS/SLAMS $O_3$ monitor network achieved an overall average bias (upper bound) of 0.2% and an overall mean precision of 3% for 2002. If special purpose and other $O_3$ monitors are also included the average upper bounds of bias and precision were 0.4% and 2.9% respectively (U.S. EPA 2004a).

### 2.3.2 CASTNET

CASTNET is the nation's primary source for data on dry acidic deposition and rural, ground-level $O_3$. Operating since 1987, CASTNET is used in conjunction with other national

monitoring networks to provide information for evaluating the effectiveness of national emission control strategies. CASTNET consists of over 80 sites across the eastern and western United States (see Figure 2-1) and is cooperatively operated and funded with the National Park Service. In 1986, EPA established the National Dry Deposition Network (NDDN) to obtain field data on rural deposition patterns and trends at different locations throughout the United States. The network consisted of 50 monitoring sites that derived dry deposition data based on measured air pollutant concentrations and modeled dry deposition velocities estimated from meteorology, land use, and site characteristic data. In 1990, amendments to the Clean Air Act necessitated a long-term, national program to monitor the status and trends of air pollutant emissions, ambient air quality, and pollutant deposition. In response, EPA, in cooperation with the National Oceanic Atmospheric Administration (NOAA), created CASTNET from NDDN. In terms of data quality, CASTNET achieved 98% to 99% of all precision and accuracy audits being within the ±10% criteria for both precision and accuracy. Overall, CASTNET $O_3$ monitors are stable and show only very small variation (U.S. EPA 2003, p.22).

## 2.4 OZONE MONITORING METHODS AND DATA QUALITY

### 2.4.1 Ozone Monitoring Methods

Ozone monitoring is conducted almost exclusively with UV absorption spectrometry with commercial short path instruments, a method that has been thoroughly evaluated in clean air. The ultimate reference method is a relatively long-path UV absorption instrument maintained under carefully controlled conditions at the National Institute of Standards and Technology (NIST) (CD, p.2-22).

Several reports in the reviewed scientific literature have investigated interferences in $O_3$ detection via UV radiation absorption and chemiluminescence. These include the effects of water vapor, VOC's, aromatic compounds and their oxidation products, and other organic and inorganic compounds. Water vapor had no significant impact on UV absorption-based instruments, but could cause a positive interference of up to 9% in chemiluminescence-based detectors at high humidities (dew point of 24° C). Aromatic compounds and their oxidation products were found to generate a positive but small interference in the UV absorption instruments. However, when the results are applied to ambient concentrations of toluene and $NO_x$, the effect appears to be very minor (about 3 percent under the study conditions). Other organic and inorganic compounds displayed interferences, but not at levels likely to interfere with accurate determination of $O_3$ in an urban environment. The possibility for substantive interferences in $O_3$ detection exists, but such interferences have not been observed even in urban plumes (CD, p.2-25).

Ozone is also measured by differential optical absorption spectroscopy (DOAS) at a variety of wavelengths in the UV and visible parts of the spectrum. Comparisons of DOAS results to those from a UV absorption instrument showed good agreement on the order of 10%. Researchers have reported a positive interference due to an unidentified absorber in the 279 to 289 nm spectral region used by many commercial short-path DOAS systems for the measurement of $O_3$. Results of that study suggest that compounds from wood burning, used for domestic heating, may be responsible (CD, p.AX2-149).

### 2.4.2 Effect of Measurement Precision on 8 hour Ozone Averages

For 2002 to 2004, the average precision in the collected $O_3$ measurements was approximately 3%. This means, for example, that a 1-hr measured concentration of 100 ppb could be between 97 ppb and 103 ppb. Staff conducted an analysis to determine the precision of an 8-hr averaged $O_3$ concentration (Cox and Camalier, 2006). Daily maximum 8-hr $O_3$ values were simulated using a Weibull distribution to yield a "true" three-year averaged $O_3$ design value without the influence of measurement error.

Utilizing site specific precision data from 900 $O_3$ monitors for the 2002 through 2004 $O_3$ seasons, a second set of 8-hr $O_3$ concentrations was generated to incorporate the precision data from the $O_3$ monitoring network to account for instrument measurement error. The result was a value which reflected the "true" $O_3$ design value plus measurement error. The difference between the value with measurement error and the "true value" reflects the impact of the instrument measurement error on the calculated 8-hr design value.

The exercise was repeated 1000 times and the differences between the two previously described design values were summarized. Table 2-3 shows the results of the analysis. The percentiles presented in the table reflect the percentage of sites at or below the corresponding 1-hour precision value. The table shows that even at a precision of approximately 4.5% of which 95% of the $O_3$ sites are at or below, the standard deviation of the difference between the 8-hr design values is less than 1 ppb.

A second exercise was performed to incorporate systematic bias error which includes the instrument drift, noise, precision and calibration error associated with the UV absorption method. It was assumed that each 8-hr measurement was subjected to this randomly occurring bias which had an average of zero and a standard deviation of approximately 4 ppb. The mean and standard deviation utilized for the simulation were believed to be reasonable estimates for monitors operating under normal conditions. The results of this exercise show that assuming a random bias of 4 ppb produced an uncertainty in the 8-hr design value of approximately 1.3 ppb.

It should be noted that the above estimate does not account for potential interferences known to exist with the UV absorption method "due to positive interference by a number of

**Table 2-3. Relationship between Precision of 1-hour Ozone Data and Corresponding Standard Deviation of 8-hour Design Values**

| Precision of 1- hour ozone value (%) | Nationwide Percentile | Standard Deviation of Difference in DV's (ppb) |
|---|---|---|
| 1.63 | 25 | 0.27 |
| 2.22 | 50 | 0.34 |
| 2.97 | 75 | 0.45 |
| 3.89 | 90 | 0.57 |
| 4.52 | 95 | 0.63 |

organic compounds, mainly those produced during the oxidation of aromatic hydrocarbons and some primary compounds such as styrene and naphthalene." These observations, however, were made during studies in Mexico City and a smog chamber where concentrations of these types of compounds were many times higher than are typically found at ambient air monitoring sites in the United States (CD, p.AX2-148).

## 2.5 CHARACTERIZATION OF GROUND-LEVEL OZONE CONCENTRATIONS

### 2.5.1 Metrics

This section characterizes ground level $O_3$ concentrations based on several metrics. Two daily maximum statistics, 1-hr and 8-hr averages, and one daily average statistic in the form of a 24-hr concentration, and one cumulative concentration weighted statistic, the SUM06, are summarized to show how $O_3$ varies over space and time. The 1-hr and 8-hr daily maximum averaging times reflect the former and current $O_3$ standards, and much of the health effects literature for $O_3$ has focused on effects associated with these averaging times. The 24-hr daily average has been used for several personal exposure studies (CD, pp.3-72 – 74). The SUM06 has been used frequently in the scientific literature and CD in studying and assessing the relationship between $O_3$ exposures and adverse effects on vegetation. The daily maximum 8-hr values are found by first calculating running or moving 8-hr values for all 24 hours in a day (for example, averaging the 1-hr concentrations from 1:00am to 8:00 am, then average the 1-hr values from 2:00am to 9:00 am, etc.). Then the maximum value for each day is found (note that any 8-hr time period that starts in a day is assigned to that day). On an annual basis, the fourth highest of these values is summarized. The daily maximum 1-hr statistic is the maximum value of all 1-hr values in a day. On an annual basis, the second highest of these values in a year is summarized. The 24-hr average is a mean of the 24 individual hourly concentrations measured from midnight to midnight. The maximum, 3 month, 12 hour SUM06 statistic is calculated by cumulating all 1-hr values greater than or equal to 0.06ppm that occur during the12 hour daytime window (8:00am to 8:00pm Local Standard Time) for each month of the $O_3$ monitoring season and then finding the largest consecutive 3-month sum of these values in an $O_3$ monitoring season according to the secondary standard proposed in 1996 (61 FR Dec 13, 1996), but not adopted in 1997 (62 FR Jul 18, 1997). The SUM06 has a weighting function that is 0 when the concentration is less than 0.06 and is 1.0 when the concentration is greater than or equal to 0.06.

### 2.5.2 Spatial Variability

This section characterizes the spatial variability of $O_3$ based on all the metrics discussed above. Spatial variability is based on maps displaying county levels of the various metrics. In this way different levels of $O_3$ for different areas of the country are displayed.

#### 2.5.2.1 Comparison of 1-hr, 8-hr, and 24-hr Ozone Metrics

Figures 2-2 to 2-4 show the distributions for measured 1-hr, 8-hr, and 24-hour daily average ozone concentrations for 12 major urban areas in the United States. The Los Angeles area clearly has a distribution which is different from the other 11 cities in that the hourly concentration interquartile range is within 0.057 to 0.089 ppm as opposed to the next highest interquartile range of Sacramento where 50% of the hourly concentrations lie between 0.056 and 0.079 ppm. In comparison, Houston which also has several 1-hr concentrations greater than 0.125 ppm has a lower interquartile range of 0.034 to 0.07 ppm with 10% of its hourly values greater than 0.089 ppm as opposed to approximately 0.106 ppm for Los Angeles. Houston also has a larger interquartile range of 0.036 ppm when compared to the average of the remaining 11 cities of 0.025 ppm. This trend is also observed in the 8-hr averaged concentrations. The remaining 9 cities all exhibit similar distributions to one another for the 1-hr and 8-hr metrics.

When examining the 24-hour daily averaged concentration distributions, the nine cities which had similar distributions for the 1-hr and 8-hr concentrations still exhibit the same similarity. However, Houston shows a lower $75^{th}$ percentile than the other cities with areas like Cleveland, Philadelphia and New York having higher distributions. The lower 24 hour concentrations in Houston indicate a wider range between the daily ozone minima and maxima unlike an area like Cleveland, which has a higher interquartile range. This implies higher overall background concentrations, possibly caused by transport from other major urban areas.

#### 2.5.2.2 8-Hour and 1-Hour Statistics

High 8-hr average $O_3$ concentrations tend to occur near larger urban areas exhibiting similar patterns as corresponding 1-hr concentrations (see Figure 2-5). Elevated 8-hr levels occurring in smaller urban and non-urban areas are most likely caused by transport (see Figure 2-6). Higher 8-hr $O_3$ levels observed in smaller urban and non-urban areas are most obvious at the end of the northeast corridor (the highly urbanized area running from Washington, DC to Boston, MA), North-central New York, and the Northern coast of Lake Michigan. Some of the highest levels occur not in California but in Texas, some counties in the Northeast Corridor, and isolated counties in the East (see Figure 2-6) (Fitz-Simons, et al., 2005). The highest 1-hr levels occur in California. (Fitz-Simons, et al., 2005).

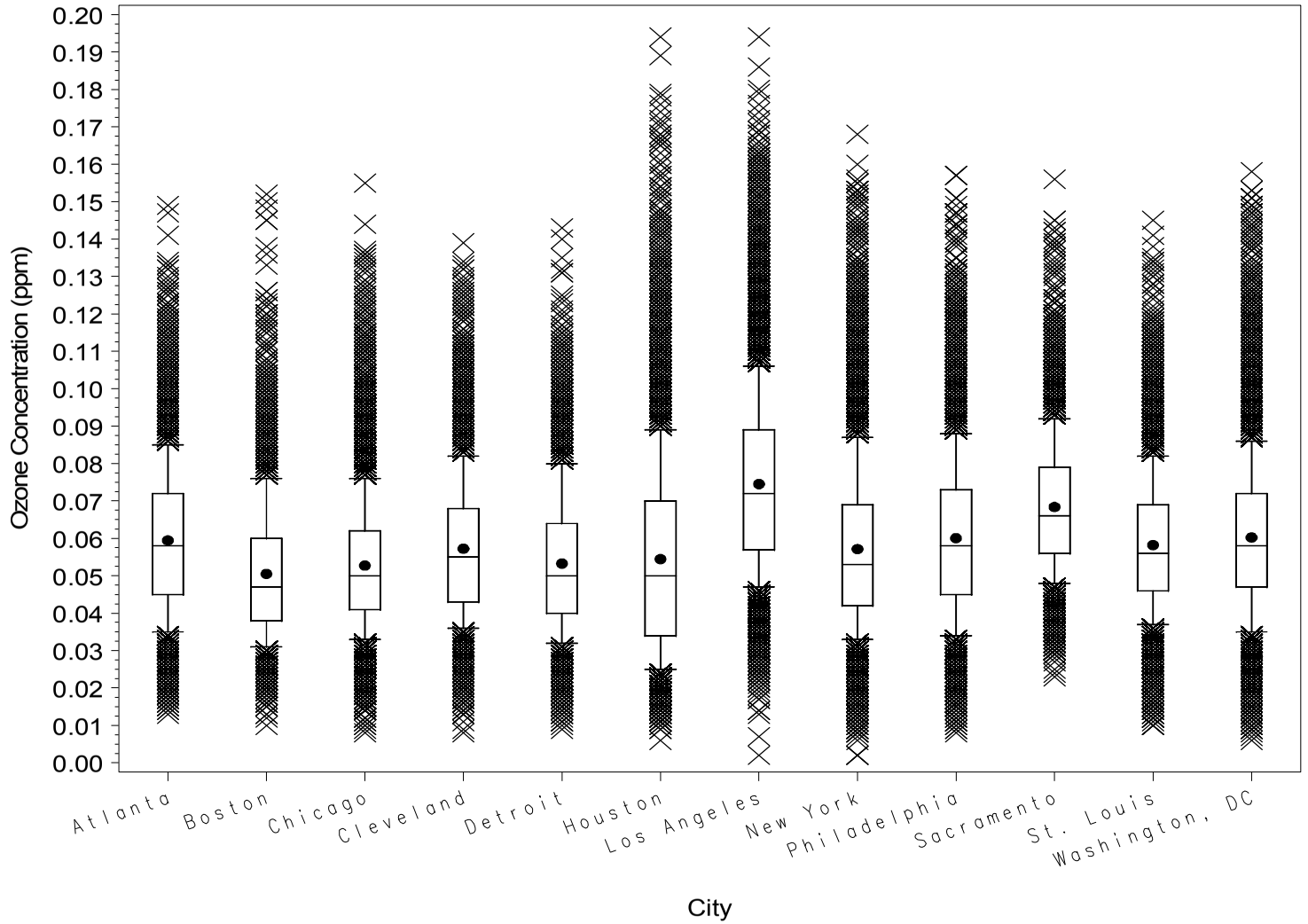


**Figure 2-2. 1-hr Ozone Distributions across 12 Risk Areas, 2002-2004.** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; and 'x' depicts values outside the 10th and 90th percentile.

Data Source: AQS

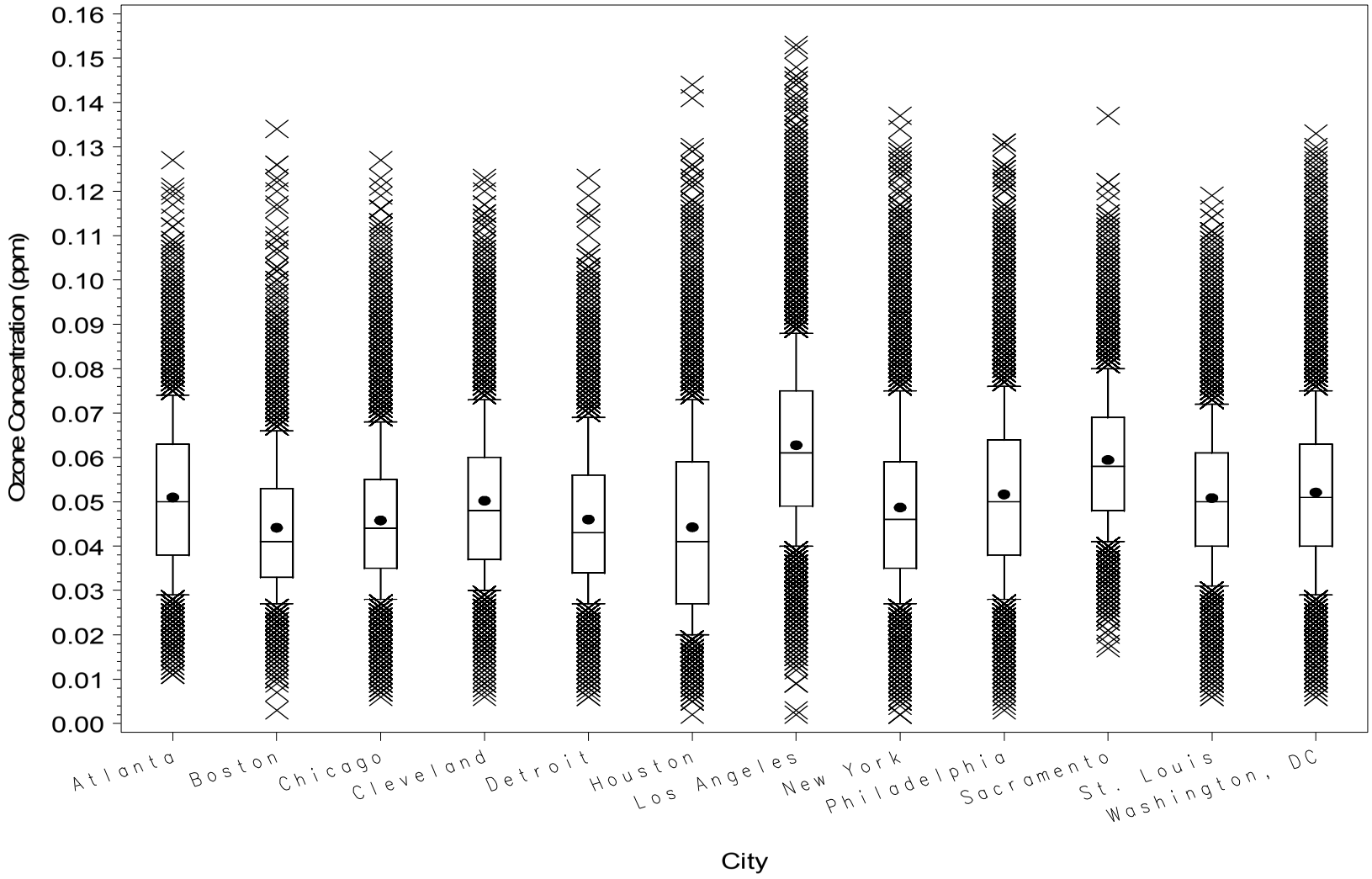


**Figure 2-3. 8-hr Ozone Distributions across 12 Risk Areas, 2002-2004.** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; and 'x' depicts values outside the 10th and 90th percentile.

Data Source: AQS

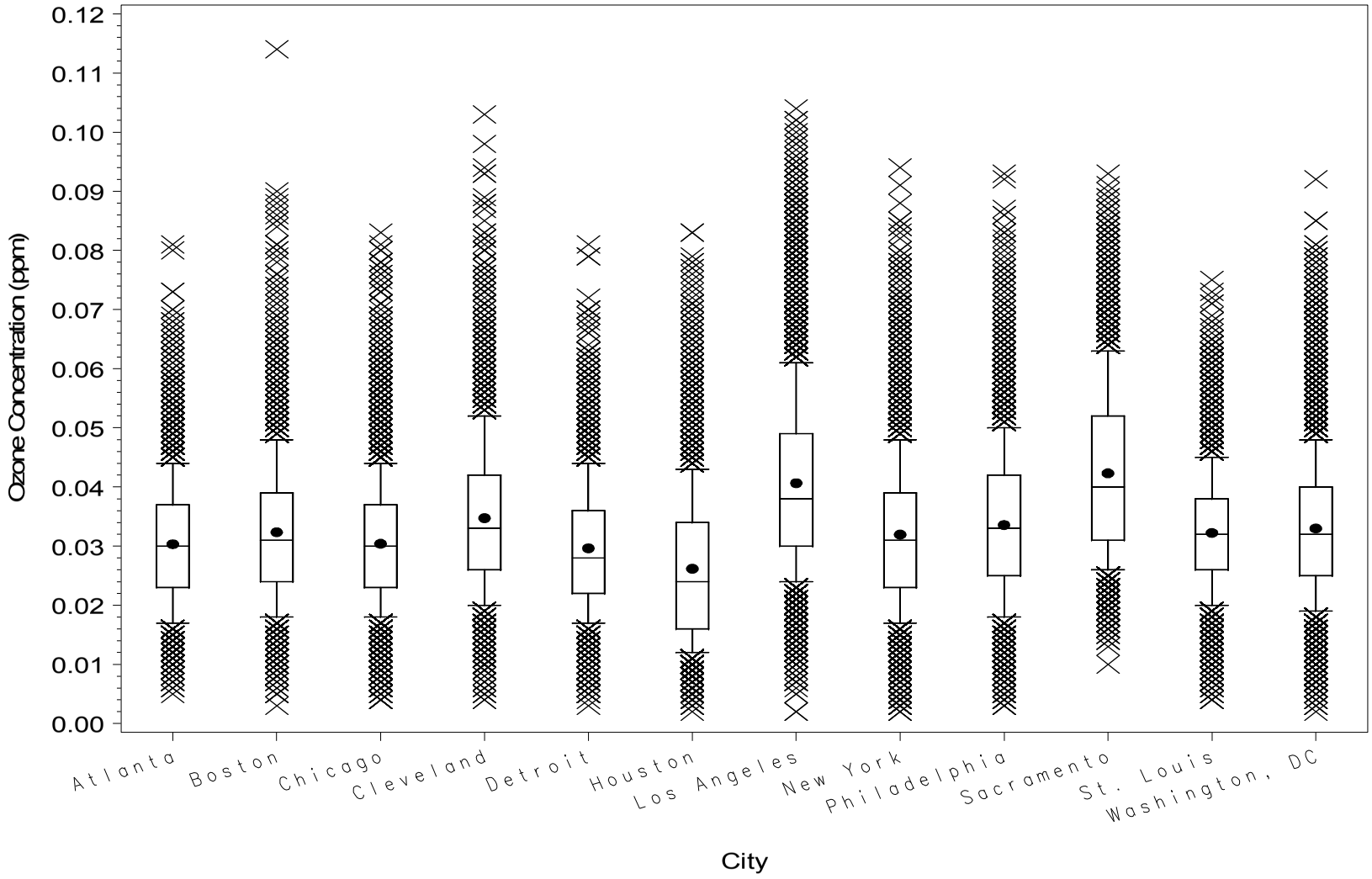


**Figure 2-4. 24-hr Ozone Distributions across 12 Risk Areas, 2002-2004.** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; and 'x' depicts values outside the 10th and 90th percentile.

Data Source: AQS

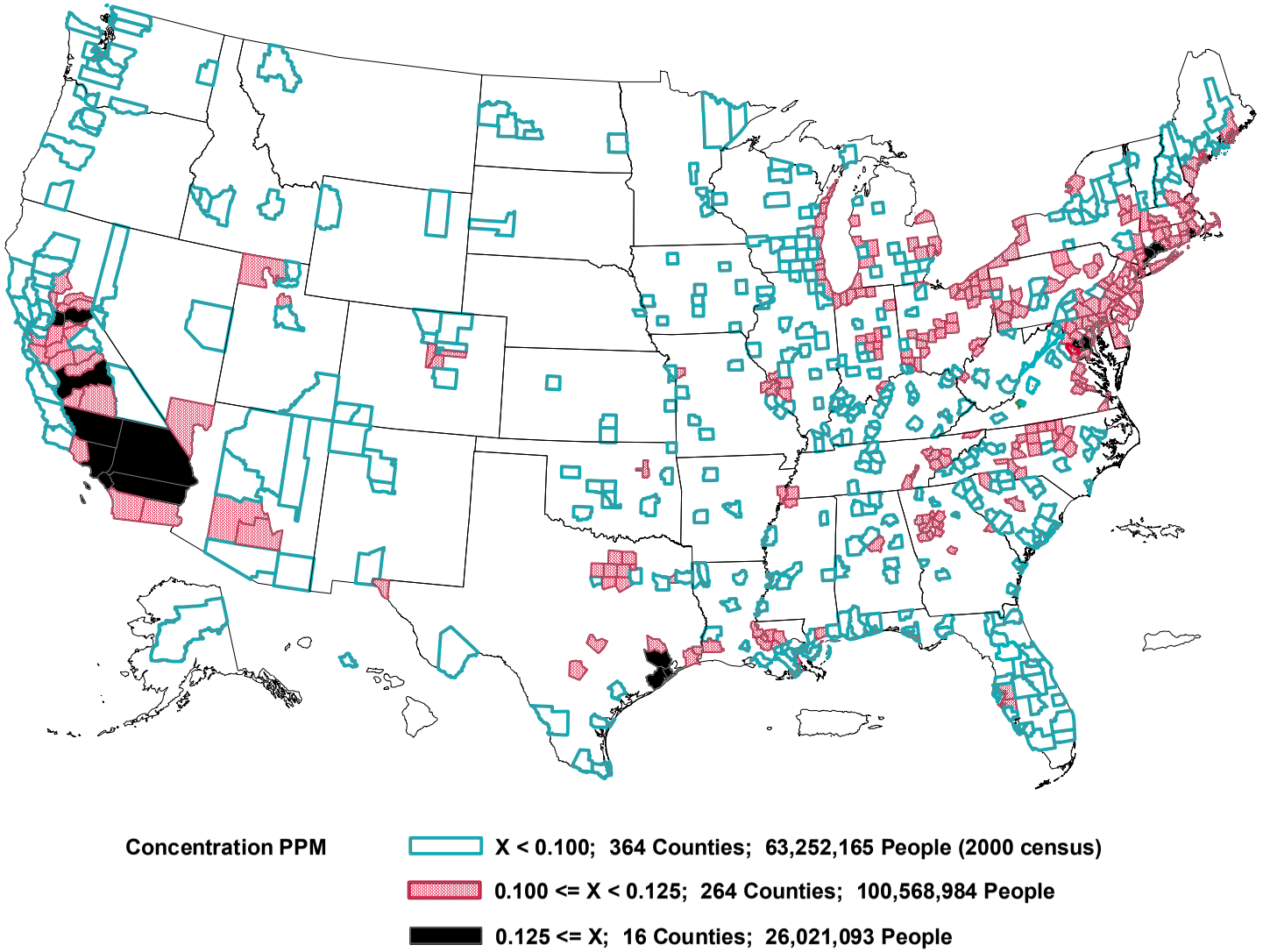


**Figure 2-5. Average 2nd Highest Daily Maximum 1-hour Values in U.S. Counties, 2002-2004 AQS Data.**

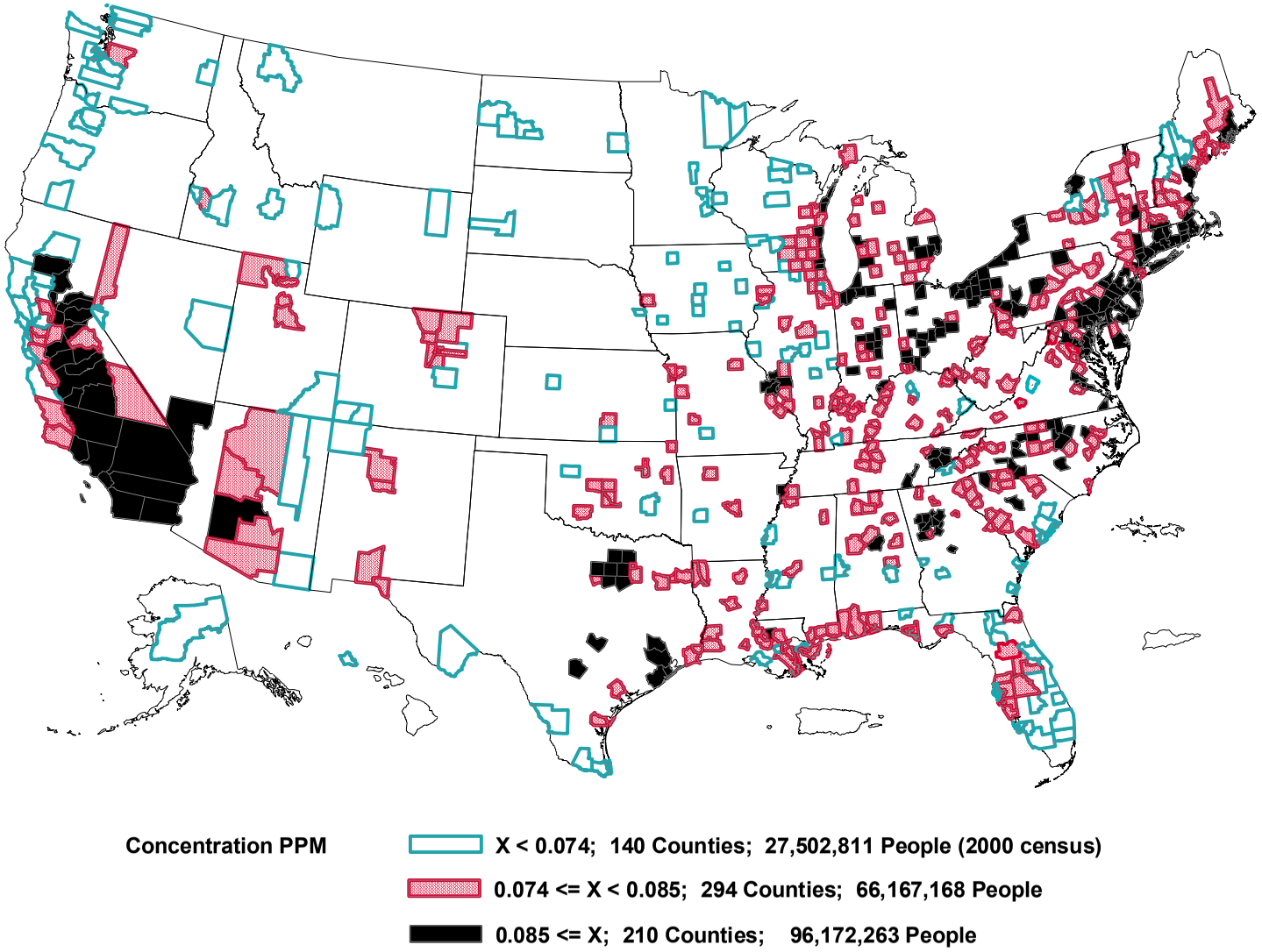


**Figure 2-6. Average 4th Highest Daily Maximum 8-hour Values in U.S. Counties, 2002-2004 AQS Data.**

#### 2.5.2.3 Cumulative Concentration-Weighted Statistics

The highest SUM06 levels in 2001 (most of the analyses in Chapter 7 center on 2001 data) occurred in most of the agricultural areas of California. When the data were from CASTNET sites, more purely rural counties showed higher values (See Figure 2-7, 2-8). (Fitz-Simons, et al., 2005). The SUM06 values experienced a sharp decline in 2004 when compared to 2002 primarily in the eastern part of the United States (See Figure 2-9, 2-10). Although there were reductions in the West, the decreases in the East were more substantial. The overall reductions across the country could possibly be due to lower temperatures experienced during the $O_3$ season. However, the eastern half of the country was also subject to the emission control requirements implemented under the $NO_x$ SIP Call which occurred after 2002. The improvements seen in 2004 for the East are most likely due to a combination of cooler weather and the emission reductions from the $NO_x$ SIP Call.

### 2.5.3 Temporal Variability

Temporal variability consists of several time frames when considering characterization of ground level air quality data. Multi-year variability characterizes long term variability or year to year variability. Trends usually provide evidence on whether or not a situation is getting better or worse over time. For the purposes of displaying long term trends, the data from both AQS and CASTNET are screened for temporally consistent data (only data from sites that meet a data completeness criteria of 12 complete years out of 15 and no gaps of more than 3 consecutive years are included). Seasonal variability characterizes month to month variability to demonstrate when in the year the highest concentrations occur. Diurnal variability characterizes hour-to-hour changes demonstrating when, in the day, the highest concentrations occur (Fitz-Simons, et al., 2005).

#### 2.5.3.1 Long Term Variability – Trends

Long term, nationwide trends for 8-hr $O_3$ values are presented in Figures 2-11 and 2-12. Figure 2-11 presents data from sites in the AQS that meet trends criteria and have locations described as Urban and Center City. Figure 2-12 presents data from CASTNET which are rural locations.

The rural and urban trends are similar, but the urban trends have more data and more variation. The rural means are slightly lower than the urban means; however the largest urban concentrations are much higher than the largest rural concentrations (Fitz-Simons, et al., 2005).

Long term trends for 1-hr $O_3$ values are presented in Figures 2-13 and 2-14. Figure 2-13 presents data from sites in the AQS that meet trends criteria and have locations described as Urban and Center City. Figure 2-14 presents data from CASTNET which are rural locations. As with the 8-hr data, the 1-hr urban trends and rural trends are similar, but urban have more data

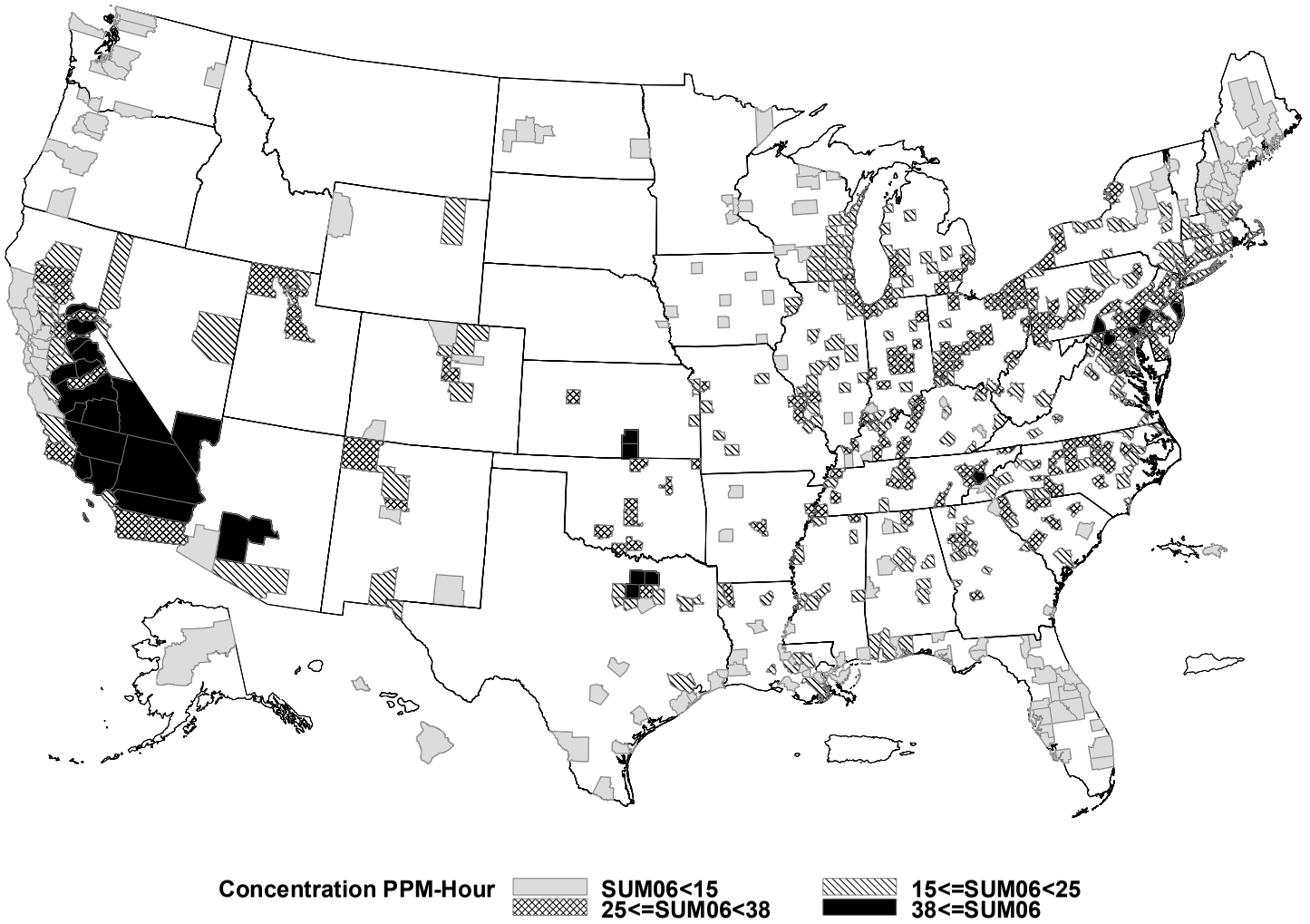


**Figure 2-7. Highest 3-month 12-hour SUM06 Exposure Index in U.S. Counties, 2001 AQS Data.**

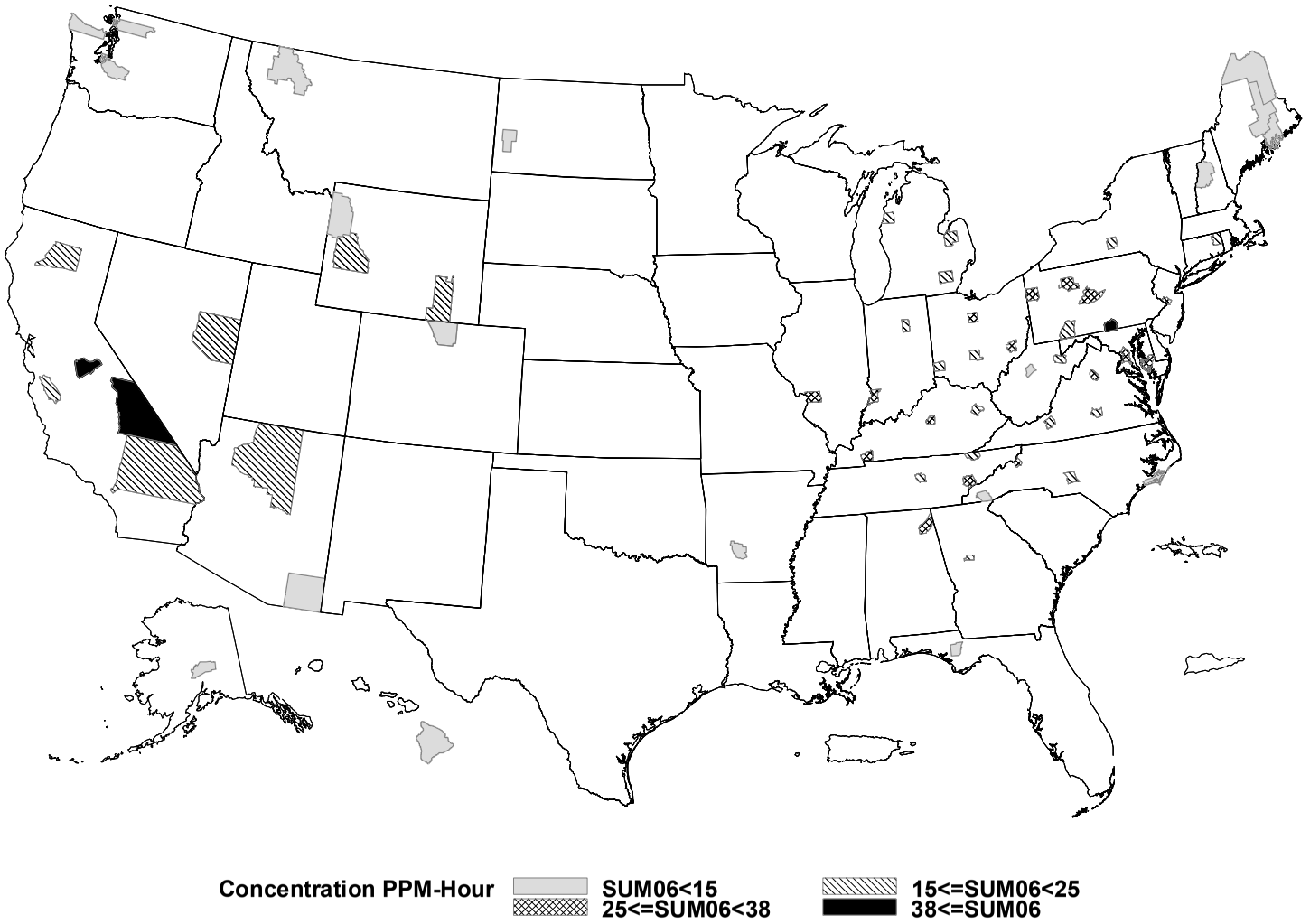


**Figure 2-8. Highest 3-month 12-hour SUM06 Exposure Index in U.S. Counties, 2001 CASTNET Data.**

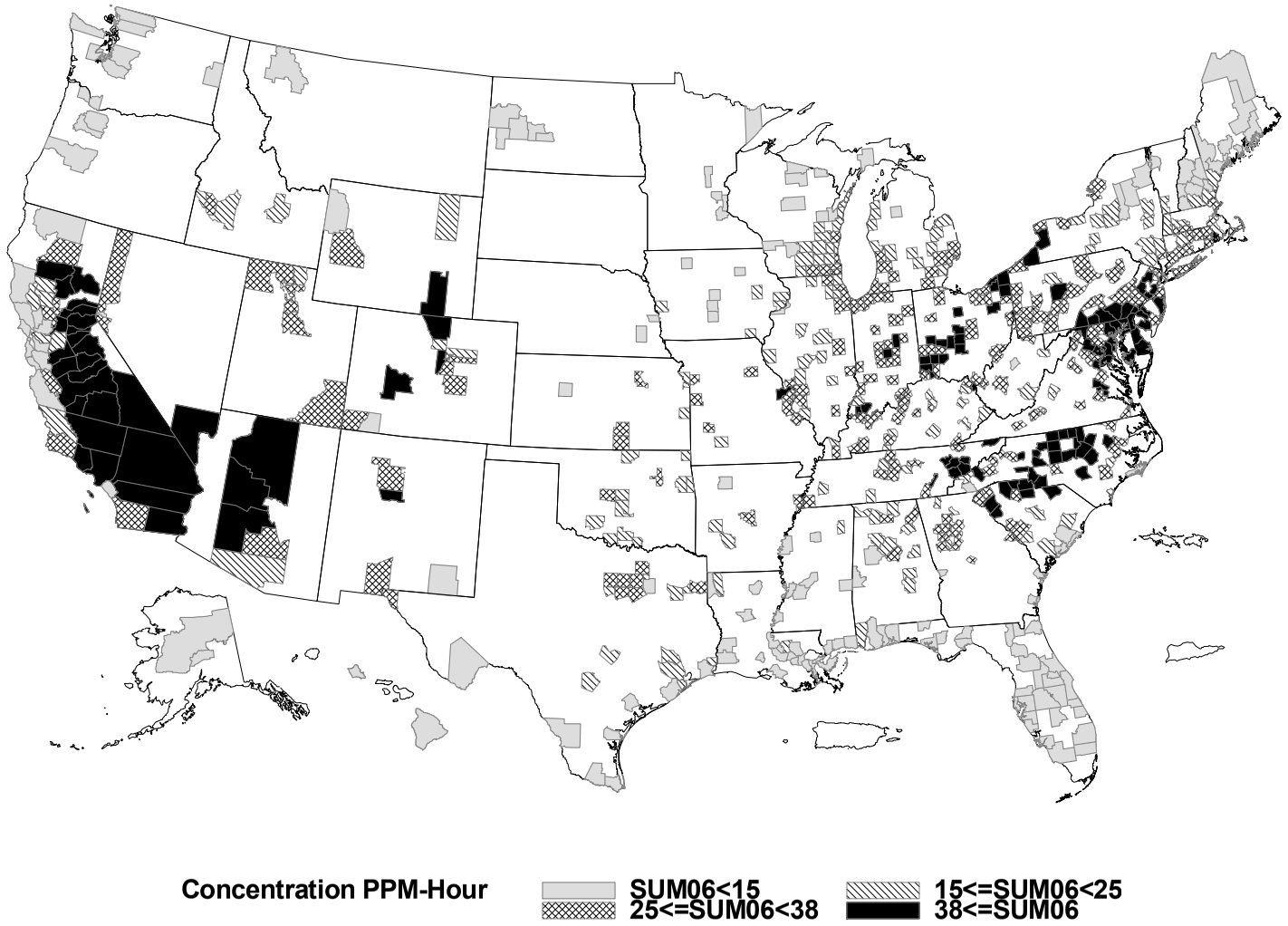


**Figure 2-9. Highest 3-month 12-hour SUM06 Exposure Index in U.S. Counties, 2002 AQS and CASTNET Data.**

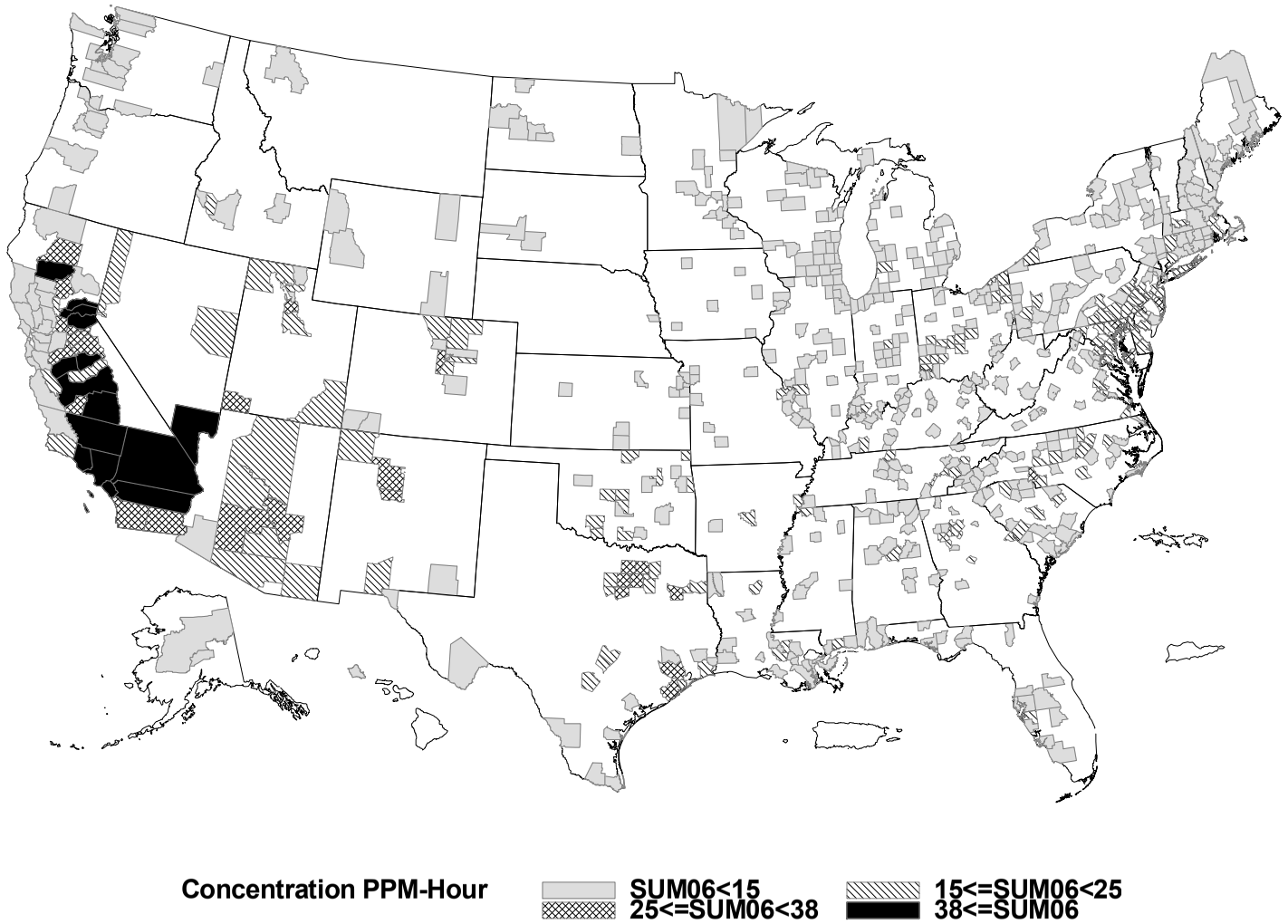


**Figure 2-10. Highest 3-month 12-hour SUM06 Exposure Index in U.S. Counties, 2004 AQS and CASTNET Data.**

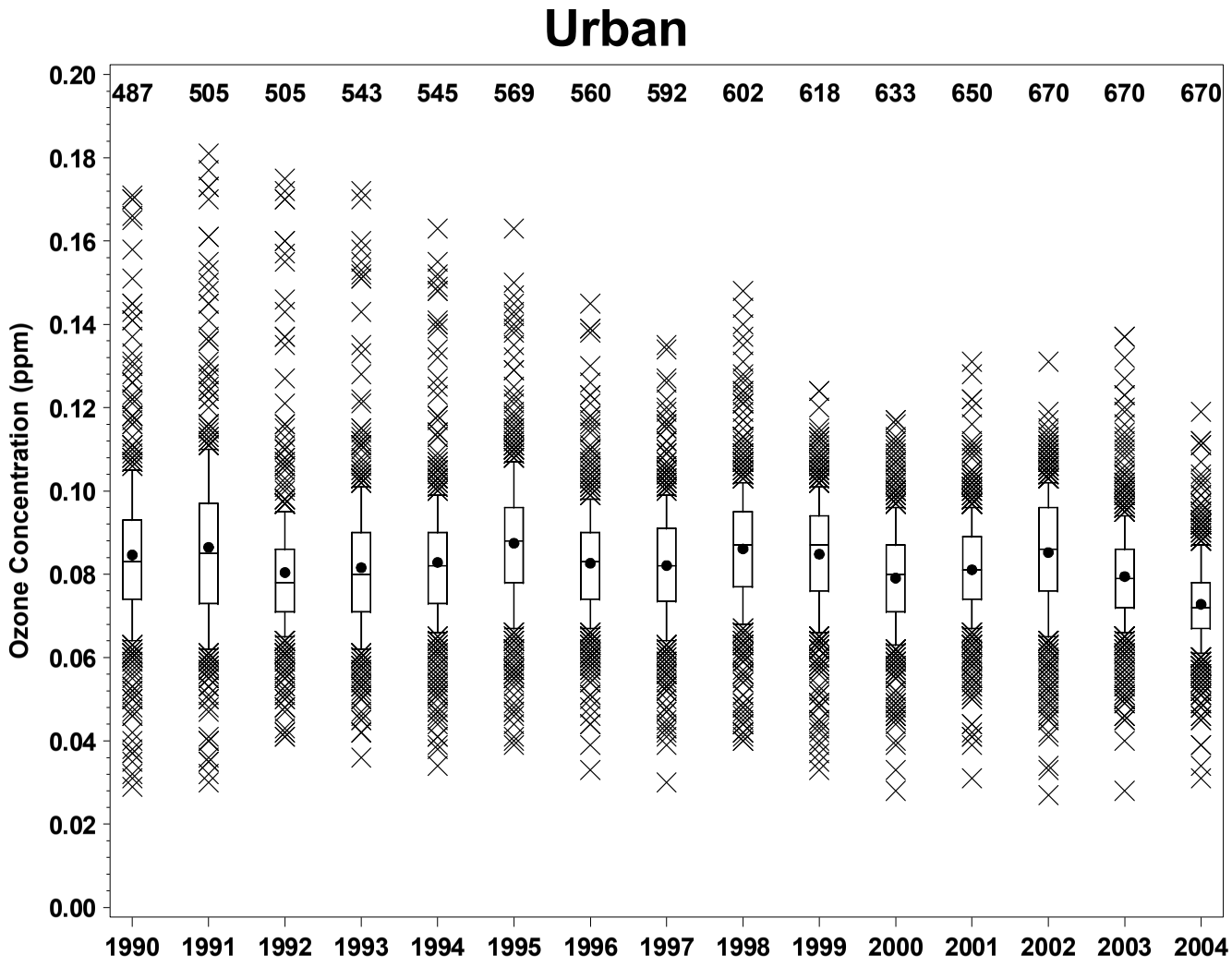


**Figure 2-11. 4th Highest Daily Maximum 8-hour Ozone Values 1990-2004 (Urban).** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; 'x' depicts values outside the 10th and 90th percentile; and numbers above the boxes depicts the number of sites.

Data Source: AQS

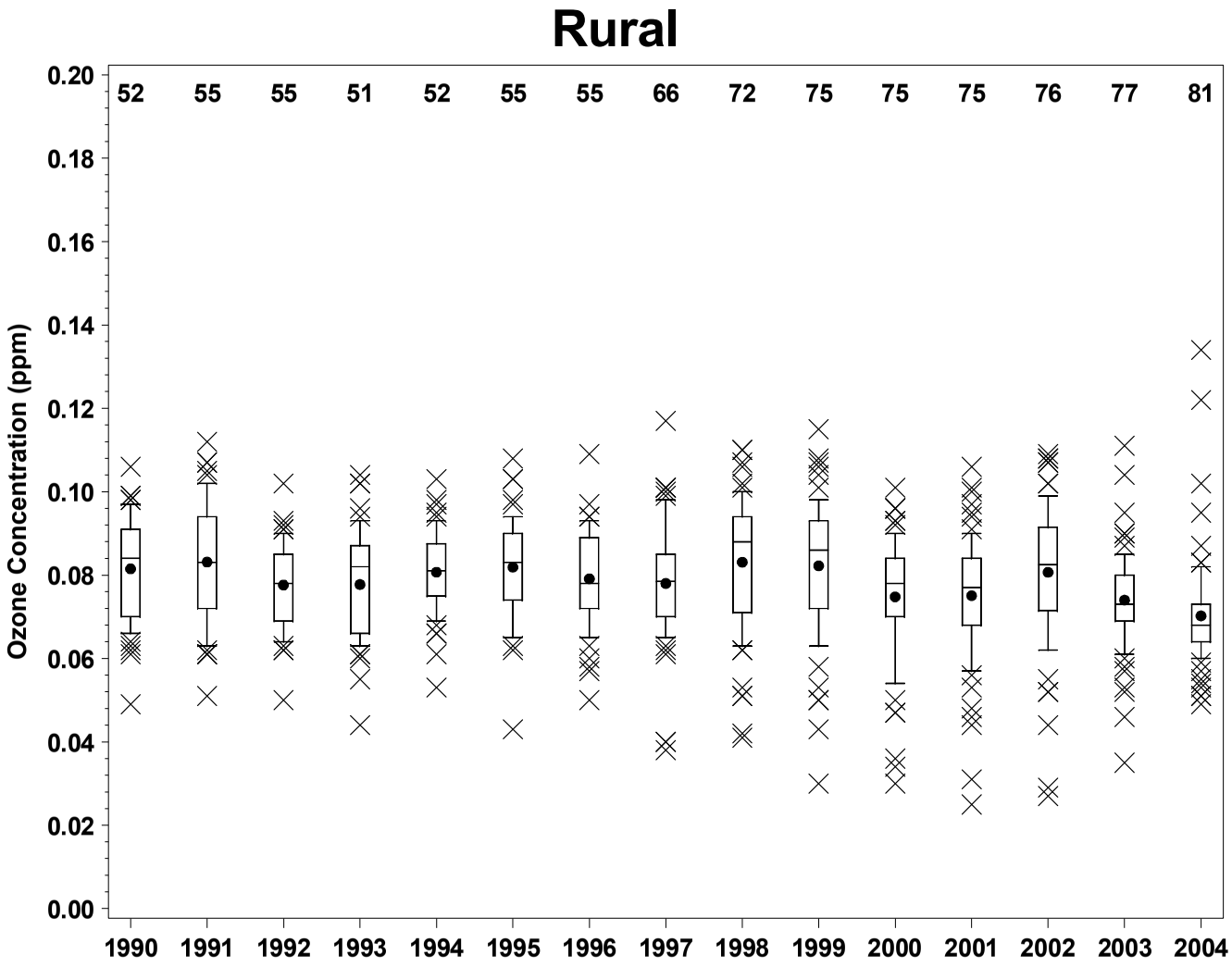


**Figure 2-12. 4th Highest Daily Maximum 8-hour Ozone Values 1990-2004 (Rural).** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; 'x' depicts values outside the 10th and 90th percentile; and numbers above the boxes depicts the number of sites.

Data Source: CASTNET

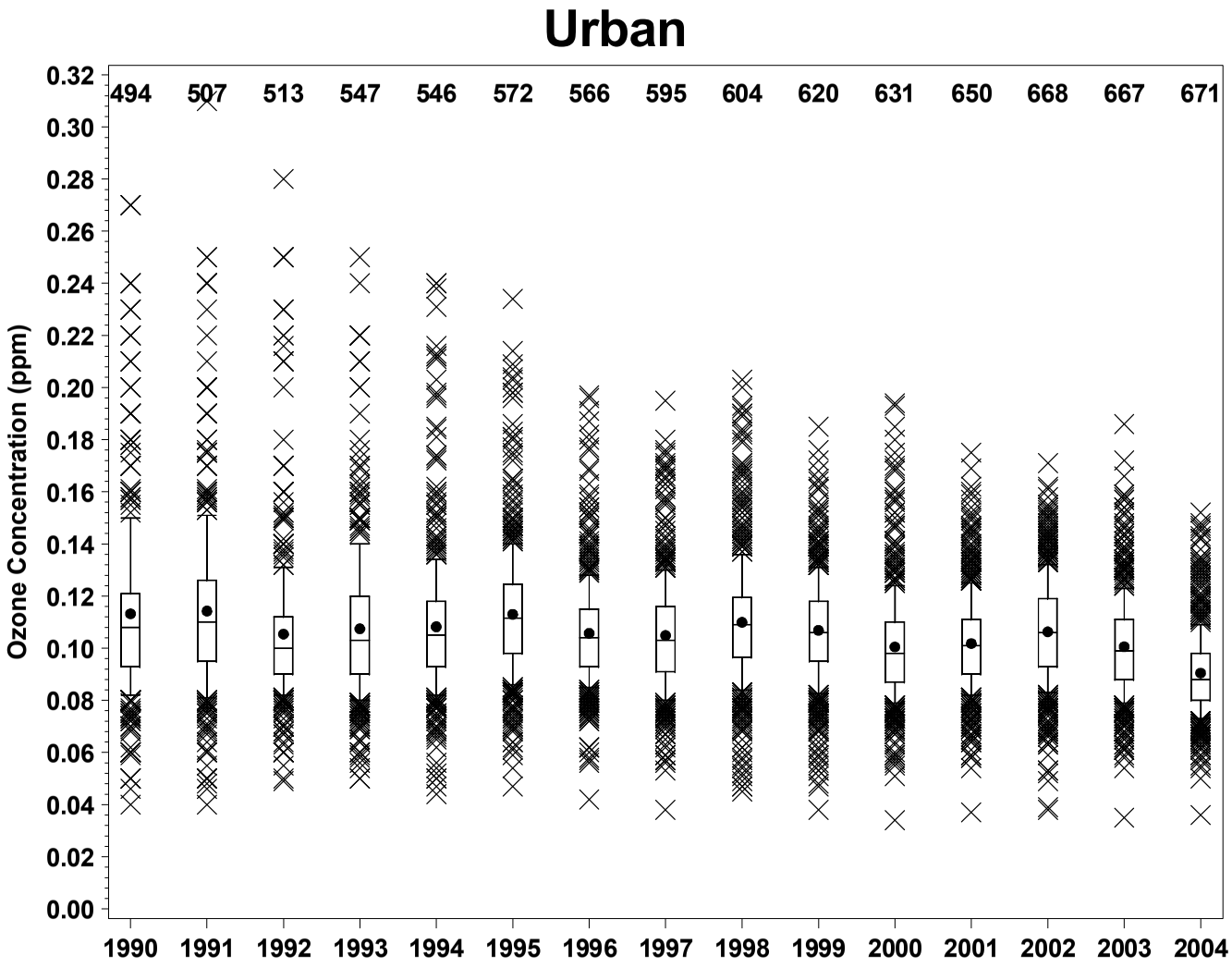


**Figure 2-13. 2nd Highest Daily Maximum 1-hour Ozone Values 1990-2004 (Urban).** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; 'x' depicts values outside the 10th and 90th percentile; and numbers above the boxes depicts the number of sites.

Data Source: AQS

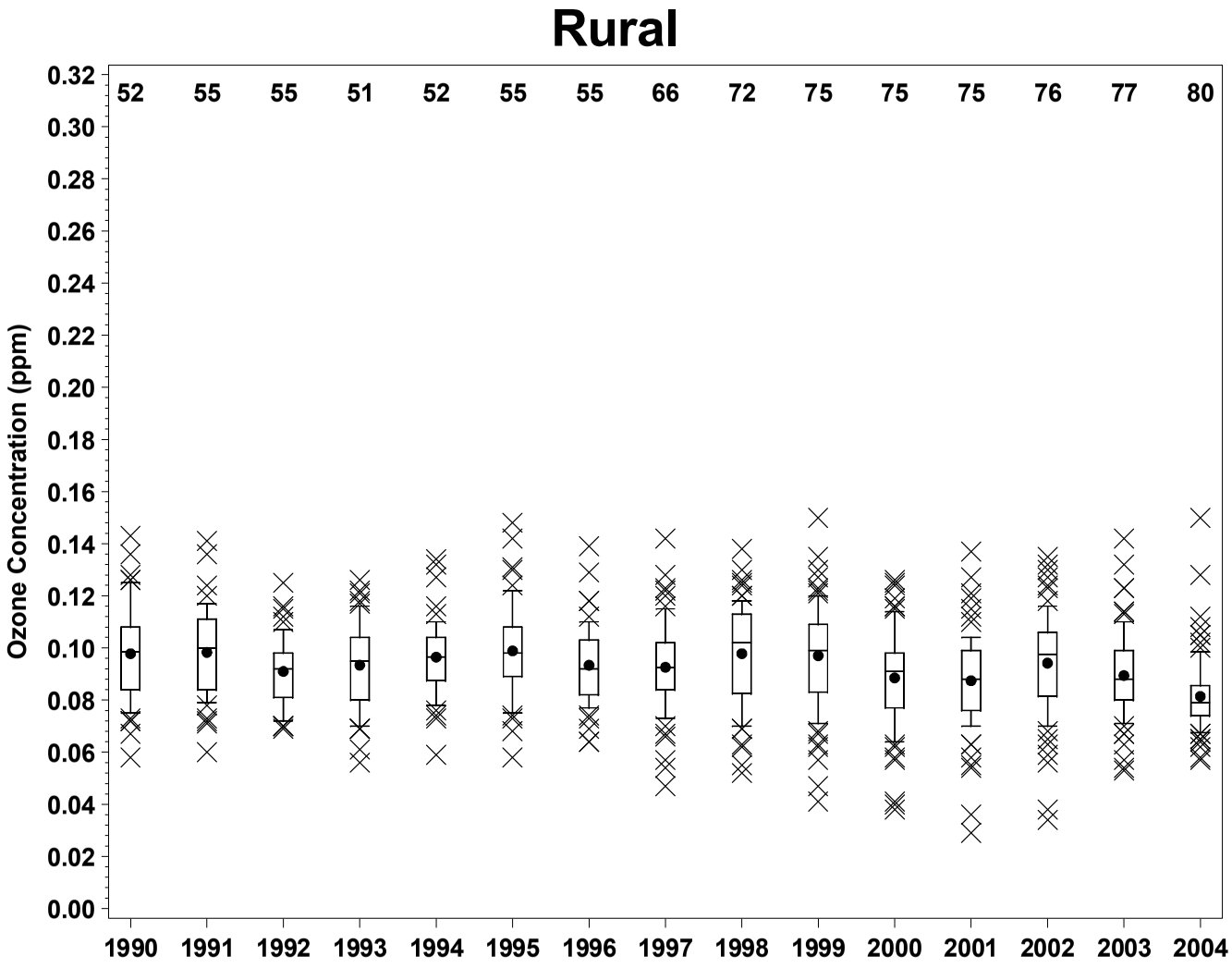


**Figure 2-14. 2nd Highest Daily Maximum 1-hour Ozone Values 1990-2004 (Rural).** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; 'x' depicts values outside the 10th and 90th percentile; and numbers above the boxes depicts the number of sites.

Data Source: CASTNET

and more variation. The 1-hr means for the urban trends are higher than the means for the rural trends. This difference is more pronounced than in the 8-hr trends (Fitz-Simons, et al., 2005).

The long term trends for both 1-hr and 8-hr $O_3$ data are similar. The 8-hr concentrations are lower, but the trends are basically parallel. The highest means occur in 1990,1991,1995, 1998 and 2002. The highest extreme values are clearly in the 1990s. In many cases, short term variation (3 years or less) is associated with meteorological conditions that are generally more or less conducive to $O_3$ formation in a particular year. One high year between two low years or one low year between two higher years are examples of this 3 years or less variation (see Evaluating Ozone Control Programs in the Eastern United States: $NO_X$ p.17, U.S. EPA, 2005b).

#### 2.5.3.2 Short Term Variability – Annual

Figure 2-15 shows a map of the number of exceedance days for 2002 and 2004 at 12 urban locations in the United States. Each grouping of two bars represents the number of exceedance days for 1-hr, 8-hr averaged and 24-hr averaged ozone concentrations. The 1-hr measured concentrations were compared to the previous 1-hr ozone standard of 0.12 ppm , 8 hour averaged concentrations were compared to the current ozone standard of 0.08 ppm and the average 24 hour concentrations were compared to 0.055 ppm which is the $95^{th}$ percentile for 24 hour ozone concentrations across the United States for 2002 through 2004. The data show that in all sites in the Midwest and the East, ozone concentrations were down dramatically in 2004 when compared to 2002. This is due in part to the fact that 2004 was much cooler than 2002, but also reflects the improvement in air quality due to $NO_x$ emission reductions in 2003 and 2004 due to the $NO_x$ SIP Call, which concentrated on reducing $NO_x$ in the eastern part of the country, thereby reducing peak $O_3$ concentrations (U.S. EPA, 2005b). However, Houston, Los Angeles and Sacramento which were not included in $NO_x$ SIP Call did not see these declines. The number of 8-hr exceedance days actually increased for Houston while remaining around the same in Los Angeles. The number of days greater than 0.055 ppm for the 24 hour averaged concentrations remained around the same or was slightly higher for 2004 than 2002 for all three cities west of the Mississippi River.

#### 2.5.3.3 Seasonal Variability

Monthly statistics are the best method to characterize seasonal variation in $O_3$ concentrations. However in many areas, monitors are not active during cooler months. As a result, data from May through September are the only universally available data for all monitors. Although this is a limited characterization of seasonal variability, it is consistent across the entire national network.

Figure 2-16 shows box-plots of all 2004 data from May through September for the second highest daily 1-hr maximums. The center of the distribution shows a slight, steady

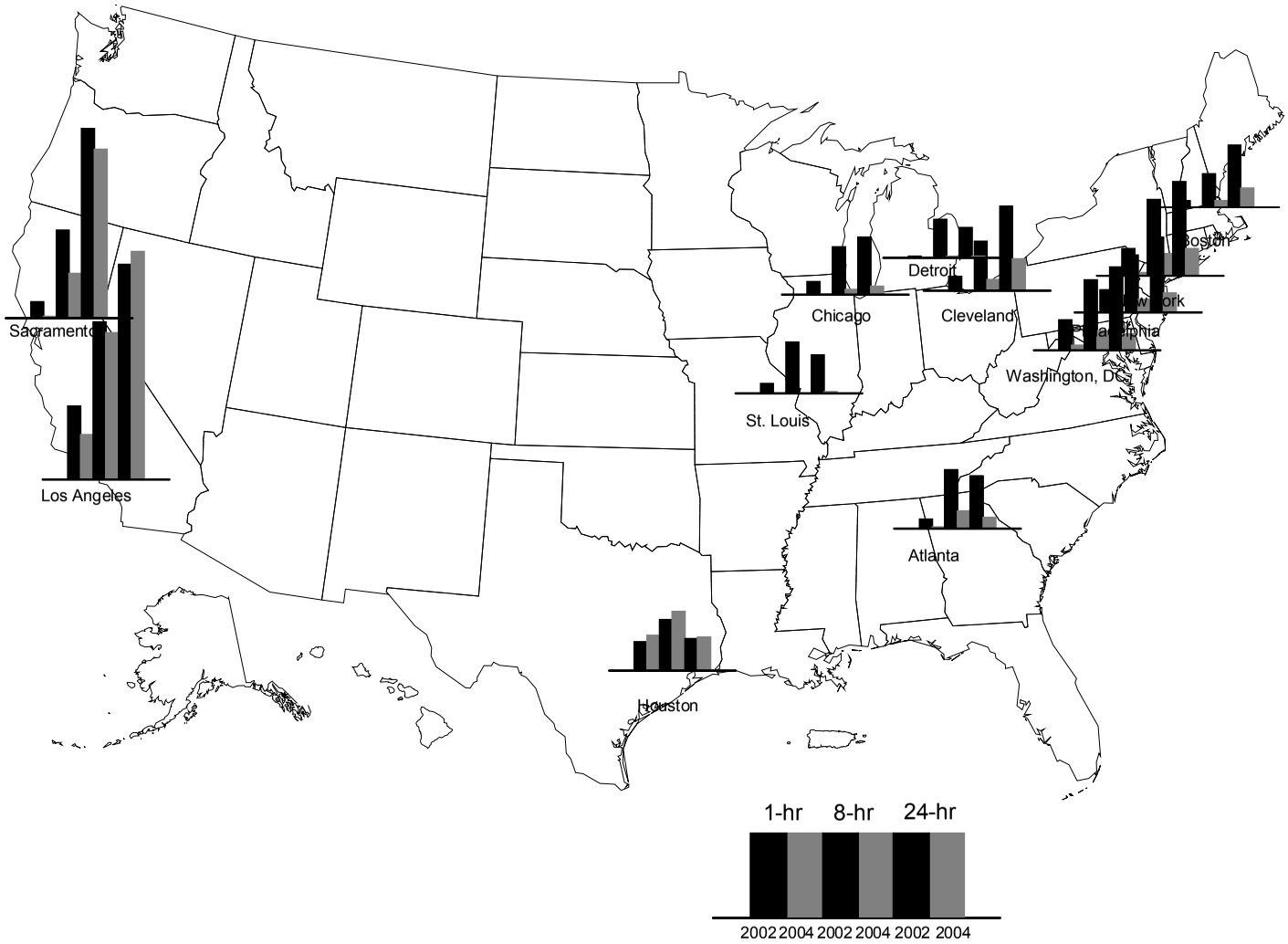


**Figure 2-15. Comparison of 1-hr, 8-hr, and 24-hr Metrics for 2002 and 2004, 12 Risk Areas**

Data Source: AQS

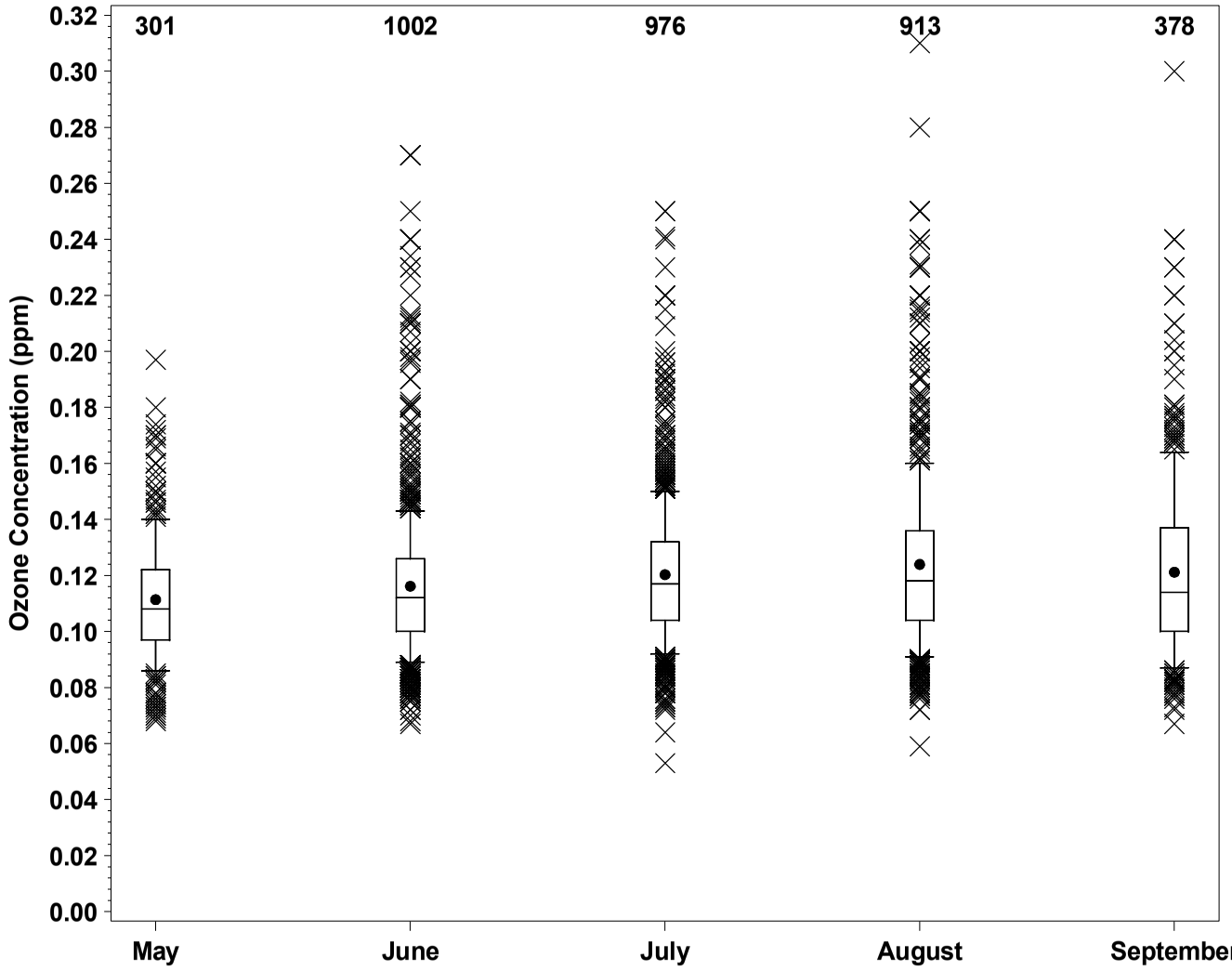


**Figure 2-16. 2nd Highest Daily Maximum 1-hour Ozone Values from 2004 by Month.** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; 'x' depicts values outside the 10th and 90th percentile; and numbers above the boxes depicts the number of sites.

Data Source: AQS

increase from May to September while the extreme values show a more pronounced but more variable increase for the same period (Fitz-Simons, et al., 2005).

Figure 2-17 shows box-plots of all 2004 data from May through September for the fourth highest daily 8-hr maximums. The center of the distribution and the extremes show a slight, steady increase from May to July followed by a slight decrease from July through September (Fitz-Simons, et al., 2005).

#### 2.5.3.4 Short Term Variability – Diurnal

The daily cycles of human activity and the solar phase drive the hour-to-hour daily cycle seen in ground level $O_3$ concentrations. The daily 1-hr peak levels generally occur in the afternoon with the lowest concentration occurring in the early morning. However, on any given day when conditions are right, this phase can be reversed with the highest values occurring at night or early morning. Ozone transport can also effect at what time peaks can occur. For example, some sites in Maine peak late in the evening due to transport.

In order to examine diurnal patterns, box-plots summarize 1-hr values and 8-hr for each hour in the day. The most recently available data, 2004, was used to generate all the box-plots. Figure 2-18 summarizes 1-hr data from AQS that was classified as urban and center city. The pattern is similar for both weekend and week day data. The pattern of the center of the distribution of values shows a smooth sinusoidal portion of the curve from 6:00AM until 8:00PM and reaches a peak at 1:00 PM to 3:00 PM. Then the pattern alters to a gradual decrease from 9:00 PM to 6:00AM (Fitz-Simons, et al., 2005).

Figure 2-19 shows the same set of summaries for 8-hr data. 8-hr values run from 0 to 23 hours. Hour1 is the average of 1-hr values from 1 to 8 while hour 2 is the average of hours 2 to 9 and so on. The main difference between the 1-hr data and the 8-hr data is that the 8-hr data exhibit a smoother sinusoidal pattern throughout the day with a peak for the center of the distribution occurring at 10:00 AM or 11:00 AM and a minimum at about 12:00 midnight. The week end pattern is similar to the week day pattern (Fitz-Simons, et al., 2005).

Figures 2-20 through 2-23 summarize 1-hr and 8-hr data from CASTNET sites which are considered rural. Several differences are noted here. The patterns for the center of the distribution are similar to the patterns for the urban sites. The largest values of the 1-hr data exhibit no pattern but the largest values for the 8-hr data have a discernable pattern that differs from the patterns for the values in the center of the distribution. The weekday pattern for the highest values, shown in figure 2-22, has a smooth sinusoidal pattern but reaches 2 peaks in the day (12:00 midnight and 12:00 noon). The weekend pattern, shown in figure 2-23, also shows a pronounced peak in the afternoon at about 1:00 PM which occurs about 2 hours after the peak for the values in the center of the distribution (Fitz-Simons, et al., 2005).

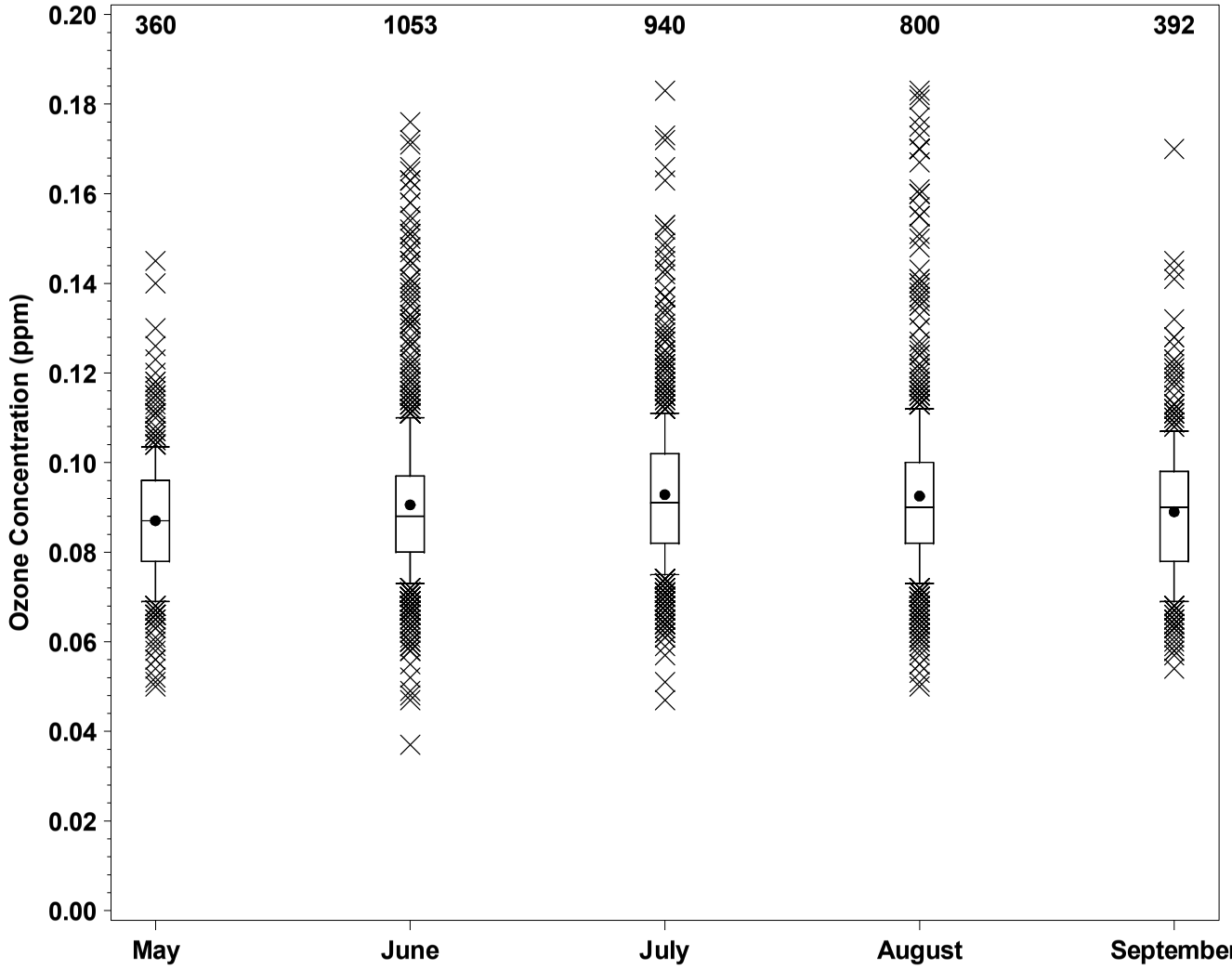


**Figure 2-17. 4th Highest Daily Maximum 8-hour Ozone Values from 2004 by Month.** Box Depicts interquartile range and median; whiskers depict 10th and 90th percentile; 'x' depicts values outside the 10th and 90th percentile; and numbers above the boxes depicts the number of sites.

Data Source: AQS

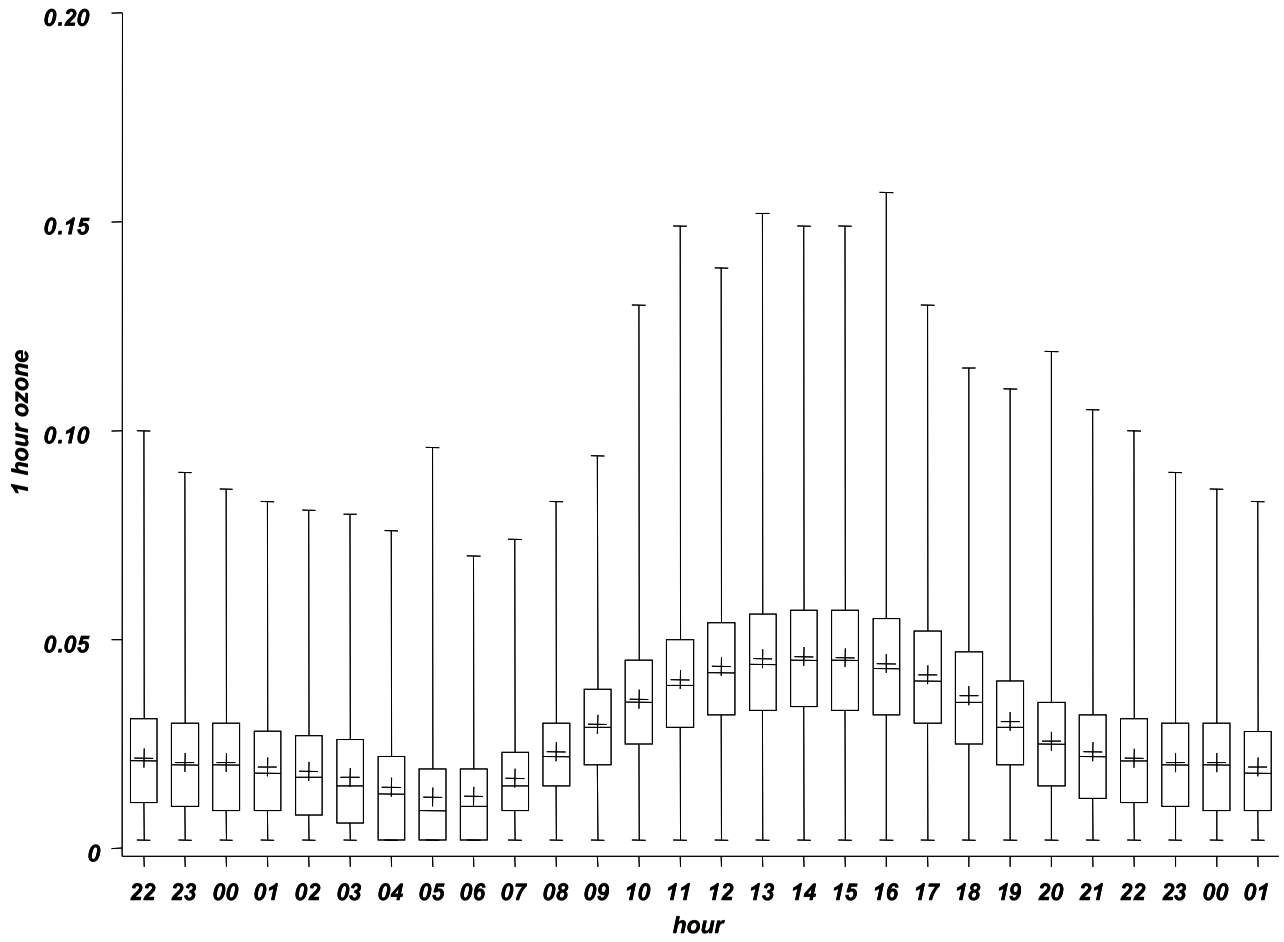


**Figure 2-18. 1-Hour Diurnal Week Day Pattern for Urban Sites, May through September 2004.**

Data Source: AQS

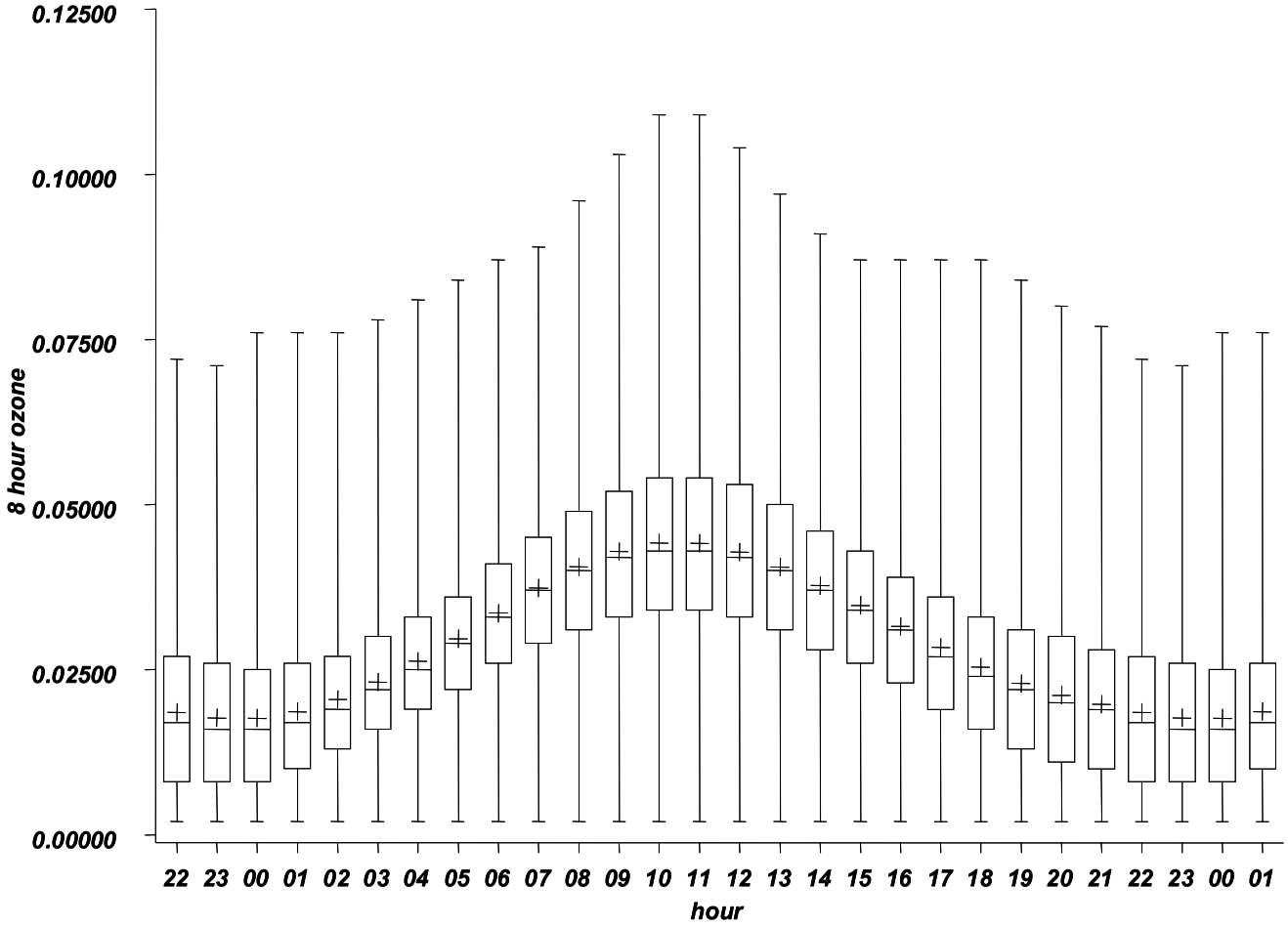


**Figure 2-19. 8-Hour Diurnal Week Day Pattern for Urban Sites, May through September 2004.** Box Depicts interquartile range and median; whiskers depict maximum and minimum values; and '+' depicts the mean.

Data Source: AQS

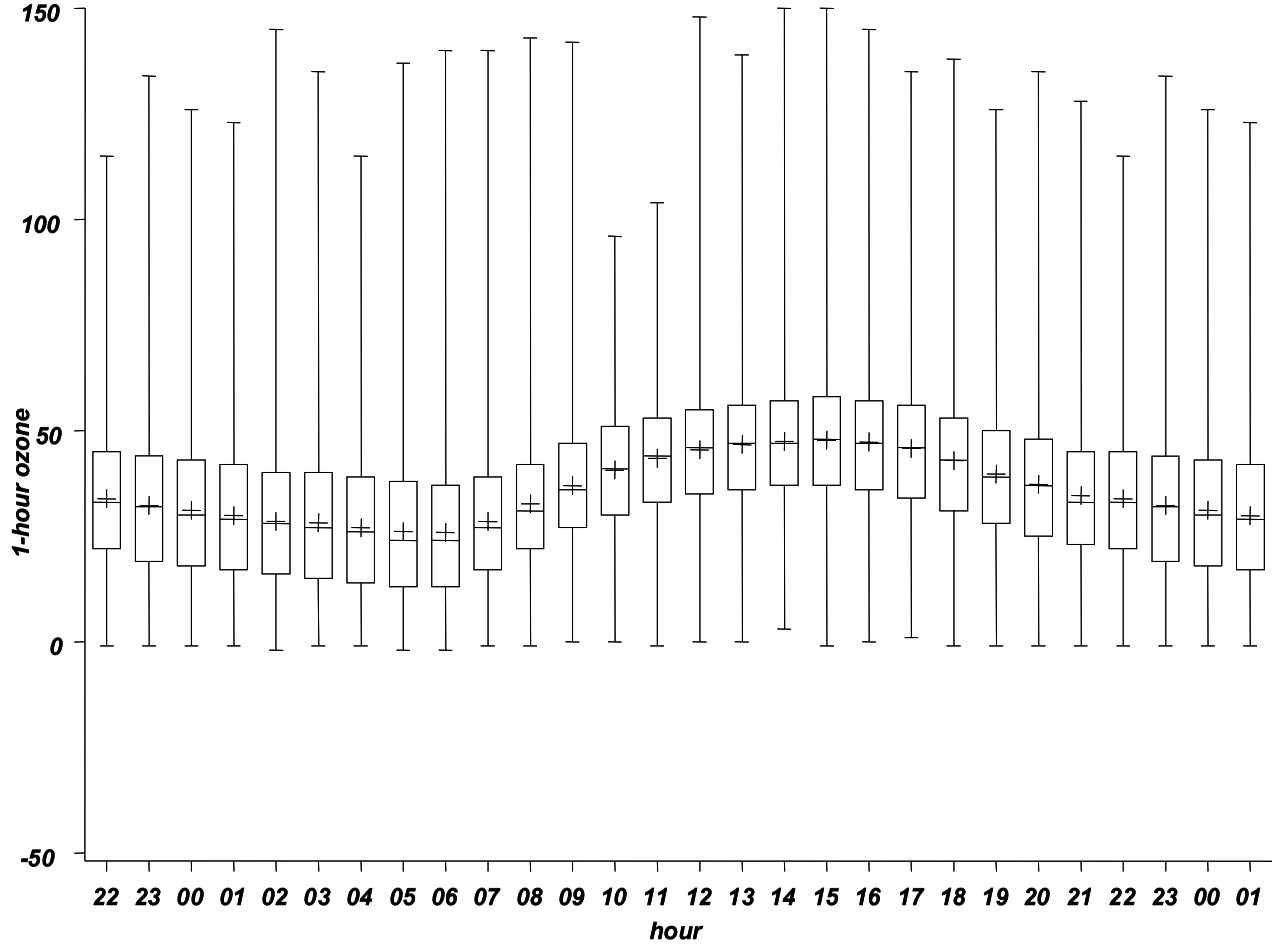


**Figure 2-20 1-Hour Week Day Diurnal Pattern for Rural Sites, May through September 2004.** Box Depicts interquartile range and median; whiskers depict maximum and minimum values; and '+' depicts the mean.

Data Source: CASTNET

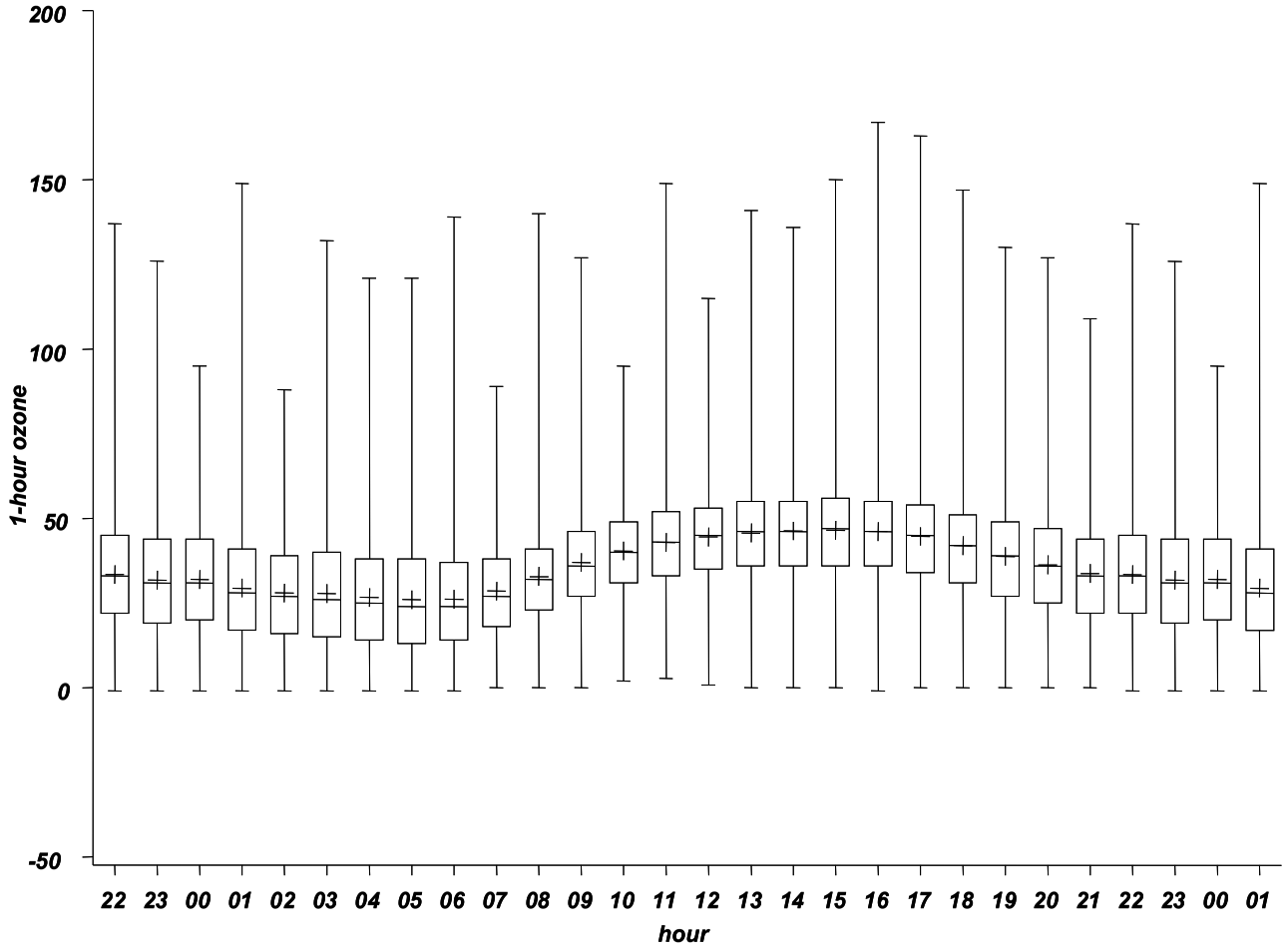


**Figure 2-21. 1-Hour Week End Diurnal Pattern for Rural Sites, May through September 2004.** Box Depicts interquartile range and median; whiskers depict maximum and minimum values; and '+' depicts the mean.

Data Source: CASTNET

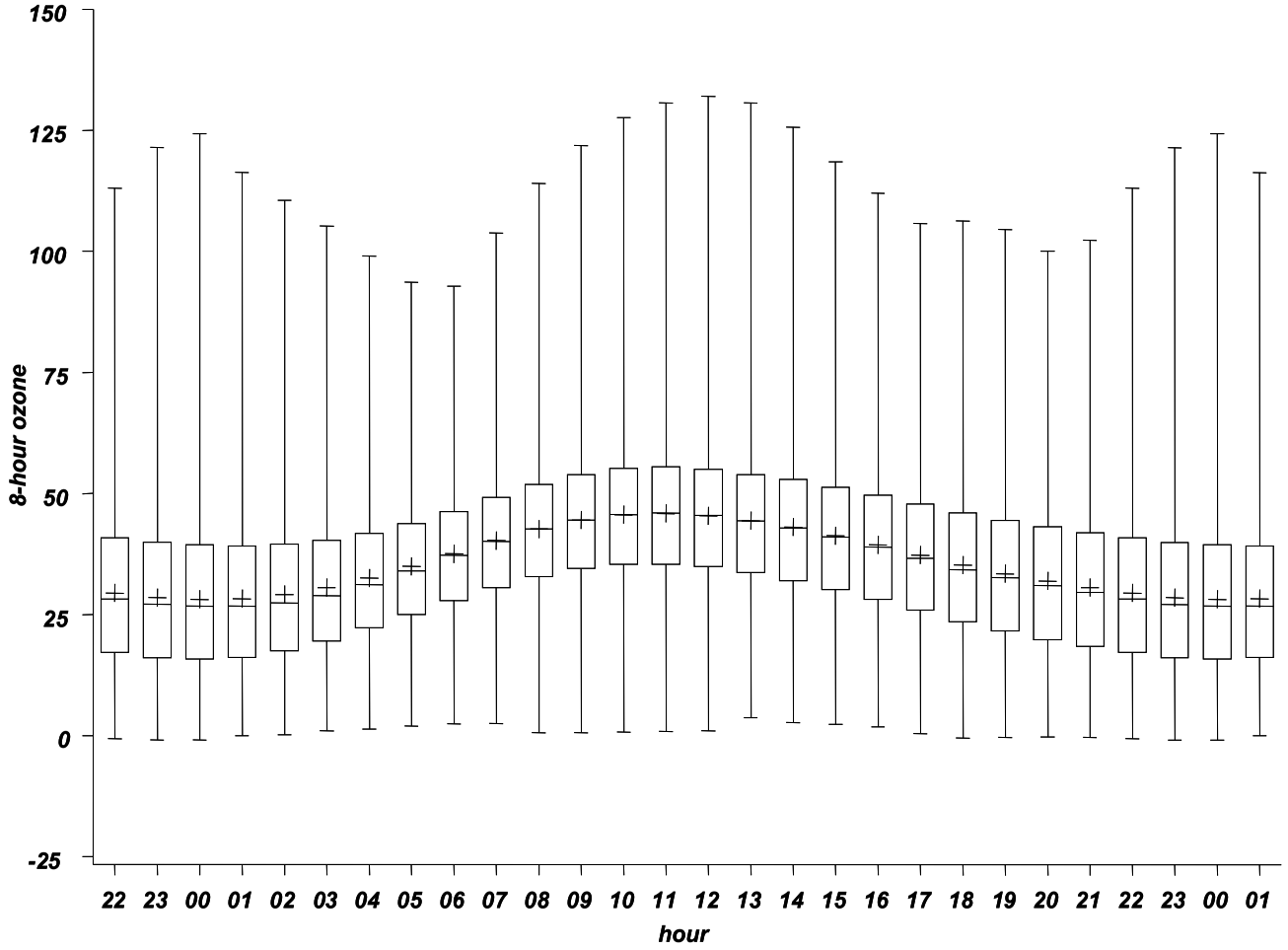


**Figure 2-22. 8-Hour Week Day Diurnal Pattern for Rural Sites, May through September 2004.** Box Depicts interquartile range and median; whiskers depict maximum and minimum values; and '+' depicts the mean.

Data Source: CASTNET

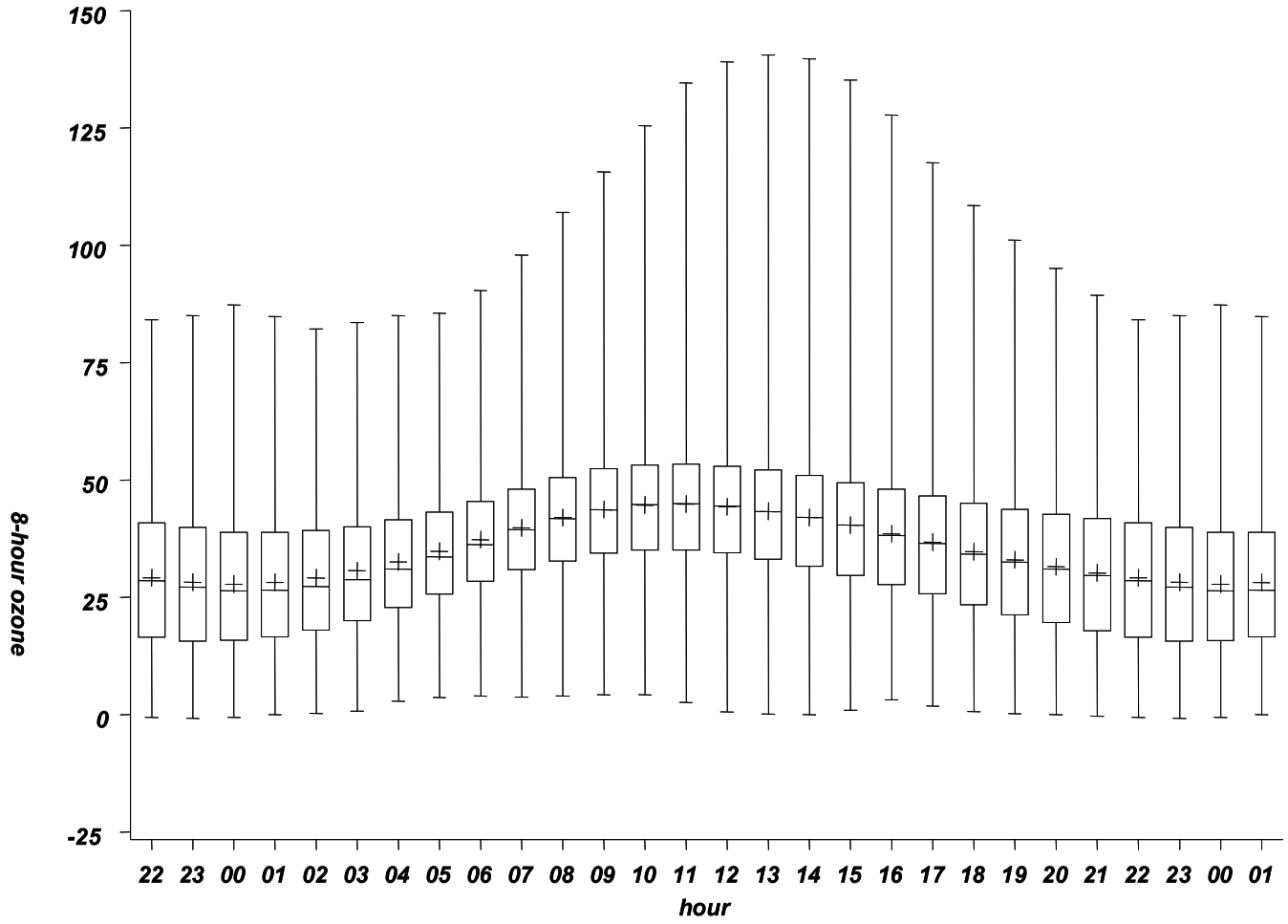


**Figure 2-23. 8-Hour Week End Diurnal Pattern for Rural Sites, May through September 2004.** Box Depicts interquartile range and median; whiskers depict maximum and minimum values; and '+' depicts the mean.

Data Source: CASTNET

## 2.6 CHARACTERIZATION OF OZONE EPISODES

Major episodes of high $O_3$ concentrations in the eastern United States are associated with slow moving, high pressure systems. High pressure systems during the warmer seasons are associated with the sinking of air, resulting in warm, generally cloudless skies, with light winds. These conditions result in the development of stable air masses near the surface which inhibit the vertical mixing of $O_3$ precursors. The combination of inhibited limited vertical mixing and light winds minimizes the dispersal of pollutants emitted in urban areas, allowing their concentrations to build up. Photochemical activity involving these precursors is also enhanced because of higher temperatures and the availability of sunlight. Downward entrainment of overnight transported ozone and precursors trapped aloft begins on the following day as the PBL starts growing. In the eastern United States, high $O_3$ concentrations during an episode can extend over hundreds of thousands of square kilometers for several days.

Episodes have two main characteristics, the concentration level reached and the length of time that this level is reached in consecutive days. The following discussion addresses how these characteristics of episodes have varied through both space and time.

Numbers of episodes defined by daily maximum 1-hr $O_3$ concentrations reaching a level of 0.12ppm for 1 day generally follow the long term trend of central values (means or medians) of the 1-hr $O_3$ data (See Figures 2-13 and 2-24). As the length of these episodes increases, the frequency of these episodes decreases. In the most recent years (1997-2004) episodes lasting 5 days or more often have not occurred at all (Fitz-Simons, et al., 2005). For this we conclude that control strategies have been reducing peak 1-hr $O_3$ across major urban areas.

Numbers of episodes defined by daily maximum 8-hr $O_3$ concentrations reaching a level of 0.08ppm for 1 day generally follow the long term trend of central values of the 8-hr $O_3$ data (See Figures 2-11 and 2-25). As the length of these episodes increase, the frequency of these episodes decreases. However, some of the longer episodes (6 days of more) continue to occur at this level even in the most recent years. In fact the episode must be defined by a level of 0.10 ppm before these longer episodes disappear in the most recent years (Fitz-Simons, et al., 2005).

As episode length and level increase for both 1-hr and 8-hr $O_3$ data the frequency decreases (Figure 2-26 and 2-27). The longer periods and higher levels disappear altogether in the period from 2000-2004 (Fitz-Simons, et al., 2005).

One final aspect of episodes to examine is the return time or the number of days between episodes. Looking at the intervals between episodes of 0.08ppm for 8-hr data, the most prevalent gap length in days is 1 day. There is a slight peak again at 4 days followed by a gradual decrease in frequency as the gap-length increases (see Figure 2-28). Looking at the same data for episodes of 0.12ppm, it appears that some periodicities appear at 1 day, 5-6 days, 21 days, and

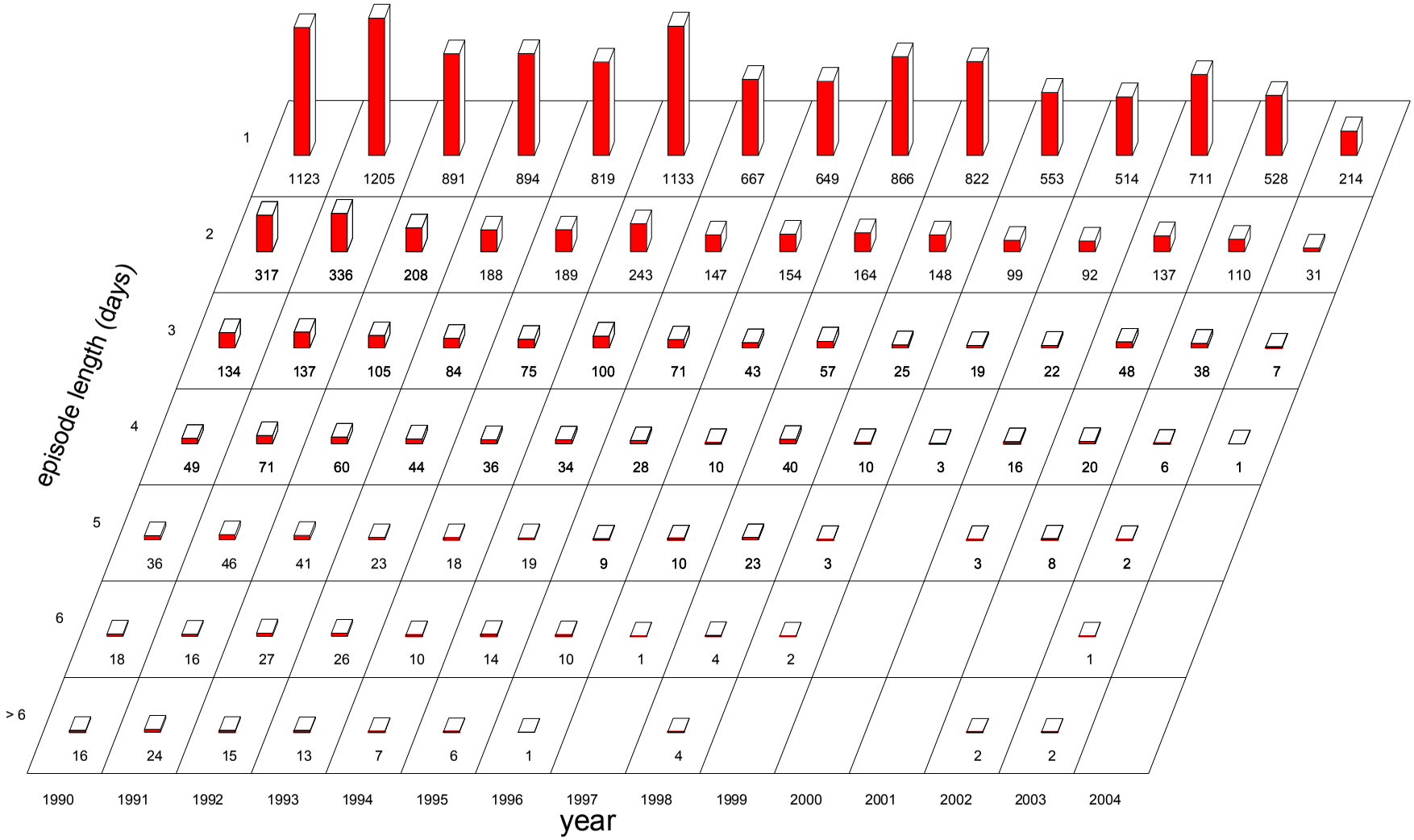


**Figure 2-24. Length of Episodes over 0.12 ppm by Year for 1-hour O3 Data.**

Data Source: AQS

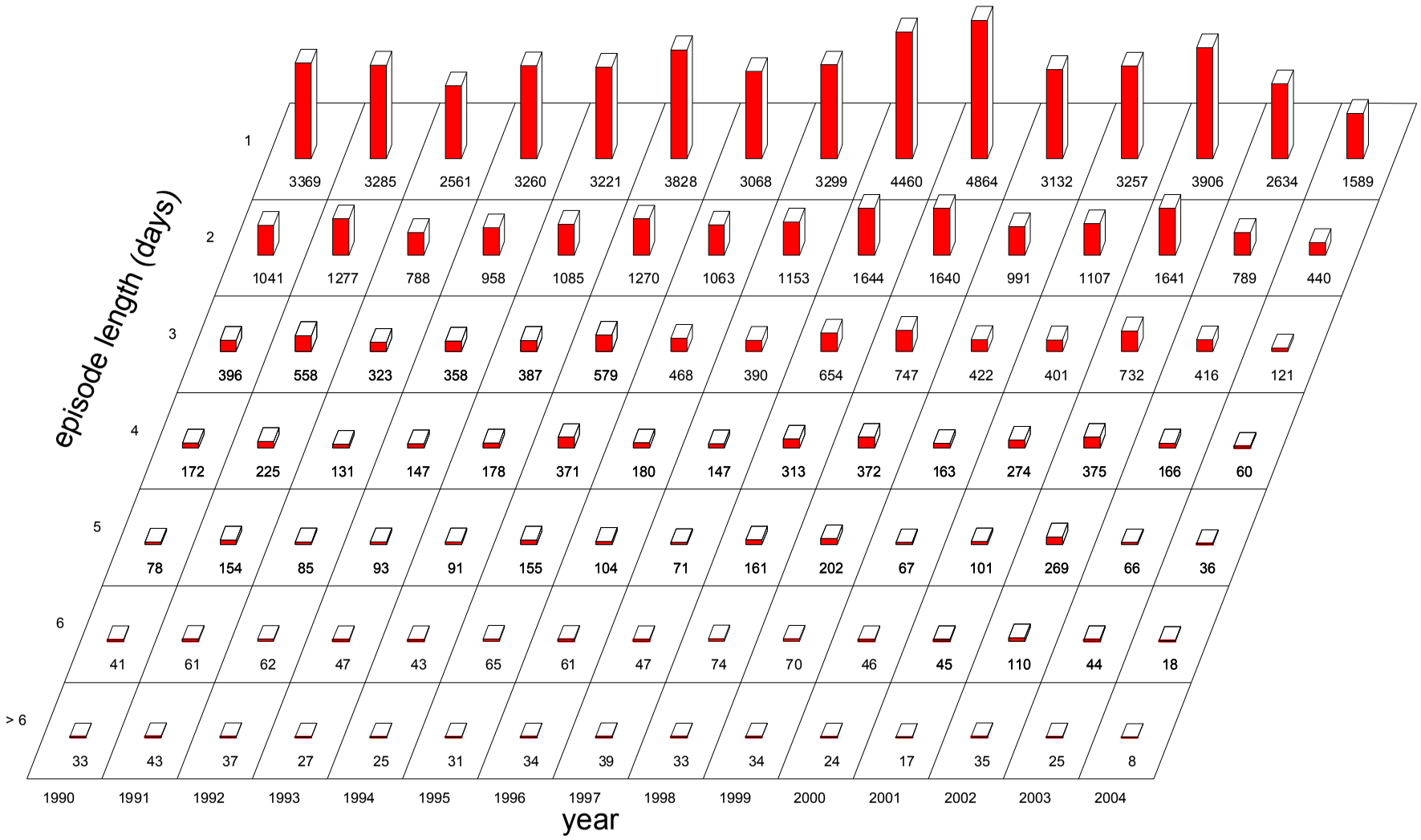


**Figure 2-25. Length of Episodes over 0.08 ppm by Year for 8-hour O3 Data.**

Data Source: AQS

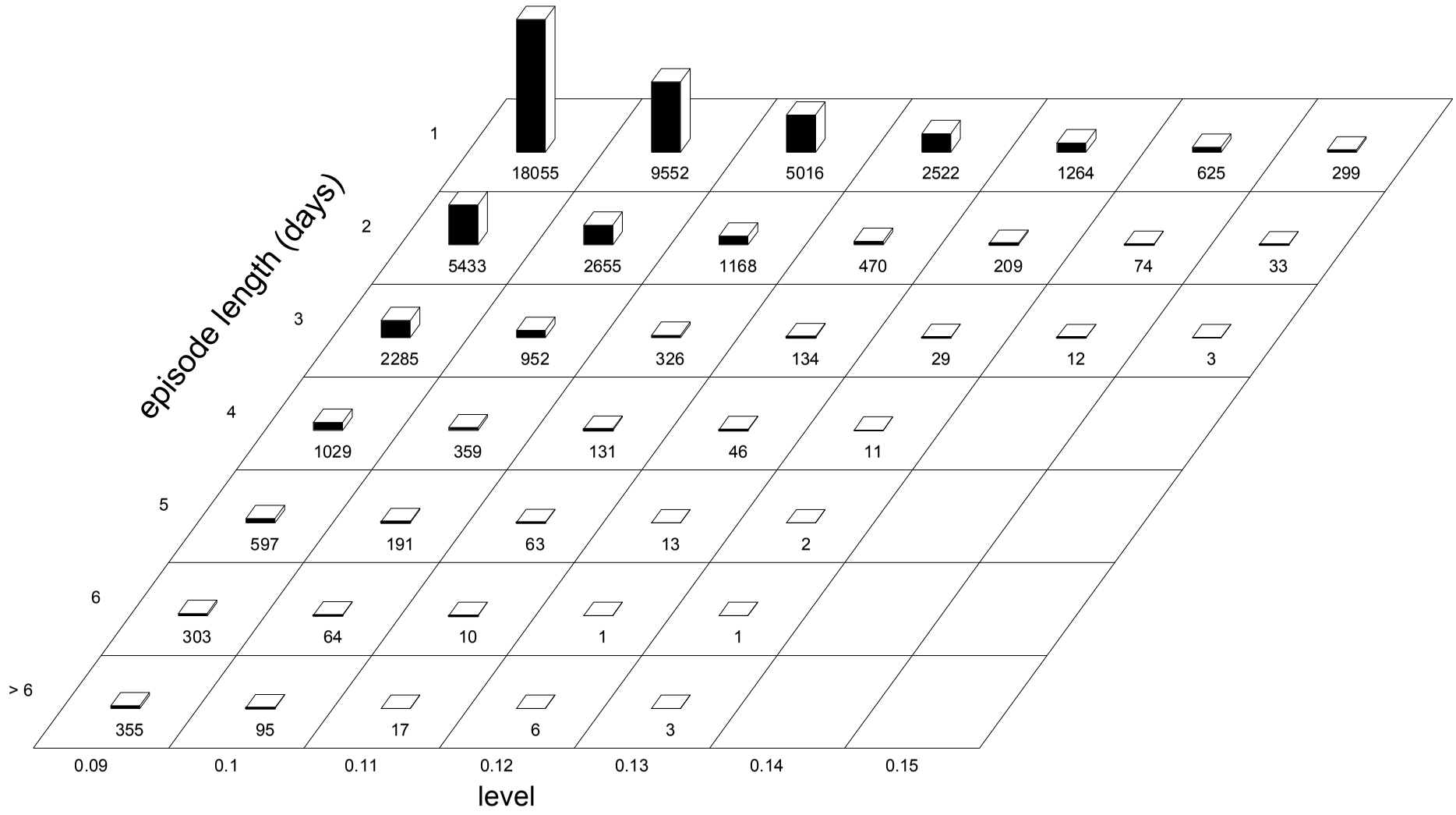


**Figure 2-26. Length of Episodes over Levels for 1-hour O3 Data (2000-2004).**

Data Source: AQS

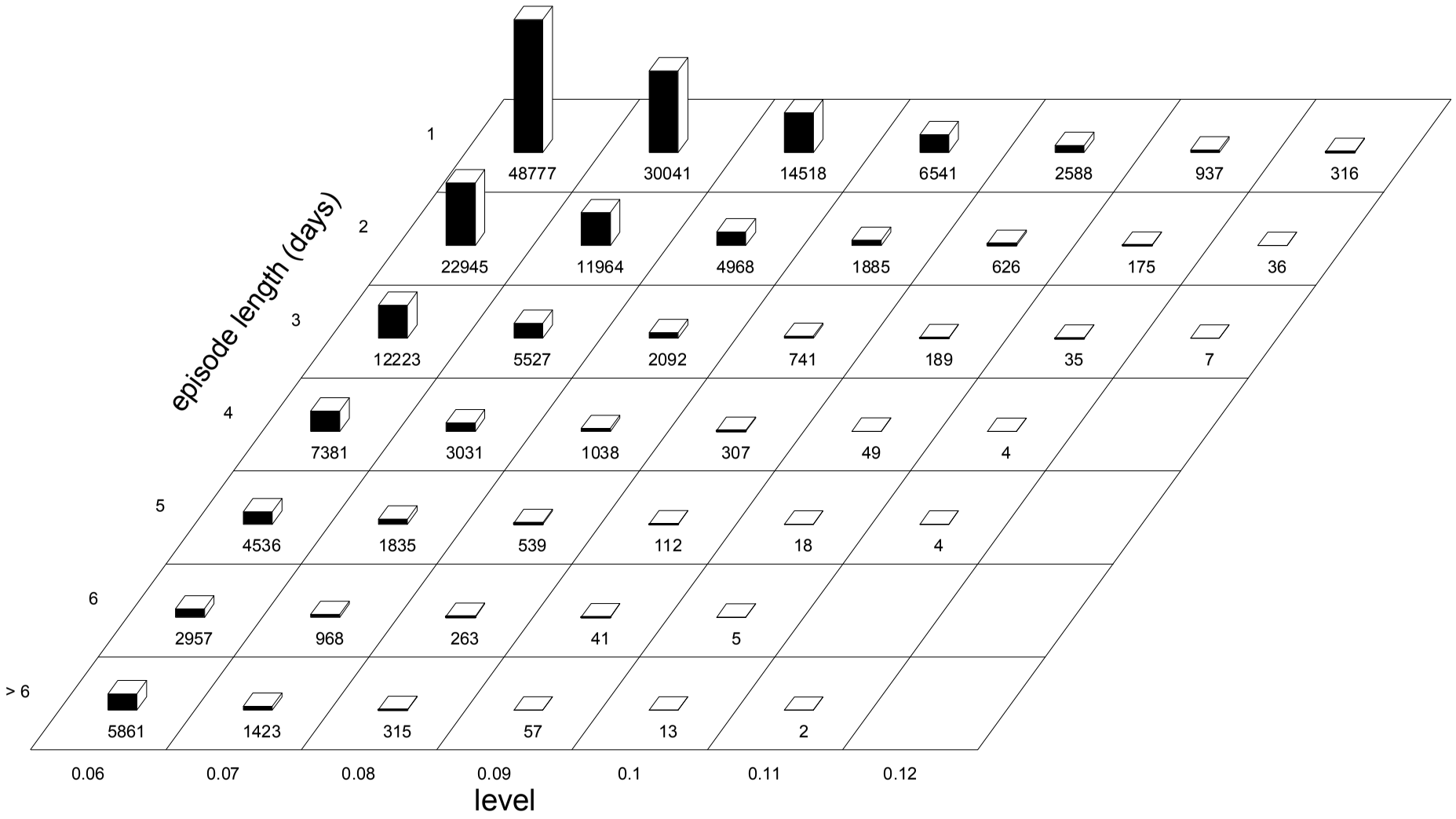


**Figure 2-27. Length of Episodes over Levels for 8-hour O3 Data (2000-2004).**

Data Source: AQS

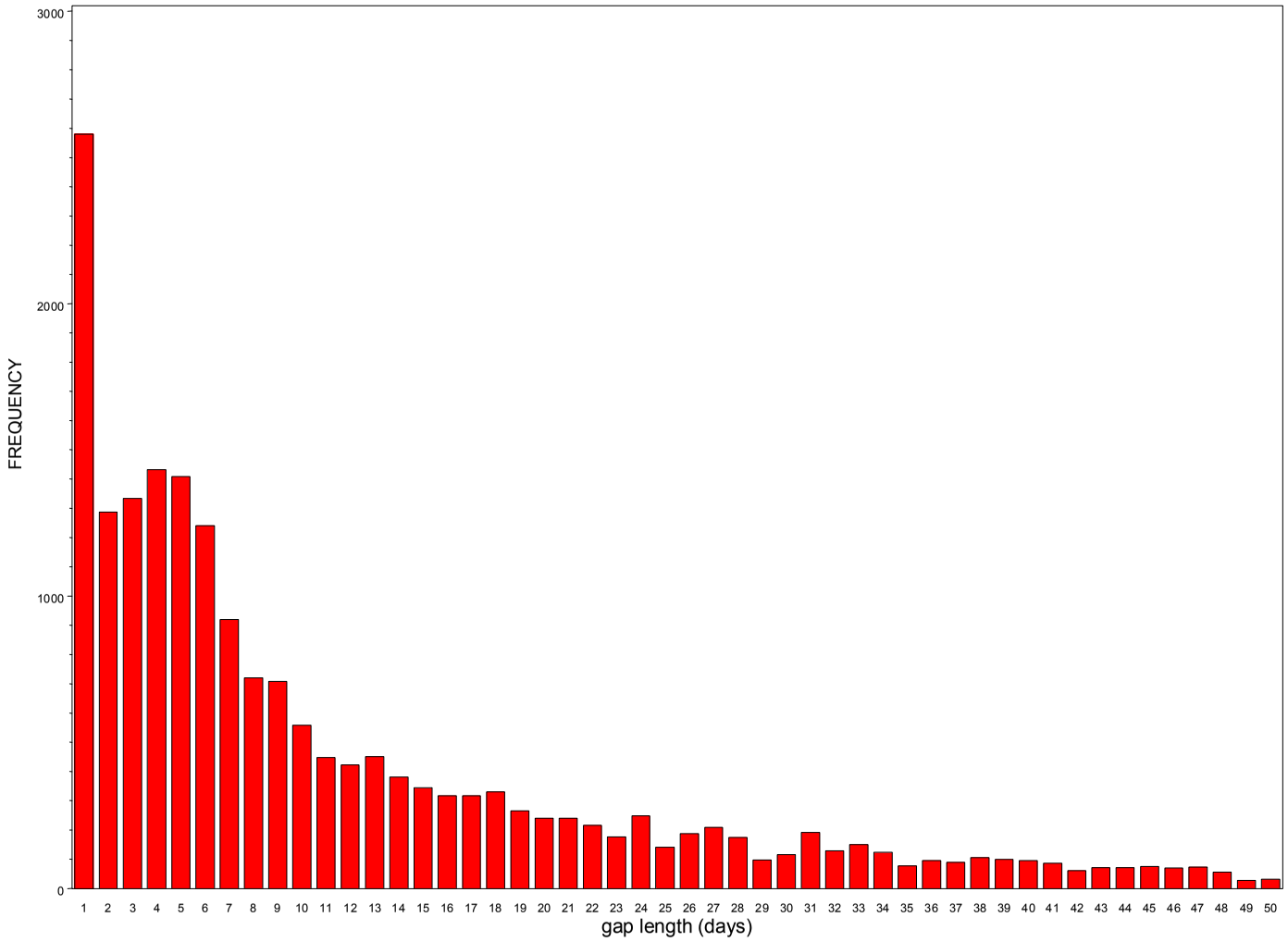


**Figure 2-28. Length of Gaps in Days Between Episodes over 0.08 ppm for 8-hour O3 Data (2000-2004).**

33-34 days. The frequencies for these episodes are so small compared to frequencies lower level episodes that these indications should not be considered real or significant indications of periodicities. The 1-hr $O_3$ data exhibit much the same lack of periodicity as the 8-hr data (Fitz-Simons, et al., 2005).

## 2.7 POLICY RELEVANT BACKGROUND LEVELS

For purposes of this document, background or policy relevant background (PRB) $O_3$ is defined as the distribution of $O_3$ concentrations that would be observed in the U.S. in the absence of anthropogenic (man-made) emissions of precursor emissions (e.g., VOC, NOx, and CO) in the U.S., Canada, and Mexico. This is referred to as policy-relevant background, since this definition of background facilitates separating pollution levels that can be controlled by U.S. regulations (or through international agreements with neighboring countries) from levels that are not generally controllable in this manner. As defined here, PRB includes (1) $O_3$ in the U.S. from natural sources of emissions in the U.S., Canada, and Mexico and (2) $O_3$ in the U.S. from the transport of $O_3$ or the transport of emissions from both natural and man-made sources, from outside of the U.S. and its neighboring countries. As discussed in Chapter 5 of this Staff Paper, PRB concentrations enter into the assessments of risk to human health.

Contributions to PRB levels of $O_3$ include: photochemical interactions involving natural emissions of VOCs, $NO_X$, and CO; the long-range transport of $O_3$ and its precursors from outside North America; and stratospheric-tropospheric exchange (STE). Processes involved in STE are described in detail in Annex AX2.3 of the CD. Natural sources of $O_3$ precursors include biogenic emissions, wildfires, and lightning. Biogenic emissions from agricultural activities are not considered in the formation of PRB (CD, p.AX2-145).

As a result of long-range transport from anthropogenic source regions within North America, estimates of PRB $O_3$ concentrations cannot be derived solely from measurements of $O_3$, and must be based on modeling. The global photochemical transport model GEOS-CHEM (Fiore et al., 2003) has been applied to estimate PRB $O_3$ concentrations across the U.S. (U.S. EPA, 2005a, AX3-131). The CD refers to a number of GEOS-Chem publications (Bey et al., 2001; Liu et al., 2002; Martin et al., 2002; Fusco and Logan, 2003; Li et al., 2002, 2005), summarizing their conclusions as "results indicate no significant bias, and agreement to generally within 5 ppbv for monthly mean concentrations at different altitudes." The CD goes on to review detailed evaluations of GEOS-Chem with ozone observations at U.S. surface sites (Fiore et al., 2002, 2003), comparisons of GEOS-Chem and MOZART global models with observations (Goldstein et al., 2004), and note that "several other papers have evaluated the GEOS-Chem simulation for surface ozone and its precursors over the United States." Summarizing their

assessment of the validity of the GEOS-Chem model, the CD states "in conclusion, we estimate that the PRB ozone values reported by Fiore et al. (2003) for afternoon surface air over the United States are likely 10 ppbv too high in the southeast in summer, and accurate within 5 ppbv in other regions and seasons."

The GEOS-Chem model shows that PRB $O_3$ concentrations are a function of season, altitude and total surface $O_3$ concentration. PRB $O_3$ concentrations at the surface are generally predicted to be in the range of 0.015 to 0.035 ppm in the afternoon, and they decline under conditions conducive to $O_3$ episodes. They are highest during spring and decline into summer. Higher values tend to occur at higher elevations during spring due to contributions from hemispheric pollution and stratospheric intrusions. The stratospheric contribution to surface $O_3$ is typically well below 0.020 ppm and only rarely elevate $O_3$ concentrations at low-altitude sites and only slightly more often elevate them at high-altitude sites (U.S. EPA, 2005a, AX3-148).

The exposure and health risk analyses described in Chapter 4 and 5 use estimates of PRB based on runs of the GEOS-CHEM model applied for the 2001 warm season (i.e., April to September). The GEOS-CHEM data consist of gridded values with latitude running from 12º to 80 º in 2 º steps and longitude running from -177.5 º to -47.5º in 2.5 º steps. These data are hourly values which have been used to create daily diurnal profiles which are fixed for each day of each month during the $O_3$ season. The model estimated the PRB and total $O_3$ concentrations at each grid point. The PRB estimates from the grid nearest each of the 12 urban areas included in the exposure and risk analyses has been used to estimate PRB in each of these areas. Appendix 2A provides plots of the PRB estimates by month for each of the 12 urban areas.

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# 3. POLICY-RELEVANT ASSESSMENT OF HEALTH EFFECTS EVIDENCE

## 3.1 INTRODUCTION

This chapter assesses key policy-relevant information on the known and potential health effects associated with exposure to ambient $O_3$, alone and in combination with other pollutants that are routinely present in ambient air. This assessment focuses specifically on the health effects evidence evaluated in Chapters 4 through 7 of the CD with particular emphasis on the integrative synthesis presented in Chapter 8. That integrative synthesis focuses on integrating newly available scientific information with that available from the last review, as well as integrating information from various disciplines, to address a set of issues central to the assessment of scientific information upon which this review of the $O_3$ NAAQS is based. This chapter also addresses key issues relevant to quantitative assessment of controlled-human exposure and epidemiological evidence, to provide a foundation for the quantitative human exposure and health risk assessments presented below in Chapters 4 and 5. Those quantitative assessments, together with this evidence-based assessment, provide the foundation for the development of staff conclusions and identification of options for consideration related to primary standards for $O_3$ presented below in Chapter 6.

The decision in the last review focused primarily on evidence from short-term and prolonged controlled-exposure studies reporting lung function decrements, respiratory symptoms, and respiratory inflammation in humans, as well as epidemiology studies reporting excess hospital admissions and emergency department (ED) visits for respiratory causes. The CD prepared for this review emphasizes a large number of epidemiological studies published since the last review with these and additional health endpoints, including acute and chronic health effects of $O_3$ for premature mortality, enhanced respiratory symptoms and lung function decrements in asthmatic individuals, school absences, and ED visits for respiratory causes. It also emphasizes important new information from toxicology, dosimetry, and controlled human exposure studies.

As discussed in more detail below (section 3.3), highlights of the new evidence include:

- New controlled human-exposure studies have examined whether lung function decrements are observed in healthy adults under moderate exertion for 6.6 hr exposures to levels as low as 0.04 ppm.
- New controlled human-exposure studies offer evidence of increased airway responsiveness to allergens in subjects with allergic asthma and allergic rhinitis exposed to $O_3$.

- Numerous controlled human-exposure studies have reported indicators of $O_3$-induced inflammatory response in both the upper respiratory tract (URT) and lower respiratory tract (LRT), while other studies have shown significant changes in host defense capability following $O_3$ exposure of healthy young adults.
- Animal toxicology studies provide new information regarding mechanisms of action, increased susceptibility to respiratory infection, and the biological plausibility of acute effects and chronic, irreversible respiratory damage.
- Numerous acute exposure epidemiological studies published during the past decade offer added evidence of ambient $O_3$-related lung function decrements and respiratory symptoms in exercising healthy subjects and asthmatic subjects, as well as evidence on new health endpoints, such as the relationships between ambient $O_3$ concentrations and school absenteeism and between ambient $O_3$ and cardiac physiologic endpoints.
- Several new studies have been published over the last decade examining the temporal associations between $O_3$ exposures and ED visits for respiratory diseases and on respiratory-related hospital admissions.
- Newly available, large multicity studies, designed specifically to examine the effects of acute exposure to PM and $O_3$ on mortality, provide much more robust and credible information than was available in the last review. The results from two key studies carried out in 95 U.S. communities (U.S. National Morbidity, Mortality Air Pollution Study [NMMAPS]) and in 23 European cities (Air Pollution and Health: European Approach [APHEA]) reported positive and significant $O_3$ effect estimates for all cause (nonaccidental) mortality.
- In a recent study, Bell et al. (2006) applied several statistical models to data on air pollution, weather, and mortality for the 98 NMMAPS communities to evaluate whether a threshold level exists for premature mortality. The results indicate that even low levels of tropospheric $O_3$ are associated with premature mortality.
- Three recent meta-analyses evaluated potential sources of heterogeneity in $O_3$-mortality associations, and these studies provide evidence of a robust association between ambient $O_3$ and mortality, especially for the warm $O_3$ season.

Section 3.2 provides an overview of mechanisms of toxicity, with more detailed discussion in Appendix 3A. Section 3.3 summarizes the nature of effects induced by $O_3$ exposure or associated with exposure to $O_3$, alone and in combination with other pollutants, drawing on information in Chapters 5-8 of the CD. Section 3.4 summarizes conclusions and judgments from the CD's integrative assessment of the epidemiological evidence regarding the extent to which causal inferences can be made about observed associations between health endpoints and exposure to $O_3$, and discusses key issues related to quantitative risk assessment based on such evidence. Section 3.5 discusses biological plausibility and coherence of evidence for $O_3$-related adverse health effects, including short-term respiratory effects, short-term cardiovascular effects,

long-term health effects, and mortality-related health endpoint. Drawing from the CD's integrative synthesis, section 3.6 discusses factors that modify responsiveness to $O_3$; potentially susceptible and vulnerable populations groups; and public health impacts of exposure to ambient $O_3$. Finally, section 3.7, summarizes key policy-relevant conclusions from the CD about $O_3$-related health effects, in the context of a discussion of issues related to our confidence in and the utility of the underlying evidence.

## 3.2 MECHANISMS OF TOXICITY

Evidence is covered in Chapters 5 and 6 of the CD on possible mechanisms by which exposure to $O_3$ may result in acute and chronic health effects. While most of the available evidence addresses mechanisms for $O_3$, we recognize that $O_3$ serves as an indicator for the total photochemical oxidant mixture found in the ambient air, which includes various reactive oxidant species (ROS). Some effects may be caused by one or more components in the overall pollutant mix, either separately of in combination with $O_3$. Evidence from dosimetry, toxicology, and human exposure studies has contributed to an understanding of the mechanisms that help to explain the biological plausibility and coherence of evidence for $O_3$-induced respiratory health effects reported in epidemiological studies. In the past, however, little information was available to help explain potential biological mechanisms which linked $O_3$ exposure to premature mortality or cardiovascular effects. More recently, however, an emerging body of animal toxicology evidence is beginning to suggest mechanisms that may mediate acute $O_3$ cardiovascular effects.

Scientific evidence discussed in the CD (section 5.2) indicates that reactions with lipids and antioxidants are the initial step in mediating deleterious health effects of $O_3$. There is subsequent activation of a cascade of events starting with inflammation, altered permeability of the epithelial barrier, impaired clearance mechanisms (including host defense), and pulmonary structural alterations that potentially exacerbate a preexisting disease status. According to the CD, the scientific evidence is still lacking for clearly establishing a role for one or a group of mechanistic pathways underlying $O_3$ health effects observed in epidemiological studies. Appendix 3A provides a further discussion of mechanisms of toxicity.

## 3.3 NATURE OF EFFECTS

The CD provides new evidence that notably enhances our understanding of short-term exposure effects, including effects on lung function, symptom, and inflammatory effects reported in controlled exposure studies. These studies support and extend the findings of the previous CD. There is also a significant body of new epidemiological evidence of associations between short-term exposure to $O_3$ and effects such as premature mortality, hospital admissions and ED

visits for respiratory (e.g., asthma) causes. Key epidemiological and human controlled exposure studies are summarized in Appendices 3B and 3C, respectively.

The following discussions of $O_3$-related health effects are based on scientific evidence critically reviewed in chapters 5, 6, and 7 of the CD, as well as the CD's integration of scientific evidence contained in Chapter 8. In addition, these health effects discussions rely on the more detailed information and tables presented in the CD's annexes AX5, AX6, and AX7. Conclusions drawn about $O_3$-related health effects depend on the full body of evidence from controlled-exposure human, epidemiological and toxicological data contained in the CD. Section 3.3.1 focuses on a broad array of morbidity effects, including both acute and chronic exposures. Section 3.3.2 focuses on the expanded body of evidence on associations between acute $O_3$ exposure and mortality, as well as the more limited evidence on chronic $O_3$ exposures and mortality.

### 3.3.1 Morbidity

This section summarizes scientific information contained in the CD on respiratory and cardiovascular effects associated with exposure to $O_3$. Evidence of $O_3$-related hospital admissions and ED visits is discussed in section 3.3.1.1, followed by discussion of the effects of short-term and long-term exposure to $O_3$ on the respiratory system in sections 3.3.1.2 and 3.3.1.3, and $O_3$-related cardiovascular effects in section 3.3.1.4.

#### 3.3.1.1 Effects on the Respiratory System from Short-term Exposures

Short-term exposures to $O_3$ have been reported to induce a wide variety of respiratory health effects. These effects include a range of effects, such as morphological changes in the respiratory tract, pulmonary function decrements, respiratory symptoms, respiratory inflammation, increased airway responsiveness, changes in host defense capability, acute morphological effects, increased ED visits and hospital admissions, and effects on exercise performance. Short-term $O_3$ exposure has also been associated with increases in restricted activity days and school absences but evidence is limited for these effects.

##### *3.3.1.1.1 Pulmonary Function Decrements, Respiratory Symptoms, and Asthma Medication Use*

A very large literature base of studies published prior to 1996, which investigated the health effects on the respiratory system from short-term $O_3$ exposures, was reviewed in the 1986 and 1996 CDs (U.S. Environmental Protection Agency, 1986, 1996). In the last review, the lowest $O_3$ concentration at which statistically significant reductions in forced vital capacity (FVC) and forced expiratory volume in 1 second ($FEV_1$) had been reported in sedentary subjects was 0.5 ppm (CD, p 6-3). During exercise, spirometric and symptomatic responses were observed at much lower $O_3$ exposures. When minute ventilation was considerably increased by

continuous exercise (CE) during $O_3$ exposures lasting 2 hr or less at $\geq$ 0.12 ppm, healthy subjects generally experienced decreases in $FEV_1$, FVC, total lung capacity (TLC), inspiratory capacity (IC), mean forced expiratory flow from 25% to 75% of FVC ($FEF_{25-75}$), and tidal volume ($V_T$); increases in specific airway resistance (sRaw), breathing frequency ($f_B$), and airway responsiveness; and symptoms such as cough, pain on deep inspiration, shortness of breath, throat irritation, and wheezing. When exposures were increased to 4- to 8-hr in duration, statistically significant spirometric and symptom responses were reported at $O_3$ concentrations as low as 0.08 ppm and at lower minute ventilation (i.e., moderate rather than high level exercise) than the shorter duration studies (CD. p. 6-6).

The most important observations drawn from studies reviewed in the 1996 CD were that: (1) young healthy adults exposed to $O_3$ concentrations $\geq$ 0.08 ppm develop significant, reversible, transient decrements in pulmonary function if minute ventilation or duration of exposure is increased sufficiently, (2) children experience similar spirometric responses but lesser symptoms from $O_3$ exposure relative to young adults, (3) $O_3$-induced spirometric responses are decreased in the elderly relative to young adults, (4) there is a large degree of intersubject variability in physiologic and symptomatic responses to $O_3$ but responses tend to be reproducible within a given individual over a period of several months, and (5) subjects exposed repeatedly to $O_3$ for several days show an attenuation of response upon successive exposures. This attenuation is lost after about a week without exposure (CD, p. 6-2).

Since 1996, there have been a number of studies published investigating spirometric and symptomatic responses, and they generally support the observations previously drawn. Recent studies for acute exposures of 1 to 2 hr and 6 to 8 hr in duration are summarized in Table AX6-1 of the CD (p. AX6-5 to AX 6-7) and reproduced here as Table 3C-1 in Appendix 3C. Among the more important of the recent studies was McDonnell et al. (1997) which examined reported changes in $FEV_1$ in 485 white males (ages 18-36) exposed for 2 hr to $O_3$ concentrations from as low as 0.08 ppm up to 0.40 ppm, at rest or with intermittent exercise (IE). Decrements in $FEV_1$ were modeled by sigmoid-shaped curve as a function of subject age, $O_3$ concentration, minute ventilation, and duration of exposure. In another study, Ultman et al. (2004) found that exposing 60 young, healthy subjects to 0.25 ppm $O_3$ for 1 hr with continuous exercise produced considerable intersubject variability in $FEV_1$ decrements ranging from 4% improvement to a 56% decrement, which was consistent with findings in the 1996 CD. One third of subjects had $FEV_1$ decrements > 15% and 7% had decrements > 40%. Foster et al. (1993, 1997) examined the effects of $O_3$ on ventilation distribution and reported results suggesting a prolonged $O_3$ effect on the small airways and ventilation distribution (CD, p. 6-5).

For prolonged exposures (4 to 8 hr) in the range of 0.08 to 0.16 ppm $O_3$ using moderate quasi-continuous exercise (QCE; 50 min exercise [minute ventilation of 35 to 40 L/min] and 10

min rest per hr), several pre- and post-1996 studies (Folinsbee et al., 1988; Folinsbee et al., 1994; Horstman et al., 1990; Adams, 2002, 2003, 2006) have reported statistically significant spirometric responses and increased symptoms in healthy adults with increasing duration of exposure, $O_3$ concentration, and minute ventilation. Based on review of several prolonged exposure studies, the CD (p. 6-6) concluded that $FEV_1$ decrements are a function of minute ventilation in 6.6 hr exposure studies and that data from recent studies do not support the contention that minute ventilation should be normalized to BSA for adults. Triangular exposure studies (Hazucha et al., 1992; Adams 2003, 2006) suggest that, depending upon the profile of the exposure, the triangular exposure, which may reflect the pattern of ambient exposures in some locations, can potentially lead to greater $FEV_1$ decrements than square wave exposures when the overall $O_3$ doses are equal (CD, p. 6-10), suggesting that peak exposures are important in terms of $O_3$ toxicology.

McDonnell (1996) and Adams (2002, 2006) used data from a series of studies to investigate the frequency distributions of $FEV_1$ decrements following 6.6 hr exposures and found that average $FEV_1$ responses were relatively small (between 5 and 10 %) at 0.08 ppm $O_3$ (CD, p. 8-17). However, about 18% of the exposed subjects had moderate functional decrements (10 to 20%), and about 8% experienced large decrements (>20%). Figure 3-1A,B,C (CD, Figures 8-1A,B and 8-2, pp. 8-17 and 8-19) demonstrates that while average responses may appear small and insignificant, some individuals can experience much more significant and severe effects that may be clinically significant. The $FEV_1$ responses illustrated in this figure were not corrected for the effect of exercise in clear air. When that is done for the Adams (2002, 2006) data, the percentage of subjects experiencing $\geq$10% $FEV_1$ decrements changes to 7%, 7% and 23% at $O_3$ concentrations of 0.04, 0.06 and 0.08 ppm, respectively in a set of studies conducted in southern California (CD, p. 8-18). The development of these effects is time-dependent during both exposure and recovery periods, with great overlap for development and disappearance of the effects. In healthy human subjects exposed to typical ambient $O_3$ levels near 0.12 ppm, spirometric responses largely resolve within 4 to 6 hr postexposure, but cellular effects persist for about 24 hr. In these healthy subjects, small residual lung function effects are almost completely gone within 24 hr, while in hyperresponsive subjects, recovery can take as much as 48 hr to return to baseline. The majority of these responses are attenuated after repeated exposure, but such attenuation to $O_3$ is lost one week postexposure (CD, p. 8-19).

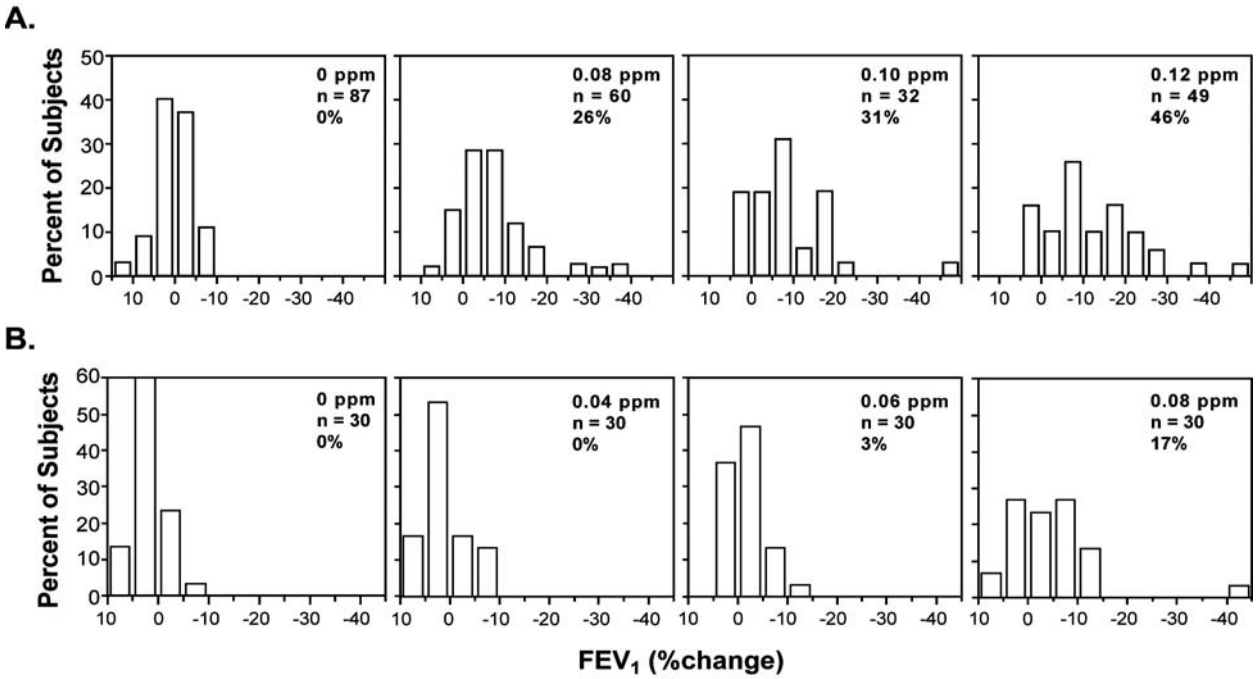



**Figure 3-1A and B. Frequency distributions of $FEV_1$ changes following 6.6-h exposures to a constant concentration of $O_3$ or filtered air. Note that the percentage in each panel indicates the portion of subjects tested having $FEV_1$ decrements in excess of 10%.**

Source:Panel A, McDonnell (1996); Panel B, Adams (2002, 2006), pre- and post-$FEV_1$ data for each subject provided by author.

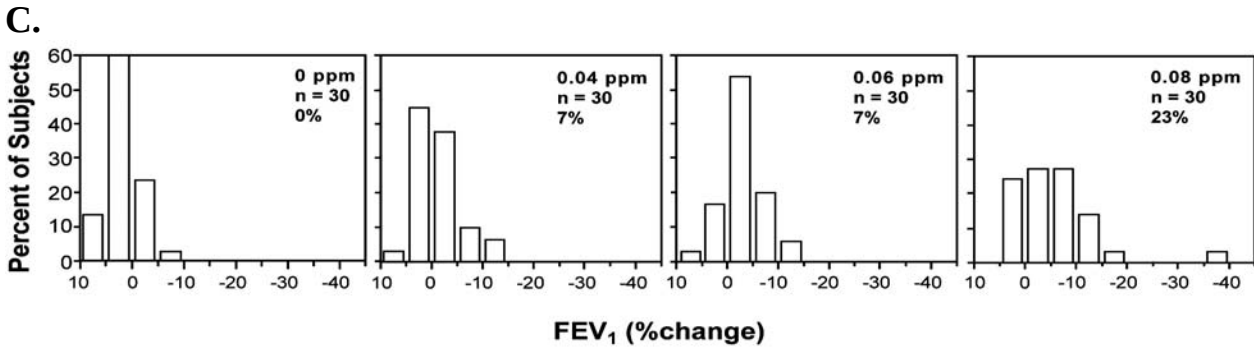



**Figure 3-1C. Frequency distributions of $FEV_1$ changes following 6.6-h exposures to a constant concentration of $O_3$ or filtered air. The $FEV_1$ changes following $O_3$ exposures have been corrected for filtered air responses, i.e., they are $O_3$-induced $FEV_1$ changes. Note that the percentage in each panel indicates the portion of subjects tested having $FEV_1$ decrements in excess of 10%.**

Source: Adams (2002, 2006), pre- and post- $FEV_1$ data for each subject provided by author.

A relatively large number of field studies investigating the effects of ambient $O_3$ concentrations, in combination with other air pollutants, on lung function decrements and respiratory symptoms have been published since 1996 (see CD, sections 7.2.3, 7.2.4, and 8.4.4.1). These newer studies support the major findings of the 1996 CD that lung function changes, as measured by decrements in $FEV_1$ or peak expiratory flow (PEF), and respiratory symptoms in healthy adults and asthmatic children are closely correlated to ambient $O_3$ concentrations. Pre-1996 field studies focused primarily on children attending summer camps and found $O_3$-related impacts on measures of lung function, but not respiratory symptoms, in healthy children. The newer studies have expanded into looking at $O_3$-related effects on outdoor workers, athletes, the elderly, hikers, school children, and asthmatics. Collectively, these studies confirm and extend clinical observations that prolonged exposure periods, combined with elevated levels of exertion or exercise, may magnify the effect of $O_3$ on lung function. The most representative data come from the hiker study (Korrick et al., 1998), which provided outcome measures stratified by several factors (e.g., gender, age, smoking status, presence of asthma) within a population capable of more than normal exertion. In this study, lung function was measured before and after hiking, and both ambient and personal $O_3$ exposure measurements were made. Decreased lung function was associated with $O_3$ exposure, with the greatest effect estimates reported for the subgroup that reported having asthma or wheezing, and for those who hiked for longer periods of time, thus increasing the exposure period (CD, p. 7-36).

Asthma panel studies, conducted both in the U.S. and in other countries, have reported that decrements in PEF are associated with $O_3$ exposures among asthmatic and healthy persons (CD, sections 7.2.3.2 and 8.4.4.1). One large U.S. multicity study (Mortimer et al., 2002) examined $O_3$-related changes in PEF in 846 asthmatic children from 8 urban areas and reported that the incidence of $\geq$ 10% decrements in morning PEF are associated with a 30 ppb increase in 8-hr average $O_3$ for a 5-day cumulative lag, suggesting that $O_3$ exposure may be associated with clinically significant changes in PEF in asthmatic children; however, no associations were reported with evening PEF (CD, p. 7-40). The authors also reported that the associations reported with morning PEF remained statistically significant when days with 8-hr $O_3$ concentrations above 80 ppb were excluded (CD, p. 7-43). Two studies (Romieu et al., 1996, 1997) carried out simultaneously in northern and southwestern Mexico City with mildly asthmatic school children reported statistically significant $O_3$-related reductions in PEF, with variations in effect depending on lag time and time of day. While several studies (Gielen et al., 1997; Jalaludin et al., 2000; Ross et al., 2002; Thurston et al., 1997) report statistically significant associations between $O_3$ exposure and reduced PEF in asthmatics, other studies (Hilterman et al., 1998; Delfino et al., 1997a) did not, possibly due to very low levels of $O_3$.

Collectively, however, these studies indicate that $O_3$ may be associated with declines in lung function in asthmatic individuals (CD, p. 7-40 to 7-43).

Mortimer et al. (2002) discussed biological mechanisms for delayed effects on pulmonary function, which included increased bronchial reactivity secondary to airway inflammation associated with irritant exposure (CD, p. 7-43). Animal toxicological and human chamber studies (CD, Chapters 5 and 6) provide supporting evidence that exposure to $O_3$ may augment cellular infiltration and cellular activation, enhance release of cytotoxic inflammatory mediators, and alter membrane permeability (CD, p.7-44). In most laboratory animals studied, biochemical markers of lung injury and associated morphological changes were not found to be attenuated, even though at similar exposures pulmonary function changes might be attenuated.

Most of the panel studies which have investigated associations between $O_3$ exposure and respiratory symptoms or increased use of asthma medication are focused on asthmatic children (CD, sections 7.2.4 and 8.4.4.1). Two large U.S. studies (Mortimer et al., 2002; Gent et al., 2003), as well as several smaller U.S. (Delfino et al., 2003; Just et al., 2002; Newhouse et al., 2004; Romieu et al., 1996, 1997; Ross et al., 2002; Thurston et al., 1997) and international studies (Hilterman et al., 1998; Desqueyroux et al., 2002a,b), have reported fairly robust associations between ambient $O_3$ concentrations and daily symptoms/asthma medication use, even after adjustment for copollutants.

The National Cooperative Inner-City Asthma Study (NCICAS) reported morning symptoms in 846 asthmatic children from 8 U.S. urban areas to be most strongly associated with a cumulative 1- to 4-day lag of $O_3$ concentrations (Mortimer et al., 2002). The NCICAS used standard protocols that included instructing caretakers of the subjects to record symptoms in the daily diary by observing or asking the child (Mitchell et al., 1997). Symptoms reported included cough, chest tightness, and wheeze. In the analysis pooling individual subject data from all eight cities, the odds ratio for the incidence of symptoms was 1.35 (95% CI: 1.04, 1.69) per 30 ppb increase in 8-hr avg $O_3$ (10 a.m.-6 p.m.). The mean 8-hr avg $O_3$ was 48 ppb across the 8 cities. Excluding days when 8-hr avg $O_3$ was greater than 80 ppb (less than 5% of days), the odds ratio was 1.37 (95% CI: 1.02, 1.82) for incidence of morning symptoms

Gent and colleagues (2003) followed 271 asthmatic children under age 12 and living in southern New England for 6 months (April through September) in a diary study of daily symptoms in relation to $O_3$ and $PM_{2.5}$. Mean 1-hr max $O_3$ and 8-hr max $O_3$ concentrations were 58.6 ppb (SD 19.0) and 51.3 ppb (SD 15.5), respectively. The data were analyzed for two separate groups of subjects, 130 who used maintenance asthma medications during the follow-up period and 141 who did not. The need for regular medication was considered to be a proxy for more severe asthma. Not taking any medication on a regular basis and not needing to use a bronchodilator would suggest the presence of very mild asthma. Effects of 1-day lag $O_3$ were

observed on a variety of respiratory symptoms only in the medication user group. Both daily 1-hr max and 8-hr max $O_3$ concentrations were similarly related to symptoms such as chest tightness and shortness of breath. Effects of $O_3$, but not $PM_{2.5}$, remained significant and even increased in magnitude in two-pollutant models. Some of the associations were noted at 1-hr max $O_3$ levels below 60 ppb. In contrast, no effects were observed among asthmatics not using maintenance medication. In terms of person days of follow-up, this is one of the larger studies currently available that address symptom outcomes in relation to $O_3$, and provides supportive evidence for effects of $O_3$ independent of $PM_{2.5}$. Study limitations include limited control for meteorological factors and the post-hoc nature of the population stratification by medication use (CD, p. 7-53).

The multicities study by Mortimer et al. (2002), which provides an asthmatic population most representative of the United States, and several single-city studies indicate a robust association of $O_3$ concentrations with respiratory symptoms and increased medication use in asthmatics. While there are a number of well-conducted, albeit relatively smaller, studies which showed only limited or a lack of evidence for symptom increases associated with $O_3$ exposure, these studies had less statistical power and/or were conducted in areas with relatively low $O_3$ levels (CD, p. 7-54). The CD (p. 7-55) concludes that the asthma panel studies, as a group, and the NCICAS in particular, indicate a positive association between ambient concentrations and respiratory symptoms and increased medication use in asthmatics. The evidence has continued to expand since 1996 and now is considered to be much stronger than in the previous review of the $O_3$ primary standard.

The association between school absenteeism and ambient $O_3$ concentrations was assessed in three relatively large field studies (CD, section 7.2.6). Chen et al. (2000) examined daily school absenteeism in 27,793 elementary school students in Nevada over a 2-year period (after adjusting for $PM_{10}$ and CO concentrations) found that ambient $O_3$ concentrations were associated with 10.41% excess rate of school absences per 40 ppb increase in 1-hr max $O_3$. Gilliland et al. (2001) studied $O_3$-related absences among 1,933 $4^{th}$ grade students in 12 southern California communities and found significant associations between 30-day distributed lag of 8-hr average $O_3$ concentrations and all absence categories, particularly for respiratory causes. Neither $PM_{10}$ nor $NO_2$ were associated with any respiratory or nonrespiratory illness-related absences in single pollutant models. The CD concludes that these studies of school absences suggest that ambient $O_3$ concentrations, accumulated over two to four weeks, may be associated with school absenteeism, particularly illness-related absences, but further replication is needed before firm conclusions can be reached regarding the effect of $O_3$ on school absences (CD, p. 7-60).

#### *3.3.1.1.2 Airway Responsiveness*

Airway hyperresponsiveness (AHR), also know as bronchial hyperreactivity, refers to a condition in which the propensity for the airways to bronchoconstrict due to a variety of stimuli (e.g., exposure to cold air, allergens, or exercise) becomes augmented (CD, section 6.8). This condition is typically quantified by measuring the decrement in pulmonary function (e.g., spirometry or plethysmography) after inhalation exposure to specific (e.g., antigen, allergen) or nonspecific (e.g., methacholine, histamine) bronchoconstrictor stimuli. Exposure to $O_3$ causes an increase in nonspecific airway responsiveness as indicated by a reduction in the concentration of methacholine or histamine required to produce a given reduction in $FEV_1$ or increase in SRaw. Increased airway responsiveness is an important consequence of exposure to $O_3$ because its presence means that the airways are predisposed to narrowing on inhalation of various stimuli, such as specific allergens, cold air or $SO_2$ (CD, p. 8-21). Significant, clinically relevant decreases in pulmonary function have been observed in early phase allergen response in subjects with rhinitis after consecutive (4-day) exposure to 0.125 ppm $O_3$ (Holz et al., 2002). Similar increased airway responsiveness in asthmatics to house dust mite antigen 16 to 18 hrs after exposure to a single dose of $O_3$ (0.16 ppm for 7.6 hrs) was observed. These observations suggest that $O_3$ exposure may be a clinically important factor that can exacerbate the response to ambient bronchoconstrictor substances in individuals with preexisting allergic asthma and that $O_3$'s influence may have an immediate impact on asthmatics as well as contribute to effects that persist for longer periods (CD, p. 8-21).

An important aspect of increased airway responsiveness after $O_3$ exposure is that it represents a plausible link between $O_3$ exposure and increased hospital admissions. Kreit et al. (1989) found that $O_3$ can induce increased airway responsiveness in asthmatic subjects to $O_3$, who typically have increased airway responsiveness at baseline. A subsequent study (Jorres et al., 1996) suggested an increase in specific (i.e., allergen-induced) airway reactivity in subjects with allergic asthma, and to a lesser extent in subjects with allergic rhinitis after exposure to 0.25 ppm $O_3$ for 3 hrs; other studies (Molfino et al., 1991; Kehrl et al., 1999) reported similar results. According to one study (Folinsbee and Hazucha, 2000), changes in airway responsiveness after $O_3$ exposure resolve more slowly than changes in $FEV_1$ or respiratory symptoms. Other studies of repeated exposure to $O_3$ suggest that changes in airway responsiveness tend to be somewhat less affected by attenuation with consecutive exposures than changes in $FEV_1$ (Dimeo et al., 1981; Folinsbee et al., 1994; Gong et al., 1997a; Kulle et al., 1982) (CD, p. 6-31).

An extensive laboratory animal data base exploring the effects of acute, long-term, and repeated exposure to $O_3$ indicates that induction of AHR occurs at relatively high ($\geq$1ppm) $O_3$ concentrations (p. 8-21). These studies provide clues to the roles of physiological and biochemical components involved in this process, but caution should be exercised in interpreting

these results, as different mechanisms may be involved in mediating high- and low-dose responses. As observed in humans, the acute changes in AHR do not persist after long-term exposure of animals exposed to near-ambient concentrations of $O_3$, and attenuation has been reported. In addition, dosimetric adjustments potentially could be made to allow better estimation of levels that would be relevant to human exposure effect levels.

The CD concludes that $O_3$ exposure is linked with increased AHR (CD, section 6.8). Both human and animal studies indicate that airway responses are not associated with inflammation, but they do suggest a likely role for neuronal involvement (CD, p. 8-21). Increases in AHR do not appear to be strongly associated with decrements in lung function or increases in symptoms (CD, p. 6-31).

#### *3.3.1.1.3 Respiratory Inflammation and Permeability*

Based on evidence from the previous review, acute inflammatory responses in the lung have been observed subsequent to 6.6 hr $O_3$ exposures to the lowest tested level of 0.08 ppm in healthy adults. Some studies suggest that inflammatory responses may be detected in some individuals following $O_3$ exposures in the absence of $O_3$-induced pulmonary decrements in those subjects. Short-term exposures to $O_3$ also can cause increased permeability in the lungs of humans and experimental animals (CD, sections 5.2.3, 6.9, 7.2.5 and 8.4.3). Not only are the newer findings consistent with the previous review, but also there is better evidence about the physiological mechanisms by which $O_3$ causes these effects.

Lung inflammation and increased permeability, which are distinct events controlled by different mechanisms, are two well characterized effects of $O_3$ exposure observed in all species studied. Disruption of the lung barrier leads to leakage of serum proteins, influx of polymorphonuclear leukocytes (PMNs), release of bioactive mediators, and movement of compounds from the airspaces into the blood.

In the animal toxicological studies discussed in the CD (Chapter 5), the lowest $O_3$ concentration that induced inflammation in the mouse lung was 0.11 ppm for 24 hr exposures. Shorter exposures of 8 hours required concentrations of 0.26 ppm to induce epithelial permeability though there was no effect on inflammation. The lowest $O_3$ concentration that affected epithelial permeability or inflammation in the rat was 0.5 ppm for a 3 hr exposure or 0.12 ppm for 6 hr (CD, p. 8-23). After acute exposures, the influence of the duration of exposure increases as the concentration of $O_3$ increases; however, dosimetric adjustments would need to be done before one can compare levels. The exact role of inflammation in causation of lung disease is not known; nor is the relationship between inflammation and lung function (CD, p. 5-23).

A number of human $O_3$-exposure studies have analyzed bronchoalveolar lavage (BAL) and nasal lavage (NL) fluids and cells for markers of inflammation and lung damage. These studies are summarized in the CD (Annex AX6, Tables AX6-12 and AX6-13). Increased lung

inflammation is demonstrated by the presence of neutrophils (PMNs) found in BAL fluid in the lungs, which has long been accepted as a hallmark of inflammation. It is apparent, however, that inflammation within airway tissues may persist beyond the point that inflammatory cells are found in the BAL fluid. Soluble mediators of inflammation, such as cytokines and arachidonic acid metabolites have been measured in the BAL fluid of humans exposed to $O_3$. In addition to their role in inflammation, many of these compounds have bronchoconstrictive properties and may be involved in increased airway responsiveness following $O_3$ exposure (CD, p. 6-31, p. 8-22). An in vitro study of epithelial cells from nonatopic and atopic asthmatics exposed to 0.01 to 0.10 ppm $O_3$ showed significantly increased permeability compared to cells from normal persons. This indicates a potentially inherent susceptibility of cells from asthmatic individuals for $O_3$-induced permeability.

In the 1996 CD, assessment of human exposure studies indicated that a single, acute (1 to 4 hrs) $O_3$ exposure (0.2 to 0.6 ppm) of subjects engaged in moderate to heavy exercise could induce a number of cellular and biochemical changes suggestive of pulmonary inflammation and lung permeability (CD, p. 8-22). These changes persisted for at least 18 hrs. Graham and Koren (1990) compared inflammatory mediators present in NL and BAL fluids of humans exposed to 0.4 ppm $O_3$ for 2 hrs and found similar increases in PMNs in both fluids, suggesting a qualitative correlation between inflammatory changes in the lower airways (BAL) and upper respiratory tract (NL). Acute airway inflammation was shown in Devlin et al. (1990) to occur among adults exposed to 0.08 ppm $O_3$ for 6.6 hr with exercise, and McBride et al. (1994) reported that asthmatic subjects were more sensitive than non-asthmatics to upper airway inflammation for $O_3$ exposures (0.24 ppm, 1.5 hr, with light IE) that did not affect pulmonary function (CD, p. 6-33).

Since 1996, a substantial number of human exposure studies have been published which have provided important new information on lung inflammation and epithelial permeability. Mudway and Kelly (2004) examined $O_3$-induced inflammatory responses and epithelial permeability with a meta-analysis of 21 controlled human exposure studies and showed that PMN influx in healthy subjects is associated with total $O_3$ dose ( product of $O_3$ concentration, exposure duration, and minute ventilation) (CD, p. 6-34). Results of the analysis suggest that the time course for inflammatory responses (including recruitment of neutrophils and other soluble mediators) is not clearly established, but differential attenuation profiles for many of these parameters are evident (CD, p. 8-22).

A number of studies (Peden et al., 1997; Scannell et al., 1996; Hilterman et al., 1999; Bosson et al., 2003) have provided evidence suggesting that asthmatics show greater inflammatory response than healthy subjects when exposed to similar $O_3$ levels (CD, section 6.9). Markers from BAL fluid following both 2-hr (Devlin et al., 1997) and 4-hr (Christian et al., 1998; Jorres et al., 2000) $O_3$ exposures repeated up to 5 days indicate that there is ongoing

cellular damage irrespective of attenuation of some cellular inflammatory responses of the airways, pulmonary function, and symptom responses (CD, p. 8-22).

The CD (p. 8-24) concludes that interaction of $O_3$ with lipid constituents of epithelial lining fluid (ELF) and cell membranes and the induction of oxidative stress is implicated in injury and inflammation. Alterations in the expression of cytokines, chemokines, and adhesion molecules, indicative of an ongoing oxidative stress response, as well as injury repair and regeneration processes, have been reported in animal toxicology and human in vitro studies evaluating biochemical mediators implicated in injury and inflammation. While antioxidants in ELF confer some protection, $O_3$ reactivity is not eliminated at environmentally relevant exposures. Further, antioxidant reactivity with $O_3$ is both species-specific and dose-dependent (CD, p. 8-24).

#### *3.3.1.1.4 Changes in Host Defense Capability*

As discussed in the CD (sections 5.2.2, 6.9.6, and 8.4.2), short-term exposures to $O_3$ have been shown to impair host defense capabilities in both humans and experimental animals by depressing alveolar macrophage (AM) functions and by altering the mucociliary clearance of inhaled particles and microbes. Short-term $O_3$ exposures also interfere with the clearance process by accelerating clearance for low doses and slowing clearance for high doses. Animal toxicological studies have reported that acute $O_3$ exposures suppress alveolar phagocytes and immune functions. Dysfunction of host defenses and subsequent increased susceptibility to bacterial lung infection in laboratory animals has been induced by short-term exposures to $O_3$ levels as low as 0.08 ppm (CD, p. 8-26).

Changes in antibacterial defenses are dependent on exposure regimens, species and strain of lab animals, species of bacteria, and age of the animals used. Acute $O_3$-induced suppression of alveolar phagocytosis and immune function in experimental animals appeared to be transient and attenuated with continuous or repeated exposures. Ozone exposure has also been shown to interfere with AM-mediated clearance in the respiratory region of the lung and with mucociliary clearance of the tracheobronchial airways. These interferences with clearance are dose dependent, with low doses accelerating clearance and high doses slowing the process (CD, p. 8-26).

A single controlled human exposure study (Devlin et al., 1991) reviewed in the 1996 CD reported that exposure to 0.08 to 0.10 ppm $O_3$ for 6.6 hrs (with moderate exercise) induced decrements in the ability of AMs to phagocytose microorganisms; several other human studies reported similar effects but with higher exposure concentrations (CD, p. 8-26). Integrating the recent study results with evidence available in the 1996 CD, the CD concludes that available evidence indicates that short-term $O_3$ exposures have the potential to impair host defenses, primarily by interfering with AM function. Any impairment in AM function may lead to

decreased clearance of microorganisms or nonviable particles. Compromised AM functions in asthmatics may increase their susceptibility to other $O_3$ effects, the effects of particles, and respiratory infections (CD, p. 8-26).

#### *3.3.1.1.5 Morphological Effects*

The 1996 CD found that short-term $O_3$ exposures cause similar alterations in lung morphology in all laboratory animal species studied, including primates. Cells in the centriacinar region (CAR) of the lung (the segment between the last conducting airway and the gas exchange region) have been recognized as a primary target of $O_3$-induced damage (epithelial cell necrosis and remodeling of respiratory bronchioles), possibly because epithelium in this region receives the greatest dose of $O_3$ delivered to the lower respiratory tract. Following chronic $O_3$ exposure, structural changes have been observed in the CAR, the region typically affected in most chronic airway diseases of the human lung (CD, p. 8-24).

Ciliated cells in the nasal cavity and airways, as well as Type I cells in the gas-exchange region, are also identified as targets. While short-term $O_3$ exposures can cause structural changes such as fibrosis in the CAR, these changes appear to be transient with recovery time after exposure, depending on species and $O_3$ dose. The potential impacts of repeated short-term and chronic morphological effects of $O_3$ exposure are discussed later in section 3.3.1.2.5.

Recent studies continue to show that short-term and sub-chronic exposures to $O_3$ cause similar alterations in lung structure in a variety of experimental animal species, at concentrations of 0.15 ppm in rats and even lower concentrations in primates (CD, section 5.2.4.). Recent work has shown that a topical anti-inflammatory corticosteroid can prevent these effects in nasal epithelia, while exposure to bacterial endotoxin can potentiate effects. Ozone-induced fibrotic changes in the CAR are maximal at 3 days of exposure and recover 3 days post-exposure with exposures of 0.2 ppm $O_3$ in rodents. One study has demonstrated variability of local $O_3$ dose and subsequent injury in the respiratory tract due to depletion of glutathione (GSH). The proximal respiratory bronchiole receives the most acute epithelial injury from exposures $\leq$ 1 ppm, while metabolic effects were greatest in the distal bronchioles and minor daughter airways (CD, p. 5-38).

Based on evidence from animal toxicological studies, short-term and sub-chronic exposures to $O_3$ can cause morphological changes in the respiratory systems, particularly in the CAR, of a number of laboratory animal species (CD, section 5.2.4).

#### *3.3.1.1.6 Emergency Department Visits/Hospital Admissions for Respiratory Causes*

The 1996 CD evaluated ED visits and hospital admissions as possible outcomes following exposure to $O_3$ (CD, section 7.3). The evidence was limited for ED visits, but results of several studies generally indicated that short-term exposures to $O_3$ were associated with

respiratory ED visits. The strongest and most consistent evidence, both below and above 0.12 ppm 1-hr max $O_3$, was found in the group of studies which investigated summertime daily hospital admissions for respiratory causes in different eastern North American cities. These studies were consistent in demonstrating that ambient $O_3$ levels were associated with increased hospital admissions and accounted for about one to three excess respiratory hospital admissions per million persons with each 100 ppb increase in 1-hr max $O_3$, with adjustment for possible confounding effects of temperature and copollutants. Overall, the 1996 CD concluded that there was strong evidence that ambient $O_3$ exposures can cause significant exacerbations of preexisting respiratory disease in the general public (CD, p. 7-66). Excess respiratory-related hospital admissions associated with $O_3$ exposures for the New York City area (based on Thurston et al., 1992) were included in the quantitative risk assessment in the prior review and are included in the current assessment along with estimates for respiratory-related hospital admissions in Cleveland, Detroit, and Los Angeles based on more recent studies (see Chapter 5). Significant uncertainties and the difficulty of obtaining reliable baseline incidence numbers resulted in ED visits not being used in the quantitative risk assessment conducted in the last $O_3$ NAAQS review.

In the past decade, a number of studies have examined the temporal being used in the quantitative risk assessment conducted in the last $O_3$ NAAQS review.associations between $O_3$ exposures and ED visits for respiratory causes (CD, section 7.3.2). These studies are summarized in the CD (Table AX7-3, Chapter 7 Annex). Respiratory causes for ED visits include asthma, bronchitis, emphysema, pneumonia, and other upper and lower respiratory infections, such as influenza, but asthma visits typically dominate the daily incidence counts. Among studies with adequate controls for seasonal patterns, many reported at least one significant positive association involving $O_3$. These studies examined ED visits for total respiratory complaints (Delfino et al., 1997b, 1998b; Hernandez-Garduno et al., 1997; Ilabaca et al., 1999; Lin et al., 1999), asthma (Friedman et al., 2001; Jaffe et al., 2003; Stieb et al., 1996; Tenias et al., 1998; Tobias et al., 1999 ; Tolbert et al., 2000 ; Weisel et al., 2002), and COPD (Tenias et al., 2002).

Figure 7-8 (CD, p. 7-68) provides effect estimates for associations between ED visits for asthma and short-term $O_3$ exposures. In general, $O_3$ effect estimates from summer only analyses tended to be positive and larger compared to results from cool season or all year analyses (CD, p. 7-67). Several of the studies reported significant associations between $O_3$ concentrations and ED visits for respiratory causes. However, inconsistencies were observed which were at least partially attributable to differences in model specifications and analysis approach among various studies. For example, ambient $O_3$ concentrations, length of the study period, and statistical methods used to control confounding by seasonal patterns and copollutants appear to affect the observed $O_3$ effect on ED visits. Thus, the CD (p. 7-71) has concluded that stratified analyses by

season generally supported a positive association between $O_3$ concentrations and ED visits for asthma in the warm season.

Unscheduled hospital admissions occur in response to unanticipated disease exacerbations and are more likely to be affected by environmental factors, such as high $O_3$ levels. Thus, hospital admissions studies focus specifically on unscheduled admissions. Results of a fairly large number of these studies published during the past decade are summarized in Table AX7-4 (CD, Chapter 7 Annex). As a group, these hospital admissions studies tend to be larger geographically and temporally than the ED visit studies and provide results that are generally more consistent. The largest and most significant associations of respiratory hospital admissions with $O_3$ concentrations were observed using short lag periods, in particular for a 0-day lag (same day exposure) and a 1-day lag (previous day exposure). Most studies in the United States and Canada indicated positive, statistically significant associations between ambient $O_3$ concentrations and respiratory hospital admissions in the warm season, including studies with 98th percentile 8-hr maximum $O_3$ levels as low as about 50 ppb. However, not all studies found a statistically significant relationship with $O_3$, possibly because of insufficient power and/or very low ambient $O_3$ levels. Analyses for confounding using multipollutant regression models suggest that copollutants generally do not confound the association between $O_3$ and respiratory hospitalizations. Ozone effect estimates were robust to PM adjustment in all-year and warm-season only data.

Overall, the CD concludes that positive and robust associations were found between ambient $O_3$ concentrations and various respiratory disease hospitalization outcomes, when focusing particularly on results of warm-season analyses. Recent studies also generally supported a positive association between $O_3$ concentrations and ED visits for asthma during the warm season (CD, p. 7-175). These observations are strongly supported by the human clinical, animal toxicologic, and epidemiologic evidence for lung function decrements, increased respiratory symptoms, airway inflammation, and increased airway responsiveness. Taken together, the overall evidence supports a causal relationship between acute ambient $O_3$ exposures and increased respiratory morbidity outcomes resulting in increased ED visits and hospitalizations during the warm season (CD, p. 8-77).

#### *3.3.1.1.7 Effects on Exercise Performance*

The effects of $O_3$ exposure on exercise performance of healthy individuals have been investigated in a number of controlled exposure studies (CD, section 6.7). Several studies discussed in the 1996 CD reported that endurance exercise performance and $VO_{2max}$ may be limited by acute exposure to $O_3$. Other studies found that significant reductions in maximal endurance exercise performance may occur in well-conditioned athletes while they perform CE ($V_E$ > 80 L/min) for 1 hr at $O_3$ concentrations $\geq$ 0.18 ppm. There are no new studies available in

the CD. Thus, as in the 1996 CD, the CD concludes that reports from studies of $O_3$ exposure during high-intensity exercise indicate that breathing discomfort associated with maximal ventilation may be an important factor in limiting exercise performance in some, but not all, subjects (CD, p. 6-30).

#### 3.3.1.2 Effects on the Respiratory System from Long-term Exposures

The 1996 CD concluded that there was insufficient evidence from the limited number of studies to determine whether long-term $O_3$ exposures resulted in chronic health effects at ambient levels observed in the U.S. However, the aggregate evidence suggested that $O_3$ exposure, along with other environmental factors, could be responsible for health effects in exposed populations (CD, section 7.5). Animal toxicological studies carried out in the 1980's and 1990's demonstrated that long-term exposures can result in a variety of morphological effects, including permanent changes in the small airways of the lungs, including remodeling of the distal airways and CAR and deposition of collagen, possibly representing fibrotic changes. These changes result from the damage and repair processes that occur with repeated exposure. Fibrotic changes were also found to persist after months of exposure providing a potential pathophysiologic basis for changes in airway function observed in children in some recent epidemiological studies. It appears that variable seasonal ambient patterns of exposure may be of greater concern than continuous daily exposures.

This section reviews studies published since 1996 in which health effects were assessed for $O_3$ exposures lasting from weeks to several years. Summaries of recent morphological effects studies of subchronic and chronic exposures are listed in Table AX5-10 (CD, Annex AX5). Summaries of recent morbidity effects epidemiological studies of long-term exposure are listed in Table AX7-6 (CD, Annex AX7).

##### *3.3.1.2.1 Seasonal Ozone Effects on Lung Function*

It is well documented in controlled human exposure and field studies that daily multi-hour exposures to $O_3$ produce transient declines in lung function; however, lung function effects of repeated exposures to $O_3$ over extended periods are far less studied. Several studies published since 1996 have investigated lung function changes over seasonal time periods (CD, section 7.5.3). One large, three-year study (Frischer et al., 1999) collected repeated lung function measurements in 1,150 young, Austrian school children and reported that there was an association between growth-related increases in lung function over the summer season and seasonal mean $O_3$ levels. Mean summertime 24-hr avg $O_3$ concentrations ranged from 32.5 to 37.3 ppb during the three summers. Growth-related increases in lung function over the summer season were reduced in relation to seasonal mean $O_3$. It was cautioned that it was difficult to attribute the reported effects to $O_3$ alone independently of copollutants (CD, p. 7-113). A one-

year extension of this study by Horak et al. (2002a,b) confirmed the results that seasonal mean $O_3$ levels are associated with a negative effect on increases in lung function in children. A study (Kopp et al., 2000) of 797 children in Austria and southwestern Germany reported smaller increases in lung function in children exposed to higher levels of ambient $O_3$ (mean $O_3$ concentration of 44 to 52 ppb) compared to children living in areas with lower ambient $O_3$ levels (25 to 33 ppb). Another Austrian study (Ihorst et al., 2000) of 2,153 young children found significantly lower FVC and $FEV_1$ increases associated with higher $O_3$ exposures in the summer but not in the winter. A pilot study (Kinney and Lippmann, 2000) of 72 young adult, military academy students provided results that are consistent with a seasonal decline in lung function that may be due, in part, to $O_3$ exposures. According to the CD (p. 7-114), these studies collectively indicate that seasonal $O_3$ exposure is associated with smaller growth-related increases in lung function in children than they would have experienced living in clean air and that there is some limited evidence that seasonal $O_3$ also may affect lung function in young adults, although uncertainty about the role of copollutants makes it difficult to attribute the effects to $O_3$ alone.

#### *3.3.1.2.2 Reduced Baseline Lung Function and Respiratory Symptoms*

Lung capacity grows during childhood and adolescence as body size increases, reaches a maximum during the twenties, and then begins to decline steadily and progressively with age. Long-term exposure to air pollution has long been thought to contribute to slower growth in lung capacity, diminished maximally attained capacity, and/or more rapid decline in lung capacity with age (CD, section 7.5.4). Toxicological findings evaluated in the 1996 CD demonstrated that repeated daily exposure of rats to an episodic profile of $O_3$ caused small, but significant, decrements in growth-related lung function that were consistent with early indicators of focal fibrogenesis in the proximal alveolar region, without overt fibrosis (CD, section 5.2.5.2). Because $O_3$ is a strong respiratory irritant and has been shown to cause inflammation and restructuring of the respiratory airways, it is plausible that long-term $O_3$ exposures might have a negative impact on baseline lung function, particularly during childhood when these exposures might have long-term risks. As noted in the current CD, however, no recent toxicological studies have been published on effects of chronic $O_3$ exposure.

Several epidemiological studies published since 1996 have examined the relationship between growth-related lung function and long-term $O_3$ exposure. The most extensive and robust study of respiratory effects in relation to long-term air pollution exposures among children in the U.S. is the Children's Health Study carried out in 12 communities of southern California starting in 1993 (Avol et al., 2001; Gauderman et al., 2000, 2002, 2004a,b; Peters et al., 1999a,b). One study (Peters et al., 1999a) examined the relationship between long-term $O_3$ exposures and self reports of respiratory symptoms and asthma in a cross sectional analysis and

found a limited relationship between outcomes of current asthma, bronchitis, cough and wheeze and a 40 ppb increase in 1-hr max $O_3$ (CD, p. 7-115). Another analysis (Peters et al., 1999b) examined the relationship between growth-related lung function at baseline and levels of air pollution in the community and reported evidence that annual mean $O_3$ levels were associated with decreases in FVC, $FEV_1$, PEF and $FEF_{25-75}$ (the latter two being statistically significant) among females but not males (CD, p. 7-116). In a separate study (Gauderman et al., 2000) of 4$^{th}$, 7$^{th}$, and 10$^{th}$ grade students, a longitudinal analysis of growth-related lung function over four years found no association with $O_3$ exposure. Subsequent studies by the same group (Gauderman et al., 2002, 2004a,b) led the authors to conclude that results provide little evidence that ambient $O_3$ at current levels is associated with chronic deficits in the rate of increase in growth-related lung function in children (CD, p. 7-116 to 7-118). Avol et al. (2001) examined children who had moved from participating communities in southern California to other states with improved air quality and found, with the exception of $FEV_1$, the $O_3$ effect estimates for all other spirometric parameters were negative, but the associations were not as strong as those observed for $PM_{10}$ (CD, p. 7-116). Collectively, the results of these reports from the children's health cohorts provide little evidence for impact of long-term $O_3$ exposures on smaller increases in growth-related lung function (CD, p. 7-116).

Evidence for a significant relationship between long-term $O_3$ exposures and decrements in maximally attained lung function was reported in a nationwide study of first year Yale students (CD, p. 7-120). Males had much larger effect estimates than females, which might reflect higher outdoor activity levels and correspondingly higher $O_3$ exposures during childhood. A similar study (Kunzli et al., 1997; Tager et al., 1998) of college freshmen at University of California at Berkeley also reported significant effects of long-term $O_3$ exposures on lung function (CD, p. 7-121). In a comparison of students whose city of origin was either Los Angeles or San Francisco, long-term $O_3$ exposures were associated with significant changes in mid- and end-expiratory flow measures, which could be considered early indicators for pathologic changes that might progress to COPD.

In summary, recent publications from the southern California children's cohort study provide no evidence for an association between long-term $O_3$ exposure and lung function in children (CD, p. 7-118), while limited evidence is available from studies of adults and college students suggest that long-term $O_3$ exposure may affect lung function or respiratory symptoms (CD, pp. 7-120, 7-121). Overall, the CD concluded that this body of evidence was inconclusive for effects of long-term $O_3$ exposure on respiratory symptoms or lung function (CD, p. 7-175).

#### *3.3.1.2.3 Long-term $O_3$ Exposure and Respiratory Inflammation*

As noted above in section 3.3.1.1.3 and in the CD (Chapter 6), chamber studies of exercising humans exposed to $O_3$ for 2 to 6.6 hrs have demonstrated inflammation in the lungs,

including the alveolar region where gas exchange takes place. The potential long-term significance of short-term exposures to $O_3$ is that they can result in the release of reactive substances from inflammatory cells that can damage the sensitive cells lining the lungs. Over time repeated inflammation can lead to permanent lung damage and restructuring of the small airways and alveoli. Also, since inflammation is a hallmark characteristic of asthma, there is the possibility that $O_3$-induced inflammation may exacerbate existing asthma or contribute to the development of asthma in genetically predisposed individuals (CD, section 7.5.5).

For subchronic exposures of animals, permeability changes are transient (and species-dependent) and return to control levels even with continuing exposure. For long-term $O_3$ exposures, persistent $O_3$-induced inflammation plays an important role in alterations of lung structure and function. Significant remodeling of the epithelium and underlying connective tissues in distal airways have been reported in rats exposed to 0.25 ppm $O_3$ (12 hr/day for 6 weeks) and in monkeys exposed to 0.2 ppm $O_3$ (8 hr/day for 90 days)(CD, p. 8-23).

In one epidemiological field study (Kinney et al., 1996), BAL fluids were taken in the summer and winter from a group of joggers in New York and were compared for evidence of acute inflammation and of enhanced cell damage (CD, p. 7-122). The mean 1-hr max concentrations for a 3-month period were 58 ppb (max 110 ppb) in the summer and 32 ppb (max 64 ppb) in the winter. There was little evidence of acute inflammation in the summer BAL fluids compared to winter, but there was evidence of enhanced cell damage. This suggests that even though inflammation may diminish over the summer, cell damage may be continuing. A cross-sectional cohort study (Calderon-Garciduenas et al., 1995) conducted in Mexico City provides evidence of inflammation and genetic damage to cells in the nasal passages of children chronically exposed to $O_3$ and other air pollutants (CD, p. 7-123). In Mexico City, the 1-hr avg $O_3$ concentrations exceeded 120 ppb for 4.4 hr/day. Significantly higher DNA damage was reported in children living in Mexico City compared to nonurban children and in older compared to younger children. Another marker of inflammation, urinary eosinophils, was analyzed in an Austrian school children study (Frischer et al., 2001), and it was reported that $O_3$ exposure (mean 30 day avg $O_3$ concentration before sample collection was 31.6 ppb) was significantly associated with eosinophil inflammation (CD, p. 7-122).

In assessing these studies, the CD (p. 7-123) concluded that specific attribution of these adverse respiratory and genotoxic effects to $O_3$ is difficult given the complex mixture in ambient air, although inflammatory changes like eosinophil levels observed in the Austrian study would be consistent with known effects of $O_3$.

#### *3.3.1.2.4 Risk of Asthma Development*

There have been a few studies investigating associations between long-term $O_3$ exposures and the onset of new cases of asthma (CD, section 7.5.6). The Adventist Health and Smog

(AHSMOG) study cohort of 3,914 was drawn from nonsmoking, non-Hispanic white adult Seventh Day Adventists living in California (Greer et al., 1993; McDonnell et al., 1999). Subjects were surveyed in 1977, 1987, and 1992. During the ten-year follow-up in 1987, it was reported that the incidence of new asthma was 2.1% for males and 2.2% for females (Greer et al., 1993). A statistically significant relative risk of 3.12 (95% CI: 1.16, 5.85) per 10 ppb increase in annual mean $O_3$ was observed in males, compared to a nonsignificant relative risk of 0.94 (95% CI: 0.65, 1.34) in females. In the 15-year follow-up in 1992, it was reported that 3.2% of eligible males and 4.3% of eligible females had developed adult asthma (McDonnell et al., 1999). For males, the relative risk of developing asthma was 2.27 (95% CI: 1.03, 4.87) per 30 ppb increase in 8-hr average $O_3$, but there was no evidence of an association in females. The lack of an association in females does not necessarily mean there is no effect but may be due to differences in time-activity patterns in males and females, which could lead to greater misclassification of exposure in females. Consistency of results in the two studies with different follow-up times provides supportive evidence of an association between long-term $O_3$ exposure and asthma incidence in adult males; however, representativeness of this cohort to the general U.S. population may be limited (CD, p. 7-125).

In a similar study (McConnell et al., 2002) of incident asthma among children (ages 9 to 16 at enrollment), annual surveys of 3,535 children initially without asthma were used to identify new-onset asthma cases as part of the Children's Health Study. Six high-$O_3$ (75.4 ppb mean 1-hr max over four years) and six low-$O_3$ (50.1 ppb, mean 1-hr max) communities were identified where the children resided. There were 265 children who reported new-onset asthma during the follow-up period. Although asthma risk was no higher for all residents of the six high-$O_3$ versus six low-$O_3$ communities, asthma risk was 3.3 times greater for children who played three or more sports as compared with children who played no sports within the high-$O_3$ communities. This association was absent in the communities with lower $O_3$ concentrations. No other pollutants were found to be associated with new-onset asthma (CD, p. 7-125)

Playing sports may result in extended outdoor activity and exposure occurring during periods when $O_3$ levels are higher. The sports activities would cause an increased ventilation rate, thus resulting in increased $O_3$ dose. It should be noted, however, that the results of the Children's Health Study (McConnell et al., 2002) were based on a small number (20 in high-$O_3$ areas and 9 in low- $O_3$ areas) of new-onset asthma cases among children who played three or more sports (CD, p. 7-125). Future replication of these findings in other cohorts would help determine whether a causal interpretation is appropriate.

#### *3.3.1.2.5 Morphological Effects*

In animal toxicology studies, the progression of morphological effects reported during and after a chronic exposure in the range of 0.5 to 1.0 ppm $O_3$ is complex, with inflammation

peaking over the first few days of exposure, then dropping, then plateauing, and finally, largely disappearing (CD, section 5.2.4.4). By contrast, fibrotic changes in the tissue increase very slowly over months of exposure, and, after exposure ceases, the changes sometimes persist or increase. Epithelial hyperplasia peaks soon after the inflammatory response but is usually maintained in both the nose and lungs with continuous exposure. Epithelial hyperplasia/metaplasia also does not repair after the end of exposure. Patterns of exposure in this same concentration range determine effects, with 18 months of daily exposure, causing less morphologic damage than exposures on alternating months. This is important as environmental $O_3$ exposure is typically seasonal. Long-term studies of Plopper and colleagues (Evans et al., 2003; Schelegle et al., 2003; Chen et al., 2003; Plopper and Fanucchi, 2000) investigated infant rhesus monkeys exposed to simulated, seasonal $O_3$ (0.5 ppm, 8 hrs/day for 5 days, every 14 days for 11 episodes) and demonstrated: 1) remodeling in the distal airways, 2) abnormalities in tracheal basement membrane; 3) eosinophil accumulation in conducting airways; and 4) decrements in airway innervation (CD, p. 5-45). As with other effects, these findings advance earlier information regarding possible injury-repair processes occurring with long-term $O_3$ exposures suggesting that these processes are only partially reversible and may progress following cessation of $O_3$ exposure and may lead to nonreversible structural damage to lung tissue; however, there is still too much uncertainty to quantitatively extrapolate these levels to human effect levels at this time (CD, p. 8-25).

#### *3.3.1.2.6 Summary*

In the past decade, important new longitudinal studies have examined the effect of chronic $O_3$ exposure on respiratory health outcomes. Evidence from recent long-term morbidity studies have suggested in some cases that chronic exposure to $O_3$ may be associated with seasonal declines in lung function, increases in inflammation, and development of asthma in children and adults. Seasonal decrements or smaller increases in lung function measures have been reported in several studies; however, it remains uncertain to what extent these changes are transient. While there is supportive evidence from animal studies involving chronic exposures, large uncertainties still remain as to whether current ambient levels and exposure patterns might cause these same effects in human populations. The CD also concludes that epidemiological studies of new asthma development and longer-term lung function declines remain inconclusive at present (CD, p. 7-134).

### 3.3.1.3 Effects on the Cardiovascular System

At the time of the 1997 review, the possibility of $O_3$-induced cardiovascular effects was a largely unrecognized issue. Since then, evidence has emerged that provides plausibility for how $O_3$ exposures could exert cardiovascular system effects. This includes direct effects such as $O_3$-

induced release from lung epithelial cells of platelet activating factor (PAF) that may contribute to blood clot formation that would increase the risk of serious cardiovascular outcomes (e.g., heart attack, stroke, mortality). Also, interactions of $O_3$ with surfactant components in epithelial lining fluid of the lung results in production of oxysterols and reactive oxygen species that may exhibit PAF-like activity contributing to clotting and also may exert cytotoxic effects on lung and heart muscle cells. Other possible mechanisms may involve $O_3$-induced secretions of vasoconstrictive substances and/or effects on neuronal reflexes that may result in increased arterial blood pressure and/or altered electrophysiologic control of heart rate or rhythm. Some animal toxicology studies have shown $O_3$-induced decreases in heart rate, mean arterial pressure, and core temperature. The only controlled human exposure study that evaluated effects of $O_3$ exposure on cardiovascular health outcomes found no significant $O_3$-induced differences in ECG, heart rate, or blood pressure in healthy or hypertensive subjects, but did observe a significant $O_3$-induced increase the alveolar-to-arterial $PO_2$ gradient in both groups resulting in an overall increase in myocardial work and impairment in pulmonary gas exchange.

Epidemiologic panel and field studies that examined associations between $O_3$ and various cardiac physiologic endpoints have yielded limited evidence suggestive of a potential association between acute $O_3$ exposure and altered heart rate variability, ventricular arrhythmias, and incidence of heart attacks. A number of epidemiological studies have also reported associations between short-term exposures and hospitalization for cardiovascular diseases. As shown in Figure 7-13 of the CD, many of the studies reported negative or inconsistent associations. Some other studies, especially those that examined the relationship when $O_3$ exposures were higher, have found robust positive associations between $O_3$ and cardiovascular hospital admissions (CD, p. 7-82). For example, one study reported a positive association between $O_3$ and cardiovascular hospital admissions in Toronto, Canada in a summer-only analysis (mean 1-hr max $O_3$ of 41.2 ppb). The results were robust to adjustment for various PM indices, whereas the PM effects diminished when adjusting for gaseous pollutants. Other studies stratified their analysis by temperature, i.e., by warms days ($\geq$20 °C) versus cool days (<20 °C). Several analyses using warms days consistently produced positive associations.

The epidemiologic evidence for cardiovascular morbidity is much more mixed than for respiratory morbidity, with only one of several U.S./Canadian studies showing statistically significant positive associations of cardiovascular hospitalizations with warm-season $O_3$ concentrations. Most of the available European and Australian studies (all of which conducted all-year $O_3$ analyses) did not find an association between short-term $O_3$ concentrations and cardiovascular hospitalizations. Overall, the currently available evidence is inconclusive regarding an association between cardiovascular hospital admissions and ambient $O_3$ exposure (CD, p. 7-83)

Based on the evidence from animal toxicology, human controlled exposure, and epidemiologic studies, the CD concludes that this generally limited body of evidence is highly suggestive that $O_3$ can directly and/or indirectly contribute to cardiovascular-related morbidity, but that much needs to be done to more fully substantiate links between ambient $O_3$ exposures and adverse cardiovascular outcomes (CD, p. 8-77).

### 3.3.2 Premature Mortality

There were only a limited number of studies which examined the relationship between $O_3$ and mortality available for review in the 1996 CD. Some studies suggested that mortality was associated with short-term exposure to $O_3$, but conclusions could not be drawn regarding such associations (CD, p. 84). Numerous recent studies have provided new and more substantial evidence supporting such an association, as discussed below in section 3.3.2.1.

At the time of the last review, little epidemiological evidence was available on potential associations between long-term exposure to $O_3$ and mortality. Among the recent studies are some that have evaluated this relationship, and these newer studies still provide limited, if any, evidence for an association between chronic $O_3$ exposure and mortality, as described in section 3.3.2.2.

#### 3.3.2.1 Mortality and Short-term $O_3$ Exposure

The 1996 CD concluded that an association between daily mortality and $O_3$ concentration for areas with high $O_3$ levels (e.g., Los Angeles) was suggested. However, due to a very limited number of studies available at that time, there was insufficient evidence to conclude that the observed association was likely causal, and thus the possibility that $O_3$ exposure may be associated with mortality was not relied upon in the 1997 decision on the $O_3$ primary standard.

The 2006 CD includes results from numerous epidemiological analyses of the relationship between $O_3$ and mortality. Key findings are available from multi-city time-series studies that report associations between $O_3$ and mortality. These studies include analyses using data from 90 U.S. cities in the National Mortality, Morbidity and Air Pollution (NMMAPS) study and from 95 U.S. cities in an extension to the NMMAPS analyses (Samet et al., 2000, reanalyzed in Dominici, 2003) and further analyses (Bell et al., 2004) using a subset of 19 U.S. cities and focusing on cause-specific mortality associations (Huang et al., 2005). An additional study (Schwartz, 2005)used case-crossover design and data from 14 U.S. cities to further investigate the influence of adjustment for weather variables in the $O_3$-mortality relationship (CD, p. 8-38). Finally, results are available from a European study, Air Pollution and Health: a European Approach (APHEA), an analysis using data from 23 cities (Gryparis et al., 2004) and 4 cities (Toulomi et al., 1997) (CD, p. 7-93).

The original 90-city NMMAPS analysis, with data from 1987 to 1994, was primarily focused on investigating effects of $PM_{10}$ on mortality. A significant association was reported between mortality and 24-hr average $O_3$ concentrations during the warm season, but the association was not significant in analyses for the full year (Samet et al., 2000) (CD, Figure 7-19; p. 7-92). This is because the estimate using all available data was about half that for the summer-only data at a lag of 1-day. The extended NMMAPS analysis included data from 95 U.S. cities and included an additional 6 years of data, from 1987-2000 (Bell et al., 2004), and significant associations were reported between $O_3$ and mortality. The effect estimate for increased mortality was 0.5% per 24-hr average $O_3$ measured on the same day (20 ppb change; 95% PI: 0.24, 0.78), and 1.04% per 24-hr average $O_3$ in a 7-day distributed lag model (20 ppb change; 95% PI: 0.54, 1.55) (CD, p. 7-88). In analyses using only data from the warm season, the results were not significantly different from the full-year results; the effect estimate for increased mortality was 0.44% per 24-hr average $O_3$ measured on the same day (20 ppb change; 95% PI: 0.14, 0.74), and 0.78% per 24-hr average $O_3$ in a 7-day distributed lag model (20 ppb change; 95% PI: 0.26, 1.30). The authors also report that $O_3$-mortality associations were robust to adjustment for PM (CD, p. 7-97).

Using a subset of the NMMAPS data set, another study focused on associations between cardiopulmonary mortality and $O_3$ exposure (24-hr avg) during the summer season only. The authors report a 1.47% increase per 20 ppb change in $O_3$ concentration measured on the same day (95% PI: 0.54, 2.39) and a 2.52% increase per 20 ppb change in $O_3$ concentration using a 7-day distributed lag model (95% PI: 0.94, 4.10)(CD, p. 7-92). These findings suggest that the effect of $O_3$ on mortality is immediate but also persists for several days.

As discussed below in section 3.4, assessment of confounding by weather, especially temperature, is complicated by the fact that higher temperatures are associated with the increased photochemical activities that are important for $O_3$ formation. Using a case-crossover study design, another study assessed associations between daily maximum concentrations and mortality, matching case and control periods by temperature, and using data only from the warm season. The reported effect estimate of 0.92% change in mortality per 40 ppb $O_3$ (1-hr max, 95% PI: 0.06, 1.80) was similar to time-series analysis results with adjustment for temperature (0.76% per 40 ppb $O_3$, 95% PI, 0.13, 1.40), suggesting that associations between $O_3$ and mortality are not sensitive to the adjustment methods for temperature (CD, p. 7-93).

An initial publication from APHEA, a European multi-city study, reported statistically significant associations between daily maximum $O_3$ concentrations and mortality, with an effect estimate of a 4.5% increase in mortality per 40 ppb $O_3$ (95% CI: 1.6, 7.7) in four cities (Toulomi et al., 1997). An extended analysis was done using data from 23 cities throughout Europe (Gryparis et al., 2004). In this report, a positive but not statistically significant association was

found between mortality and 1-hr daily maximum $O_3$ in a full year analysis (CD, p. 7-93). Gryparis et al. (2004) noted that there was a considerable seasonal difference in the $O_3$ effect on mortality; thus, the small effect for the all-year data might be attributable to inadequate adjustment for confounding by seasonality. Focusing on analyses using summer measurements, the authors report statistically significant associations with total mortality [1.8% increase per 30 ppb 8-hr $O_3$ (95% CI: 0.8, 2.9)], cardiovascular mortality [2.7% increase per 30 ppb 8-hr $O_3$ (95% CI: 1.2, 4.3)] and with respiratory mortality (6.8% increase per 30 ppb 8-hr $O_3$, 95% CI: 4.5, 9.2) (CD, p. 7-93, 7-99).

Two of the recent multi-city mortality studies (Bell et al., 2004; Gryparis et al., 2004) have also reported associations for multiple averaging times (CD, p. 8-38). Bell and colleagues (2004) reported associations between mortality and 1-hr daily max, 8-hr daily max and 24-hr avg $O_3$ concentrations. Effect estimates for associations with 1-hr $O_3$ was slightly larger than that reported for 8-hr $O_3$ concentrations, and both were distinctly larger than the association with 24-hr avg $O_3$, but the effect estimates did not differ statistically. The APHEA study (Gryparis et al., 2004) also reported effect estimates that were slightly larger with 1-hr than with 8-hr $O_3$ concentrations, but not significantly so.

Numerous single-city analyses have also reported associations between mortality and short-term $O_3$ exposure, especially for those analyses using warm season data. As shown in Figure 7-18 of the CD, the results of recent publications show a pattern of positive, often statistically significant associations between short-term $O_3$ exposure and mortality during the warm season (CD, p. 7-91). For example, statistically significant associations were reported in southern California (Ostro et al., 1995), Philadelphia (Moolgavkar et al., 1995), Dallas (Gamble et al., 1998), and Vancouver (Vedal et al.,2003), as well as numerous studies conducted in other countries. However, no evidence of an association was seen in a study conducted in Pittsburgh (Chock et al., 2000). In considering results from year-round analyses, there remains a pattern of positive results but the findings are less consistent. For example, statistically significant associations were reported in Philadelphia (Moolgavkar et al., 1995) and Dallas (Gamble et al., 1998), while positive but not statistically significant associations were reported in Detroit (Lippmann et al., 2000, reanalyzed in Ito, 2003), San Jose (Fairley, 1999, reanalyzed Fairley, 2003), and Atlanta (Klemm et al., 2004). No evidence for associations was reported in Los Angeles (Kinney et al., 1995), Coachella Valley (Ostro et al., 2003), and St. Louis and Eastern Tennessee (Dockery et al., 1992). In most single-city analyses, effect estimates were not substantially changed with adjustment for PM (CD Figure 7-19, p. 7-92).

In addition, several meta-analyses have been conducted on the relationship between $O_3$ and mortality. As described in section 7.4.4 of the CD, these analyses reported fairly consistent and positive combined effect estimates ranging from 1.5 to 2.5% increase in mortality for a

standardized change in $O_3$ (CD, Figure 7-20, p. 7-95). Three recent meta-analyses evaluated potential sources of heterogeneity in $O_3$-mortality associations (Bell et al., 2005; Ito et al., 2005; Levy et al., 2005). The CD (p. 7-96) observes common findings across all three analyses, in that all reported that effect estimates were larger in warm season analyses, reanalysis of results using default GAM criteria did not change the effect estimates, and there was no strong evidence of confounding by PM (CD, p. 7-97). Bell et al. (2005) and Ito et al. (2005) both provided suggestive evidence of publication bias, but $O_3$-mortality associations remained after accounting for that potential bias. The CD (7-97) concludes that the "positive $O_3$ effects estimates, along with the sensitivity analyses in these three meta-analyses, provide evidence of a robust association between ambient $O_3$ and mortality."

For standardized increments, effect estimates range from 0.5 to 2.5% increases in mortality in the multi-city studies and from 0.5 to 5% in single-city studies. For most studies that conducted season-specific analyses, effects were larger and more precise in warm-season analyses (CD, p. 7-97).

In the CD (p. 7-101), Figure 7-22 shows the $O_3$ risk estimates with and without adjustment for PM indices using all-year data in studies that conducted two-pollutant analyses. Approximately half of the $O_3$ risk estimates increased slightly, whereas the other half decreased slightly with the inclusion of PM in the models. In general, the $O_3$-mortality risk estimates were robust to adjustment for PM in the models, with the exception of Los Angeles, CA data with $PM_{10}$ (Kinney et al., 1995) and Mexico City data with TSP (Borja-Aburto et al., 1997). The U.S. 95 communities study (Bell et al., 2004) examined the sensitivity of acute $O_3$-mortality effects to potential confounding by $PM_{10}$ (CD, 7-100). Restricting analysis to days when both $O_3$ and $PM_{10}$ data were available, the community-specific $O_3$-mortality effect estimates as well as the national average results indicated that $O_3$ was robust to adjustment for $PM_{10}$ (Bell et al., 2004).

Several $O_3$-mortality studies examined the effect of confounding by PM indices in different seasons (CD, p. 7-102, Figure 7-23). In analyses using all-year data and warm-season only data, $O_3$ effect estimates were once again fairly robust to adjustment for PM indices, with values showing both slight increases and decreases with the inclusion of PM in the model. In the analyses using cool season data only, the $O_3$ effect estimates all increased slightly with the adjustment of PM indices, although none reached statistical significance.

The three recent meta-analyses (Bell et al., 2005; Ito et al., 2005; Levy et al., 2005) all examined the influence of PM on $O_3$ risk estimates. No substantial influence was observed in any of these studies. In the analysis by Bell et al. (2005), the combined estimate without PM adjustment was 1.7% (95% PI: 1.10, 2.37) from 41 estimates, and the combined estimate with PM adjustment was 1.95% (95% PI: 1.06, 4.00) from 11 estimates per 20 ppb increase in 24-hr avg $O_3$. In the meta-analysis of 15 cities (Ito et al., 2005), the combined estimate was 1.6%

(95% PI: 1.1, 2.2) and 1.5% (95% PI: 0.8, 2.2) per 20 ppb in 24-hr avg $O_3$ without and with PM adjustment, respectively (CD, p. 7-103). The additional time-series analysis of six cities by Ito et al. (2005) found that the influence of PM by season varied across alternative weather models but was never substantial. Levy et al. (2005) examined the regression relationships between $O_3$ and PM indices ($PM_{10}$ and $PM_{2.5}$) with $O_3$-mortality effect estimates for all year and by season. Positive slopes, which might indicate potential confounding, were observed for $PM_{2.5}$ on $O_3$ effect estimates in the summer and all-year periods, but the relationships were weak. The effect of one causal variable (i.e., $O_3$) is expected to be overestimated when a second causal variable (e.g., PM) is excluded from the analysis, if the two variables are positively correlated and act in the same direction. However, the results from these meta-analyses, as well as several single- and multiple-city studies, indicate that copollutants generally do not appear to substantially confound the association between $O_3$ and mortality (CD, p. 7-103).

Finally, from those studies that included assessment of associations with specific causes of death, it appears that effect estimates for associations with cardiovascular mortality are larger than those for total mortality; effect estimates for respiratory mortality are less consistent in size, possibly due to reduced statistical power in this subcategory of mortality (CD, p. 7-108). In addition to all-cause mortality, several studies examined broad underlying causes of mortality, such as cardiovascular and respiratory causes. The U.S. 95 communities study (1987-2000) analyzed $O_3$ effect estimates from cardiovascular and respiratory mortality. The analysis by Bell et al. (2005) used all available data, which included all-year data from 55 communities and warm-season only data from 40 communities. The national average estimate from the constrained distributed lag model was slightly greater for cardiopulmonary deaths than deaths from all causes, with an excess risk of 1.28% (95% PI: 0.62, 1.97) compared to1.04% (95% PI: 0.54, 1.55) per 20 ppb increase in 24-hr avg $O_3$ in the preceding week.

A related study (Huang et al., 2005) examined $O_3$ effects on cardiopulmonary mortality during the summers (June to September) of 1987 to 1994 in 19 large U.S. cities from the NMMAPS database. Figure 7-24 in the CD (p. 7-104), presents the Bayesian city-specific and overall average $O_3$ effect estimates for cardiopulmonary mortality per 20 ppb increase in 24-hr avg $O_3$ from a constrained 7-day distributed lag model. The $O_3$ effect estimate was 2.52% (95% PI: 0.94, 4.10) excess risk in cardiopulmonary mortality per 20 ppb increase in 24-hr avg $O_3$ in the preceding week for the combined analysis of all cities. For analyses of summer data, confounding of the $O_3$ effect by PM is of concern as daily variations in $O_3$ may be correlated to PM during the summer months. Huang et al. (2005) observed that when $PM_{10}$ was included in the model, the $O_3$ effect estimate, on average, remained positive and significant. As $PM_{10}$ measurements were available only every 1 to 6 days, only single-day lags were examined. At a 0-day lag, $O_3$ was associated with a 1.47% (95% PI: 0.54, 2.39) excess risk versus a 1.49% (95%

PI: 0.66, 3.47) excess risk in cardiopulmonary mortality in the $O_3$-only model and after adjustment for $PM_{10}$, respectively. The slight sensitivity of the $O_3$ health effects to the inclusion of $PM_{10}$ in the model may indicate a true confounding effect. However, as only the days with $PM_{10}$ data available were included in the analysis, the lack of significance is likely attributable to higher statistical uncertainty due to the lack of daily $PM_{10}$ measurements (CD, p. 7-105).

Figure 7-25 in the CD (p., 7-106), presents effect estimates for associations between $O_3$ and cardiovascular mortality for all-year and warm-season analyses. All studies, with the exception of Ponka et al. (1998), showed positive associations between $O_3$ and cardiovascular mortality (CD, p. 7-105). As with all-cause mortality, there appears to be heterogeneity in the effect estimates across studies. The cardiovascular mortality estimate from one meta-analysis appears to be close to the mode of the effect estimates from the various studies, as shown in Figure 7-25, in the CD (p. 7-105). This is expected, given that many of these studies were also included in the meta-analysis. This study observed that the posterior mean estimate for cardiovascular causes (2.23% excess risk per 20 ppb increase in 24-hr avg $O_3$ from 25 estimates) was slightly larger than that for total mortality (1.75% excess risk from 41 estimates). However, since cardiovascular deaths account for the largest fraction (over 40%) of total deaths, it is not surprising that the risk estimates for cardiovascular mortality are somewhat similar to those from all-cause mortality. Overall, the cardiovascular mortality risk estimates in the current literature show consistently positive associations with some heterogeneity (most estimates fall within the range of 1 to 8% per 40 ppb increase in 1-hr avg $O_3$ (CD, p. 7-107).

Several studies observed that the risk estimates for the respiratory category were larger than the cardiovascular and total nonaccidental categories (Anderson et al., 1996; Gouveia and Fletcher, 2000b; Gryparis et al., 2004; Zmirou et al., 1998). The apparent inconsistencies across studies may be due in part to the differences in model specifications, but they may also reflect the lower statistical power associated with the smaller daily counts of the respiratory category (usually accounting for less than 10% of total deaths) compared to the larger daily counts for the cardiovascular category (approximately 40 to 50% of total deaths). Thus, an examination of the differences in risk estimates across specific causes requires a large population and/or a long period of data collection. In one meta-analysis (Bell et al., 2005), which combined 23 estimates from 17 studies for respiratory mortality, the effect estimate for respiratory causes was smaller (0.94% excess risk per 20 ppb increase in 24-hr avg $O_3$ ) compared to the estimates for total mortality (1.75% excess risk) and cardiovascular mortality (2.23% excess risk) (CD, p. 7-107).

In summary, several single-city studies observed positive associations between ambient $O_3$ concentrations and cardiovascular mortality. In addition, a meta-analysis that examined specific causes of mortality found that the cardiovascular mortality risk estimates were higher than those for total mortality. The findings regarding the effect size for respiratory mortality

have been less consistent, possibly because of lower statistical power in this subcategory of mortality. The CD finds that the results from U.S. multi-city time-series studies, along with the meta-analyses, provide strong evidence for associations between short-term $O_3$ exposure and mortality (CD, p. 7-84). The results of these analyses show that the effects of ozone on mortality are generally robust to confounding by copollutants (CD, p. 7-149, 8-54). For cardiovascular mortality, the CD reports that effect estimates are consistently positive, and are more likely to be larger and statistically significant in the warm season analyses (CD, p. 7-108, Figure 7-22). The findings regarding the effects size for respiratory mortality are less consistent, possibly due to lower statistical power in this group (CD, p. 7-94). Overall, the CD concludes that these findings suggest a likely causal association between short-term $O_3$ exposure and mortality particularly in the warm season (CD, p. 8-78).

#### 3.3.2.2 Mortality and Long-term $O_3$ Exposure

Little evidence was available in the last review on the potential for associations between mortality and long-term exposure to $O_3$. In the Harvard Six City prospective cohort analysis, the authors report that mortality was not associated with long-term exposure to $O_3$ (Dockery et al., 1993). The authors note that the range of $O_3$ concentrations across the six cities was small (19.7 to 28.0 ppb in average 24-hr concentrations over the 7-year study period), which may have limited the power of the study to detect associations between mortality and $O_3$ levels (CD, p. 7-127).

As discussed in section 7.5.8 of the CD, in this review there are results available from three prospective cohort studies: the American Cancer Society (ACS) study, the Adventist Health and Smog (AHSMOG) study, and the U.S. Veterans Cohort study. In addition, a major reanalysis report includes evaluation of data from the Harvard Six City cohort study (Krewski et al., 2000). This reanalysis also includes additional evaluation of data from the initial ACS cohort study report that had only reported results of associations between mortality and long-term exposure to fine particles and sulfates (Pope et al., 1995).[1]

In this reanalysis of data from the previous Harvard Six City prospective cohort study, the investigators replicated and validated the findings of the original studies, and the report included additional quantitative results beyond those available in the original report (Krewski et al., 2000). In the reanalysis of data from the Harvard Six Cities study, the effect estimate for the association between long-term $O_3$ concentrations (8.3 ppb between the highest and lowest concentrations in the cities) and mortality was negative and nearly statistically significant (relative risk = 0.87, 95% CI: 0.76, 1.00).

[1] This reanalysis report and the original prospective cohort study findings are discussed in more detail in section 8.2.3 in *Air Quality Criteria for Particulate Matter* (EPA, 2004).

The ACS study is based on health data from a large prospective cohort of approximately 500,000 adults and air quality data from about 150 U.S. cities. The initial report (Pope et al., 1995) focused on associations with fine particles and sulfates, for which significant associations had been reported in the earlier Harvard Six Cities study (Dockery et al., 1993). As part of the major reanalysis of these data, results for associations with other air pollutants were also reported, and the authors report that no significant associations were found with $O_3$. However, results of seasonal analyses show a small positive association between long-term $O_3$ concentrations in the warm months (April-September) with a relative risk of 1.02 for all-cause mortality (95% CI: 0.96-1.07) and a stronger association was reported for cardiopulmonary mortality (relative risk=1.08, 95% CI: 1.01, 1.16) (Krewski et al., 2000, p. 174). For some specifications of $O_3$ exposure in the ACS study, there was an effect in the warm quarter, as there was in the reanalysis of the Harvard Six Cities study.

The ACS II study (Pope et al., 2002) reported results of associations with an extended data base; the mortality records for the cohort had been updated to include 16 years of follow-up (compared with 8 years in the first report) and more recent air quality data were included in the analyses. Results are presented for full-year analyses, and show no evidence for a significant association between long-term exposure to $O_3$ and mortality. As shown in Figure 7-27 of the CD, the effect estimates are near zero and sometimes negative (though not statistically significant) for associations between long-term $O_3$ exposure and all-cause, cardiopulmonary, and lung cancer mortality (CD, p. 7-128).

The Adventist Health and Smog (AHSMOG) cohort includes about 6,000 adults living in California. In two studies from this cohort, a significant association has been reported between long-term $O_3$ exposure and increased risk of lung cancer mortality among males only (Beeson et al., 1998; Abbey et al., 1999). No significant associations were reported between long-term $O_3$ exposure and mortality from all causes or cardiopulmonary causes. Due to the small numbers of lung cancer deaths (12 for males, 18 for females) and the precision of the effect estimate (i.e., the wide confidence intervals), the CD raised concerns about the plausibility of the reported association with lung cancer (CD, p. 7-130).

The U.S. Veterans Cohort study (Lipfert et al., 2000b, 2003) of approximately 50,000 middle-aged males diagnosed with hypertension, reported some positive associations between mortality and peak $O_3$ exposures ($95^{th}$ percentile level for several years of data). The analysis included numerous analyses using subsets of exposure and mortality follow-up periods which spanned the years 1960 to 1996. In the results of analyses using deaths and $O_3$ exposure estimates concurrently across the study period, there were positive, statistically significant associations between peak $O_3$ and mortality, with a 9.4% excess risk (95% CI: 0.4, 18.4) per mean 95% percentile $O_3$ (CD, p. 7-129).

Thus, the results from all-year analyses in the Harvard Six Cities and ACS cohorts provide no evidence for associations between long-term $O_3$ exposure and mortality, though the warm-season results in the reanalysis of the ACS cohort study suggest a potential association. Imprecise and inconclusive associations were reported in analyses for the AHSMOG cohort study. Significant associations between long-term $O_3$ exposure and mortality were only reported for the Veterans cohort study; while this study used an indicator of peak $O_3$ concentrations, the cohort is also a rather specific subgroup of the U.S. population. Overall, the CD concludes that consistent associations have not been reported between long-term $O_3$ exposure and all-cause, cardiopulmonary or lung cancer mortality (CD, p. 7-130).

### 3.3.3 Ozone Effects on UV-B Flux

The CD (Chapter 10) provides a thorough analysis of the current understanding of the relationship between reducing tropospheric $O_3$ concentrations and the potential impact these reductions might have on increasing UV-B surface fluxes and indirectly contributing to increased UV-B related health effects. It is clear that there are many factors that influence UV-B radiation penetration to the earth's surface, including cloud cover, surface albedo, PM concentration and composition, and gas phase pollution. A risk assessment of UV-B related health effects would need to take into account human habits, such as outdoor activities, dress and skin care. However, little is known about the impact of these factors on individual exposure to UV-B, and detailed information does not exist regarding type (e.g., peak or cumulative) and time period (e.g., childhood, lifetime, current) of exposure, wavelength dependency of biological responses, and interindividual variability in UV-B resistance. In fact there have been recent reports indicating the necessity of UV-B in producing vitamin D, suggesting that increased risks of human disease due to slight excess UV-B exposure may be offset by the benefits of enhanced vitamin D production. However, as with other impacts of UV-B on human health, this beneficial effect of UV-B radiation has not been studied in sufficient detail to allow for a credible health benefits or risk assessment. The CD (p. 10-38) concluded that the effects of changes in surface-level $O_3$ concentrations on UV-induced health effects cannot be critically assessed given the significant uncertainties summarized above.

### 3.3.4 Summary

The CD (Chapters 4-8) summarizes and assesses substantial new evidence which builds upon what was previously known about the health effects of $O_3$. The new information supports previous findings that short-term $O_3$ is associated with lung function decrements and respiratory symptoms, as well as numerous more subtle effects on the respiratory system such as morphological changes and altered host defense mechanisms. Short-term $O_3$ exposure has also

been associated with hospital admissions for respiratory causes in numerous new studies that further confirm the findings evaluated in the 1996 CD. The CD reports that warm-season studies show evidence for positive and robust associations between ambient $O_3$ concentrations and respiratory hospital admissions, respiratory symptoms and lung function effects in asthmatic children, and positive but less conclusive evidence for associations with respiratory ED visits (CD, p. 7-175).

Some new studies have suggested associations between increased incidence of asthma or reduced lung function and long-term exposure to elevated ambient $O_3$ levels. The findings of this small group of studies are inconsistent, however, and the CD concludes that the evidence for this group of associations is inconclusive (CD, p. 7-175).

A new body of studies has suggested associations between short-term $O_3$ exposure and effects on the cardiovascular system, including changes in heart rate variability, cardiac arrhythmia, incidence of MI and hospitalization for cardiovascular diseases. The CD finds this body of evidence to be limited but supportive of potential effects of $O_3$ on the cardiovascular system (CD, p. 7-175).

A major area where new information presented in the CD has significantly expanded our knowledge on health effects is evidence of an elevated risk of mortality associated with acute exposure to $O_3$, especially in the summer or warm season when $O_3$ levels are typically high. Results from recent large U.S. multicity time-series studies and meta-analyses provide the strongest evidence for associations between short-term $O_3$ exposure and mortality (CD, p. 7-175). The risk estimates shown are consistent across studies and robust to control for potential confounders. This overall body of evidence is highly suggestive that $O_3$ directly or indirectly contributes to nonaccidental and cardiopulmonary-related mortality, but additional research is needed to more fully establish underlying mechanisms by which such effects occur (CD, p. 8-78).

## 3.4 ASSESSMENT OF EVIDENCE FROM EPIDEMIOLOGICAL STUDIES

In Chapter 8, the CD assesses the new health evidence, integrating findings from experimental (e.g., toxicological, dosimetric and controlled human exposure) and epidemiological studies, to make judgments about the extent to which causal inferences can be made about observed associations between health endpoints and exposure to $O_3$. Section 8.4.4.3 of the CD indicates that *strength* of epidemiologic evidence (including the magnitude and precision of reported $O_3$ effect estimates and their statistical significance), *consistency* of effects associations (looking across results of multiple- and single-city studies conducted by different investigators in different places and times), and *robustness* of epidemiological associations (i.e.,

stability in the effect estimates after considering a number of factors) are all important in forming judgments as to the likely causal significance of observed associations (CD, p. 8-40).

In evaluating the evidence from epidemiological studies in sections 7.1.3 and 8.4.4.3, the CD focuses on well-recognized criteria, including: (1) the *strength* of reported associations, including the magnitude and precision of reported effect estimates and their statistical significance; (2) the *robustness* of reported associations, or stability in the effect estimates after considering factors such as alternative models and model specification, potential confounding by co-pollutants, as issues related to the consequences of exposure measurement error; and (3) the *consistency* of the effects associations as observed by looking across results of multi-le- and single-city studies conducted by different investigators in different places and time (CD, p. 8-40). Integrating more broadly across epidemiological and experimental evidence, the CD also focuses on the *coherence* and *plausibility* of observed $O_3$-related health effects to reach judgments about causality (CD, section 8.6).

Subsequent to the final CD being published, CASAC sent a letter to the Administrator (Henderson, 2006) providing additional advice on some key issues in order to inform specifically the preparation of this draft Staff Paper specifically and the review of the $O_3$ NAAQS in general. The issues related to assessment of epidemiological studies are addressed in this section and more generally in section 3.5, and include the general issue of the utility of time-series epidemiological studies in assessing the risks from exposure to $O_3$ and other criteria pollutants, as well as related issues about exposure measurement error in $O_3$ mortality time-series studies and $O_3$ as a surrogate for the broader mix of photochemical oxidant pollution in time-series studies. Implications of these issues for staff conclusions about the adequacy of the current $O_3$ NAAQS and the identification of options for consideration will be considered below in Chapter 6.

The following discussion summarizes the conclusions and judgments from the CD's summary of epidemiologic evidence and integrative assessment, focusing in particular on discussions of strength, robustness, and consistency in the epidemiological evidence; judgments in the CD about coherence and plausibility are summarized below in section 3.5. This section also addresses issues related to lag periods between $O_3$ ambient exposure levels and health outcomes, the nature of $O_3$-health effect concentration-response relationships, and the assessment of air pollutant mixtures containing $O_3$ in time-series epidemiological studies.

### 3.4.1 Strength of Associations

The strength of associations most directly refers to the magnitude of the reported relative risk estimates. Taking a broader view, the CD draws upon the criteria summarized in a recent report from the U.S. Surgeon General, which define strength of an association as "the magnitude

of the association and its statistical strength" which includes assessment of both effect estimate size and precision, which is related to the statistical power of the study (CDC, 2004). In general, when associations are strong in terms of yielding large relative risk estimates, it is less likely that the association could be completely accounted for by a potential confounder or some other source of bias (CDC, 2004). With associations that yield small relative risk estimates it is especially important to consider potential confounding and other factors in assessing causality.

Effect estimates between $O_3$ and many health outcomes are generally small in size and could thus be characterized as weak. For example, effect estimates for associations with mortality generally range from 0.5 to 5% increases per 40 ppb increase in 1-hr max $O_3$ or equivalent, whereas associations for hospitalization range up to 50% increases per standardized $O_3$ increment. The CD particularly notes that there are several multicity studies for associations between short-term $O_3$ exposure and mortality or morbidity that, although small in size, have great precision due to the statistical power of the studies, concluding that such associations are strong relative to the precision of the studies (CD, p.8-40). That is, the associations were strong enough to have been reliably measured by the studies such that many of the associations can be distinguished from the null hypothesis with statistical confidence.

### 3.4.2 Robustness of Associations

Factors considered in assessing *robustness* include impact of exposure error, potential confounding by copollutants, and alternative models and model specifications, as evaluated in the CD (sections 7.1.3 and 8.4.4.3) and discussed below.

#### 3.4.2.1 Exposure Error

In time-series epidemiological studies, concentrations measured at ambient monitoring stations are generally used to represent a community's exposure to ambient $O_3$. For time-series studies, the emphasis is on the temporal (e.g., daily or hourly) changes in ambient $O_3$. In cohort or cross-sectional studies, air quality data averaged over a period of months to years are used as indicators of a community's long-term exposure to ambient $O_3$ and other pollutants. In both types of analyses, exposure error is an important consideration, as actual exposures to individuals in the population will vary across the community. As described in the CD, there are few sources of $O_3$ exposure for most people other than ambient air; potential indoor sources of $O_3$ include office equipment, air cleaners, and small electric motors (CD, p. 7-6). Exposure to ambient $O_3$ for individuals is influenced by factors related to the infiltration of $O_3$ into buildings, air exchange rate, indoor circulation rate, and $O_3$ removal processes, as well as the time spent out of doors by the individuals, particularly for those individuals who engage in exercise or other activities which induce increased respiration (e.g., sports, construction work).

In a study describing the relationships between panel studies and time-series studies, Sheppard (2005) noted that non-ambient exposures varied across individuals and were not likely to have strong temporal correlations, whereas ambient concentrations across individuals should be highly correlated. In the case of $O_3$, there are limited non-ambient sources, thus, the non-ambient sources are likely to be independent of the ambient sources. A related simulation study by Sheppard et al. (2005) examining non-reactive pollutants found no noticeable difference between effects estimates using either total personal exposure or ambient concentration data when non-ambient sources exposures were independent of ambient source exposures in times series studies. Since $O_3$ is a reactive pollutant, an additional assumption needs to be made in applying these conclusions to $O_3$, i.e., that its chemical reactivity does not induce strong temporal correlations.

The seasonal variation of personal behaviors and building ventilation practices can modify exposure, thereby obscuring the relationship between personal exposures and ambient concentrations. In addition, that relationship may be affected by temperature. For example, high temperatures may increase air conditioning use, which can reduce $O_3$ penetration indoors, further complicating the role of temperature as a confounder of $O_3$ health effects. It should be noted that the pattern of exposure misclassification error and the influence of confounders may differ across the outcomes of interest as well as in susceptible populations. Those who suffer from chronic cardiovascular or respiratory conditions may tend to protect themselves more from environmental threats by reducing their exposure to both $O_3$ and its confounders, such as high temperature and PM, than those who are healthy.

The CD discusses the potential influence of exposure error on epidemiological study results in section 7.1.3.1. Three components to exposure measurement error are outlined: (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 (CD, p. 7-7). These components are expected to have different effects, with the first and third likely not causing bias in a particular direction ("nondifferential error") but increasing the standard error, while the second component may result in downward bias, or attenuation of the risk estimate (CD, pp. 7-7 to 7-8).

Some recent studies have evaluated the impact of exposure measurements error on $O_3$ effect estimates. Navidi et al. (1999) used data from a children's cohort study to compare effect estimates from a simulated "true" exposure level to results of analyses from $O_3$ exposures determined by several methods. The results indicated that the use of $O_3$ exposures from personal sampling or microenvironmental approaches is associated with nondifferential error in $O_3$ effect estimates, compared with effect estimates from "true" exposures. However, $O_3$ exposures based

on the use of ambient monitoring data overestimates the individual's $O_3$ exposure and thus generally results in $O_3$ effect estimates that are biased downward (CD, p. 7-8). Similarly, Zidek (1997) noted that a statistical analysis must balance bias and imprecision (error variance). For example, in a reanalysis of a study by Burnett et al. (1994) on the acute respiratory effects of ambient air pollution, Zidek et al. (1998) noted that accounting for measurement error, as well as making a few additional changes to the analysis, resulted in qualitatively similar conclusions, but the effects estimates were considerably larger in magnitude (CD, p. 7-8).

In addition to overestimation of exposure and the resulting underestimation of effects, the use of ambient $O_3$ concentrations may obscure the presence of thresholds in epidemiologic studies (CD p. 7-9). Brauer et al. (2002) concluded that surrogate measures of exposure, such as those from centrally located ambient monitors, that were not highly correlated with personal exposures obscured the presence of thresholds in epidemiologic studies at the population level, even if a common threshold exists for individuals within the population.

As discussed in the CD Section 3.9, $O_3$ concentrations measured at central ambient monitoring sites may explain, at least partially, the variance in individual exposures; however, this relationship is influenced by other factors such as air exchange rates in housing and time spent outdoors which may vary from city to city. Other studies conducted in various cities observed that the daily averaged personal $O_3$ exposures from the population were well correlated with ambient $O_3$ concentrations, although substantial variability existed among the personal measurements. Thus, there is supportive evidence that ambient $O_3$ concentrations from central monitors may serve as valid surrogate measures for mean personal exposures experienced by the population, which is of the most relevance for time-series studies. This is especially true for respiratory hospital admission studies, for which much of the response is attributable to $O_3$ effects on people with asthma. Ambient monitors are more likely to correlate reasonably well with the personal exposures of children, who spend more time outdoors in the warm season and who are also more likely to have asthma than adults. Conversely, there is some concern about the extent to which ambient concentrations are representative of personal $O_3$ exposures of another particularly susceptible group of individuals, the debilitated elderly, and what impact that may have on mortality and hospitalization time-series studies. The correlation between ambient concentrations and personal exposure measurements has not been examined in this population. A better understanding of the relationship between ambient concentrations and personal exposures, as well as of the other factors that affect relationship will improve the interpretation of concentration-population health response associations observed with ambient $O_3$ concentrations.

Existing epidemiologic models may not fully take into consideration all of the biologically relevant exposure history or reflect the complexities of all of the underlying

biological processes. As discussed in the CD, Section 3.9, using ambient concentrations to determine exposure generally overestimates true personal $O_3$ exposures by approximately 2- to 4-fold in available studies, resulting in biased descriptions of underlying concentration-response relationships and attenuated risk estimates. The implication is that the effects being estimated occur at fairly low exposures and the potency of $O_3$ is greater than these effects estimates indicate. As very few studies evaluating $O_3$ health effects with personal $O_3$ exposure measurements exist in the literature, effect estimates determined from ambient $O_3$ concentrations must be evaluated and used with caution to assess the health risks of $O_3$. Until more data on personal $O_3$ exposure becomes available, the use of routinely monitored ambient $O_3$ concentrations as a surrogate for personal exposures is not generally expected to change the principal conclusions from $O_3$ epidemiologic studies. Thus, the CD concludes that "there is supportive evidence that ambient $O_3$ concentrations from central monitors may serve as surrogate measures for mean personal $O_3$ exposures experienced by the population, which is of most relevance to time-series studies" (CD, p. 7-9). Therefore, population health risk estimates derived using ambient $O_3$ levels from currently available observational studies, with appropriate caveats about personal exposure considerations, remain useful.

In using epidemiological study results for quantification of health risks for certain health outcomes, staff recognizes that the risk estimates may be underestimating true public health risk. However, staff observes that the use of risk estimates for comparing relative risk reductions between alternative $O_3$ standards considered in the risk assessment is less likely to suffer from this concern. In addition, as discussed in Chapter 5, staff has conducted an exposure assessment in conjunction with a portion of the health risk assessment that incorporates estimated population exposures in developing risk estimates for health outcomes based on controlled human exposure studies.

#### 3.4.2.2 Confounding by Copollutants

Confounding occurs when a health effect that is caused by one risk factor is attributed to another variable that is correlated with the causal risk factor; epidemiological analyses attempt to adjust or control for potential confounders. Copollutants (e.g., PM, CO, $SO_2$ and $NO_2$) can meet the criteria for potential confounding in $O_3$-health associations if they are potential risk factors for the health effect under study and are correlated with $O_3$. Effect modifiers include variables that may influence the health response to the pollutant exposure (e.g., co-pollutants, individual susceptibility, smoking or age). Both are important considerations for evaluating effects in a mixture of pollutants, but for confounding, the emphasis is on controlling or adjusting for potential confounders in estimating the effects of one pollutant, while the emphasis for effect modification is on identifying and assessing the level of effect modification.

The CD observes that $O_3$ is generally not highly correlated with other criteria pollutants (e.g., $PM_{10}$, CO, $SO_2$ and $NO_2$), but may be more highly correlated with secondary fine particles, especially during the summer months (CD, p. 7-148). In addition, the correlation between $O_3$ and other pollutants may vary across seasons, since $O_3$ concentrations are generally higher in the summer months. This may lead to negative correlations between $O_3$ and other pollutants during the cooler months, but positive associations between $O_3$ and pollutants such as fine particles during the warmer months (CD, p. 7-17). Thus, the CD pays particular attention to the results of season-specific analyses and studies that assess effects of PM in potential confounding of $O_3$-health relationships in its discussions in section 7.6.4.

Multipollutant models are commonly used to assess potential confounding in epidemiological studies. As discussed in the CD, the limitations to the use of multipollutant models include the difficulty in interpreting results where the copollutants are highly colinear, or where correlations between pollutants change by season (CD, p. 7-150). This is particularly the situation where $O_3$ and a copollutant, such as sulfates, are formed under the same atmospheric condition; in such cases multipollutant models would produce unstable and possibly misleading results (CD, p. 7-152).

For mortality, the results from numerous multi-city and single-city studies are shown in Figure 7-22 of the CD. These results indicate that $O_3$-mortality associations do not appear to be substantially changed in multipollutant models including $PM_{10}$ or $PM_{2.5}$ (CD, p. 7-88). Focusing on results of warm season analyses, Figure 7-23 of the CD shows effect estimates for $O_3$-mortality associations that are fairly robust to adjustment for PM in multipollutant models (CD, p. 7-90). In general, based on results from several single- and multiple-city studies, and on recent meta-analyses, the CD (p. 7-103) concludes that "copollutants generally do not appear to substantially confound the association between $O_3$ and mortality."

Similarly, multipollutant models are presented for associations between short-term $O_3$ exposures and respiratory hospitalization in Figure 7-12 of the CD; the CD concludes that copollutants generally do not confound the relationship between $O_3$ and respiratory hospitalization (CD, p. 7-70, 7-71). Multipollutant models were not used as commonly in studies of relationships between respiratory symptoms or lung function with $O_3$, but the CD reports that results of available analyses indicate that such associations generally were robust to adjustment for $PM_{2.5}$ (CD, p. 7-134). For various co-pollutant models, in a large multicity study of asthmatic children (Mortimer et al., 2002), the $O_3$ effect was attenuated, but there was still a positive association. In Gent et al. (2003), effects of $O_3$, but not $PM_{2.5}$, remained statistically significant and even increased in magnitude in two-pollutant models (CD, p. 7-53).

Considering this body of studies, the CD concludes: "Multipollultant regression analyses indicated that $O_3$ risk estimates, in general, were not sensitive to the inclusion of copollutants,

including $PM_{2.5}$ and sulfate. These results suggest that the effects of $O_3$ on respiratory health outcomes appear to be robust and independent of the effects of other copollutants (CD, p. 7-154)." We use the results of single-pollutant model results in presentation of results in this chapter and in quantitative risk assessments conducted as part of this review (see Chapter 5) for purposes of comparing results from different studies. However, we also include the use of multi-pollutant model results in presenting risk estimates, when available, to more completely characterize the quantitative health risks associated with ambient $O_3$ levels.

#### 3.4.2.3 Model Specification

The CD observes that one challenge of time-series epidemiological analysis is assessing the relationship between $O_3$ and health outcomes while avoiding bias due to confounding by other time-varying factors, particularly seasonal trends and weather variables. (CD, p. 7-12) These variables are of particular interest because $O_3$ concentrations have a well-characterized seasonal pattern (see Chapter 2) and are also highly correlated with changes in temperature. Thus it can be difficult to distinguish whether effects are associated with $O_3$ or with seasonal or weather variables in statistical analyses.

Section 7.1.3.4 of the CD discusses statistical modeling approaches that have been used to adjust for time-varying factors, highlighting a series of analyses that were done in a Health Effects Institute-funded reanalysis of numerous time-series studies. While the focus of these reanalyses was on associations with PM, a number of investigators also examined the sensitivity of $O_3$ coefficients to the extent of adjustment for temporal trends and weather factors. In addition, several recent studies, including U.S. multi-city studies (Bell et al., 2005; Huang et al., 2005; Schwartz et al., 2005) and a meta-analysis study (Ito et al., 2005), evaluated the effect of model specification on $O_3$-mortality associations (CD, p. 7-14). As discussed in the CD (section 7.6.3.1), these studies generally report that associations reported with $O_3$ are not substantially changed with alternative modeling strategies for adjusting for temporal trends and meteorologic effects. However, significant confounding can occur when strong seasonal cycles are present, suggesting that season-specific results are more generally robust than year-round results in such cases. The CD concludes that "seasonal dependence of $O_3$-mortality effects complicates interpretation of $O_3$ risk estimates calculated from year-round data without adequate adjustment of temporal trends" (CD, p. 7-99), and that more work is needed in this area to reduce the uncertainty involved in the epidemiologic interpretation of $O_3$ effect estimates (CD, p. 7-141).

A number of epidemiological studies have conducted season-specific analyses, as discussed in section 7.6.3.2 of the CD. As observed above in section 3.3, such studies have generally reported stronger and more precise effect estimates for $O_3$ associations in the warm season than in analyses conducted in the cool seasons or over the full year. For assessing

relationships between $O_3$ and health outcomes, the CD highlights several reasons to focus on warm season analyses: (1) the seasonal nature of $O_3$ concentrations; (2) the relationship between $O_3$ formation and temperature; (3) correlations between other pollutants, particularly fine particles, and $O_3$ variations across seasons in some areas; and (4) factors affecting exposure to ambient $O_3$, such as air conditioning use, varies seasonally in most areas of the U.S.. We have therefore focused on epidemiological findings from warm season analyses, where available, for qualitative assessments and for the quantitative risk assessment discussed in Chapter 5.

### 3.4.3 Consistency

Consistency refers to the persistent finding of an association between exposure and outcome in multiple studies of adequate power in different persons, places, circumstances and times (CDC, 2004). In considering results from multicity studies and single-city studies in different areas, the CD observes general consistency in effects of short-term $O_3$ exposure on mortality, respiratory hospitalization and other respiratory health outcomes (CD, p. 8-41). The variations in effects that are observed may be attributable to differences in relative personal exposure to $O_3$, as well as varying concentrations and composition of copollutants present in different regions. Thus, the CD concludes that "consideration of consistency or heterogeneity of effects is appropriately understood as an evaluation of the similarity or general concordance of results, rather than an expectation of finding quantitative results with a very narrow range" (CD, p.8-41).

### 3.4.4 Lag Structure in Short-term Exposure Studies

In the short-term exposure epidemiological studies, many investigators have tested associations for a range of lag periods between the health outcome and $O_3$ concentration (see CD, sections 7.1.3.3). The CD observes that the selection of an appropriate lag period can depend on the health outcome under study. For example, if cough is resulting from the irritant action of $O_3$, that would be expected to occur with a short lag time; however, exacerbation of asthma through an inflammatory response might occur up to several days after initial exposure (CD, p. 7-12). For both mortality and respiratory hospital admissions, the CD reports that most significant associations between $O_3$ and mortality were observed with $O_3$ measured on the same day or a 1-day lag period in studies using individual lag periods (CD, p. 7-14). In U.S. multi-city studies, larger effect estimate sizes were reported for the $O_3$-mortality relationship with the distributed lag structure (CD, p. 7-88). Field studies of lung function or respiratory symptoms reported associations with $O_3$ across a range of lag periods from the exposure on the same day to exposures averaged over several days (CD, Sections 7.2.3 and 7.2.4). Cardiovascular effects appeared to be associated with $O_3$ at shorter lag periods; cardiovascular health outcomes such as

changes in cardiac autonomic control were associated with $O_3$ measured on the same day (CD, section 7.2.7.1). In addition, Peters et al. (2001) reported a positive but not statistically significant association between myocardial infarction onset and $O_3$ with very short lag times of 1- to 4 hr (CD, p. 7-64).

In focusing on an effect estimate reported for any individual lag period, the CD observes that it is important to consider the pattern of results across the series of lag periods. If there is an apparent pattern of results across the different lags, then selecting the single-day lag with the largest effect from a series of positive associations is likely to underestimate the overall effect size, since single-day lag effect estimates do not fully capture the risk that may be distributed over adjacent or other days (CD, p. 7-13). However, if the reported effect estimates vary substantially across lag periods, any result for a single day may well be biased (CD, p. 7-14). If the effect of $O_3$ on health outcomes persists over several days, distributed lag model results can provide more accurate effect estimates for quantitative assessment than an effect estimate for a single lag period (CD, p. 7-12). Conversely, if the underlying $O_3$-health relationship is truly an acute effect, then a distributed lag model would likely result in a reduced effect estimate size that may underestimate the effect (CD, p. 7-12).

On this basis, the CD focuses on effect estimates from models using 0- or 1-day lag periods, with some consideration of multi-day lag effects (CD, p. 7-14). For quantitative assessments, we conclude that it is appropriate to use results from lag period analyses consistent with those reported in the CD, focusing on single day lag periods of 0-1 days for associations with mortality or respiratory hospitalization, depending on availability of results (CD, p. 7-14). When available, distributed lag model results also have been used in the quantitative risk assessment. However, for those few studies that show inconsistent patterns, the use of single-day lag results is not appropriate for inclusion in the quantitative assessment.

### 3.4.5 Concentration-Response Relationships and Potential Thresholds

It has been recognized that it is reasonable to expect that there likely are biological thresholds for different health effects in individuals or groups of individuals with similar innate characteristics and health status. For $O_3$ exposure, individual thresholds would presumably vary substantially from person to person due to individual differences in genetic susceptibility, pre-existing disease conditions and possibly individual risk factors such as diet or exercise levels (and could even vary from one time to another for a given person). Thus, it would be difficult to detect a distinct threshold at the population level, below which no individual would experience a given effect, especially if some members of a population are unusually sensitive even down to very low concentrations (U.S. EPA, 2004, p. 9-43, 9-44).

Some studies have tested associations between $O_3$ and health outcomes after removal of days with higher $O_3$ levels from the data set; such analyses do not necessarily indicate the presence or absence of a threshold, but provide some information on whether the relationship is found using only lower-concentration data. For example, using data from 95 U.S. cities, Bell et al. (2004) found that the effect estimate for an association between short-term $O_3$ exposure and mortality was little changed when days exceeding 60 ppb (24-hr average) were excluded in the analysis (CD, p. 8-43). Using data from 8 U.S. cities, Mortimer and colleagues (2002) also reported that associations between $O_3$ and both lung function and respiratory symptoms remained statistically significant and of the same or greater magnitude in effect size when concentrations greater than 80 ppb (8-hr avg) were excluded (CD, p. 7-46). Several single-city studies are also summarized in section 7.6.5 of the CD that report similar findings of associations that remain or are increased in magnitude and statistical significance when data at the upper end of the concentration range are removed.

Other time-series epidemiological studies have used statistical modeling approaches to evaluate whether thresholds exist in associations between short-term $O_3$ exposure and mortality. As discussed in section 7.6.5 of the CD, one European multi-city study included evaluation of the shape of the concentration-response curve, and observed no deviation from a linear function across the range of $O_3$ measurements from the study (Gryparis et al., 2004; CD p. 7-154). Several single-city studies also observed a monotonic increase in associations between o $O_3$ and morbidity that suggest that no population threshold exists (CD, p. 7-159).

On the other hand, a study in Korea used several different modeling approaches and reported that a threshold model provided the best fit for the data. The results suggested a potential threshold level of about 45 ppb (1-hr maximum concentration; < 35 ppb, 8-hr avg) for an association between mortality and short-term $O_3$ exposure during the summer months (Kim et al., 2004; CD, p. 8-43). The authors reported larger effect estimates for the association for data above the potential threshold level, suggesting that an $O_3$-mortality association might be underestimated in the non-threshold model. A threshold analysis recently reported by Bell et al. (2006) for 98 U.S. communities, including the same 95 communities in Bell et al. (2004), indicated that if a population threshold existed for mortality, it would likely fall below a 24-h average $O_3$ concentration of 15 ppb (< 25 ppb, 8-hr avg). In addition, Burnett and colleagues (1997) plotted the relationships between air pollutant concentrations and both respiratory and cardiovascular hospitalization, and it appears in these results that the associations with $O_3$ are found in the concentration range above about 30 ppb (1-hr maximum; < 25 ppb, 8-hr avg).

Vedal and colleagues (2003) reported a significant association between $O_3$ and mortality in British Columbia where $O_3$ concentrations were quite low (mean concentration of 27.3 ppb). The authors did not specifically test for threshold levels, but the fact that the association was

found in an area with such low $O_3$ concentrations suggests that any potential threshold level would be quite low in this data set.

In summary, the CD finds that, taken together, the available evidence from toxicological, clinical and epidemiological studies suggests that no clear conclusion can now be reached with regard to possible threshold levels for $O_3$-related effects (CD, p. 8-44). Further, recognizing that limitations in epidemiological studies make discerning thresholds in populations difficult, the evidence suggests that if a population threshold level does exist, it is likely near the lower limit of ambient $O_3$ concentrations in the U.S. (CD, p. 8-44). We recognize, however, the possibility that thresholds for individuals may exist in reported associations at fairly low levels within the range of air quality observed in the studies but not be detectable as population thresholds in epidemiological analyses. Based on the CD's conclusions, we judge that there is insufficient evidence to support use of potential threshold levels in quantitative risk assessments and that it is appropriate to estimate risks within the range of air quality concentrations down to estimated policy-relevant background level.

### 3.4.7 Health Effects of Pollutant Mixtures Containing $O_3$

The potential for $O_3$-related enhancements of PM formation, particle uptake, and exacerbation of PM-induced cardiovascular effects underscores the importance of considering contributions of $O_3$ interactions with other often co-occurring air pollutants to health effects due to $O_3$-containing pollutant mixes. Chapters 4, 5, and 6 of the CD provide a discussion of experimental studies that evaluate interactions of $O_3$ with other co-occurring pollutants. Some examples of important pollutant mixture effects noted there are highlighted below.

In Chapter 4, the CD noted some important interactive effects of coexposures to $O_3$, and $NO_2$ and $SO_2$, two other common gaseous copollutants found in ambient air mixes. A study by Rigas et al. (1997) showed that continuous exposure of healthy human adults to $SO_2$ or to $NO_2$ increased inhaled bolus $O_3$ absorption, while continuous exposure to $O_3$ alone decreased bolus absorption of $O_3$. This suggests enhancement of $O_3$ uptake by $NO_2$ or $SO_2$ coexposure in ambient air mixes. Another study by Jenkins et al. (1999) showed that asthmatics exhibited enhanced airway responsiveness to house dust mite following exposures to $O_3$, $NO_2$, and the combination of the two gases (CD, Chapter 6). Spirometric responses, however, were impaired only by $O_3$ and $O_3$+$NO_2$ at higher concentrations. On the other hand, animal toxicology studies (CD, Chapter 5) that evaluated exposures to $O_3$ in mixture with $NO_2$, formaldehyde, and PM demonstrated additive, synergistic or antagonistic effects, depending on the exposure regimen and the specific health endpoints evaluated.

Several studies have demonstrated the enhancement by $O_3$ exposure of various respiratory responses of sensitive individuals to allergens. For example, Peden et al. (1995) showed $O_3$-induced increased response to nasal allergen challenge among allergic asthmatic subjects, and

Michelson et al. (1999) showed promotion by 0.4 ppm $O_3$ exposure of inflammatory cell influx in response to nasal allergen challenge in asymptomatic dust-mite sensitive asthmatics. In addition, Jörres et al. (1996) demonstrated enhancement by 0.25 ppm $O_3$ exposure of airway responsiveness in mildly allergic asthmatics that was increased in response to an individual's historical allergen (grass and birch pollen, house dust mite, animal dander). These results were further extended by Holz et al. (2002) who showed that repeated daily exposure to 0.125 ppm $O_3$ for 4 days exacerbated lung function decrements (e.g., decreased $FEV_1$) in response to bronchial allergen challenges among subjects with preexisting allergic airway disease, with or without asthma (see Chapter 6 of the CD). This suggests that $O_3$ exposure can place allergic people who do not have asthma, as well as people who do have asthma, at increased risk for allergic respiratory effects. Consistent with and supporting the above findings are animal toxicology studies reviewed in detail by Harkema and Wagner (2005), which indicate that (a) $O_3$-induced epithelial and inflammatory responses in laboratory rodents are markedly enhanced by coexposure to inhaled biogenic substances (e.g., bacterial endotoxin or ovalbumin, an experimental aeroallergen) and (b) adverse airway effects of biogenic substances can be exacerbated by coexposure to $O_3$.

Also of much note is a newly emerging literature which indicates that $O_3$ can modify the biological potency of certain types of ambient PM, as shown by experimental tests. For example, as described in the CD, Section 5.4.2, the reaction of diesel PM with 0.1 ppm $O_3$ for 48 hr increased the potency (compared to non-exposed or air-exposed diesel PM) to induce neutrophil inflex, total protein, and LDH in lung lavage fluid in response to intratracheal PM instillation in rats (Madden et al., 2000). However, the potency of carbon black particles was not enhanced by exposure to $O_3$, suggesting that $O_3$ reaction with organic components of the diesel PM were responsible for the observed increased diesel PM effects.

Potential interaction of $O_3$ with fine PM in aged rats was examined by Kleinman et al. (2000). In this study the effects of fine PM containing two common toxic constituents, ammonium bisulfate (ABS, 0.3 μm 70 $\mu g/m^3$) and elemental carbon (C, 0.3 μm 50 $\mu g/m^3$) and a mixture (ABS + C) with 0.2 ppm $O_3$ was evaluated on aged rat lung structure and macrophage function. Exposures of $O_3$, elemental carbon or ABS alone did not cause significant lung injury, lung tissue collagen content or respiratory burst activity. On the other hand, mixtures (ABS + C + $O_3$) caused significant lung injury as assessed by increased cell proliferation response in lung epithelial and interstitial cells, loss of lung tissue collagen and increase in respiratory burst and phagocytic activity.

The majority of toxicological studies discussed in the CD evaluated effects of individual pollutants or simple mixtures of the constituents of urban smog mixtures, and these toxicology studies may not fully explain epidemiologic findings that have increasingly shown ambient $O_3$,

other gaseous pollutants, and/or PM to be associated with various health effects at relatively low concentrations. In a recent report, Sexton et al (2004) utilized "smog chambers", i.e., environmental irradiation chambers to generate synthetic photochemical oxidants mixtures similar to urban smog, and studied the toxicity of such mixtures on the inflammatory response of A549 cells in an in vitro exposure system. In this preliminary study, the authors found the simulated urban photochemical oxidant mixture generated with the addition of $O_3$ to have enhanced toxicity (as assessed by the expression of IL-8 mRNA). Additional toxicology studies using similar realistic air pollution smog mixtures in the future may provide more relevant biological understanding for the potential interactions that occur in the ambient air among various pollutants.

All of the above types of interactive effects of $O_3$ with other co-occurring gaseous and nongaseous viable and nonviable PM components of ambient air mixes argue for not only being concerned about direct effects of $O_3$ acting alone, but also the need for viewing $O_3$ as a surrogate indicator for air pollution mixes which may enhance risk of adverse effects due to $O_3$ acting in combination with other pollutants. Viewed from this perspective, those epidemiologic findings of morbidity and mortality associations, with ambient $O_3$ concentrations extending to concentrations below 0.08 ppm, become more understandable and plausible.

## 3.5 BIOLOGICAL PLAUSIBILITY AND COHERENCE OF EVIDENCE

This section summarizes material contained in section 8.4.3 and section 8.6 of the CD, which integrates epidemiological studies with mechanistic information from controlled human exposure studies and animal toxicological studies to draw conclusions regarding the coherence of evidence and biological plausibility of $O_3$-related health effects. For its assessment, the CD's discussion draws from epidemiological evidence on a range of relevant health endpoints (from cardiopulmonary and physiological changes to morbidity and mortality) and assessment of available toxicological and biochemical evidence on potential plausible causal relationships for the observed epidemiological associations (CD, p. 8-45).

### 3.5.1 Animal-to-Human Extrapolation Issues

Table 3-1 (Table 8-1, CD, p. 8-29) summarizes physiological and biochemical observations which represent the knowledge base available from toxicological studies in humans and animals that support conclusions drawn about biological alterations that cause acute $O_3$-induced health effects. Table 3-1 was based upon experimental data (contained in CD Chapters 5 and 6, as well as the chapter annexes), which used environmentally relevant exposure regimens. Although most of the acute $O_3$-induced biological alterations are transient and attenuate over time, this does not mean that injury at the cellular and tissue level does not

continue. Most inflammatory markers (e.g., PMN influx) attenuate after 5 days of exposure, but markers of cell damage (e.g., LDH enzyme activity) do not attenuate and continue to increase. Also, the time-line for resolution of many of the physiological and biological parameters presented in Figure 3-2 (Figure 8-3, CD, p. 8-30) differ for healthy human subjects and those with underlying cardiopulmonary diseases. The CD further notes that alterations in acute $O_3$-induced cellular and molecular changes observed in human airway epithelium evolve over time, as depicted in Figure 3-3 (Figure 8-4, CD, p. 8-31), and that the knowledge of this profile is important in assessing biological plausibility to integrate across evidence of various health endpoints.

The similarities in physiological, biochemical and pathological processes between humans and many animal species are due to the high level of genome sequence homology that exists across species (CD, p. 8-28). It is this homology that supports the use of knowledge gained on initiation, progression, and treatment regimes for disease processes across species, especially on the acute $O_3$-induced effects in the respiratory tracts of humans and various animal species, as depicted in CD Table 3-1 and Figures 3-2 and 3-3. The similarities observed in human and rat respiratory system effects (e.g., in spirometry, ventilatory response, host defense), attenuation, and at higher levels of cellular organization (e.g., neutrophilic inflammation, macrophage phagocytosis processes) lend support to animal-to-human extrapolation. This is particularly important in collecting information that would not be possible to gather in human exposure or epidemiological studies but may corroborate data from both types of studies.

Quantitative extrapolation requires a combination of dosimetry, end point homology, and species sensitivity. Although uncertainties continue to exist, animal-to-human extrapolation can be done for a number of health endpoints with sufficient accuracy to be useful in evaluating the potential for human health effects. For example, the amount of protein in lavage fluid shows a striking relationship when interspecies dosimetric adjustments are applied to the individual species and exposure studies. One study (Hatch et al., 1994) of inflammatory markers suggests that a 2 ppm $O_3$ exposure in sedentary rats approximates a 0.4 ppm exposure in exercising humans (i.e., if one considers the dosimetry, the sensitivities of rats and humans are consistent). This supports the use of some animal data collected at higher $O_3$ exposures to help understand molecular changes in acutely exposed humans (CD, 8-31). Also of importance are the chronic exposure studies (12 to 24 months) reporting lesions in animals caused by long-term $O_3$ exposures that may analogously occur in humans with long-term (months, years) exposure to relatively high levels of $O_3$. However, specific exposure patterns of $O_3$ concentrations that could produce comparable alterations in human lungs remain to be substantiated (CD, p. 8-32).

**Table 3-1. Acute $O_3$-induced Physiological and Biochemical Changes in Human and Animals**

| Physiological/Biochemical Alterations | Human Exposure Studies [1,2] | Animal Toxicology Studies [3,4] |
|---|---|---|
| Pulmonary Function: | ↓ $FEV_1$<br>↑ Frequency of breathing (rapid, shallow )<br>↓ FVC<br>(cough, breathing discomfort, throat irritation, wheezing)<br>Mild bronchoconstriction | ↑ Frequency of breathing (rapid, shallow )<br>↓ FVC |
| Airway Responsiveness: | ↑ (neuronal involvement)<br>Change in lung resistance | ↑ (vagal mediation)<br>Change in lung resistance |
| Inflammation: | Yes<br>↑ inflammatory mediators | Yes<br>↑ inflammatory mediators |
| Reactive Oxygen Species: | ↑ | ↑ |
| Host Defense: | ↑ particle clearance<br>↑ permeability<br>↓ AM phagocytosis | ↑ particle clearance<br>↑ permeability<br>↓ clearance of bacteria<br>↑ severity of infection<br>↑ mortality & morbidity |
| Lung Injury:<br>Morphology: | Yes | Yes |
| Susceptibility: | Age,<br>Interindividual variability<br>Disease status<br>Polymorphism in certain genes being recognized | Species-specific differences<br>Genetic basis for susceptibility indicated |
| Cardiovascular Changes: | Impairment in arterial $O_2$ transfer<br>Ventilation-perfusion mismatch (suggesting potential arterial vasoconstriction)<br>↑ rate pressure product[5]<br>↑ myocardial work[5] | Heart rate<br>↓ core body temperature<br>↑ atrial natriuretic factor<br>Role for platelet activity factor (PAF) indicated<br>Increased pulmonary vascular resistance |

[1] Controlled chamber exposure studies in human volunteers were carried out for a duration of 1 to 6.6 h with $O_3$ concentration in the range of 0.08-0.40 ppm with intermittent exercise.
[2] Data on some of the biochemical parameters were obtained from in vitro studies using cells recovered from BALF.
[3] Responses were observed in animal toxicology studies with exposure for a duration of 2 to 72 h with $O_3$ concentration in the range of 0.1 to 2.0 ppm.
[4] Various species (mice, rat, guinea pigs and rabbit) and strains.
[5] In hypertensive subjects.

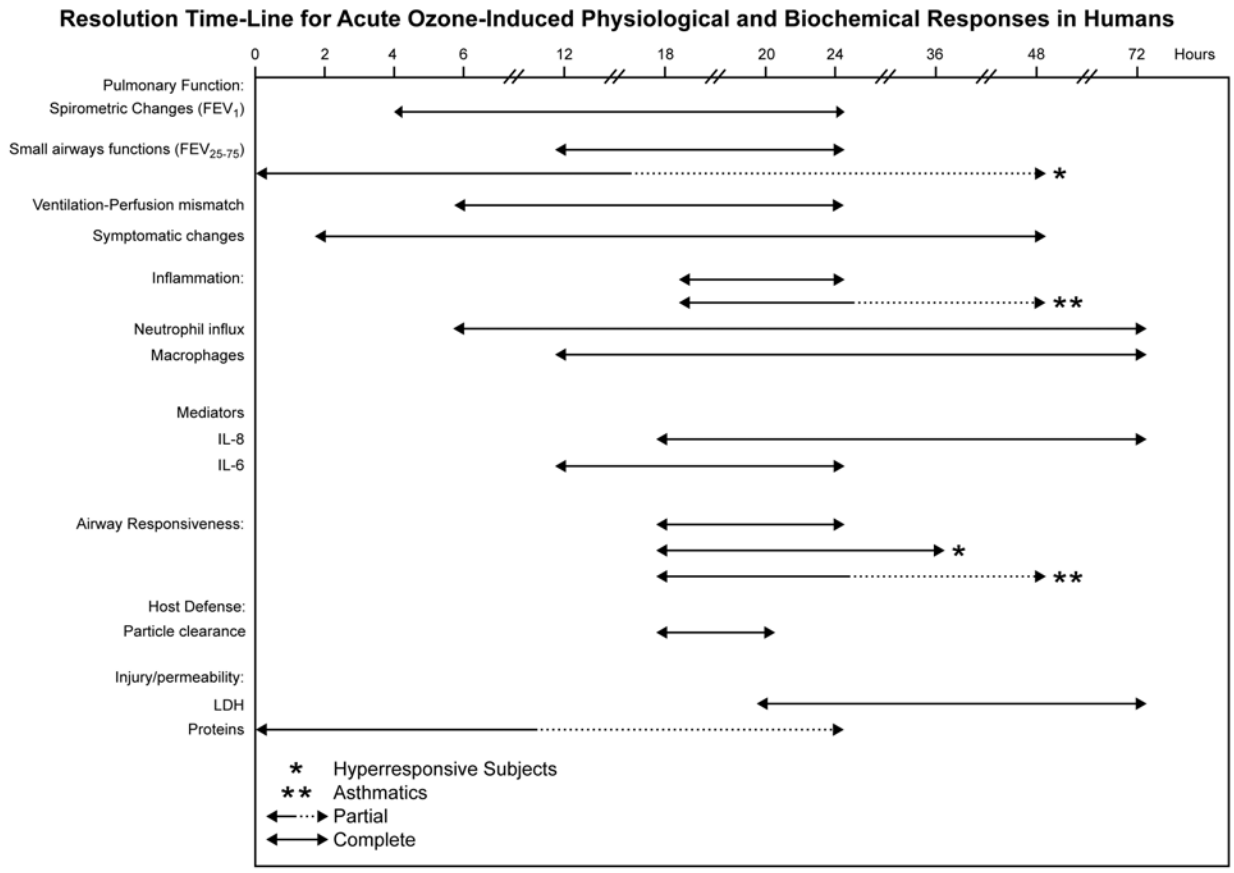



**Figure 3-2. Resolution time-line for the respiratory, physiological, and biochemical parameters are derived from studies reported in the CD, Chapter 6 and Chapter 6 Annex.**

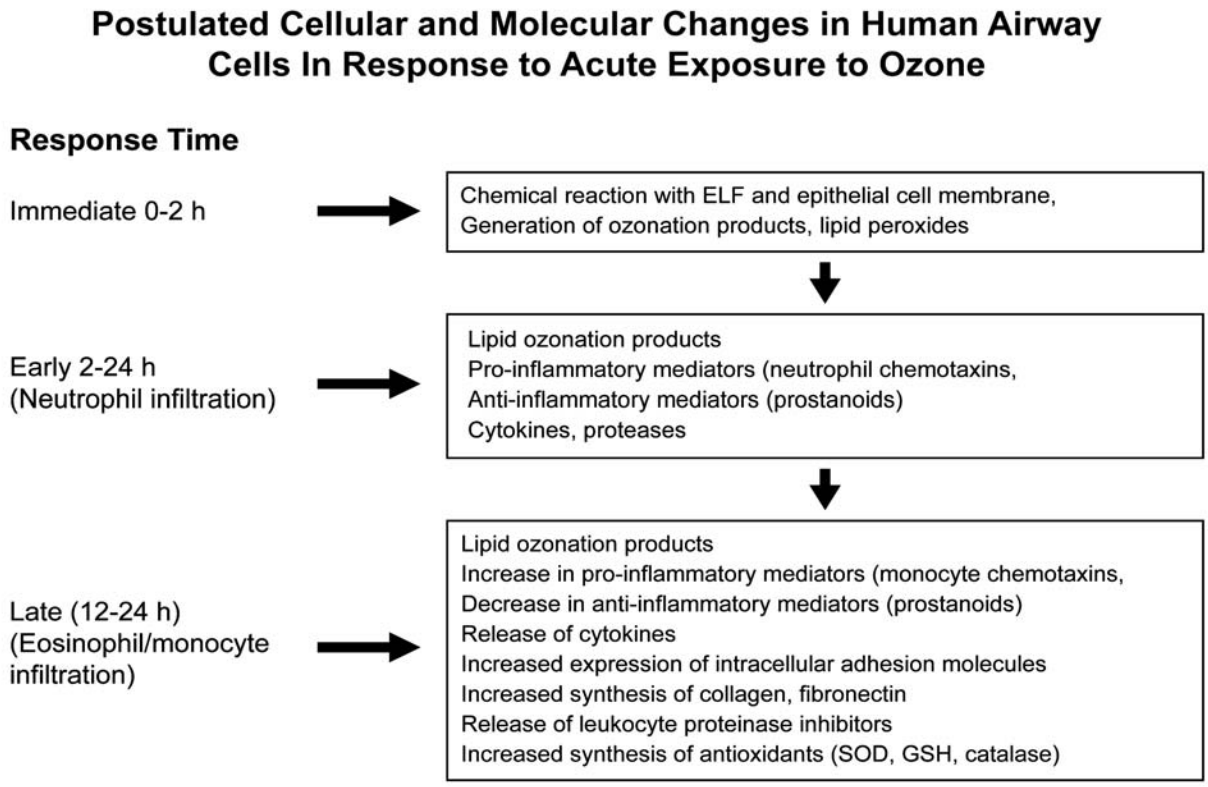



**Figure 3-3. Acute (1-8 h) $O_3$ exposure-induced cellular and molecular changes and timelines for their resolution depicted here are derived from the data reported in Leikauf et al. (1995) and Mudway and Kelly (2000)3-4.Acute (1-8 h) $O_3$ exposure-induced cellular and molecular changes and timelines for their resolution depicted here are derived from the data reported in Leikauf et al. (1995) and Mudway and Kelly (2000).**

### 3.5.2 Coherence and Plausibility of Short-term Effects on the Respiratory System

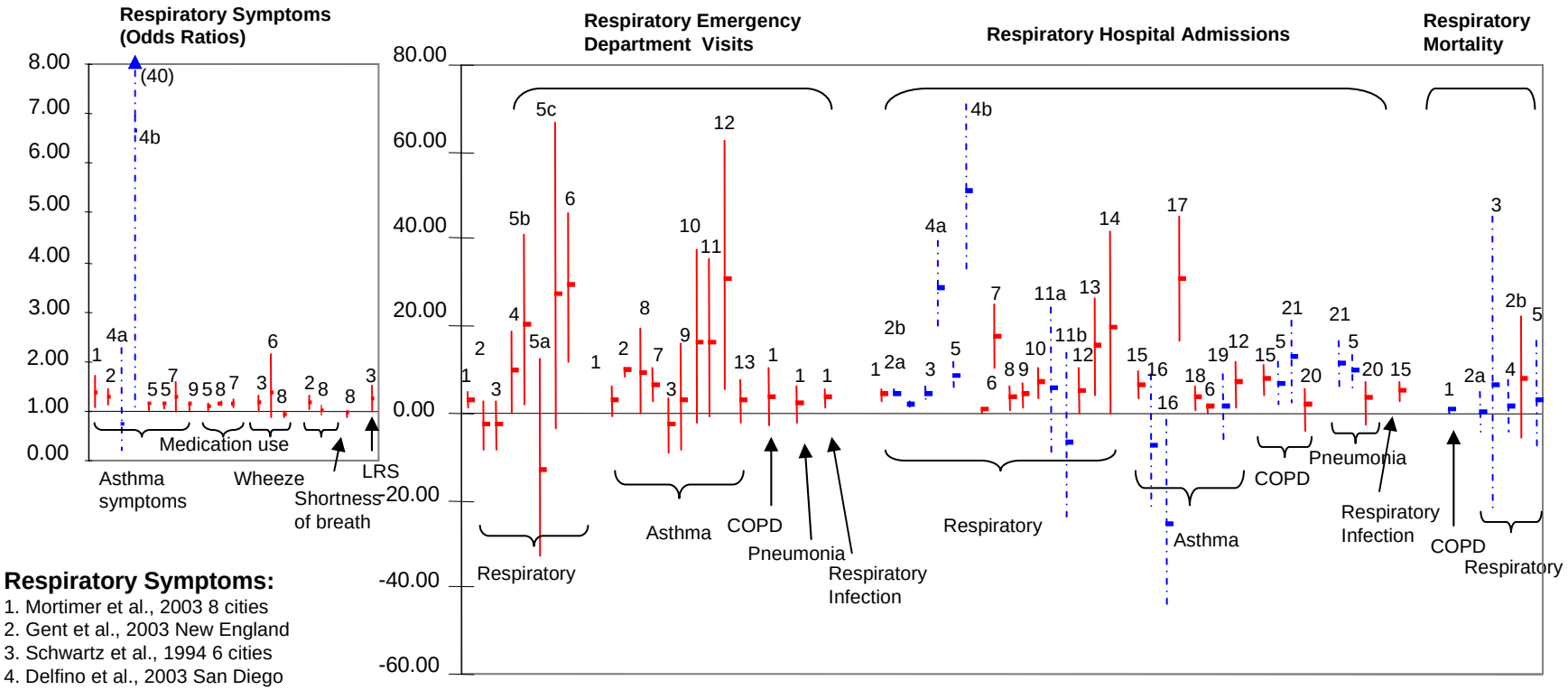
Acute respiratory morbidity effects that have been associated with short-term exposure to $O_3$ include such health endpoints as decrements in lung function, increased airway responsiveness, airway inflammation, epithelial injury, immune system effects, ED visits for respiratory diseases, and hospitalization due to respiratory illness

Recent epidemiological studies have supported evidence available in the previous $O_3$ NAAQS review on associations between ambient $O_3$ exposure and decline in lung function for children. Earlier observations that children and asthmatic individuals are particularly susceptible to ambient $O_3$ are supported by a meta-analysis (Kinney et al., 1996) of summer camp studies. The CD (p. 8-34) concludes that exposure to ambient $O_3$ has a significant effect on lung function, is associated with increased respiratory symptoms and medication use, particularly in asthmatics.

Short-term exposure to $O_3$ has also been associated with more severe morbidity endpoints, such as ED visits and hospital admissions for respiratory cases, including specific respiratory illness (e.g., asthma) (CD, sections 7.3.2 and 7.3.3). In addition, a few epidemiological studies have reported positive associations between short-term $O_3$ exposure and respiratory mortality, though the associations are not generally statistically significant, possibly due to a lack of statistical power for this mortality subcategory (CD, p. 7-109).

Considering the evidence from epidemiological studies, the results described above provide evidence for coherence in $O_3$-related effects on the respiratory system. Effect estimates from U.S. and Canadian studies are shown in Figure 3-4, where it can be seen that mostly positive associations have been reported with respiratory effects ranging from respiratory symptoms, such as cough or wheeze, to hospitalization for various respiratory diseases, and there is suggestive evidence for associations with respiratory mortality. Many of the reported associations are statistically significant.

Considering also evidence from toxicological, chamber, and field studies, the CD (section 8.6) discusses biological plausibility and coherence of evidence for acute $O_3$-induced respiratory health effects. Inhalation of $O_3$ for several hours while subjects are physically active can elicit both acute adverse pathophysiological changes and subjective respiratory tract symptoms (CD, section 8.4.2). Acute pulmonary responses observed in healthy humans exposed to $O_3$ at ambient concentrations include: decreased inspiratory capacity; mild bronchoconstriction; rapid, shallow breathing during exercise; subjective symptoms of tracheobronchial airway irritation, including cough and pain on deep inspiration; decreases in measures of lung function (e.g., FVC and $FEV_1$); and increased airway resistance ($SR_{aw}$). The severity of symptoms and magnitude of response depends on inhaled dose, individual $O_3$ sensitivity, and the degree of attenuation or




**Respiratory Symptoms:**

1. Mortimer et al., 2003 8 cities
2. Gent et al., 2003 New England
3. Schwartz et al., 1994 6 cities
4. Delfino et al., 2003 San Diego (a=score>1; b=score>2)
5. Ross et al., 2002 East Moline
6. Neas et al., 1995 Uniontown
7. Delfino et al., 1998 San Diego
8. Ostro et al., 2001 S. California
9. Thurston et al., 1997 Connecticut

**Emergency Department Visits:**

1. Peel et al., 2005 Atlanta
2. Wilson et al., 2005 Portland NH
3. Wilson et al., 2005 Manchester NH
4. Stieb et al., 1996 St. John Canada
5. Jones et al., 1995 Baton Rouge (a=0-17 yo; b=18-60 yo; c=>60 yo)
6. Delfino et al., 1997 Montreal
7. Tolbert et al., 2000 Atlanta
8. Jaffe et al., 2003 3 Ohio cities
9. Jaffe et al., 2003 Cleveland
10. Jaffe et al., 2003 Columbus
11. Jaffe et al., 2003 Cincinnati
12. Friedman et al., 2001 Atlanta
13. Zhu et al., 2003 Atlanta

**Hospital Admissions:**

1. Burnett et al., 1994 Toronto
2. Gwynn et al., 2001 New York City (a=nonwhite; b=white)
3. Gwynn et al., 2000 Buffalo
4. Yang et al., 2003 Vancouver (a=<3 yo; b=65+ yo)
5. Moolgavkar et al., Minneapolis/St. Paul
6. Thurston et al., 1992 New York City
7. Burnett et al., 1997 Toronto
8. Schwartz et al., 1996 Cleveland
9. Delfino et al., 1994 Montreal
10. Burnett et al., 1997 16 Canadian cities
11. Luginaah et al., 2003 Windsor (a=males; b=females)
12. Thurston et al., 1992 Buffalo
13. Thurston et al., 1994 Toronto
14. Schwartz et al., 1996 Spokane
15. Burnett et al., 1999 Toronto
16. Lin et al., 2003 Windsor
17. Burnett et al., 2001Toronto
18. Sheppard et al., 2003 Seattle
19. Nauenberg and Basu, 1999 Los Angeles
20. Ito, 2003 Detroit
21. Schwartz et al., 1994 Detroit

**Respiratory Mortality:**

1. Moolgavkar, 2003 Cook County
2. Ito, 2003 Detroit (a=1986-1990; b=1992-1994)
3. Vedal et al., 2003 Vancouver
4. Villeneuve et al., 2003 Vancouver
5. Ostro et al., 2003, Coachella Valley

**Figure 3-4. Effect estimates (with 95% confidence intervals) for associations between short-term ozone exposure and respiratory health outcomes.**

**Effect estimates expressed as odds ratios for associations with respiratory symptoms and % increase for other outcomes, per standardized increments: 20 ppb for 24-hr $O_3$, 30 ppb for 8-hr $O_3$, and 40 ppb for 1-hr $O_3$, presented in order of decreasing statistical power from left to right in each category. Dotted line (blue) indicates all year analyses; solid line (red) indicates warm season results. LRS=lower respiratory symptoms; COPD=chronic obstructive pulmonary disease**

enhancement of response resulting from previous $O_3$ exposures. Lung function studies of several animal species acutely exposed to relatively low $O_3$ levels (0.25 to 0.4 ppm) show responses similar to those observed in humans, including increased breathing frequency, decreased tidal volume, increased resistance, and decreased FVC. Alterations in breathing pattern return to normal within hours of exposure, and attenuation in functional responses following repeated $O_3$ exposures is similar to those observed in humans.

Physiological and biochemical alterations investigated in controlled human exposure and animal toxicology studies tend to support certain hypotheses of underlying pathological mechanisms which lead to the development of respiratory-related effects reported in epidemiology studies (e.g., increased hospitalization and medication use). Some of these are: (a) decrements in lung function, (b) bronchoconstriction, (c) increased airway responsiveness, (d) airway inflammation, (e) epithelial injury, (f) immune system activation, (g) host defense impairment, and sensitivity of individuals, such as age, genetic susceptibility, and the degree of attenuation present due to prior exposures. The time sequence, magnitude, and overlap of these complex events, both in terms of development and recovery (as depicted in Figures 3-2 and 3-3), illustrate the inherent difficulty of interpreting the biological plausibility of $O_3$-induced cardiopulmonary health effects (CD, p. 8-48).

The interaction of $O_3$ with airway epithelial cell membranes and epithelial lining fluid (ELF) to form lipid ozonation products and ROS is supported by numerous human, animal and in vitro studies. Ozonation products and ROS initiate a cascade of events that lead to oxidative stress, injury, inflammation, airway epithelial damage and increased epithelial damage and increased alveolar permeability to vascular fluids. Repeated respiratory inflammation can lead to a chronic inflammatory state with altered lung structure and lung function and may lead to chronic respiratory diseases such as fibrosis and emphysema (CD, section 8.6.2). Continued respiratory inflammation also can alter the ability to respond to infectious agents, allergens and toxins. Acute inflammatory responses to $O_3$ are well documented, and lung injury can become apparent within 3 hr after exposure in humans. Ozone-induced lung injury and subsequent disruption of the airway epithelial barrier has been implicated in increased mucociliary clearance of particles in human subjects.

Taken together, the CD concludes that the evidence from experimental human and animal toxicology studies indicates that acute $O_3$ exposure is causally associated with respiratory system effects, including $O_3$-induced pulmonary function decrements, respiratory symptoms, lung inflammation, and increased lung permeability, airway hyperresponsiveness, increased uptake of nonviable and viable particles, and consequent increased susceptibility to PM-related toxic effects and respiratory infections (CD, p. 8-48).

### 3.5.3 Coherence and Plausibility of Effects on the Cardiovascular System

Only a few experimental studies of animals and humans have evaluated possible mechanisms or physiological pathways by which acute $O_3$ exposures may induce cardiovascular system effects. Ozone induces lung injury, inflammation, and impaired mucociliary clearance, with a host of associated biochemical changes all leading to increased lung epithelial permeability. As discussed in Section 3.2.2, the generation of lipid ozonation products and reactive oxygen species in lung tissues can influence pulmonary hemodynamics, and ultimately the cardiovascular system.

Other potential mechanisms by which $O_3$ exposure may be associated with cardiovascular disease outcomes have been described. Laboratory animals exposed to relatively high $O_3$ concentrations (≥ 0.5 ppm) demonstrate tissue edema in the heart and lungs. Ozone-induced changes in heart rate, edema of heart tissue, and increased tissue and serum levels of ANF found with 8-h 0.5 ppm $O_3$ exposure in animal toxicology studies (Vesely et al., 1994a,b,c) also raise the possibility of potential cardiovascular effects of acute ambient $O_3$ exposures

Animal toxicology studies have found both transient and persistent ventilatory responses with and without progressive decrease in heart rate (Arito et al., 1997). Observations of $O_3$-induced vasoconstriction in a controlled human exposure study by Brook et al. (2002) suggests another possible mechanism for $O_3$-related exacerbations of preexisting cardiovascular disease. One controlled human study (Gong et al., 1998) evaluated potential cardiovascular health effects of $O_3$ exposure. The overall results did not indicate acute cardiovascular effects of $O_3$ in either the hypertensive or control subjects. The authors observed an increase in rate-pressure product and heart rate, a decrement for $FEV_1$, and a >10 mm Hg increase in the alveolar/arterial pressure difference for $O_2$ following $O_3$ exposure. The mechanism for the decrease in arterial oxygen ($O_2$) tension study could be due to an $O_3$-induced ventilation-perfusion mismatch. Foster et al. (1993) demonstrated that even in relatively young healthy adults, $O_3$ exposure can cause ventilation to shift away from the well-perfused basal lung. This effect of $O_3$ on ventilation distribution may persist beyond 24-hr post-exposure (Foster et al., 1997). These findings suggest that $O_3$ may exert cardiovascular effects indirectly by impairing alveolar-arterial $O_2$ transfer and potentially reducing $O_2$ supply to the myocardium. Ozone exposure may increase myocardial work and impair pulmonary gas exchange to a degree that could perhaps be clinically important in persons with significant preexisting cardiovascular impairment.

As noted in Section 3.3.1.3, a limited number of new epidemiological studies have reported associations between short-term $O_3$ exposure and effects on the cardiovascular system. Among these studies, three were population-based and involved relatively large cohorts. Two studies, the ARIC (Liao at al, 2004) and the NAS (Parks et al., 2005) evaluated associations between $O_3$ and HRV. The other study, MONICA (Ruidavets et al., 2005) evaluated the

association between $O_3$ levels and the relative risk of MI. Such studies may offer more informative results based on their large subject-pool and design. Results from these three studies were suggestive of an association between $O_3$ exposure and the cardiovascular endpoints studies. In other recent studies on incidence of myocardial infarction and some more subtle cardiovascular health endpoints, such as changes in heart rate variability or cardiac arrhythmia, some but not all studies reported associations with short-term exposure to $O_3$ (CD, section 7.2.7.1). From these studies, the CD concludes that the "current evidence is rather limited but suggestive of a potential effect on HRV, ventricular arrhythmias, and MI incidence" (CD, p. 7-65).

An increasing number of studies have evaluated the association between $O_3$ exposure and cardiovascular hospital admissions. As shown in Figure 7-13 and discussed in section 7.3.4 of the CD, many reported negative or inconsistent associations, whereas other studies, especially those that examined the relationship when $O_3$ exposures were higher, have found positive and robust associations between $O_3$ and cardiovascular hospital admissions. The CD finds that the overall evidence from these studies remains inconclusive regarding the effect of $O_3$ on cardiovascular hospitalizations (CD, p. 7-83).

The CD notes that the suggestive positive epidemiologic findings of $O_3$ exposure on cardiac autonomic control, including effects on HRV, ventricular arrhythmias and MI, and reported associations between $O_3$ exposure and cardiovascular hospitalizations in the warm season gain credibility and scientific support from the results of experimental animal toxicology and human clinical studies, which are indicative of plausible pathways by which $O_3$ may exert cardiovascular effects (CD, Section 8.6.1).

### 3.5.4 Coherence and Plausibility of Effects Related to Long-Term $O_3$ Exposure

As discussed in section 8.6.2 of the CD, previous epidemiological studies have provided only inconclusive evidence for either mortality or morbidity effects of long-term $O_3$ exposure. The CD observes that the inconsistency in findings may be due to a lack of precise exposure information, the possibility of selection bias, and the difficulty of controlling for confounders (CD, p. 8-50). Several new longitudinal epidemiology studies have evaluated associations between long-term $O_3$ exposures and morbidity and mortality and suggest that these long-term exposures may be related to changes in lung function in children; however, little evidence is available to support a relationship between chronic $O_3$ exposure and mortality or lung cancer incidence (CD, p. 8-50).

Although human chamber studies have not evaluated effects with long-term exposures to $O_3$, there is some evidence available from toxicological studies. While early animal toxicology studies of long-term $O_3$ exposures were conducted using continuous exposures, more recent

studies have focused on exposures which mimic diurnal and seasonal patterns and more realistic $O_3$ exposure levels (CD, p. 8-50). Studies of monkeys that compared these two exposure scenarios found increased airway pathology only with the latter design. Persistent and irreversible effects reported in chronic animal toxicology studies suggest that additional complementary human data are needed from epidemiologic studies (CD, p. 8-50).

A long-term study of infant rhesus monkeys exposed to simulated seasonal $O_3$ (0.5 ppm , 8 hr/day for 5 days every 14 days for 11 episodes) reported remodeling of the distal airways, abnormalities in tracheal basement membrane, accumulation of eosinophils in conducting airways, and decrements in airway innervation. Another long-term exposure study of monkeys exposed to 0.61 ppm $O_3$ for a year and studies of rats exposed for 20 months (0.5-1.0 ppm $O_3$ for 6 hr/day) reported increased deposition of collagen and thickening of the CAR, suggestive of irreversible long-term $O_3$ impacts on the lungs. Although some earlier seasonal exposure studies of rats reported small, but significant, decrements in lung function consistent with focal fibrogenesis in the proximal alveolar region, other chronic exposure studies with exposures of 0.5 to 1.0 ppm $O_3$ report epithelial hyperplasia that disappears in a few days. At this time, however, there is little evidence from human studies for long-term $O_3$–induced effects on lung function .

The CD (p. 8-51) concludes that evidence from animal toxicology studies strongly suggests that chronic $O_3$ exposure is capable of damaging the distal airways and proximal alveoli, resulting in lung tissue remodeling leading to apparent irreversible changes. Such structural changes and compromised pulmonary function caused by persistent inflammation may exacerbate the progression and development of chronic lung disease. Together with the limited evidence available from epidemiological studies, these findings offer some insight into potential biological mechanisms for suggested associations between long-term or seasonal exposures to $O_3$ and reduced lung function development in children which have been observed in epidemiologic studies (CD, p. 8-51).

### 3.5.5 Coherence and Plausibility of Mortality-Related Health Endpoints

An extensive epidemiological literature on air pollution related mortality risk estimates from the U.S., Canada, and Europe is discussed in the CD (sections 7.4 and 8.6.3). These single- and multi-city mortality studies coupled with meta-analyses generally indicate associations between acute $O_3$ exposure and elevated risk for all-cause mortality, even after adjustment for the influence of season and PM. Several single-city studies that specifically evaluated the relationship between $O_3$ exposure and cardiopulmonary mortality also reported results suggestive of a positive association (CD, p. 8-51). These mortality studies suggest a pattern of effects for causality that have biologically plausible explanations, but our knowledge regarding potential

underlying mechanisms is very limited at this time and requires further research. Most of the physiological and biochemical parameters investigated in human and animal studies suggest that $O_3$-induced biochemical effects are relatively transient and attenuate over time. The CD (p. 8-52) hypothesizes a generic pathway of $O_3$-induced lung damage, potentially involving oxidative lung damage with subsequent inflammation and/or decline in lung function leading to respiratory distress in some sensitive population groups (e.g., asthmatics), or other plausible pathways noted below that may lead to $O_3$-related contributions to cardiovascular effects that ultimately increase risk of mortality.

The third National Health and Nutrition Examination Follow-up data analysis indicates that about 20% of the adult population has reduced $FEV_1$ values, suggesting impaired lung function. Most of these individuals have COPD, asthma or fibrotic lung disease (Manino et al., 2003), which are associated with persistent low-grade inflammation. Furthermore, patients with COPD are at increased risk for cardiovascular disease, and lung disease with underlying inflammation may be linked to low-grade systemic inflammation associated with atherosclerosis, independent of cigarette smoking (CD, p. 8-52). Lung function decrements in persons with cardiopulmonary disease have been associated with inflammatory markers, such as C-reactive protein (CRP) in the blood. At a population level it has been found that individuals with the lowest $FEV_1$ values have the highest levels of CRP, and those with the highest $FEV_1$ values have the lowest CRP levels (Manino et al., 2003; Sin and Man, 2003). This complex series of physiological and biochemical reactions following $O_3$ exposure may tilt the biological homeostasis mechanisms which could lead to adverse health effects in people with compromised cardiopulmonary systems.

Of much interest are several other types of newly available data that support reasonable hypotheses that may help to explain the findings of $O_3$-related increases in cardiovascular mortality observed in some epidemiological studies. These include the direct effect of $O_3$ on increasing PAF in lung tissue that can then enter the general circulation and possibly contribute to increased risk of blood clot formation and the consequent increased risk of MI, cerebrovascular events (stroke), or associated cardiovascular-related mortality. Ozone reactions with cholesterol in lung surfactant to form epoxides and oxysterols that are cytotoxic to lung and heart muscles and that contribute to atherosclerotic plaque formation in arterial walls represent another potential pathway. Stimulation of airway irritant receptors may lead to increases in tissue and serum levels of ANF, changes in heart rate, and edema of heart tissue. A few new field and panel studies of human adults have reported associations between ambient $O_3$ concentrations and changes in cardiac autonomic control (e.g., HRV, ventricular arrhythmias, and MI). These represent plausible pathways that may lead to $O_3$-related contributions to cardiovascular effects that ultimately increase the risk of mortality.

In addition, $O_3$-induced increases in lung permeability allow more ready entry for inhaled PM into the blood stream, and $O_3$ exposure would increase the risk of PM-related cardiovascular effects. Furthermore, increased ambient $O_3$ levels contribute to ultrafine PM formation in the ambient air and indoor environments. Thus, the contributions of elevated ambient $O_3$ concentrations to ultrafine PM formation and human exposure, along with the enhanced uptake of inhaled fine particles, consequently contribute to exacerbation of PM-induced cardiovascular effects in addition to those more directly induced by $O_3$ (CD, p. 8-53).

## 3.6 OZONE-RELATED IMPACTS ON PUBLIC HEALTH

The following discussion draws from section 8.7 of the CD to characterize factors which modify responsiveness to $O_3$, subpopulations potentially at risk for $O_3$-related health effects, and potential public health impacts associated with exposure to ambient $O_3$. Providing appropriate protection of public health requires that a distinction be made between those effects that are considered adverse health effects and those that are not adverse. What constitutes an adverse health effect depends not only on the type and magnitude of effect but also on the population group being affected. While some changes in healthy individuals would not be considered adverse, similar changes in susceptible individuals would be seen as adverse. In order to estimate the potential public health impact, it is important to consider both the susceptible subpopulations for $O_3$ exposure and the definition of adversity for $O_3$ health effects.

### 3.6.1 Factors which Modify Responsiveness to Ozone

There are numerous factors which can modify individual responsiveness to $O_3$. These include: influence of physical activity; age; gender and hormonal influences; racial, ethnic and socioeconomic status (SES) factors; environmental factors; and oxidant-antioxidant balance. These factors are discussed in more detail in section 6.5 of the CD.

It is well established that physical activity increases an individual's minute ventilation and will thus increase the dose of $O_3$ inhaled (CD, section 6.5.4). Increased physical activity results in deeper penetration of $O_3$ into more peripheral regions of the lungs, which are more sensitive to acute $O_3$ response and injury. This will result in greater lung function decrements for acute exposures of individuals during increased physical activity. Research has shown that respiratory effects are observed at lower $O_3$ concentrations if the level of exertion is increased and/or duration of exposure and exertion are extended. Predicted $O_3$-induced decrements in lung function have been shown to be a function of exposure duration and exercise level for healthy, young adults (McDonnell et al., 1997)

Most of the studies investigating the influence of age have used lung function decrements and symptoms as measures of response. For healthy adults, lung function and symptom

responses to $O_3$ decline as age increases. The rate of decline in $O_3$ responsiveness appears greater in those 18 to 35 years old compared to those 35 to 55 years old, while there is very little change after age 55. In one study (Seal et al., 1996) analyzing a large data set, a 5.4% decrement in $FEV_1$ was estimated for 20 year old individuals exposed to 0.12 ppm $O_3$, whereas similar exposure of 35 year old individuals were estimated to have a 2.6% decrement. While healthy children tend not to report respiratory symptoms when exposed to low levels of $O_3$, for subjects 18 to 36 years old symptom responses induced by $O_3$ tend to decrease with increasing age (McDonnell et al., 1999).

Limited evidence of gender differences in response to $O_3$ exposure has suggested that females may be predisposed to a greater susceptibility to $O_3$. Lower plasma and NL fluid levels of the most prevalent antioxidant, uric acid, in females relative to males may be a contributing factor (Housley et al., 1996). Consequently, reduced removal of $O_3$ in the upper airways may promote deeper penetration. However, most of the evidence on gender differences appears to be equivocal, with one study (Hazucha et al., 2003) suggesting that physiological responses of young healthy males and females may be comparable (CD, section 6.5.2).

A few studies have suggested that ethnic minorities might be more responsive to $O_3$ than Caucasian population groups (CD, section 6.5.3). This may be more the result of a lack of adequate health care and socioeconomic status than any differences in sensitivity to $O_3$. The limited data available, which have investigated the influence of race, ethnic or other related factors on responsiveness to $O_3$, prevent drawing any clear conclusions at this time.

Few human studies have examined the potential influence of environmental factors such as the sensitivity of individuals who voluntarily smoke tobacco (i.e., smokers) and the effect of high temperatures. New controlled human exposure studies have confirmed that smokers are less responsive to $O_3$ than nonsmokers; however, time course of development and recovery of these effects, as well as reproducibility, was not different from nonsmokers (CD, section 6.5.5). Influence of ambient temperature on pulmonary effects induced by $O_3$ has been studied very little, but additive effects of heat and $O_3$ exposure have been reported.

Antioxidants, which scavenge free radicals and limit lipid peroxidation in the ELF, are the first line of defense against oxidative stress. Ozone exposure leads to absorption of $O_3$ in the ELF with subsequent depletion of ELF antioxidant level in the nasal ELF, but concentration and antioxidant enzyme activity in ELF or plasma don't appear related to $O_3$ responsiveness (CD, section 6.5.6). Controlled studies of the protective effects of dietary antioxidant supplements have shown some protective effects of lung function but not of subjective symptoms or inflammatory response. Dietary antioxidant supplements have provided some protection to asthmatics by attenuating post-exposure airway hyperresponsiveness. Animal studies have also supported the protective effects of ELF antioxidants.

### 3.6.2 Susceptible Population Groups

Several characteristics that may increase the extent to which a population group shows sensitivity to $O_3$ have been discussed in the CD, in the sections on clinical studies in Chapter 6, epidemiological studies in Chapter 7, and in the integrated assessment in Chapter 8; this section will draw on all of these. The characteristics that likely increase susceptibility to $O_3$ are based on: (1) activity patterns; (2) lung disease; (3) age; and (4) biological responsiveness to $O_3$. Other groups that might have enhanced sensitivity to $O_3$, but for which there is currently very little evidence, include: people with heart disease; groups based on race, gender and socioeconomic status; and those with nutritional deficiencies.

#### 3.6.2.1 Active People

A large group of individuals at risk from $O_3$ exposure consists of outdoor workers and children, adolescents, and adults who engage in outdoor activities involving exertion or exercise during summer daylight hours when ambient $O_3$ concentrations tend to be higher. This conclusion is based on a large number of controlled-exposure human studies which have been conducted with healthy children and adults and those with preexisting respiratory diseases (CD, sections 6.2 and 6.3). These studies show a clear $O_3$ exposure-response relationship with increasing spirometric and symptomatic response as exercise level increases. Furthermore, $O_3$-induced response increases as time of exposure increases. Studies of outdoor workers and others who participate in outdoor activities indicate that extended exposures to $O_3$ at elevated exertion levels can produce marked effects on lung function.

The effects of $O_3$ on the respiratory health of outdoor workers and others who participate in outdoor activities have been investigated in several recent epidemiologic studies. These individuals may experience increased vulnerability for $O_3$ health effects, because they are typically exposed to high doses of $O_3$ as they spend long hours outdoors often at elevated exertion levels. In a group of berry pickers in Fraser Valley, Canada, large decrements in lung function (~5% decrease in $FEV_1$ per 40 ppb increase in 1-hr max $O_3$) were associated with acute exposure to $O_3$ (Brauer et al., 1996). The mean ambient 1-hr max $O_3$ was 40.3 ppb (SD 15.2) over the study period of June to August 1993. The berry pickers worked outdoors for an average of 11 hr at elevated heart rates (on average, 36% higher than resting levels). These results indicate that extended exposures to $O_3$ at elevated exertion levels can produce marked effects on lung function among outdoor workers.

Höppe et al. (1995) examined forestry workers for $O_3$-related changes in pulmonary function in Munich, Germany. Ventilation rates, estimated from their average activity levels, were elevated. When comparisons were made between high $O_3$ days (mean ½-hr max $O_3$ of 64 ppb) and low $O_3$ days (mean ½-hr max $O_3$ of 32 ppb), 59% of the forestry workers experienced a notable decrement in lung function (i.e., at least a 20% increase in specific airway resistance or

at least a 10% decrease in $FEV_1$, FVC, or PEF) on high $O_3$ days. None experienced improved lung function. This study also examined athletes following a 2-hr outdoor training period in the afternoon yielding a ventilation rate double the estimate for the forestry workers. Though a significant association between ambient $O_3$ levels and decrements in $FEV_1$ was observed overall, a smaller percentage of the athletes (14%) experienced a notable decrement in lung function on high $O_3$ days compared to the forestry workers; and 19% of the athletes actually showed an improvement.

A large field study by Korrick et al. (1998) examined the effects of multi-hour $O_3$ exposures (on average, 8 hr) on adults hiking outdoors on Mount Washington, in NH. The mean of the hourly $O_3$ concentrations during the hike was 40 ppb (range 21-74). After the hike, all subjects combined experienced a relatively small mean decline in $FEV_1$ (1.5% decrease per 30 ppb increase in mean hourly $O_3$ concentrations) during the hike. Ozone-related changes in lung function parameters were estimated. Stratifying the data by hiking duration indicated that individuals who hiked 8 to 12 hr experienced a >2-fold decline in $FEV_1$ versus those only hiking 2 to 8 hr.

Results from the above field studies are consistent with those from earlier summer camp studies (Avol et al., 1990; Higgins et al., 1990; Raizenne et al., 1987, 1989; Spektor et al., 1988, 1991), which also observed strong associations between acute $O_3$ exposure and decrements in lung function among children who spent long hours outdoors. In a recent analysis by the Southern California Children's Health Study, a total of 3,535 initially nonasthmatic children (ages 9 to 16 years at enrollment) were followed for up to 5 years to identify new-onset asthma cases associated with higher long-term ambient $O_3$ concentrations (McConnell et al., 2002). Communities were stratified by pollution levels, with six high-O $O_3$ communities (mean 1-hr max $O_3$ of 75.4 ppb [SD 6.8] over four years) and six low-$O_3$ communities (mean 50.1 ppb [SD 11.0]). In the combined analysis using all children, asthma risk was not found to be higher for residents of the six high-$O_3$ communities versus those from the six low-$O_3$ communities. However, within the high-$O_3$ communities, asthma risk was more than 3 times greater for children who played three or more sports versus those who played no sports, an association not observed in the low-$O_3$ communities. Therefore, among children repeatedly exposed to higher $O_3$ levels, increased exertion outdoors (and resulting increased $O_3$ dose) was associated with excess asthma risk.

These field studies with subjects at elevated exertion levels support the extensive evidence derived from controlled human exposure studies. The majority of human chamber studies have examined the effects of $O_3$ exposure in subjects performing continuous or intermittent exercise for variable periods of time. Significant $O_3$-induced respiratory responses have been observed in clinical studies of exercising individuals. The epidemiologic studies

discussed above also indicate that prolonged exposure periods, combined with elevated levels of exertion or exercise, may magnify $O_3$ effects on lung function. Thus, outdoor workers and others who participate in higher exertion activities outdoors during the time of day when high peak $O_3$ concentrations occur appear to be particularly vulnerable to $O_3$ effects on respiratory health. Although these studies show a wide variability of response and sensitivity among subjects and the factors contributing to this variability continue to be incompletely understood, the effect of increased exertion is consistent.

#### 3.6.2.2 People with Lung Disease

People with preexisting pulmonary disease are likely to be among those at increased risk from $O_3$ exposure. Altered physiological, morphological and biochemical states typical of respiratory diseases like asthma, COPD and chronic bronchitis may render people sensitive to additional oxidative burden induced by $O_3$ exposure. The new results from controlled exposure and epidemiologic studies continue to indicate that asthmatics are a sensitive subpopulation for $O_3$ health effects.

A number of epidemiological studies have been conducted using asthmatic study populations. The majority of epidemiological panel studies that evaluated respiratory symptoms and medication use related to $O_3$ exposures focused on children. These studies suggest that $O_3$ exposure may be associated with increased respiratory symptoms and medication use in children with asthma. Other reported effects include respiratory symptoms, lung function decrements, and ED visits, as discussed in the CD (section 7.6.7.1). Strong evidence from a large multi-city study (Mortimer et al., 2002), along with support from several single-city studies suggest that $O_3$ exposure may be associated with increased respiratory symptoms and medication use in children with asthma. With regard to ambient $O_3$ levels and increased hospital admissions and ED visits for asthma and other respiratory causes, strong and consistent evidence establishes a correlation between $O_3$ exposure and increased exacerbations of preexisting respiratory disease for 1-hr maximum $O_3$ concentrations <0.12 ppm. Several hospital admission and ED visit studies in the U.S. (Peel et al., 2005), Canada (Burnett et al., 1997a; Anderson et al., 1997), and Europe (Anderson et al., 1997) have reported positive associations between increase in $O_3$ and increased risk of ED visits and hospital admissions, especially during the warm season.

Several clinical studies reviewed in the 1996 CD on atopic and asthmatic subjects had suggested but not clearly demonstrated enhanced responsiveness to acute $O_3$ exposure compared to healthy subjects. The majority of the newer studies reviewed in Chapter 6 of the CD indicate that asthmatics are as sensitive as, if not more sensitive than, normal subjects in manifesting induced pulmonary function decrements.

Ozone-induced increases in neutrophils, protein, and IL-8 were found to be significantly higher in the BAL fluid from asthmatics compared to healthy subjects, suggesting mechanisms for the increased sensitivity of asthmatics. Similarly, subjects with allergic asthma exhibited increased airway responsiveness to inhaled allergens upon acute $O_3$ exposure. Asthmatics present a differential response profile for cellular, molecular, and biochemical parameters (CD, Figure 8-1) that are altered in response to acute $O_3$ exposure. Increases in $O_3$-induced nonspecific airway responsiveness incidence and duration could have important clinical implications for asthmatics.

Bronchial constriction following provocation with allergens presents a two-phase response. The early response is mediated by release of histamine and leukotrienes that leads to contraction of smooth muscle cells in the bronchi, narrowing the lumen and decreasing the airflow. In asthmatics, these mediators also cause accumulation of eosinophils, followed by production of mucus and a late-phase bronchial constriction and reduced airflow. Holz et al. (2002) reported an early phase response in subjects with rhinitis after a consecutive 4-day exposure to 0.125 ppm $O_3$ that resulted in a clinically relevant (>20%) decrease in $FEV_1$. Allergen challenge in mild asthmatics 24 hr postexposure to 0.27 ppm $O_3$ for 2 hr resulted in significantly increased eosinophil counts in BALF compared to healthy subjects (Vagaggini et al., 2002). Epithelial cells from mucosal biopsies of allergic asthmatics indicated significant increases in the expression of IL-5, IL-8 and GM-CSF, suggesting increased neutrophilic inflammation compared to healthy subjects (Bosson et al., 2003).

Several human exposure studies have shown differences between asthmatics and healthy human subjects with regard to PMN influx in BAL fluid. In vitro studies (Schierhorn et al., 1999) of nasal mucosal biopsies from atopic and nonatopic subjects exposed to 0.1 ppm $O_3$ found significant differences in release of IL-4, IL-6, IL-8, and *TNF*-α. Another study by Schierhorn et al. (2002) found significant differences in the $O_3$-induced release of the neuropeptides neurokinin A and substance P for allergic patients in comparison to nonallergic controls, suggesting increased activation of sensory nerves by $O_3$ in the allergic tissues. Another study by Bayram et al. (2002) using in vitro culture of bronchial epithelial cells recovered from atopic and nonatopic asthmatics also found significant increases in epithelial permeability in response to $O_3$ exposure. In addition, some controlled human $O_3$ exposure studies in asthmatics (Hiltermann et al., 1999; Scannell et al., 1996) reported increased secretion of IL-8, suggesting increased neutrophilic inflammation. Two studies (Jörres et al., 1996; Holz et al., 2002) observed increased airway responsiveness to repeated daily $O_3$ exposure to bronchial allergen challenge in subjects with preexisting allergic airway disease.

Newly available reports from controlled human exposure studies (see Chapter 6 in the CD) utilized subjects with preexisting cardiopulmonary diseases such as COPD, asthma, allergic

rhinitis, and hypertension. The data generated from these studies that evaluated pulmonary function changes in spirometry did not find clear differences between filtered air and $O_3$ exposure in COPD and asthmatic subjects. However, the new data on airway responsiveness, inflammation, and various molecular markers of inflammation and bronchoconstriction indicate that people with atopic asthma and allergic rhinitis comprise susceptible groups for $O_3$-induced adverse health effects.

Although controlled human exposure studies have not found evidence of larger spirometric changes in people with COPD relative to healthy subjects, this may be due to the fact that most people with COPD are older adults who would not be expected to have such changes based on their age. However, in Section 8.7.1, the CD notes that new epidemiological evidence indicates that people with COPD may be more likely to experience other effects, including emergency room visits, hospital admissions, or premature mortality. For example, results from an analysis of five European cities indicated strong and consistent $O_3$ effects on unscheduled respiratory hospital admissions, including COPD (Anderson et al., 1997). Also, an analysis of a 9-year data set for the whole population of the Netherlands provided risk estimates for more specific causes of mortality, including COPD (Hoek et al., 2000, 2001; reanalysis Hoek, 2003); a positive, but nonsignificant, excess risk of COPD-related mortality was found to be associated with short-term $O_3$ concentrations. Moreover, as indicated by Gong et al. (1998), the effects of $O_3$ exposure on alveolar-arterial oxygen gradients may be more pronounced in patients with preexisting obstructive lung diseases. Relative to healthy elderly subjects, COPD patients have reduced gas exchange and low $SaO_2$. Any inflammatory or edematous responses due to $O_3$ delivered to the well-ventilated regions of the COPD lung could further inhibit gas exchange and reduce oxygen saturation. In addition, $O_3$-induced vasoconstriction could also acutely induce pulmonary hypertension. Inducing pulmonary vasoconstriction and hypertension in these patients would perhaps worsen their condition, especially if their right ventricular function was already compromised (CD, Section 6.10).

#### 3.6.2.3 Children and Older Adults

Supporting evidence exists for heterogeneity in the effects of $O_3$ by age. As discussed in section 6.5.1 of the CD, children, adolescents, and young adults (<18 yrs of age) appear, on average, to have nearly equivalent spirometric responses to $O_3$, but have greater responses than middle-aged and older adults when exposed to comparable $O_3$ doses. Symptomatic responses to $O_3$ exposure, however, do not appear to occur in healthy children, but are observed in asthmatic children, particularly those who use maintenance medications. For adults (>17 yrs of age) symptoms gradually decrease with increasing age. In contrast to young adults, the diminished symptomatic responses in children and symptomatic and spirometric responses in the elderly may put them at an increased risk for continued exposure.

As described in the section 7.6.7.2 of the CD, many epidemiological field studies focused on the effect of $O_3$ on the respiratory health of school children. In general, children experienced decrements in pulmonary function parameters, including PEF, $FEV_1$, and FVC. Increases in respiratory symptoms and asthma medication use were also observed in asthmatic children. In one German study, children with and without asthma were found to be particularly susceptible to $O_3$ effects on lung function. Approximately 20% of the children, both with and without asthma, experienced a greater than 10% change in $FEV_1$, compared to only 5% of the elderly population and athletes (Höppe et al., 2003).

The American Academy of Pediatrics (2004) notes that children and infants are among the population groups most susceptible to many air pollutants, including $O_3$. This is in part because their lungs are still developing. For example, eighty percent of alveoli are formed after birth, and changes in lung development continue through adolescence (Dietert et al., 2000). Children are also likely to spend more time outdoors than adults do, which results in increased exposure to air pollutants (Wiley et al., 1991a,b). Moreover, children have high minute ventilation rates and high levels of physical activity which also increases their dose (Plunkett et al., 1992).

Several mortality studies have investigated age-related differences in $O_3$ effects. Among the studies that observed positive associations between $O_3$ and mortality, a comparison of all age or younger age ($\leq$65 years of age) $O_3$-mortality effect estimates to that of the elderly population (>65 years) indicates that, in general, the elderly population is more susceptible to $O_3$ effects (Borja-Aburto et al. 1997; Bremner et al., 1999; Gouveia and Fletcher 2000b; O'Neill et al., 2004; Simpson et al., 1997; Sartor et al., 1995; Sunyer et al., 2002). For example, a study by Gouveia and Fletcher (2000b) examined the $O_3$-mortality effect by age in São Paulo, Brazil. Among all ages, $O_3$ was associated with a 0.6% excess risk in all cause mortality per 40 ppb increase in 1-hr max $O_3$. In comparison, in the elderly population, the $O_3$-mortality risk estimate was nearly threefold greater, at 1.7%. Similarly, a Mexico City study found that $O_3$-mortality effect estimates were 1.3% and 2.8% per 20 ppb increase in 24-hr average $O_3$ concentration in all ages and the elderly, respectively (O'Neill et al., 2004).

The meta-analysis by Bell et al. (2005) found a larger effect estimate for the elderly (2.92% per 20 ppb increase in 24-hr average $O_3$) than for all ages (1.75%). In the large U.S. 95 communities study (Bell et al., 2004), effect estimates were slightly higher for those aged 65 to 74 years, 1.40% excess risk per 20 ppb increase in 24-hr average $O_3$, compared to individuals less than 65 years and 75 years or greater, 1.00% and 1.04%, respectively, using a constrained distributed 7-day lag model. Bell et al. (2004) note that despite similar effects estimates, the absolute effect of $O_3$ is substantially greater in the elderly population due to the higher underlying mortality rates, which lead to a larger number of extra deaths for the elderly compared to the general population. The CD concludes that the elderly population (>65 years of age) appear to be at greater risk of $O_3$-related mortality and hospitalizations compared to all ages or younger populations (CD, p. 7-177).

The CD notes that, collectively, there is supporting evidence of age-related differences in susceptibility to $O_3$ health effects. The elderly population (>65 years of age) appear to be at increased risk of $O_3$-related mortality and hospitalizations, and children (<18 years of age) experience other potentially adverse respiratory health outcomes with increased $O_3$ exposure (CD, section 7.6.7.2).

#### 3.6.2.4 People with Increased Responsiveness to Ozone

Biochemical and molecular parameters extensively evaluated in animal toxicology and controlled human exposure experiments were used to identify specific loci on the chromosomes and, in some cases, to relate the differential expression of specific genes to biochemical and physiological differences observed among these species. Utilizing $O_3$-sensitive and $O_3$-resistant species, it has been possible to identify the involvement of AHR and inflammation processes in $O_3$ susceptibility. However, most of these studies were carried out using relatively high doses of $O_3$, making the relevance of these studies questionable in human health effects assessment. The molecular parameters identified in these studies may serve as useful biomarkers with the availability of suitable technologies and, ultimately, can likely be integrated with epidemiological studies. Interindividual differences in $O_3$ responsiveness have been observed across a spectrum of symptoms and lung function responses but do not yet allow identification of important underlying factors, except a significant role for age.

#### 3.6.2.5 Other Population Groups

There is limited, new evidence supporting associations between short-term $O_3$ exposures and a range of effects on the cardiovascular system. Some but not all, epidemiological studies have reported associations between short-term $O_3$ exposures and the incidence of myocardial infarction and more subtle cardiovascular health endpoints, such as changes in heart rate variability and cardiac arrhythmia. Others have reported associations with hospitalization or ED visits for cardiovascular diseases, although the results across the studies are not consistent. Studies also report associations between short-term $O_3$ exposure and mortality from cardiovascular or cardiopulmonary causes. Based on epidemiological study results, the CD concludes that the current evidence from field studies is rather limited but supportive of a potential effect of short-term $O_3$ exposure and heart rate variability, cardiac arrhythmia and incidence of myocardial infarction (CD, p. 7-66). In the CD's evaluation of studies of hospital admissions for cardiovascular disease (CD, section 7.3.4), it is concluded that evidence from this growing group of studies is generally inconsistent but is suggestive of an association with $O_3$ in studies conducted during the warm season (CD, p. 7-83). This body of evidence suggests that people with heart disease may be at increased risk from short-term exposures to $O_3$; however, more evidence is needed to conclude that people with heart disease are a susceptible population.

Other groups that might have enhanced sensitivity to $O_3$, but for which there is currently very little evidence, include groups based on race, gender and socioeconomic status, and those

with nutritional deficiencies, as discussed above in section 3.6.1 about factors which modify responsiveness to $O_3$, above.

### 3.6.3 What Constitutes an Adverse Health Impact from Ozone Exposure?

In making judgments as to when various $O_3$-related effects become regarded as adverse to the health of individuals, in previous NAAQS reviews staff has relied upon the guidelines published by the American Thoracic Society (ATS) and the advice of CASAC. While recognizing that perceptions of "medical significance" and "normal activity" may differ among physicians, lung physiologists and experimental subjects, the ATS (1985) defined adverse respiratory health effects as "medically significant physiologic changes generally evidenced by one or more of the following: (1) interference with the normal activity of the affected person or persons, (2) episodic respiratory illness, (3) incapacitating illness, (4) permanent respiratory injury, and/or (5) progressive respiratory dysfunction."

During the 1997 review, it was concluded that there was evidence of causal associations from controlled human exposure studies for effects in the first of these five ATS-defined categories, evidence of statistically significant associations from epidemiological studies for effects in the second and third categories, and evidence from animal toxicology studies, which could be extrapolated to humans only with a significant degree of uncertainty, for the last two categories. For the current review, the evidence of $O_3$-related effects is stronger across all the categories. For ethical reasons, clear causal evidence from controlled human exposure studies still covers only effects in the first category. However, for this review there are results from epidemiological studies, upon which to base judgments about adversity, for effects in all of the categories. Statistically significant and robust associations have been reported in epidemiology studies falling into the second and third categories. These more serious effects include respiratory illness that may require medication (e.g., asthma), but not necessarily hospitalization, as well as respiratory hospital admissions. Less conclusive, but still positive associations have been reported for school absences, ED visits for respiratory causes, and cardiovascular hospital admissions. Human health effects for which associations have been suggested through evidence from epidemiological and animal toxicology studies, but have not been conclusively demonstrated still fall primarily into the last two categories. In the last review of the $O_3$ standard, evidence for these more serious effects came from studies of effects in laboratory animals, and could be extrapolated to humans only with a significant degree of uncertainty. Evidence from animal studies evaluated in this CD strongly suggests that $O_3$ is capable of damaging the distal airways and proximal alveoli, resulting in lung tissue remodeling leading to apparently irreversible changes. Recent advancements of dosimetry modeling also provide a better basis for extrapolation from animals to humans. Information from epidemiological studies

provides supporting, but limited evidence of irreversible respiratory effects in humans (as described in section 6.3.3.2 below). Moreover, the CD concludes that the findings from single-city and multi-city time-series epidemiology studies and meta-analyses of these epidemiology studies support a likely causal association between short-term $O_3$ exposure and mortality particularly in the warm season.

While $O_3$ has been associated with effects that are clearly adverse, application of these guidelines, in particular to the least serious category of effects related to ambient $O_3$ exposures, involves judgments about which medical experts on the CASAC panel and public commenters have in the past expressed diverse views. To help frame such judgments, we have defined gradations of individual functional responses (e.g., decrements in $FEV_1$ and airway responsiveness) and symptomatic responses (e.g., cough, chest pain, wheeze), together with judgments as to the potential impact on individuals experiencing varying degrees of severity of these responses, that have been used in previous NAAQS reviews. These gradations and impacts are summarized in Tables 3-2 and 3-3.

For active healthy people, moderate levels of functional responses (e.g., $FEV_1$ decrements of $\geq$10% but < 20%, lasting up to 24 hrs) and/or moderate symptomatic responses (e.g., frequent spontaneous cough, marked discomfort on exercise or deep breath, lasting up to 24 hrs) would likely interfere with normal activity for relatively few sensitive individuals; whereas large functional responses (e.g., $FEV_1$ decrements $\geq$ 20%, lasting longer than 24 hrs) and/or severe symptomatic responses (e.g., persistent uncontrollable cough, severe discomfort on exercise or deep breath, lasting longer than 24 hrs) would likely interfere with normal activities for many sensitive individuals and therefore would be considered adverse under ATS guidelines. However, for people with lung disease, even moderate functional (e.g., $FEV_1$ decrements $\geq$ 10% but < 20%, lasting up to 24 hrs) or symptomatic responses (e.g., frequent spontaneous cough, marked discomfort on exercise or with deep breath, wheeze accompanied by shortness of breath, lasting up to 24 hrs) would likely interfere with normal activity for many individuals, and would likely result in additional and more frequent use of medication. For people with lung disease, large functional responses (e.g., $FEV_1$ decrements $\geq$ 20%, lasting longer than 24 hrs) and/or severe symptomatic responses (e.g., persistent uncontrollable cough, severe discomfort on exercise or deep breath, persistent wheeze accompanied by shortness of breath, lasting longer than 24 hrs) would likely interfere with normal activity for most individuals and would increase the likelihood that these individuals would seek medical treatment or go to an ED for relief.

In judging the extent to which these impacts represent effects that should be regarded as adverse to the health status of individuals, an additional factor that has been considered in previous NAAQS reviews is whether such effects are experienced repeatedly during the course of a year or only on a single occasion. While some experts would judge single occurrences of

**Table 3-2. Gradation of Individual Responses to Short-Term Ozone Exposure in Healthy Persons**[1]

| Functional Response | None | Small | Moderate | Large |
|---|---|---|---|---|
| $FEV_1$ | Within normal range (±3%) | Decrements of 3 to ≤10% | Decrements of >10 but <20% | Decrements of ≥20% |
| Nonspecific bronchial responsiveness[2] | Within normal range | Increases of <100% | Increases of ≤300% | Increases of >300% |
| Duration of response | None | <4 hrs | >4 hrs but ≤24 hrs | >24 hrs |
| **Symptom Response** | **Normal** | **Mild** | **Moderate** | **Severe** |
| Cough | Infrequent cough | Cough with deep breath | Frequent spontaneous cough | Persistent uncontrollable cough |
| Chest pain | None | Discomfort just noticeable on exercise or deep breath | Marked discomfort on exercise or deep breath | Severe discomfort on exercise or deep breath |
| Duration of response | None | <4 hrs | >4 hrs but ≤24 hrs | >24 hrs |
| **Impact of Responses** | **Normal** | **Normal** | **Mild** | **Moderate** |
| Interference with normal activity | None | None | A few sensitive individuals choose to limit activity | Many sensitive individuals choose to limit activity |



[1] This table is reproduced from the 1996 $O_3$ AQCD (Table 9-1, page 9-24) (U.S. Environmental Protection Agency, 1996).
[2] An increase in nonspecific bronchial responsiveness of 100% is equivalent to a 50% decrease in $PD_{20}$ or $PD_{100}$.

**Table 3-3. Gradation of Individual Responses to Short-Term Ozone Exposure in Persons with Impaired Respiratory Systems**

| **Functional Response** | **None** | **Small** | **Moderate** | **Large** |
|---|---|---|---|---|
| $FEV_1$ change | Decrements of <3% | Decrements of 3 to ≤10% | Decrements of >10 but <20% | Decrements of ≥20% |
| Nonspecific bronchial responsiveness [3] | Within normal range | Increases of <100% | Increases of ≤300% | Increases of >300% |
| Airway resistance (SRaw) | Within normal range (±20%) | SRaw increased <100% | SRaw increased up to 200% or up to 15 cm H2O/s | SRaw increased >200% or more than 15 cm H2O/s |
| Duration of response | None | <4 hr | >4 hr but ≤24 hr | >24 hr |
| **Symptom Response** | **Normal** | **Mild** | **Moderate** | **Severe** |
| Wheeze | None | With otherwise normal breathing | With shortness of breath | Persistent with shortness of breath |
| Cough | Infrequent cough | Cough with deep breath | Frequent spontaneous cough | Persistent uncontrollable cough |
| Chest pain | None | Discomfort just noticeable on exercise or deep breath | Marked discomfort on exercise or deep breath | Severe discomfort on exercise or deep breath |
| Duration of response | None | < 4 hr | >4 hr but ≤24 hr | >24 hr |
| **Impact of Responses** | **Normal** | **Mild** | **Moderate** | **Severe** |
| Interference with normal activity | None | Few individuals choose to limit activity | Many individuals choose to limit activity | Most individuals choose to limit activity |
| Medical treatment | No change | Normal medication as needed | Increased frequency of medication use or additional medication | Physician or emergency room visit |

[3] An increase in nonspecific bronchial responsiveness of 100% is equivalent to a 50% decrease in $PD_{20}$ or $PD_{100}$.

moderate responses to be a "nuisance," especially for healthy individuals, a more general consensus view of the adversity of such moderate responses emerges as the frequency of occurrence increases. Thus it has been judged that repeated occurrences of moderate responses, even in otherwise healthy individuals, may be considered to be adverse since they could well set the stage for more serious illness (61 FR 65723). The CASAC panel in the last review expressed a consensus view that these "criteria for the determination of an adverse physiological response was reasonable" (Wolff, 1995b).

In 2000, the American Thoracic Society (ATS) published an official statement on "What Constitutes an Adverse Health Effect of Air Pollution?" (ATS, 2000), which updated its earlier guidance (ATS, 1985). The revised guidance was intended to address new investigative approaches used to identify the effects of air pollution, and to reflect the concern for the impacts of air pollution on specific groups that had been expressed through the environmental justice movement.

The new guidance builds upon and expands the 1985 definition of adversity in several ways. There is an increased focus on quality of life measures as indicators of adversity. There is also a more specific consideration of population risk. Exposure to air pollution that increases the risk of an adverse effect to the entire population is adverse, even though it may not increase the risk of any individual to an unacceptable level. For example, a population of asthmatics could have a distribution of lung function such that no individual has a level associated with significant impairment. Exposure to air pollution could shift the distribution to lower levels that still do not bring any individual to a level that is associated with clinically relevant effects. However, this would be considered to be adverse because individuals within the population would have diminished reserve function, and therefore would be at increased risk if affected by another agent.

Of the various effects of $O_3$ exposure that have been studied, many would meet the ATS definition of adversity. Such effects include, for example, any detectible level of permanent lung function loss attributable to air pollution, including both reductions in lung growth or acceleration of the age-related decline of lung function; exacerbations of disease in individuals with chronic cardiopulmonary diseases; reversible loss of lung function in combination with the presence of symptoms; as well as more serious effects such as those requiring medical care including hospitalization and, obviously, mortality.

As discussed above, relatively small, reversible declines in lung function parameters may be of questionable significance in healthy people. However, a 5 to 15 % change in $FEV_1$ is considered to have clinical importance to asthma morbidity (ATS 1991; Lebowitz et al. 1987; Lippmann, 1988). The National Institutes of Health (1997) has stated that a PEF below 80% of a person's personal best indicates a need for continued medication use in asthmatics. In Mortimer

et al. (2002), $O_3$ was associated with increased incidence of $\geq$ 10% declines in morning PEF as well as morning symptoms, suggesting that $O_3$ exposure may have clinically significant effects on asthmatic children.

Reflecting new investigative approaches, the ATS statement describes the potential usefulness of research into the genetic basis for disease, including responses to environmental agents that will provide insights into the mechanistic basis for susceptibility, and provide markers of risk status. Likewise biomarkers, that are indicators of exposure, effect or susceptibility, may someday be useful in defining the point at which a response should be equated with an adverse effect. Based on concern for segments of the population that may be disproportionately exposed to environmental contaminants, or have other factors that may increase susceptibility (e.g., genetic or nutritional factors), there was a call for increased research in these areas.

Overall, the new guidance does not fundamentally change the approach previously taken to define adversity, nor does it suggest a need at this time to change the structure or content of the tables describing gradation of severity and adversity of effects in Tables 3-2 or 3-3 above.

### 3.6.4 Estimation of Potential Numbers of People in At-Risk Susceptible Population Groups in the United States

Although $O_3$-related health risk estimates may appear to be numerically small, their significance from an overall public health perspective is affected by the large numbers of individuals in potential risk groups. Several subpopulations may be identified as having increased susceptibility or vulnerability to adverse health effects from $O_3$, including: older adults, children, individuals with preexisting pulmonary disease, and those with higher exposure levels, such as outdoor workers.

One consideration in the assessment of potential public health impacts is the size of various population groups that may be at increased risk for health effects associated with $O_3$-related air pollution exposure. Table 8-4 in the CD summarizes information on the prevalence of chronic respiratory conditions in the U.S. population in 2002 and 2003 (Dey and Bloom, 2005; Lethbridge-Çejku et al., 2004). Individuals with preexisting cardiopulmonary disease constitute a fairly large proportion of the population, with tens of millions of people included in each disease category. Of most concern here are those individuals with preexisting respiratory conditions, with approximately 11% of U.S. adults and 13% of children having been diagnosed with asthma and 6% of adults having COPD (chronic bronchitis and/or emphysema). Table 8-5 in the CD provides further information on the number of various specific respiratory conditions per 100 persons by age among the U.S. population during the mid-1990s. Asthma prevalence tends to be higher in children than adults.

In addition, subpopulations based on age group also comprise substantial segments of the population that may be potentially at risk for $O_3$-related health impacts. Based on U.S. census data from 2003, about 26% of the U.S. population are under 18 years of age and 12% are 65 years of age or older. Hence, large proportions of the U.S. population are included in age groups that are considered likely to have increased susceptibility and vulnerability for health effects from ambient $O_3$ exposure.

The health statistics data illustrate what is known as the "pyramid" of effects. At the top of the pyramid, there are approximately 2.5 millions deaths from all causes per year in the U.S. population, with about 100,000 deaths from chronic lower respiratory diseases (Kochanek et al., 2004). For respiratory health diseases, there are nearly 4 million hospital discharges per year (DeFrances et al., 2005), 14 million ED visits (McCaig and Burt, 2005), 112 million ambulatory care visits (Woodwell and Cherry, 2004), and an estimated 700 million restricted activity days per year due to respiratory conditions (Adams et al., 1999). Combining small risk estimates with relatively large baseline levels of health outcomes can result in quite large public health impacts. Thus, even a small percentage reduction in $O_3$ health impacts on cardiopulmonary diseases would reflect a large number of avoided cases.

Another key input for public health impact assessment is the range of concentration response functions for various health outcomes. Epidemiologic studies have reported associations between short-term exposure to $O_3$ with mortality, hospitalizations for pulmonary diseases, ED visits for asthma, reduced lung function, and incidence of respiratory symptoms. Effect estimates for morbidity responses to short-term changes in $O_3$ tend to be larger and more variable in magnitude than those for mortality.

In addition to attribution of risks for various health outcomes related to $O_3$ and other copollutants, important considerations in assessing the impact of $O_3$ on public health include the size of population groups at risk, as well as the concentration-response relationship and potential identification of threshold levels. Taken together, based on the above information, it can be concluded that exposure to ambient $O_3$ likely has a significant impact on public health in the U.S.

## 3.7 SUMMARY AND CONCLUSIONS FOR OZONE HEALTH EFFECTS

Based on dosimetric, experimental, and epidemiological evidence assessed in the 1996 CD, a set of findings and conclusions were drawn regarding potential health effects of $O_3$ exposure as of 1996. These conclusions are integrated into the Summary and Conclusions for Ozone Health Effects in the 2006 CD (section 8.8). (The revised CD will be referred to as the "2006 CD" in this section to be more easily distinguished from the "1996 CD.") Section 8.8 of the 2006 CD also has summarized the main conclusions derived from the integrated analysis of

animal toxicology (2006 CD, Chapter 5), human experimental (2006 CD, Chapter 6) and epidemiological (2006 CD, Chapter 7) studies that evaluated evidence of health effects associated with short-term, prolonged, and long-term exposures to $O_3$ alone or in combination with other pollutants commonly found in the ambient air. This section summarizes conclusions drawn from section 8.8 of the 2006 CD with respect to the health effects associated with exposure to $O_3$ that are most relevant to our assessment of the adequacy of the current primary $O_3$ standard and the identification of options to consider concerning potential alternative standards to protect public health with an adequate margin of safety.

### 3.7.1 Respiratory Morbidity Effects of Short-term Exposures to Ozone

In the 1996 CD, it was concluded from assessment of controlled human exposure studies that short-term $O_3$ exposures to $O_3$ concentrations of $\geq$ 0.08 ppm for 6.6 to 8 hr under moderate exertion and $\geq$ 0.12 ppm for 1 hr under heavy exertion cause decrements in lung function in children and increased lung function and respiratory symptoms in healthy adults and asthmatic individuals exposed (2006 CD, p. 8-73). Lung inflammatory responses have been observed in healthy human adults following 6.6 hr $O_3$ exposures as low as 0.08 ppm (2006 CD, p. 8-75). Changes in lung function, respiratory symptoms, and lung inflammatory responses occur as a function of exposure concentration, duration, and level of exertion. Such experimentally demonstrated effects were consistent with and helped support the plausibility of epidemiological findings assessed in the 1996 CD regarding daily hospital admissions and ED visits for respiratory causes.

The 1996 CD concluded that group mean data from numerous controlled human exposure and field studies of healthy subjects (18 to 45 years of age) exposed for 1 to 3 hr indicate that, in general, statistically significant pulmonary function decrements beyond the range of normal measurement variability (e.g., 3 to 5% for $FEV_1$) occur

- at >0.12 ppm $O_3$ with very heavy exercise (competitive running).
- at >0.18 ppm $O_3$ with heavy exercise (easy jogging),
- at >0.30 ppm $O_3$ with moderate exercise (brisk walking),
- at >0.37 ppm $O_3$ with light exercise (slow walking), and
- at >0.50 ppm $O_3$ when at rest.

Small group mean changes (e.g., <5%) in $FEV_1$ have been observed in healthy young adults at levels as low as 0.12 ppm $O_3$ for 1 to 3 hr exposure periods. Also, lung function decrements have been observed in children and adolescents at concentrations of 0.12 and 0.14 ppm $O_3$ with heavy exercise. Some individuals within a study may experience $FEV_1$ decrements in excess of 15% under these conditions, even when group mean decrements are less than 5%.

For exposures of healthy, young adult subjects performing moderate exercise during longer duration exposures (6 to 8 hr), 5% group mean decrements in $FEV_1$ were observed at

- 0.08 ppm after $O_3$ 5.6 hr,
- 0.10 ppm after $O_3$ 4.6 hr, and
- 0.12 ppm after $O_3$ 3 hr.

For these same subjects, 10% group mean $FEV_1$ decrements were observed at 0.12 ppm $O_3$ after 5.6 and 6.6 hr. As in the shorter duration studies, some individuals experience changes larger than those represented by group mean changes.

The 2006 CD (section 8.8) concludes that newer meta-analyses confirmed interindividual differences in lung function decrements reported in the 1996 CD. Age-specific differences in lung function responses were also observed. Spirometric responses (due to decrements in lung function) in healthy adults exposed to near ambient $O_3$ levels typically resolve to near baseline within 4-6 hr. Meta-analyses of four controlled human exposure studies (two new and two assessed in the 1996 CD) reporting the effects of prolonged (6.6 hr) exposures to 0.08 ppm $O_3$ during moderate exertion on lung function in young healthy adults (M=90, F=30; mean age 23 years) indicate an absolute $FEV_1$ decrease of 6%, whereas $FEV_1$ increased by 1% following fresh air exposures. Newer studies from Adams (2002, 2006), as illustrated earlier in Figure 3-1B, demonstrate notable interindividual variability for $O_3$ exposure concentrations of 0.04, 0.06 and 0.08 ppm. In these studies, following a continuous exposure to 0.08 ppm $O_3$ during intermittent, moderate exertion, the group mean $FEV_1$ decrement was 5%, but 17 % of subjects had $FEV_1$decrements of 10% or more. Following exposure to 0.06 ppm $O_3$, the group mean $FEV_1$ decrement was less than 2%, but five subjects had greater than 5% $FEV_1$ decrements, with only one experiencing this magnitude of effect when exposed to filtered air (2006 CD, p. 8-18). A few controlled human exposure studies (Adams, 2003; 2006; Hazucha et al., 1992) investigated a triangular exposure pattern at $O_3$ concentrations that had 6.6 to 8-hr averages between 0.08 and 0.12 ppm in order to more closely mimic typical ambient $O_3$ exposure patterns. Greater overall $FEV_1$ decrements were observed with triangular exposures compared to the constant or square-wave exposures. Furthermore, peak $FEV_1$ decrements observed during triangular exposures were greater than those observed during square-wave patterns. At a lower average $O_3$ concentration of 0.06 ppm, no temporal (i.e., hour by hour responses) differences were observed in $FEV_1$ decrements between square-wave and triangular exposure patterns. Results of these studies suggest the potential for somewhat greater effects on lung function in ambient $O_3$ exposure scenarios that typically involve gradually increasing daily exposure up to a peak in the late afternoon and a subsequent gradual decline (2006 CD, p. 8-19). The quantitative risk assessment, discussed below in Chapter 5, provides estimates addressing what percentage of

active school age children are estimated to experience $FEV_1$ decrements greater than or equal to 10, 15, and 20% after 8-hr exposures to $O_3$ while engaged in moderate exertion.

Decrements in lung function associated with ambient $O_3$ levels have also been found in children attending summer camps in southern Ontario, Canada, in the northeastern U.S., and in southern California (2006 CD, p. 8-74). Meta-analyses indicate that a 0.50-mL decrease in $FEV_1$ is associated with a 1 ppb increase in $O_3$ concentration. For preadolescent children exposed to 120 ppb (0.12 ppm) ambient $O_3$, this amounts to an average decrement of 2.4 to 3.0% in $FEV_1$. Similar responses are reported for exercising children and adolescents exposed to $O_3$ in ambient air or $O_3$ in purified air for 1-2 hours.

The 1996 CD concluded that an increase in the incidence of cough has been reported at $O_3$ concentrations as low as 0.12 ppm in healthy adults during 1 to 3 hr of exposure with very heavy exercise. Other respiratory symptoms, such as pain on deep inspiration, shortness of breath, and lower respiratory scores (i.e., a combination of several symptoms), have been observed at 0.16 ppm to 0.18 ppm $O_3$, 1-hr average, with heavy and very heavy exertion. Respiratory symptoms also have been observed following exposure to 0.08, 0.10 and 0.12 ppm $O_3$ for 6.6 hr with moderate exertion levels. Also, increases in nonspecific airway responsiveness in healthy adults at rest have been observed after 1 to 3 hr of exposures to 0.40 ppm but not to 0.20 ppm $O_3$; during very heavy exertion, these increases were observed at concentrations as low as 0.18 ppm but not at 0.12 ppm $O_3$. Increases in nonspecific airway responsiveness during the 6.6 hr exposures with moderate levels of exertion have been observed at 0.08, 0.10 and 0.12 ppm $O_3$.

The majority of asthma panel studies evaluated the associations of ambient $O_3$ with lung function and respiratory symptoms in asthmatic children. Results obtained from these studies show some inconsistencies, with some indicating significant positive associations and other smaller studies not finding such effects. Overall, however, the multicity study by Mortimer et al. (2002) and several credible single-city studies (e.g., Gent et al., 2003) indicate a fairly robust association between ambient $O_3$ concentrations and increased respiratory symptoms in moderate to severe asthmatic children (2006 CD, p. 8-35).

The 2006 CD (p. 8-75) concludes that lung inflammatory responses have been observed in healthy human adults following 6.6 hr $O_3$ exposures as low as 0.08 ppm. These responses have been found even in the absence of $O_3$-induced lung function decrements for some individuals. Attenuation of most inflammatory markers occurs with repeated exposures over several days, but none of the several markers of lung injury and permeability show attenuation, which is indicative of continued lung tissue damage during repeated exposure. Laboratory animal studies have reported that 1 to 3 hr $O_3$ exposures as low as 0.1 to 0.5 ppm can cause (1) lung inflammatory responses (e.g., increased ROS and inflammatory cytokines, influx of PMNs, and activation of AMs); (2) damage to epithelial airway tissues, (3) increases in permeability of

both lung endothelium and epithelium, and (4) increases in susceptibility to infectious diseases due to modulation of lung host defenses. Consistent with the above results of human and animal experimental studies, there is limited epidemiologic evidence of an association between acute ambient $O_3$ exposure (1-hr max of about 0.1 ppm) and airway inflammation in children, all of which taken together is indicative of a causal role for $O_3$ in inflammatory responses in the airways (2006 CD, p. 8-76). See Table 3.4 for a summary of short-term health effects of $O_3$ based on clinical studies assessed in both the 1996 CD and 2006 CD.

The 1996 CD concluded that increased $O_3$ levels are associated with increased hospital admissions and ED visits for respiratory causes. Analyses from data in the northeastern U.S. suggested that $O_3$ air pollution is associated with a substantial portion of all summertime respiratory hospital visits and admissions. The 2006 CD concludes (CD, p. 8-36) that a large multi-city and several single-city studies have indicated a positive association between increased $O_3$ levels (especially during the warm season) and increased risk for hospital admissions.

**Table 3-4. Summary of Ozone-Induced Respiratory Health Effects from Clinical Studies[2]**

| Health Effect | Exercise Level | Prolonged Exposure | Short-term Exposure | Lowest Ozone Effect Level |
|---|---|---|---|---|
| Pulmonary Function Decrements | Moderate | 6.6 hr | | 0.08 ppm |
| | Moderate | 4.6 hr | | 0.10 ppm |
| | Moderate | 3.0 hr | | 0.12 ppm |
| | Competitive | | 1 hr | 0.12-0.14 ppm |
| | Very Heavy | | 1-3 hr | 0.16 ppm |
| | Heavy | | 1-3 hr | 0.18 ppm |
| | Moderate | | 1-3 hr | 0.30 ppm |
| | Light | | 1-3 hr | 0.37 ppm |
| | At rest | | 1-3 hr | 0.50 ppm |
| Increased Respiratory Symptoms | Moderate | 6.6 hr | | 0.08 ppm |
| | Very Heavy | | 1-3 hr | 0.12 ppm |
| Airway Responsiveness | Moderate | 6.6 hr | | 0.08 ppm |
| | Very Heavy | | 1-3 hr | 0.18 ppm |
| | At rest | | 1-3 hr | 0.40 ppm |
| Respiratory Inflammation | Moderate | 6.6 hr | | 0.08 ppm |
| | Very Heavy | | 1-3 hr | 0.20 ppm |
| Changes in Host Defenses | Moderate | 6.6 hr | | 0.08 ppm |
| Decreased Exercise Performance | Competitive | | 1 hr | 0.18 ppm |

[2] Information contained in this table is based on scientific data assessed in Chapters 6 and 8 of the 2006 CD.

### 3.7.2 Cardiovascular Morbidity Effects of Short-term Exposures to Ozone

One health endpoint that was unrecognized in the 1996 CD, but is addressed in the 2006 CD, is $O_3$-induced cardiovascular effects. Newly available evidence has emerged since 1996 which provides considerable plausibility for how $O_3$ could exert cardiovascular effects (2006 CD, p. 8-77). Examples of such $O_3$-induced cardiovascular effects include: (1) $O_3$-induced release from lung epithelial cells of PAF that may contribute to blood clot formation that would increase the risk of serious cardiovascular outcomes (e.g., heart attack, stroke, mortality); (2) interactions of $O_3$ with surfactant components in ELF of the lung resulting in production of oxysterols and ROS that may exhibit PAF-like activity contributing to clotting and/or exerting cytotoxic effects on lung and heart cells; (3) possible mechanisms that may involve $O_3$-induced secretions of vasoconstrictive substances and/or effects on neuronal reflexes that may result in increased arterial blood pressure and/or altered electrophysiologic of heart rate or rhythm; (4) associations between $O_3$ and various cardiac physiologic endpoints suggesting a potential relationship between $O_3$ exposure and altered HRV, ventricular arrhythmias, and incidence of MI; and (5) positive associations during the warm season only between ambient $O_3$ concentrations and cardiovascular hospitalizations. While the only controlled human exposure study that evaluated effects of $O_3$ exposure on the cardiovascular system found no $O_3$-induced differences in ECG, heart rate, or blood pressure in healthy or hypertensive subjects, the study did report an overall increase in myocardial work and impairment in pulmonary gas exchange.

Also, animal toxicological studies have reported $O_3$-induced decreases in heart rate, mean arterial pressure and core temperature. Overall, the 2006 CD (p. 8-77) concludes that this generally limited body of evidence is highly suggestive that $O_3$ directly and/or indirectly contributes to cardiovascular-related morbidity, but much remains to be done to more fully substantiate links between short-term ambient $O_3$ exposures and adverse cardiovascular effects.

### 3.7.3 Mortality-Related Effects of Short-term Exposures to Ozone

The 1996 CD concluded that an association between daily mortality and $O_3$ concentration for areas with high $O_3$ levels (e.g., Los Angeles) was suggested. However, due to a very limited number of studies available at that time, there was insufficient evidence to conclude that the observed association was likely causal. Since 1996, new data are available from large multicity studies conducted in the U.S. and several single-city studies conducted all over the world, as well as from several meta-analyses that have combined information from multiple studies. The majority of these studies suggest an elevated risk of total nonaccidental mortality associated with acute exposure to $O_3$, especially in the summer or warm season when $O_3$ levels are typically high, with somewhat larger effect estimate sizes for associations with cardiovascular mortality (2006 CD, p. 7-175). The 2006 CD finds that the results from U.S. multicity time-series studies

provide the strongest evidence to-date for associations between short-term $O_3$ exposure and mortality. These studies, along with recent meta-analyses, showed consistent effect estimates that are unlikely to be confounded by PM, though the 2006 CD observes that future work is needed to better understand the influence of model specifications on the effect estimates (2006 CD, p. 7-175). For cardiovascular mortality, the 2006 CD reports that effect estimates are consistently positive, falling in the range of 1 to 8% increases per 40 ppb in 1-hr $O_3$ (2006 CD, p. 7-107). Overall, the 2006 CD concludes that these findings appear to be consistent with a causal association between short-term $O_3$ exposure and mortality particularly in the warm season when $O_3$ levels are typically high (2006 CD, p. 7-175).

### 3.7.4 Health Effects of Repeated Short-term Exposures to Ozone

The 1996 CD drew several conclusions regarding repeated short-term $O_3$ exposures (2006 CD, p. 8-15). Partial or complete attenuation is observed for some of the $O_3$-induced responses after more than 2 days of exposure. After 5 days of exposure, lung function changes return to control levels with the greatest changes usually occurring on the second day, but the attenuation was reversed after 7 to 10 days without $O_3$ exposure. Most inflammatory markers (e.g., PMN influx) attenuate after 5 days of exposure, but markers of cell damage (e.g., LDH enzyme activity) do not attenuate and continue to increase. Recovery of some inflammatory markers occurred a week to 10 days after exposure ceased, but some responses were not normal after 20 days. Animal studies suggest underlying cell damage continues throughout the attenuation process. Also, attenuation may alter normal distribution of $O_3$ within the lungs, allowing more $O_3$ to reach sensitive regions, possibly affecting lung defenses. Newer studies assessed in the 2006 CD (p. 8-74 and 8-75) supported all of these conclusions in addition to which it was concluded that repeated daily, multi-hour exposure to lower concentrations of $O_3$ (0.125 ppm for 4 days) causes an increased response to bronchial allergen challenge in subjects with preexisting allergic airway disease, with or without asthma. In these subjects, changes in airway responsiveness after $O_3$ exposure appear to be resolved more slowly than changes in $FEV_1$ or respiratory symptoms.

### 3.7.5 Confidence in Various Health Outcomes Associated with Short-term Exposures to Ozone

In characterizing the extent to which relationships between the various health outcomes discussed above and short-term exposures to ambient $O_3$ are likely causal, we note that several different factors have informed the judgments made in the CD and here. These factors include the nature of the evidence (i.e., controlled human exposure, epidemiological, and/or toxicological studies) and the weight of evidence, including such considerations as biological plausibility, coherence of evidence, strength of association, and consistency of evidence.

In assessing the health effects data base for $O_3$, it is clear that human studies provide the most directly applicable information because they are not limited by the uncertainties of dosimetry differences and species sensitivity differences, which would need to be addressed in extrapolating animal toxicology data to human health effects. Controlled human exposure studies provide data with the highest level of confidence since they provide human effects data under closely monitored conditions and can provide clear exposure-response relationships. Epidemiological data provide evidence of associations between ambient $O_3$ levels and more serious acute and chronic health effects (e.g., hospital admissions and mortality) that cannot be assessed in controlled human exposure studies. For these studies the degree of uncertainty regarding potential confounding variables (e.g., other pollutants, temperature) and other factors affects the level of confidence that the health effects being investigated are attributable to $O_3$ exposures, alone and in combination with other copollutants.

In using a weight of evidence approach to inform judgments about the degree of confidence that various health outcomes are likely caused by exposure to $O_3$, our increases as the number of studies and other factors, such as strength, consistency, and coherence of evidence, consistently reporting a particular health endpoint grows. For example, there is a very high level of confidence that $O_3$ induces lung function decrements in healthy adults and children due in part to the dozens of studies consistently showing that these effects were observed. As noted above, the 2006 CD (p. 8-74) states that studies provide clear evidence of causality for associations between short-term $O_3$ exposures and statistically significant declines in lung function in children, asthmatics and adults who exercise outdoors. An increase in respiratory symptoms (e.g., cough, shortness of breath) has been observed in controlled human exposure studies of short-term $O_3$ exposures, and significant associations between ambient $O_3$ exposures and a wide variety of symptoms have been reported in epidemiology studies (2006 CD, p. 8-75). Aggregate population time-series studies showing robust associations with respiratory hospital admissions and ED visits are strongly supported by human clinical, animal toxicologic, and epidemiologic evidence for lung function decrements, respiratory symptoms, airway inflammation, and airway hyperreactivity. Taken together, the 2006 CD (p. 8-77) concludes that the overall evidence supports the inference of a causal relationship between acute ambient $O_3$ exposures and increased respiratory morbidity outcomes resulting in increased ED visits and hospitalizations during the warm season. Recent epidemiologic evidence has been characterized in the CD (p. 8-78) as highly suggestive that $O_3$ directly or indirectly contributes to non-accidental and cardiopulmonary-related mortality.

As discussed above in section 3.5 and in section 8.6 of the 2006 CD, conclusions regarding biological plausibility, consistency, and coherence of evidence of $O_3$-related health effects are drawn from the integration of epidemiological studies with mechanistic information

from controlled human exposure studies and animal toxicological studies. This type of mechanistic linkage has been firmly established for several respiratory endpoints (e.g., lung function decrements, lung inflammation) but remains far more equivocal for cardiovascular endpoints (e.g., cardiovascular-related hospital admissions). Finally, for epidemiological studies, strength of association refers to the magnitude of the association and its statistical strength, which includes assessment of both effects estimate size and precision (section 3.4.1). In general, when associations yield large relative risk estimates, it is less likely that the association could be completely accounted for by a potential confounder or some other bias. Consistency refers to the persistent finding of an association between exposure and outcome in multiple studies of adequate power in different persons, places, circumstances and times (section 3.4.3). For example, the magnitude of effect estimates is relatively consistent across recent studies showing association between short-term, but not long-term, $O_3$ exposure and mortality.

Figure 3-5 summarizes our judgments for the various health outcomes discussed above concerning the extent to which relationships between various health outcomes and ambient $O_3$ exposures are likely causal. These judgments are informed by the conclusions and discussion in the CD and in earlier sections of this chapter, reflecting the nature of the evidence and overall weight of the evidence, and are taken into consideration in our quantitative risk assessment, presented below in Chapter 5.

### 3.7.6 Health Effects of Long-term Exposures to Ozone

In the 1996 CD, available data, primarily from animal toxicology studies, indicated that exposure to $O_3$ for periods of months to years causes structural changes in several regions of the respiratory tract (2006 CD, p. 8-79). Effects may be of greatest importance in the CAR, where the alveoli and conducting airways meet. This region of the lungs is typically affected in most human airway diseases. However, data from epidemiological and clinical studies is lacking, and most information on chronic $O_3$ effects in the distal lungs continues to come from animal toxicology studies.

What had been previously been viewed as an apparent lack of reversibility of effects during clean air exposures has been investigated since 1996 with animal toxicology studies using exposure regimens simulating a seasonal exposure pattern. One long-term study exposed rhesus monkeys to a simulated seasonal $O_3$ pattern (0.5 ppm $O_3$ 8hr/day for 5 days, every 14 days for 11 episodes) and reported: (1) remodeling in the distal airways; (2) abnormalities in tracheal basement membrane; (3) eosinophil accumulation in conducting airways; and (4) decrements in airway innervation. These findings support and advance the earlier information suggestive of injury and repair processes which are caused by seasonal $O_3$ exposures (2006 CD, p.8-79). Although adverse physiological changes associated with long-

**Figure 3-5. Qualitative Characterization of Ozone-Related Health Effect Outcomes**

| Characterization | Overall Confidence in Causal Relationship With Ambient Ozone |
|---|---|
| Causal ↓ | -Lung function decrements in healthy children<br>-Lung function decrements in asthmatic children<br>-Lung function decrements in healthy adults<br>-Respiratory symptoms in asthmatic children<br>-Respiratory symptoms in healthy adults<br>-Increased lung inflammation<br>-Aggravation of asthma (i.e., increased medication usage, increased asthma attacks)<br><br>-Respiratory-related hospital admissions<br>-Respiratory related emergency department visits<br>-Respiratory-related doctors visits<br>-Increased school absences<br>-Respiratory-related mortality during the $O_3$ season<br><br>-Cardiorespiratory-related mortality during the $O_3$ season<br>-Total nonaccidental mortality during the $O_3$ season |
| Suggestive | -Cardiovascular-related hospital admissions |

term $O_3$ exposures reported in animal studies suggest similar changes in humans, interspecies differences in sensitivity to chronic effects of $O_3$ continue to be a limiting factor in extrapolation of effect responses in animals to levels at which these responses would be expected to occur in human health effects.

Epidemiological studies investigating chronic effects in humans following long-term exposures to $O_3$ previously provided only limited suggestive evidence. However, recent studies of lung function changes observed in children living in cities with high $O_3$ levels support the conclusion that long-term $O_3$ exposure may play a role in causing irreversible lung damage. Further investigation, however, is necessary before we are able to draw firmer conclusions about chronic health effects of $O_3$ in human populations.

### 3.7.7 Health Effects of Pollutant Mixtures Containing Ozone

In the 1996 CD, it was recognized that coexposure of humans and animals to $O_3$ and other pollutants, such as $NO_2$, $SO_2$, $H_2SO_4$, $HNO_3$, or CO, showed additive response for lung spirometry or respiratory symptoms (2006 CD, p. 8-82). Since 1996, most animal toxicology studies investigating $O_3$ in a mixture with $NO_2$ and $H_2SO_4$ have shown that effects can be additive, synergistic, or even antagonistic, depending on the exposure regimen and the endpoint studied. Ozone has served for a long time as a surrogate or indicator for the overall photochemical oxidant mix. It is well recognized that the observed effects may be due to components of that mix alone or in combination with $O_3$ and other gases and PM in the ambient air. Although the issue of exposure to copollutants was previously described as poorly understood, especially with regard to chronic effects, newer information from human and animal studies of binary mixtures containing $O_3$ suggest potential interactions depending on the exposure regimen and pollutant mix (CD, p. 8-82). Examples of this newer information include: (1) continuous exposure to $SO_2$ and $NO_2$ increased inhaled $O_3$ bolus absorption, while continuous exposure to $O_3$ decreased $O_3$ bolus absorption; (2) asthmatics exhibited enhanced airway reactivity to house dust mite allergen following exposures to $O_3$, $NO_2$ and the combination of the two gases; however, spirometric response was impaired only by $O_3$ and $O_3$+ $NO_2$ at higher concentrations; and (3) animal toxicology studies with $O_3$ in mixture with $NO_2$, formaldehyde, and PM demonstrated additive, synergistic, or antagonistic effects depending on the exposure regimen and the endpoints evaluated.

One controlled-exposure study of children, designed to approximate conditions of an epidemiological study by matching population and exposure atmosphere (0.1 ppm $O_3$, 0.1 ppm $SO_2$, and 101 ug/$m^2$ $H_2SO_4$), failed to support the findings of the epidemiological study. This demonstrates the difficulty of trying to link outcomes of epidemiological studies and controlled-exposure studies with pollutant mixtures.

### 3.7.8 Populations at Risk/Susceptibility Factors Associated with Ozone Exposure

The 1996 CD (2006 CD, p. 8-80) identified several factors that may increase sensitivity to $O_3$ of population groups, including: (1) biological variation in responsiveness to $O_3$; (2) preexisting lung disease (e.g., asthma); (3) activity patterns (e.g., exertion levels); (4) personal exposure history (e.g., time spent indoors v. outdoors); and (5) personal factors (e.g., age, nutritional status, gender, smoking history, ethnicity). Based on the information assessed in the 1996 CD (2006 CD, p. 8-80), population groups that demonstrated increased responsiveness to ambient concentrations of $O_3$ consisted of exercising, healthy and asthmatic individuals, including children, adolescents, and adults. Since 1996, evidence from controlled-exposure human and animal studies, as well as from epidemiological studies, has provided further support for these and other susceptibility factors and populations at risk. For example, controlled-exposure human studies continue to show differential biological response to $O_3$ based on physical activity (exertion) and age. These studies demonstrate a large variation in sensitivity and responsiveness to $O_3$, although specific factors that contribute to this intersubject variability are yet to be identified. Associations of increased summertime hospital admissions for asthma and COPD with ambient $O_3$ levels suggest that individuals with these respiratory diseases are populations at risk to $O_3$ exposure effects. Also, based on $O_3$-induced differential response in lung inflammation and airway responsiveness, asthmatic adults and children appear to have potentially increased susceptibility to $O_3$. There is no evidence from controlled-exposure human studies which suggests that individuals with COPD are more sensitive to health effects of $O_3$.

There is some animal toxicology evidence which has demonstrated the importance of genetic background in $O_3$ susceptibility. Genetic and molecular characterization studies of experimental animals have identified genetic loci responsible for both sensitivity and resistance.

Taking all of this information into account, the CD (p. 8-80 to 8-81) concludes that all exercising (moderate to high physical exertion) healthy and asthmatic adults, adolescents, and children appear to exhibit increased responsiveness to ambient $O_3$ levels and continue to be considered at increased risk of $O_3$-induced health effects. Also, any individual with respiratory or cardiovascular disease or any healthy individual who is engaged in vigorous physical activity outdoors during periods when $O_3$ levels are high (e.g., active outdoor children) is potentially at increased risk to $O_3$-induced health effects. In addition, healthy individuals and those with cardiorespiratory impairment (e.g., those with COPD or cardiovascular disease) who are "hyperresponsive" to $O_3$ exposure (i.e., exhibit much higher than normal lung function decrements and/or respiratory symptoms) would be considered at greater risk to $O_3$ exposure. Finally, individuals who are more likely to be exposed to air pollution while engaged in physical

activity (e.g., outdoor workers) and those with genetic polymorphisms for antioxidant enzymes and inflammatory genes may be at heightened risk of effects of $O_3$ (2006 CD, p. 8-81).

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# 4. CHARACTERIZATION OF HUMAN EXPOSURE TO OZONE

## 4.1 INTRODUCTION

As part of the last $O_3$ NAAQS review, EPA conducted exposure analyses for the general population, children who spent more time outdoors, and outdoor workers. Exposure estimates were generated for nine urban areas for "as is" (i.e., a recent year) air quality and for just meeting the existing 1-hr standard and several alternative 8-hr standards. EPA also conducted a health risk assessment that produced risk estimates for the number of children and percent of children experiencing lung function and respiratory symptoms associated with the exposures estimated for these same nine urban areas.

The exposure analysis conducted for the current review builds upon the methodology and lessons learned from the exposure analyses conducted for the last review (US EPA, 1996a). The methodology used to conduct the exposure analysis as well as summary results from the exposure analysis are described in this chapter. The exposure analysis technical support document, *Ozone Population Exposure Analysis for Selected Urban Areas* (US EPA, 2006a) (hereafter cited as "draft Exposure Analysis TSD") presents a detailed description of the exposure analysis methodology.

Population exposures to ambient $O_3$ levels are modeled for 12 urban areas located across the U.S. using the Air Pollutants Exposure (APEX) model, also referred to as the Total Risk Integrated Methodology Inhalation Exposure (TRIM.Expo) model (US EPA, 2006c,d). Exposure estimates are developed for $O_3$ levels in recent years, based on 2002 and 2004 ambient air quality measurements. Exposures are also estimated for $O_3$ levels associated with just meeting the current 8-hr $O_3$ NAAQS and several potential alternative standards, based on adjusting data derived from the ambient monitoring network as described in section 4.5.8. Exposures to background levels of $O_3$ are also estimated, based on $O_3$ concentrations predicted by the GEOS-CHEM atmospheric photochemical model.

Exposures are modeled for 1) the general population, 2) all school-age children (ages 5-18), 3) active school-age children (defined below), and 4) asthmatic school-age children. The strong emphasis on children reflects the finding of the last $O_3$ NAAQS review that children, especially those who are active outdoors, are an important at-risk group.

This chapter provides a brief overview of the types of studies that provide data on which this analysis is based, followed by a description of the exposure model used for this analysis, the model input data, and the results of the analysis. The final sections of this chapter compare the exposure estimates with those from the prior review and summarize the sensitivity analyses and

model evaluation that have been conducted for the $O_3$ exposure model described in this chapter. The uncertainty assessment and a technical description of the modeling effort are provided in separate documents (Langstaff, 2006; US EPA, 2006a).

## 4.2 OZONE EXPOSURE STUDIES

Many studies have produced information and data supporting the development of methods for estimating human exposure to ambient $O_3$ over the past several decades. These studies have been reviewed in the current and previous EPA Ozone Air Quality Criteria Documents (US EPA, 1986, 1996b, 2006b).

The types of studies which provide the basis for modeling human exposure to $O_3$ include studies of people's activities, work and exercise patterns, physiology, physics and $O_3$-related chemistry in microenvironments, atmospheric modeling of $O_3$, chamber studies of atmospheric chemistry, and modeling of meteorology. Measurements that have proven to be useful for understanding and estimating exposure obtained from personal exposure assessment studies include fixed-site ambient concentrations, concentrations in specific indoor and outdoor microenvironments, personal exposure levels, personal activity patterns, air exchange rates, infiltration rates, deposition and decay rates, and meteorology.

### 4.2.1 Exposure Concepts and Definitions

*Human exposure* to a contaminant is defined as "contact at a boundary between a human and the environment at a specific contaminant concentration for a specific interval of time," and has units of concentration times time (National Research Council, 1991). For airborne pollutants the contact boundary is nasal and oral openings in the body, and *personal exposure* of an individual to a chemical in the air for a discrete time period is quantified as (Lioy, 1990; National Research Council, 1991):

$$E_{[t_1, t_2]} = \int_{t_1}^{t_2} C(t)dt \qquad (4\text{-}1)$$

where $E_{[t_1,t_2]}$ is the personal exposure during the time period from $t_1$ to $t_2$, and $C(t)$ is the concentration at time $t$ in the breathing zone. We refer to the *exposure concentration* to mean the concentration to which one is exposed. The breathing rate (ventilation rate) at the time of exposure is an important determinant of the dose received by the individual. Although we do not estimate dose, we refer to *intake* as the total amount of $O_3$ inhaled (product of exposure concentration, duration, and minute ventilation rate).

Personal exposure to $O_3$ can be estimated directly by monitoring the concentration of $O_3$ in the person's breathing zone (close to the nose/mouth) using a personal exposure monitor. Exposure can also be estimated indirectly, by estimating or monitoring the concentrations over

time in locations in which the individual spends time and estimating the time and duration the individual spends in each location. In both of these methods, Equation 4-1 is used to calculate an estimate of personal exposure. A key concept in modeling exposure is the *microenvironment*, a term that refers to the immediate surroundings of an individual. A microenvironment is a location in which pollutant concentrations are relatively homogeneous for short periods of time. Microenvironments can be outdoors or indoors; some examples are outdoors near the home, outdoors near the place of work, bedrooms, kitchens, vehicles, stores, restaurants, street-corner bus stops, schools, and places of work. A bedroom may be treated as a different microenvironment than a kitchen if the concentrations are significantly different in the two rooms. The concentrations in a microenvironment typically change over time; for example, $O_3$ concentrations in a kitchen while cooking with a gas stove may be lower than when these activities are not being performed, due to scavenging of $O_3$ by $NO_x$ emissions from the gas burned.

An important factor affecting the concentrations of $O_3$ indoors is the degree to which the ambient outdoor air is transported indoors. This can be modeled using physical factors such as air exchange rates (AERs), deposition and decay rates, and penetration factors. The *volumetric exchange rate* ($m^3$/hour) is the rate of air exchange between the indoor and outdoor air. The *AER* between indoors and outdoors is the number of complete air exchanges per hour and is equal to the volumetric exchange rate divided by the volume of the well-mixed indoor air. Indoor concentrations of $O_3$ can be decreased by uptake of $O_3$ by surfaces and by chemical reactions. The *deposition* and *chemical decay rates* are the rates (per hour) at which $O_3$ is removed from the air by surface uptake and chemical reactions. Some exposure models employ an infiltration factor, which is conceptually useful if distinguishing between the air exchange processes of air blowing through open doors and windows and the infiltration of air through smaller openings. Since measurements of AERs account for both of these processes (including infiltration), this distinction is not useful in applied modeling of $O_3$ exposures and will not be discussed further here. Simpler exposure models use a "factor model" approach to estimate indoor $O_3$ concentrations by multiplying the ambient outdoor concentrations by an indoor/outdoor concentration ratio, referred to as a *penetration factor*.

### 4.2.2 Monitoring Equipment Considerations

Exposure assessment studies involve monitoring airborne $O_3$ and/or other pollutants, and monitor design and placement play a critical role in interpreting the results of these studies. For exposure assessment purposes there are two general classes of monitors, personal exposure monitors (PEMs) and fixed site monitors.

PEMs are designed to be worn or carried easily by individuals and to measure the concentrations experienced by individuals over a period of hours, days, or weeks. The placement of PEMs is important; the desired placement is usually in the breathing zone near the mouth and nose, but where the monitor will not be excessively impacted by exhaled air. This placement is intended to represent the concentrations the individual breathes in. PEMs typically report continuously measured $O_3$ concentrations with averaging times ranging from 1 to 24 hours.

The CD reviews $O_3$ PEMS (CD, Appendix AX3, p. 163-5) and notes that humidity, wind velocity, badge placement, and interference with other pollutants may result in measurement error. The CD reports PEM detection limits ranging from 5 to 23 ppb for averaging times from 24-hr to 1- hr.

Fixed-site monitors measure concentrations over time at a given location. There are numerous fixed-site $O_3$ monitors which are part of national, state, and local air monitoring networks. In addition to their role of being used to determine which areas are in compliance with existing $O_3$ NAAQS, these are also useful for alerting the public to high $O_3$ days, providing air quality data in support of photochemical modeling and exposure assessments for a study area, for tracking $O_3$ levels and trends, and for studying the representativeness of measurements at these monitors for the study area. Existing fixed-site monitors usually report hourly averaged concentrations, and are in operation over a period of years. Federal reference and equivalent $O_3$ monitoring methods are required to have a lower detectable limit of 0.01 ppm and precision of 0.01 ppm for 1-hr average concentrations (40 CFR Ch. 1, §53.21). A discussion of monitoring equipment and networks can be found in Chapter 2 of this draft Staff Paper and in section 2.6 in the CD.

There are also stationary monitors expressly set up for particular exposure field studies. These are used to measure concentrations over time in microenvironments, such as rooms in a home, just outside a home, roadsides, and so forth. The stationary monitors which are outdoors can provide information about community-scale representativeness of routinely operated fixed-site monitors in or near the community.

### 4.2.3 Personal Ozone Exposure Assessment Studies

The most useful PEM studies have data collected repeatedly from each individual in the study over a period of time, yielding a longitudinal time series of concentrations each individual is exposed to. These studies permit analysis of both the temporal and spatial variability of each person's personal exposure to $O_3$.

Some studies are designed so that the data are sampled randomly from the population, which reduces bias and allows one to make inferences about exposure in the broader population.

Most studies addressing $O_3$ exposure have not been random. They might have specific goals for which randomness is not required, or be subject to constraints which do not allow for random sampling. Some studies draw upon data from existing measurement systems or historical data collection efforts. These non-random studies can be very helpful in the development of models of exposure; however, we recognize that they may not be representative of the broader population.

### 4.2.4 Microenvironmental Studies

The focus of microenvironmental studies is on measuring concentrations in different locations that people spend time in, as well as on measuring the movement of pollutants from one microenvironment to another and on measuring other parameters that contribute to variability in exposure. Typically, microenvironmental measurements include indoor and outdoor concentrations of $O_3$ and other pollutants, AERs, infiltration factors, deposition rates, decay rates, emissions of $O_3$, $NO_x$, VOCs, and other pollutants, operating characteristics of air conditioning systems, and meteorological data such as wind velocity, temperature, and humidity. The CD discusses several studies of microenvironments that contribute to our understanding of the factors and processes that affect exposure to $O_3$ (CD Appendix AX3, p. 191-216).

There is a great deal of variability among individuals in the amount of time spent indoors, but the majority of people spend most of their time indoors (Graham & McCurdy, 2004), and therefore the concentrations of $O_3$ indoors can be an important determinant of people's exposure to $O_3$. There are several factors affecting $O_3$ concentrations indoors. The ambient outdoor concentration of $O_3$ and the AER are the primary determinants of the indoor concentrations. Removal processes are also significant, the most important of which is deposition onto indoor surfaces such as carpets, furnishings, and ventilation ductwork. Chemical reactions of $O_3$ with other compounds, such as solvents from consumer products or $NO_x$ emissions from gas stoves, also deplete $O_3$ indoors. (Weschler, 2000; Monn, 2001.)

The primary sources of $O_3$ indoors are $O_3$-generating air cleaners and some photocopiers and laser printers. Ozone generators can increase indoor concentrations by more than 50 ppb. Some older photocopiers, if run continuously in an enclosed area, can increase $O_3$ concentrations by as much as 150 ppb. Older laser printers can produce concentrations of up to 180 ppb. (US EPA, 1995; CARB, 2005.)

## 4.3 EXPOSURE MODELING

Models of human exposure to airborne pollutants are typically driven by estimates of ambient outdoor concentrations of the pollutants, which vary by time of day as well as by location. These concentration estimates may be provided by measurements, by air quality models, or by a combination of these. It is only possible to address hypothetical future scenarios using modeling. The main purpose of this exposure analysis is to allow comparisons of population exposures to $O_3$ within each urban area, associated with current air quality levels and with several potential alternative air quality standards or scenarios. Human exposure, regardless of the pollutant, depends on where an individual is located and what they are doing. Exposure models are useful in realistically estimating personal exposures and intake based on activity-specific ventilation rates, particularly when recognizing that these measurements cannot be performed for a given population. This section provides a brief overview of the model used by EPA to estimate $O_3$ population exposure. Details about the application of the model to estimate $O_3$ population exposure are provided in the following sections and in the draft Exposure Analysis TSD (EPA, 2006a).

### 4.3.1 The APEX Model

The EPA has developed the APEX model for estimating human population exposure to criteria and air toxic pollutants. APEX also serves as the human inhalation exposure model within the Total Risk Integrated Methodology (TRIM) framework (Richmond et al., 2002; EPA 2005c). APEX is conceptually based on the probabilistic NAAQS Exposure Model (pNEM) that was used in the last $O_3$ NAAQS review (Johnson et al., 1996a; 1996b: 1996c). Since that time the model has been restructured, improved, and expanded to reflect conceptual advances in the science of exposure modeling and newer input data needed for the model. Key improvements to algorithms include replacement of the cohort approach with a probabilistic sampling approach focused on individuals, accounting for fatigue and oxygen debt after exercise in the calculation of ventilation rates, and a new approach for construction of longitudinal activity patterns for simulated persons. Major improvements to data input to the model include updated AERs, census and commuting data, and the daily time-activities database. These improvements are described later in this chapter.

APEX is a probabilistic model designed to account for the numerous sources of variability that affect people's exposures. APEX simulates the movement of individuals through time and space and their exposure to a given pollutant in indoor, outdoor, and in-vehicle microenvironments. Figure 4-1 provides a schematic overview of the APEX model. The model stochastically generates simulated individuals using census-derived probability distributions for

demographic characteristics (Figure 4-1, steps 1-3). The population demographics are drawn from the year 2000 Census at the tract level, and a national commuting database based on 2000 census data provides home-to-work commuting flows between tracts.[1] Any number of simulated individuals can be modeled, and collectively they approximate a random sampling of people residing in a particular study area.

Daily activity patterns for individuals in a study area, an input to APEX, are obtained from detailed diaries that are compiled in the Consolidated Human Activity Database (CHAD) (McCurdy et al., 2000; EPA, 2002). The diaries are used to construct a sequence of activity events for simulated individuals consistent with their demographic characteristics, day type, and season of the year, as defined by ambient temperature regimes (Graham & McCurdy, 2004) (Figure 4-1, step 4). APEX calculates the concentration in the microenvironment associated with each event in an individual's activity pattern and sums the event-specific exposures within each hour to obtain a continuous series of hourly exposures spanning the time period of interest (Figure 4-1, steps 5, 6).

APEX has a flexible approach for modeling microenvironmental concentrations, where the user can define the microenvironments to be modeled and their characteristics. Typical indoor microenvironments include residences, schools, and offices. Outdoor microenvironments include near roadways, at bus stops, and playgrounds. Inside cars, trucks, and mass transit vehicles are microenvironments which are classified separately from indoors and outdoors.

Activity-specific simulated breathing rates of individuals are used in APEX to characterize intake received from an exposure. These breathing, or ventilation, rates are derived from energy expenditure estimates for each activity included in CHAD and are adjusted for age- and gender-specific physiological parameters associated with each simulated individual. Energy expenditure estimates themselves are derived from METS (metabolic equivalents of work) distributions associated with every activity in CHAD (McCurdy et al., 2000), largely based upon the Ainsworth et al. (1993) "Compendium of Physical Activities." METS are a dimensionless ratio of the activity-specific energy expenditure rate to the basal or resting energy expenditure rate, and the metric is used by exercise physiologists and clinical nutritionists to estimate work undertaken by individuals as they go through their daily life (Montoye et al., 1996). This approach is discussed more thoroughly in McCurdy (2000).

[1] There are approximately 65,400 census tracts in the ~3,200 counties in the U.S.

**Figure 4-1. Overview of the APEX Model**

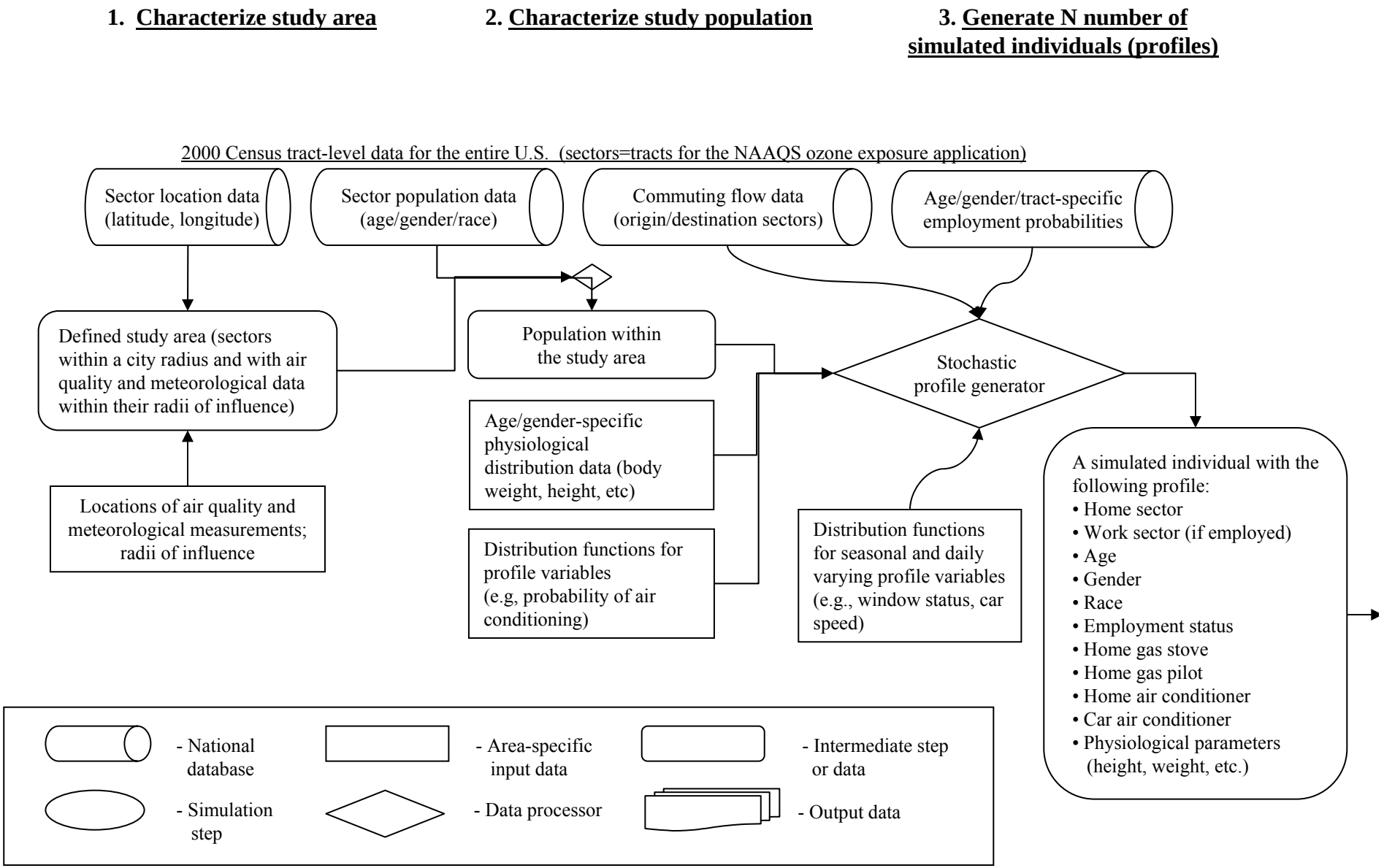


**Figure 4-1. Overview of the APEX Model, continued**

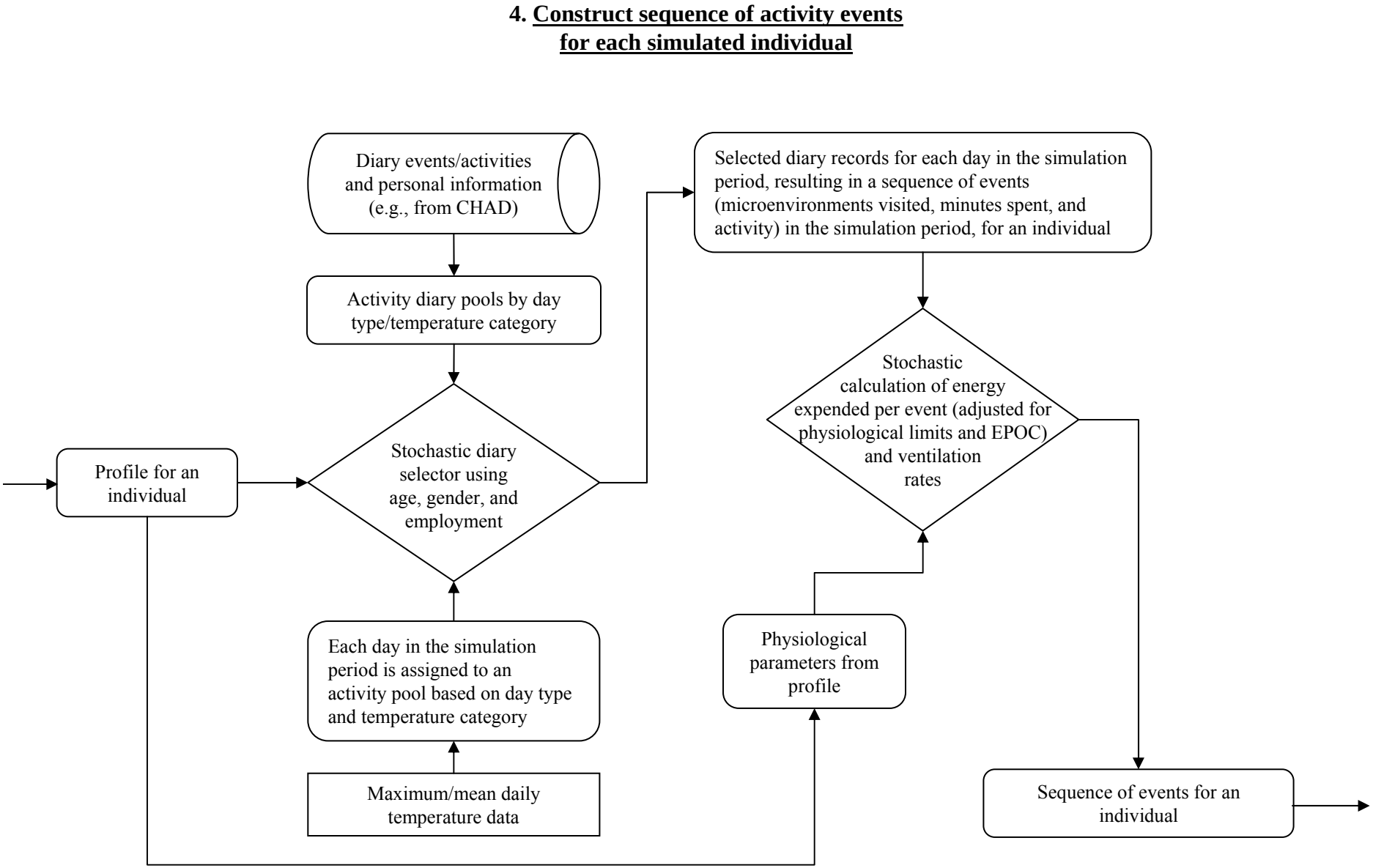
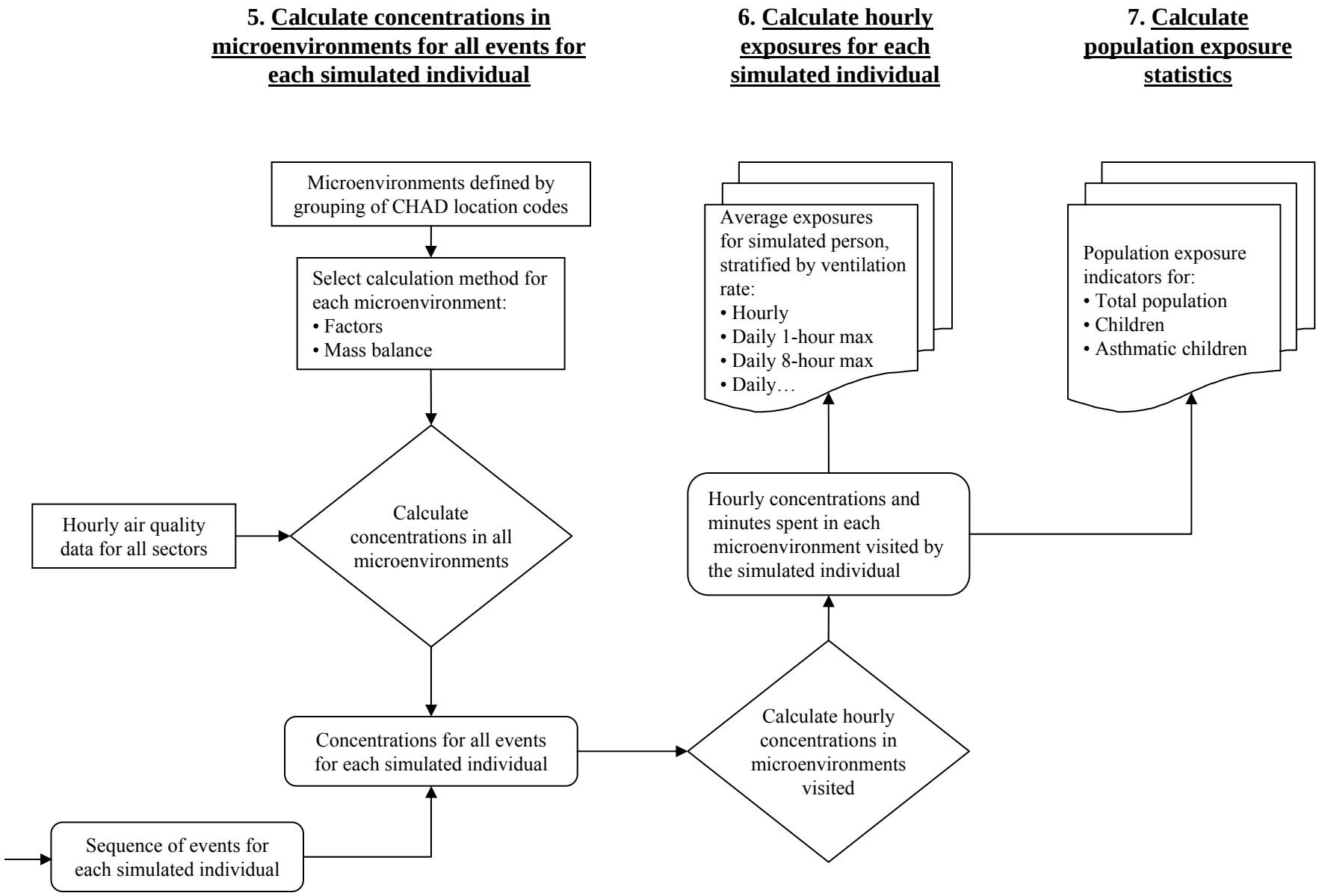


**Figure 4-1. Overview of the APEX Model, concluded**



### 4.3.2 Key Algorithms

Ozone concentrations in each microenvironment are estimated using either a mass-balance or transfer factors approach, and the user specifies probability distributions for the parameters that are used in the microenvironment model that reflect the observed variabilities in the parameters. These distributions can depend on the values of other variables calculated in the model or input to APEX. For example, the distribution of AERs in a home, office, or car can depend on the type of heating and air conditioning present, which are also stochastic inputs to the model, as well as the ambient temperature. The user can choose to keep the value of a stochastic parameter constant for the entire simulation (which would be appropriate for the volume of a house), or can specify that a new value shall be drawn hourly, daily, or seasonally from specified distributions. APEX also allows the user to specify diurnal, weekly, or seasonal patterns for various microenvironmental parameters. The distributions of parameters input to APEX characterize the variability of parameter values, and are not intended to reflect uncertainties in the parameter estimates.

The mass balance method used within APEX assumes that the air in an enclosed microenvironment is well-mixed and that the air concentration is fairly spatially uniform at a given time within the microenvironment. The following four processes are modeled to predict the concentration of an air pollutant in such a microenvironment:

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

The transfer factors model is simpler than the mass balance model, however, still most parameters are derived from distributions rather than single values, to account for observed variability. It does not calculate concentration in a microenvironment from the concentration in the previous hour and it has only two parameters, a proximity factor, used to account for proximity of the microenvironment to sources or sinks of pollution, or other systematic differences between concentrations just outside the microenvironment and the ambient concentrations (at the measurements site), and a penetration factor, which quantifies the degree to which the outdoor air penetrates into the microenvironment and is essentially the ratio of the concentration in the microenvironment to the outdoor concentration.

Regardless of the method used to estimate the microenvironmental concentrations, APEX calculates a time series of exposure concentrations that a simulated individual experiences during the modeled time period. APEX estimates the exposure using the concentrations calculated for each microenvironment and the time spent in each of a sequence of microenvironments visited

according to the "activity diary" of each individual. The hourly average exposures of each simulated individual are time-weighted averages of the within-hour exposures. From hourly exposures, APEX calculates the time series of 8-hr and daily average exposures that simulated individuals experience during the simulation period. APEX then statistically summarizes and tabulates the hourly, 8-hr, and daily exposures.

### 4.3.3 Model Output

There are several useful indicators of exposure and intake of people to $O_3$ air pollution. Factors that are important include the magnitude and duration of exposure, frequency of repeated high exposures, and the breathing rate of individuals at the time of exposure. In this analysis, exposure indicators include daily maximum 1-hr and 8-hr average $O_3$ exposures, stratified by a measure of the level of exertion at the time of exposure. The level of exertion of individuals engaged in particular activities is measured by an equivalent ventilation rate (EVR), ventilation normalized by body surface area (BSA), which is calculated as Ve/BSA, where Ve is the ventilation rate. Table 4-1 lists the ranges of EVR corresponding to "moderate" and "heavy" levels of exertion.

**Table 4-1. Exertion levels in terms of equivalent ventilation rates (liters/min-$m^2$)**

| Averaging time | Moderate exertion | Heavy exertion |
|---|---|---|
| 1 hour | 16-30 EVR | ≥ 30 EVR |
| 8-hr | 13-27 EVR | ≥ 27 EVR |

from Whitfield et al., 1996, page 15.

APEX calculates two general types of exposure estimates: counts of the estimated number of people exposed to a specified $O_3$ concentration level and the number of times per $O_3$ season that they are so exposed; the latter metric is in terms of "person-occurrences." The former highlights the number of individuals exposed *one or more* times per $O_3$ season to the exposure indicator of interest. In the case where the exposure indicator is a benchmark concentration level, the model estimates the number of people who are expected to experience exposures to that level of air pollution, or higher, at least once during the modeled period. APEX also reports counts of individuals with multiple exposures. The person-occurrences measure estimates the number of times per season that individuals are exposed to the exposure indicator of interest and then accumulates these estimates for the entire population residing in an area. This metric conflates people and occurrences: one occurrence for each of 10 people is counted the same as 10 occurrences for one person.

APEX tabulates and displays the two measures for exposures above levels ranging from 0 to 0.16 ppm by 0.01 ppm increments, where the exposures are:

- Daily maximum 1-hr average exposures
- Daily maximum 8-hr average exposures
- Daily average exposures.

These results are tabulated for the following population groups:

- All ages and activity levels
- Children at all activity levels
- Active people of all ages
- Active children
- Asthmatic children.

Separate output tables are produced for different levels of exertion concomitant with the exposures:

- All exertion levels
- Moderate exertion levels
- Heavy exertion levels.

APEX also produces tables of the time spent in different microenvironments, stratified by exposure levels.

### 4.3.4 Limitations of the Model

APEX has a strong scientific foundation and incorporates several significant algorithmic improvements and updates to input data since it's predecessor, pNEM, was used in the last review. However, significant uncertainties in the predictions of APEX remain.

In the future, we expect to have better tools and data for characterizing personal exposure to $O_3$ and other pollutants and integrating these with controlled human exposure health studies and with epidemiological analyses. Important research needs to reduce uncertainties associated with the current $O_3$ exposure analysis include conducting studies to provide better information for refining methods for assessing exposure to $O_3$ as well as other pollutants. E.g., activity diaries for sensitive groups; distributions of short-term $O_3$ concentrations near roadways and inside homes (as a function of influential covariates). There is also a need for personal exposure monitors with shorter averaging times and lower detection limits. The most pressing need at this time is for evaluation of existing exposure models and specific algorithms which make up these models. This would greatly improve our understanding of how well current models perform and aid in prioritizing future data collection and model development efforts.

In this section we discuss qualitatively some of the limitations of this application of APEX to model population exposures to $O_3$ pollution. We divide our discussion of the limitations of APEX into four areas: estimation of ambient air quality, estimation of

concentrations in microenvironments, characterization of population demographics and activity patterns, and modeling physiological processes. In general, limitations and uncertainties result from variability not modeled or modeled incorrectly, erroneous or uncertain inputs, errors in coding, simplifications of physical, chemical, and biological processes to form the conceptual model, and flaws in the conceptual model. We restrict the discussion here to limitations of the modeling of variability and the quality of input data. The implications of these limitations for the uncertainty of the APEX results is discussed in Langstaff (2006).

#### 4.3.4.1 Estimation of Ambient Air Quality

For estimating ambient $O_3$ concentrations to use in the exposure model, the urban areas modeled have several monitors measuring hourly $O_3$ concentrations. The primary uncertainties in the air quality data input to the model result from errors in estimating concentrations at locations which are not close to monitoring sites (spatial interpolation) and from the estimation of missing data. Concentrations of $O_3$ near roadways are particularly difficult to estimate due to the rapid reaction of $O_3$ with $NO_x$ emitted from motor vehicles.

If a single $O_3$ season is modeled, another source of uncertainty results from the year-to-year variability of $O_3$ concentrations. We have modeled the year 2004, the most recent year with air quality and meteorological data. For most of the 12 areas modeled, $O_3$ concentrations were lower than previous years, due to a combination of reduced emissions of precursors and weather patterns less conducive to the formation of $O_3$. Therefore, we also modeled the year 2002, to account for year-to-year variability of air quality and meteorology.

Modeling exposures for an unspecified future year simulated to just meet alternative air quality standards has, in addition to the uncertainties involved with modeling historical scenarios, the uncertainties of the complex process of projecting to future years air quality, population demographics, activity patterns, and other changing parameters. For the purpose of estimating population exposure as an input to decisions about the appropriate level of a NAAQS, EPA has historically not incorporated any projections in population demographics, activity patterns, or other factors (e.g., air conditioning use, changes in housing types, etc). This allows policy makers to focus on the impact of changing the allowed air quality distribution on population exposure and public health while avoiding the additional uncertainties that inclusion of these other factors would introduce.

#### 4.3.4.2 Estimation of Concentrations in Indoor Microenvironments

The importance of estimation of concentrations in indoor microenvironments (homes, offices, schools, restaurants, vehicles, etc.) is underscored by the finding that personal exposure

measurements of $O_3$ are often not well-correlated with ambient measurements (CD, pages 3-59 to 3-61).

The microenvironmental characteristics used to model the concentrations in microenvironments tend to be highly variable, both between microenvironments (e.g., different houses have varying characteristics) and within microenvironments (e.g., the characteristics of a given house can vary over time). Since APEX is a probabilistic model, if data accurately characterizing this variability could be provided to the model, such variabilities would not result in uncertainties. However, input data are always a limiting factor. In addition to accurately characterizing the distributions of each individual microenvironmental parameter, we also need to account for the relationships between the different parameters, as well as the relationships between the microenvironmental parameters, human activities, physiology, and other components of the exposure model.

#### 4.3.4.3 Air Exchange Processes

The AER is the single most important factor in determining the ratio of outdoor to indoor concentrations of $O_3$. AERs are highly variable, both within a microenvironment over time and between microenvironments of the same type. AERs depend on the physical characteristics of a microenvironment and also on the behavior of the occupants of the microenvironment. There is also some dependence on the atmospheric conditions. APEX uses probabilistic distributions of AERs which were derived from several measurement studies in a number of locations, thought to be sufficient to adequately characterize AERs for this analysis (see Appendix A of the draft Exposure Analysis TSD).

#### 4.3.4.4 Deposition Processes

The rate of deposition of $O_3$ to a surface depends on the material the surface is made of, the humidity, and the concentration of $O_3$. The rate of removal of $O_3$ from a microenvironment depends on the dimensions, the ratio of surface area to volume, surface coverings, and furnishings in the microenvironment. Deposition is modeled in APEX by a distribution of decay rates based on a study which measured decay rates in 26 homes in Southern California (Lee et al., 1999). Although we do not expect inter-city differences in decay rates to be more important than differences between homes within cities, there is some uncertainty associated with the small sample size of this study. We do not expect this to be a major contributor to the uncertainty of the modeling results. There can be additional $O_3$ loss, which is not currently modeled, due to the use of HVAC systems, which significantly increase the effective surface area as air recirculates through ductwork and filters.

#### 4.3.4.5 Chemical Reaction Processes

Ozone reacts with a number of indoor pollutants, such as $NO_x$ from gas stoves and VOCs from consumer products. However, $O_3$ reacts slowly with most indoor pollutants, and this is typically a less influential removal process than air exchange and surface removal (Weschler, 2000). The lack of a better treatment of indoor air chemistry is not considered to be a significant limitation of APEX for modeling $O_3$, until we have sufficient information characterizing intermittent personal activities such as using terpene-containing cleaners or cooking with a gas stove (which have the potential to significantly modify short-term $O_3$ exposures) to allow them to be modeled.

#### 4.3.4.6 Characterization of Population Demographics and Activity Patterns

In addition to the uncertainty inherent in the human activity data input to APEX, there are a number of population characteristics or attributes that contribute to the variability of exposures which are modeled in APEX, but for which the assignment to simulated individuals is not entirely reflective of the modeled population:

- Occupational category
- Longitudinal stability in occupation, exercise levels, and leisure activities
- Geographical locations of activities away from the home
- The specific microenvironments visited away from home
- Representativeness of CHAD diaries (numbers of diaries used (20,000 used to represent several million people over long periods of time), age of diaries (some are more than 20 years old), diary structure differences, etc.)

In addition, the extent to which the human activity database provides a balanced representation of the population being modeled is likely to vary across areas. Although the algorithm that constructs activity sequences accounts to some extent for the effects of population demographics and local climate on activity, this adjustment procedure is unlikely to fully account for all intercity differences in people's activities. Our choice of parameters for the new procedure for constructing multi-day activity patterns is based on very limited longitudinal activity data on children only (discussed in Section 4.5.3). Thus, there remains considerable uncertainty due to the uncertainty about within-person variance and between-person variance in key variables (e.g., time spent outdoors). Activity patterns are likely to be affected by many local factors, including topography, land use, traffic patterns, mass transit systems, and recreational opportunities.

#### 4.3.4.7 Modeling Physiological Processes

The modeling of physiological processes that are relevant to the exposure and intake of $O_3$ is a complicated endeavor. APEX currently uses a built-in physiological model to simulate activity-specific ventilation rate ($V_E$) which primarily drives $O_3$ intake dose rates. See Section 2.5 of the draft Exposure Assessment TSD for a discussion of this model. These $V_E$ estimates, when normalized by BSA, are used to characterize exertion in compiling the summary exposure tables. In addition, the physiological model is used to develop a daily-averaged indicator of each child's Physical Activity Index (PAI), which itself is used to characterize the simulated children as sedentary, moderately active, and active (McCurdy 2000).

There is uncertainty in using PAI values derived from the CHAD database of human activities for this classification purpose. Using the CHAD database to classify children as being sedentary, moderately active, and active is problematic due mostly to the manner in which the daily activity diaries were constructed. A child, or her or his caregiver if younger than eight years old, would code an activity being undertaken with a start and end time, with no relationship to the exertion level involved with the activity. Exertion level, as MET (metabolic equivalent), was inferred by developers of the CHAD database using standard values and distributions of those values reported in the "Compendium of physical activities" developed by a expert panel of exercise physiologists (Ainsworth et al., 1993). The process used by the CHAD developers to assign MET distributions to activities in the database is described in McCurdy et al. (2000). While care was used to apply the proper exertion levels to the coded activities, for children their activity levels fluctuate widely within a single activity category; their pattern is often characterized as having "bursts" of high energy expenditure movement within a longer time frame of less energy expenditure (Freedson, 1989). This behavior is not well captured by the MET assignment procedure since the diary data cannot distinguish between different activity levels within a single event (i.e., the same activity occurring within one location).

When activity-specific MET values are averaged over a day, the resultant is the child's PAI value for the simulated day. This is equivalent to total daily energy expenditure in a day divided by the child's basal, or resting, metabolic rate. PAI is the metric used by exercise physiologists and clinical nutritionists to define inactive/active children, where a PAI>1.75 is considered to be an active child (see McCurdy 2000 for a discussion of this metric). Children having a PAI value lower than that are considered to be sedentary or "low active." Children >2.00 are considered to be (very) active. We use the 1.75 criterion as an indicator of an active child.

The uncertainty of the MET values carries over to the uncertainty of the modeled ventilation rates. The ventilation rates are important, since they are used to characterize exertion levels in the clinical studies of responses of exposure to ozone, and consequently we use them to classify exposures of potentially greater risk. The classification of children as active is used to evaluate

whether a larger percentage of this subgroup of children is likely to experience more occurrences of exposures of concern at moderate or greater exertion. However, there is no evidence that an active child is at higher risk than an inactive child for any given exposure to $O_3$ at the same high level of exertion.

## 4.4 SCOPE OF EXPOSURE ASSESSMENT

### 4.4.1 Selection of Urban Areas to be Modeled

The selection of urban areas to include in the exposure analysis takes into consideration the location of $O_3$ epidemiological studies, the availability of ambient $O_3$ data, and the desire to represent a range of geographic areas, population demographics, and $O_3$ climatology. These selection criteria are discussed further in Chapter 5. Based on these criteria, we chose the 12 urban areas listed in Table 4-2 to develop population exposure estimates.[2] The geographic extent of each modeled area consists of the census tracts in the combined statistical area (CSA) as defined by OMB (OMB, 2005).

### 4.4.2 Time Periods Modeled

The exposure periods modeled are the $O_3$ seasons for which routine hourly $O_3$ monitoring data are available. The time periods modeled for both 2002 and 2004 for each area are listed in Table 4-2.

**Table 4-2. Urban areas and time periods modeled**

| Urban Area (CSA) | Period modeled |
|---|---|
| **Atlanta**-Sandy Springs-Gainesville, GA-AL | March 1 to Oct. 31 |
| **Boston**-Worcester-Manchester, MA-NH | April 1 to Sept. 30 |
| **Chicago**-Naperville-Michigan City, IL-IN-WI | April 1 to Sept. 30 |
| **Cleveland**-Akron-Elyria, OH | April 1 to Oct. 31 |
| **Detroit**-Warren-Flint, MI | April 1 to Sept. 30 |
| **Houston**-Baytown-Huntsville, TX | Jan. 1 to Dec. 30 |
| **Los Angeles**-Long Beach-Riverside, CA | Jan. 1 to Dec. 30 |
| **New York**-Newark-Bridgeport, NY-NJ-CT-PA | April 1 to Sept. 30 |
| **Philadelphia**-Camden-Vineland, PA-NJ-DE-MD | April 1 to Oct. 31 |
| **Sacramento**--Arden-Arcade--Truckee, CA-NV | Jan. 1 to Dec. 30 |
| **St. Louis**-St. Charles-Farmington, MO-IL | April 1 to Oct. 31 |
| **Washington**-Baltimore-N. Virginia, **DC**-MD-VA-WV | April 1 to Oct. 31 |

[2] In the remainder of this chapter the city name in bold in Table 4-2 is used to represent the entire CSA.

### 4.4.3 Populations Modeled

Exposure modeling is conducted for the general population residing in each area modeled, as well as for school-age children (ages 5 to 18), active school-age children, and asthmatic school-age children. Due to the increased amount of time spent outdoors engaged in relatively high levels of physical activity (which increases intake), school-age children as a group are particularly at risk for experiencing $O_3$-related health effects. We report results for school-age children down to age five, but there is a trend for younger children to attend school. Some states allow 4-year-olds to attend kindergarten, and more than 40 states have preschool programs for children younger than five (Blank and Mitchell, 2001). In 2000, six percent of U.S. children ages 3 to 19 who attend school were younger than five years old (2000 Census Summary File 3, Table QT-P19: School Enrollment).

Levels of physical activity are categorized by a daily physical activity index (PAI), a time integrated measure of METS (discussed in section 4.3.1 above). Children are characterized as active if their median daily PAI over the period modeled is greater than 1.75, a level characterized by exercise physiologists as being "moderately active" (McCurdy, 2000). With this particular definition of "active," about 45 percent of the children are classified as active.

The populations of asthmatic children are calculated using asthma prevalence data from the National Health Interview Survey (NHIS) for 2003 (Dey and Bloom, 2005). Asthma prevalence rates for children aged 0 to 17 years were calculated for each age, gender, and region. The regions defined by NHIS are "Midwest," "Northeast," "South," and "West." For this analysis, asthma prevalence was defined as the probability of a "Yes" response to the question: "Ever been told that … had asthma?" among those that responded "Yes" or "No" to this question. The responses were weighted to take into account the complex survey design of the NHIS survey. Standard errors and confidence intervals for the prevalence were calculated using a logistic model, taking into account the survey design. A scatter plot smoothing technique using the LOESS smoother was applied to smooth the prevalence curves and compute the standard errors and confidence intervals for the smoothed prevalence estimates. Logistic analysis of the prevalence curves shows statistically significant differences in prevalence by gender and by region. Therefore we did not combine the prevalence rates for different genders or regions. A detailed description of this analysis is presented in the draft Exposure Analysis TSD.

Table 4-3 lists the year 2000 populations of the modeled areas. The 12 modeled areas combined represent 40 percent of the total U.S. urban population (approximately 222 million in 2000).

**Table 4-3. Population coverage of modeled areas (2002 analysis)**

| Urban Area (CSA) | Modeled population (thousands) | Modeled children[1] (thousands) | Active children[2] (thousands) | Asthmatic children (thousands) |
|---|---|---|---|---|
| Atlanta | 4,548 | 943 | 446 | 117 |
| Boston | 5,714 | 1,096 | 475 | 182 |
| Chicago | 9,311 | 1,951 | 850 | 279 |
| Cleveland | 2,945 | 594 | 244 | 279 |
| Detroit | 5,357 | 1,110 | 479 | 162 |
| Houston | 4,815 | 1,089 | 476 | 136 |
| Los Angeles | 16,371 | 3,667 | 1,632 | 457 |
| New York | 21,357 | 4,147 | 1,808 | 643 |
| Philadelphia | 5,832 | 1,186 | 532 | 193 |
| Sacramento | 1,930 | 412 | 151 | 51 |
| St. Louis | 2,754 | 582 | 268 | 83 |
| Washington, DC | 7,572 | 1,485 | 682 | 187 |
| Population in all 12 areas | 88,506 | 18,262 | 8,043 | 2769 |

[1] ages 5-18. [2] PAI > 1.75

## 4.5 INPUTS TO THE EXPOSURE MODEL

The data inputs to the APEX model are briefly described in this section. A more detailed description of the development of these data and the derivation of input distributions can be found in the draft Exposure Analysis TSD.

### 4.5.1 Population Demographics

APEX takes population characteristics into account to develop accurate representations of study area demographics. Population counts and employment probabilities by age and gender are used to develop representative profiles of hypothetical individuals for the simulation. Tract-level population counts by age in one-year increments, from birth to 99 years, come from the 2000 Census of Population and Housing Summary File 1. The Summary File 1 contains the 100-percent data, which is the information compiled from the questions asked of all people and about every housing unit.

Employment data from the 2000 Census provide employment probabilities for each gender and specific age groups for every Census tract. The employment age groupings are: 16-19, 20-21,

22-24, 25-29, 30-34, 35-44, 45-54, 55-59, 60-61, 62-64, 65-69, 70-74, and >75 years of age. Children under the age of 16 are assigned employment probabilities of zero.

### 4.5.2 Population Commuting Patterns

To ensure that individual's daily activities are accurately represented within APEX, it is important to integrate working patterns into the assessment. The APEX commuting data are derived from the 2000 Census and collected as part of the Census Transportation Planning Package (CTPP). CTPP contains tabulations by place of residence, place of work, and the flows between the residence and work. These data are available from the U.S. Department of Transportation, Bureau of Transportation Statistics (U.S. Department of Transportation and U.S. Census Bureau, 2000).

For school age children we have not included commuting to and from school. We are assuming that children attend a school in the same census tract as their residence. To the extent that the highest ozone levels are generally in the period June through August when most students are not in school, the absence of school commuting is less likely to have a significant impact on the exposure estimates.

It was assumed that all persons with home-to-work distances up to 120 km are daily commuters, and that persons who travel further than 120 km do not commute daily. Therefore the list of commuting destinations for each home tract is restricted to only those work tracts that are within 120 km of the home tract.

APEX allows the user to specify how to handle individuals who commute to destinations outside the study area. One option is to drop them from the simulation. If they are included, the user specifies values for two additional parameters, called $L_M$ and $L_A$ (Multiplicative and Additive factors for commuters who Leave the area). While a commuter is at work, if the workplace is outside the study area, then the ambient concentration cannot be determined from any air district (since districts are inside the study area). Instead, it is assumed to be related to the average concentration $C_{AVE}(t)$ over all air districts at the time in question. The ambient concentration outside the study area at time $t$, $C_{OUT}(t)$, is estimated as:

$$C_{OUT}(t) = L_M * C_{AVE}(t) + L_A \qquad (4\text{-}2)$$

The microenvironmental concentration (for example, in an office outside the study area) is determined from this ambient concentration by the same model (mass balance or factor) as applies inside the study area. The parameters $L_M$ and $L_A$ were both set to zero for this modeling analysis; thus, exposures to individuals are set to zero when they are outside of the study area. This was done since we have not estimated ambient concentrations of $O_3$ in counties outside of the modeled areas.

### 4.5.3 Human Activity Data

The human activity data are drawn from the most recent version (December 2000) of the Consolidated Human Activity Database (CHAD) (McCurdy et al., 2000; EPA, 2002), developed

and maintained by the Office of Research and Development's (ORD) National Exposure Research Laboratory (NERL). The CHAD includes data from several surveys covering specific time periods at city, state, and national levels, with varying degrees of representativeness. Table 4-4 summarizes the studies in CHAD used in this modeling analysis, providing almost 16,000 diary-days of activity data (3,075 diary-days for ages 5-18) collected between 1982 and 1998.

A key issue in this assessment is the development of an approach for creating $O_3$-season or year-long activity sequences for individuals based on a cross-sectional activity data base of 24-hour records. The average subject in the time/activity studies in CHAD provided less than two days of diary data. For this reason, the construction of a season-long activity sequence for each individual requires some combination of repeating the same data from one subject and using data from multiple subjects. An appropriate approach should adequately account for the day-to-day and week-to-week repetition of activities common to individuals while maintaining realistic variability between individuals. The method in APEX for creating longitudinal diaries captures the tendency of individuals to repeat activities, based on reproducing realistic variation in a key diary variable, which is a user-selected function of diary variables. For this analysis the key variable is set to the amount of time an individual spends outdoors each day, which is one of the more important determinants of exposure to $O_3$.

The actual diary construction method targets two statistics, a population diversity statistic (***D***) and a within-person autocorrelation statistic (***A***). The ***D*** statistic reflects the relative importance of within-person variance and between-person variance in the key variable. The ***A*** statistic quantifies the lag-one (day-to-day) key variable autocorrelation. Desired ***D*** and ***A*** values for the key variable are selected by the user and set in the APEX parameters file, and the method algorithm constructs longitudinal diaries that preserve these parameters. Longitudinal diary data from a field study of school-age children (Geyh et al., 2000) and subsequent analyses (Xue et al., 2004) suggest that ***D*** and ***A*** are stable over time (and perhaps over cohorts as well). Based on these studies, appropriate target values for the two statistics for outdoor time for children are determined to be 0.2 for ***D*** and 0.2 for ***A***. In the absence of data for estimating these statistics for younger children and for adults, these values are also used for adults. This new method for constructing longitudinal diaries from the CHAD data is described in detail in the draft Exposure Analysis TSD.

**Table 4-4. Studies in CHAD Used in This Analysis**

| Study name | Geographic coverage | Study time period | Subject ages | Diary-days | Diary-days (ages 5-18) | Diary type and study design | Reference |
|---|---|---|---|---|---|---|---|
| Baltimore | One building in Baltimore | 01/1997-02/1997, 07/1998-08/1998 | 72-93 | 292 | 0 | Diary | Williams et al, 2000 |
| California Adolescents (CARB) | California | 10/1987-09/1988 | 12-17 | 181 | 181 | Recall; Random | Robinson et al. (1989), Wiley et al. (1991a) |
| California Adults (CARB) | California | 10/1987-09/1988 | 18-94 | 1,552 | 36 | Recall; Random | Robinson et al. (1989), Wiley et al. (1991a) |
| California Children (CARB) | California | 04/1989- 02/1990 | 0-11 | 1,200 | 683 | Recall; Random | Wiley et al. (1991b) |
| Cincinnati (EPRI) | Cincinnati metro. area | 03/1985-04/1985, 08/1985 | 0-86 | 2,587 | 740 | Diary; Random | Johnson (1989) |
| Denver (EPA) | Denver metro. area | 11/1982- 02/1983 | 18-70 | 791 | 7 | Diary; Random | Johnson (1984), Akland et al. (1985) |
| Los Angeles: Elementary School | Los Angeles | 10/1989 | 10-12 | 51 | 51 | Diary | Spier et al. (1992) |
| Los Angeles: High School | Los Angeles | 09/1990-10/1990 | 13-17 | 42 | 42 | Diary | Spier et al. (1992) |
| National: NHAPS-Air | National | 09/1992-10/1994 | 0-93 | 4,326 | 634 | Recall; Random | Klepeis et al. (1996), Tsang and Klepeis (1996) |
| National: NHAPS-Water | National | 09/1992-10/1994 | 0-93 | 4,332 | 691 | Recall; Random | Klepeis et al. (1996), Tsang and Klepeis (1996) |
| Washington, D.C. (EPA) | Wash., D.C. metro. area | 11/1982-02/1983 | 18-98 | 639 | 10 | Diary; Random | Hartwell et al. (1984), Akland et al. (1985) |

### 4.5.4 Physiological Data

APEX requires values for various physiological parameters for subjects in order to accurately model their metabolic processes that affect pollutant intake. This is because physiological differences may cause people with the same exposure and activity scenarios to have different pollutant intake levels. The physiological parameters file distributed with APEX contains physiological data or distributions by age and gender for maximum ventilatory capacity (in terms of age- and gender-specific maximum oxygen consumption potential), body mass, resting metabolic rate, and oxygen consumption-to-ventilation rate relationships.

### 4.5.5 Microenvironments Modeled

In APEX, microenvironments provide the exposure locations for modeled individuals. For exposures to be measured accurately, it is important to have realistic microenvironments that are matched closely to where people are physically located on a daily basis. As discussed in Section 4.3.2 above, the two methods available in APEX for calculating pollutant concentrations within microenvironments are a mass balance model and a transfer factor approach. Table 4-5 lists the 12 microenvironments selected for this analysis and the exposure calculation method for each. The parameters used in this analysis for modeling these microenvironments are described in this section.

**Table 4-5. Microenvironments Modeled**

| Microenvironment | Calculation Method | Parameters[1] |
|---|---|---|
| Indoors – Residence | Mass balance | AER and DE |
| Indoors – Bars and restaurants | Mass balance | AER and DE |
| Indoors – Schools | Mass balance | AER and DE |
| Indoors – Day-care centers | Mass balance | AER and DE |
| Indoors – Office | Mass balance | AER and DE |
| Indoors – Shopping | Mass balance | AER and DE |
| Indoors – Other | Mass balance | AER and DE |
| Outdoors – Near road | Factors | PR |
| Outdoors – Public garage/parking lot | Factors | PR |
| Outdoors – Other | Factors | None |
| In-vehicle – Cars and Trucks | Factors | PE and PR |

[1] AER=air exchange rate, DE=decay-deposition rate, PR=proximity factor, PE=penetration factor

#### 4.5.5.1 Air Exchange Rates for Indoor Residential Environments

Distributions of AERs for the indoor microenvironments were developed using data from several studies. The analysis of these data and the development of the distributions used in the modeling is described in detail in the draft Exposure Analysis TSD. This analysis showed that the AER distributions for the residential microenvironments depend on the type of air conditioning (A/C) and on the outdoor temperature, as well as other variables for which we do not have sufficient data to estimate. This analysis clearly demonstrates that the AER distributions vary greatly across cities and A/C types and temperatures, so that the selected AER distributions for the modeled cities should also depend upon the city, A/C type, and temperature. For example, the mean AER for residences with A/C ranges from 0.39 for Los Angeles between 30 and 40 ºC to 1.73 for New York between 20 and 25 ºC. The mean AER for residences without A/C ranges from 0.46 for San Francisco on days with temperature between 10 and 20 ºC to 2.29 for New York on days with temperature between 20 and 25 ºC. The need to account for the city as well as the A/C type and temperature is illustrated by the result that for residences with A/C on days with temperature between 20 and 25 ºC, the mean AER ranges from 0.52 for Research Triangle Park to 1.73 for New York. For each combination of A/C type, city, and temperature with a minimum of 11 AER values, exponential, lognormal, normal, and Weibull distributions were fit to the AER values and compared. Generally, the lognormal distribution was the best-fitting of the four distributions, and so, for consistency, the fitted lognormal distributions are used for all the cases.

One limitation of this analysis was that distributions were available only for selected cities, and yet the summary statistics and comparisons demonstrate that the AER distributions depend upon the city as well as the temperature range and A/C type. Another important limitation of the analysis was that distributions were not able to be fitted to all of the temperature ranges due to inadequate data. A description of how these limitations were addressed can be found in the draft Exposure Analysis TSD.

City-specific AER distributions were used where possible; otherwise data for a similar city were used. We obtained estimates of A/C prevalence from the American Housing Survey (AHS, 2003) for each metropolitan area. The final AER distributions used for the exposure modeling are given the draft Exposure Analysis TSD.

Some residences, particularly in the Southwest, use evaporative coolers, also known as "swamp coolers," for cooling. We performed an analysis of AER distributions of residences without A/C, with and without evaporative coolers, using data from three AER measurement studies. This comparison is described in Appendix F in the draft Exposure Analysis TSD. This analysis showed no improvement in the statistical air exchange model when the data were also

stratified by evaporative cooler presence or absence, given that they are already stratified by CSA, air conditioner presence or absence, and outdoor temperature range.

#### 4.5.5.2 AER Distributions for Other Indoor Environments

To estimate AER distributions for non-residential, indoor environments (e.g., offices and schools), we obtained and analyzed two AER data sets: "Turk" (Turk et al., 1989); and "Persily" (Persily and Gorfain, 2004; Persily et al., 2005). The earlier "Turk" data set (Turk et al., 1989) includes 40 AER measurements from offices (25 values), schools (7 values), libraries (3 values), and multi-purpose buldings (5 values), each measured using an $SF_6$ tracer over two or four hours in different seasons of the year. The more recent "Persily" data (Persily and Gorfain, 2004; Persily et al., 2005) were derived from the U.S. EPA Building Assessment Survey and Evaluation (BASE) study, which was conducted to assess indoor air quality, including ventilation, in a large number of randomly selected office buildings throughout the U.S. This data base consists of a total of 390 AER measurements in 96 large, mechanically ventilated offices; each office was measured up to four times over two days, Wednesday and Thursday, AM and PM. The office spaces were relatively large, with at least 25 occupants, and preferably 50 to 60 occupants. AERs were measured both by a volumetric method and by a $CO_2$ ratio method, and included their uncertainty estimates. For these analyses, we used the recommended "Best Estimates" defined by the values with the lower estimated uncertainty; in the vast majority of cases the best estimate was from the volumetric method.

Due to the small sample size of the Turk data, the data were analyzed without stratification by building type and/or season. For the Persily data, the AER values for each office space were averaged, rather using the individual measurements, to account for the strong dependence of the AER measurements for the same office space over a relatively short period. The mean values are similar for the two studies, but the standard deviations are about twice as high for the Persily data. The proposed AER distributions were derived from the more recent Persily data only.

We fitted exponential, lognormal, normal, and Weibull distributions to the 96 office space average AER values, and the best fitting of these was the lognormal. The fitted parameters for this distribution, used for AER distributions for the indoor, non-residential microenvironments, can be found in the draft Exposure Analysis TSD.

#### 4.5.5.3 Proximity and Penetration Factors For Outdoors and In-vehicle

For the outdoors near-road, public garage/parking lot, and in-vehicle proximity factors, and for the in-vehicle penetration factors, we use distributions developed from the Cincinnati Ozone Study (American Petroleum Institute, 1997, Appendix B; Johnson et al., 1995). This field

study was conducted in the greater Cincinnati metropolitan area in August and September, 1994. Vehicle tests were conducted according to an experimental design specifying the vehicle type, road type, vehicle speed, and ventilation mode. Vehicle types were defined by the three study vehicles: a minivan, a full-size car, and a compact car. Road types were interstate highways (interstate), principal urban arterial roads (urban), and local roads (local). Nominal vehicle speeds (typically met over one minute intervals within 5 mph) were at 35 mph, 45 mph, or 55 mph. Ventilation modes were as follows:

- Vent Open: Air conditioner off. Ventilation fan at medium. Driver's window half open. Other windows closed.
- Normal A/C: Air conditioner at normal. All windows closed.
- Max A/C: Air conditioner at maximum. All windows closed.

Ozone concentrations were measured inside the vehicle, outside the vehicle, and at six fixed-site monitors in the Cincinnati area.

The draft Exposure Analysis TSD documents the distributions and the rationale for the selection of distributions of penetration and proximity factors for outdoors and in-vehicle microenvironments used in this modeling analysis.

#### 4.5.5.4 Ozone Decay and Deposition Rates

A distribution for combined $O_3$ decay and deposition rates was obtained from the analysis of measurements from a study by Lee et al. (1999). This study measured decay rates in the living rooms of 43 residences in Southern California. Measurements of decay rates in a second room were made in 24 of these residences. The 67 decay rates range from 0.95 to 8.05 $hour^{-1}$. A lognormal distribution was fit to the measurements from this study, yielding a geometric mean of 2.5 and a geometric standard deviation of 1.5. This distribution is used for all indoor microenvironments.

### 4.5.6 Meteorological Data

Daily average and maximum 1-hr temperatures are computed from hourly surface temperature measurements obtained from the National Weather Service. APEX uses the data from the closest weather station to each Census tract. Temperatures are used in APEX both in selecting human activity data and in estimating AERs for indoor microenvironments.

### 4.5.7 Ambient Ozone Concentrations

APEX requires hourly ambient $O_3$ concentrations at a set of locations in the study area. Data from EPA's AIRS Air Quality Subsystem were used to prepare the ambient air quality input files for 2002 and 2004. The hourly $O_3$ concentrations at the AIRS sites in each CSA were used as input to APEX to represent the ambient concentrations within each urban area. For near

road and parking garage microenvironments the ambient concentrations are adjusted by proximity factors.

### 4.5.8 Modeling Alternative Standards

In addition to modeling exposures based on historical air quality, an analysis was conducted using air quality representative of just meeting the current 8-hr $O_3$ NAAQS of 0.08 ppm. Seven alternative standards, reflecting different combinations of standard levels and form are also being considered. Two of the alternatives examined are intended to reflect a different rounding convention, where the rounding convention would use three instead of two decimal places (in ppm) (e.g., 0.080 ppm for the current standard level instead of the current rounding convention which uses 0.084 ppm as the highest level that is considered as meeting the current 0.08 ppm standard). Similarly, the alternatives analyzed also include a 0.070 ppm, average 4th daily maximum 8-hr average scenario to reflect this alternative rounding convention. A 3$^{rd}$ high form is considered for 0.08 and 0.07 ppm levels, and a 5$^{th}$ high for the 0.07 level. These alternative scenarios are modeled using a quadratic rollback approach to adjust the hourly $O_3$ concentrations observed in 2002-2004 to yield a design value corresponding to the standard being modeled. Table 4-6 shows the alternative standards, their corresponding attainment thresholds (which the design values are rolled back to), the form of the standard used for each scenario, and the notation used in the remainder of the Staff Paper. Design values for the current 8-hr $O_3$ NAAQS are calculated as the 3-year averages of the annual 4$^{th}$ daily maximum 8-hr average concentration based on the maximum monitor within an urban area. These are given in Table 4-7 for the 2002-2004 period.

The quadratic rollback technique combines both linear and quadratic elements to reduce higher concentrations more than lower concentrations near ambient background levels. The quadratic rollback adjustment procedure was considered in a sensitivity analysis during the last review of the $O_3$ NAAQS and has been shown to be more realistic than the linear proportional rollback method, where all of the ambient measurements are reduced by a constant multiplicative factor regardless of their individual magnitudes. The quadratic rollback approach and evaluation of this approach are described by Johnson (1997), Duff, Horst, and Johnson (1998), and Rizzo (2005, 2006).

**Table 4-6. Alternative 8-hr ozone standard scenarios**

| Alternative Standard | Attain. Threshold | Form of Standard | Notation |
|---|---|---|---|
| 0.08 ppm (rounding[1] to 0.01 ppm) | 0.084 ppm | 3$^{rd}$ daily maximum<br>4$^{th}$ daily maximum | 84/3<br>84/4 |
| 0.08 ppm (rounding to 0.001 ppm) | 0.080 ppm | 4$^{th}$ daily maximum | 80/4 |
| 0.07 ppm (rounding to | 0.074 ppm | 3$^{rd}$ daily maximum | 74/3 |

| | | | |
|---|---|---|---|
| 0.01 ppm) | | 4th daily maximum<br>5th daily maximum | 74/4<br>74/5 |
| 0.07 ppm (rounding to 0.001 ppm) | 0.070 ppm | 4th daily maximum | 70/4 |
| 0.06 ppm (rounding to 0.01 ppm) | 0.064 ppm | 4th daily maximum | 64/4 |

[1] The rounding convention applied here involves truncating the design value to the nearest 0.001 ppm and then rounding according to the first column of this table.

**Table 4-7. 2002-2004 8-hr ozone design values for the modeled areas**

| Urban Area (CSA) | 2002-2004 design value (ppm) | Ratio of 0.084 to the design value |
|---|---|---|
| Atlanta | 0.093 | 0.90 |
| Boston | 0.091 | 0.92 |
| Chicago | 0.094 | 0.89 |
| Cleveland | 0.095 | 0.88 |
| Detroit | 0.092 | 0.91 |
| Houston | 0.101 | 0.83 |
| Los Angeles | 0.127 | 0.66 |
| New York | 0.094 | 0.89 |
| Philadelphia | 0.094 | 0.89 |
| Sacramento | 0.102 | 0.82 |
| St. Louis | 0.089 | 0.94 |
| Washington, DC | 0.089 | 0.94 |

## 4.6 EXPOSURE ASSESSMENT RESULTS

In this section we present results for children exposed to $O_3$ while engaged in moderate or greater exertion. The results of the exposure analysis are presented as graphs of the numbers of persons who experience daily maximum 8-hr average exposures above 0.06, 0.07, and 0.08 ppm-8hr (expressed as percentages of the population), while experiencing moderate or greater levels of exertion during the same 8-hr period that the exposure occurred. Exertion is characterized by breathing rates, as described in Section 4.3.3. The exposure levels of 0.06, 0.07, and 0.08 ppm-8hr are levels at which there is clear evidence of health effects in controlled human exposure

studies for some healthy individuals engaged in moderate exertion over a 6.6 hour period. The Adams (2006) study demonstrated that exposure to 0.06 ppm $O_3$ over a 6.6 hour period caused >10% $FEV_1$ lung function decline in seven percent of the healthy adult subjects, and effects on lung function were seen at concentrations as low as 0.04 ppm (CD, p. 8-18).

The patterns of exposures in each city are similar for the different population groups, so in this chapter we present results only for the group of all children exposed while engaged in moderate or greater exertion. The similarity of patterns for different groups is illustrated in Figures 4-1 and 4-2, which present the same exposure measures for three groups: all children, active children, and asthmatic children.

Table 4-8 presents counts of children (ages 5-18) with one or more 8-hr $O_3$ exposures above 0.07 ppm-8hr, concomitant with moderate or greater exertion, for 2002 air quality scenarios reflecting the current standard and four of the alternative standards considered (the standards with the $4^{th}$ high forms). As discussed in section 3.6.3, multiple exposures pose a greater health concern than single exposures. Table 4-9 gives counts analogous to Table 4-8, but for children with three or more exposures during the $O_3$ season.

Figures 4-3 through 4-20 illustrate the effect of the current and several potential alternative standards on the percentages of children experiencing 1, 2, and 3 or more repeated exposures above 0.08, 0.07, and 0.06 ppm-8hr concomitant with moderate or greater exertion, for each of the cities modeled, based on rollback of 2002 and 2004 $O_3$ concentrations. The notation in these figures for the alternative standards is defined in Table 4-6. These figures are in terms of percents of the children ages 5-18 who have at least one instance of 8-hr moderate or greater exertion at any exposure during the modeled period (total counts are listed in Table 4-8).

Inspection of these figures and Table 4-8 show marked differences between cities in the levels of exposures under alternative standards. For example, under the same 0.074 ppm, $4^{th}$ daily maximum 8-hr average alternative standard, almost 5 percent of the Boston children but less than 0.05 percent of the Los Angeles children experience 8-hr $O_3$ exposures above 0.07 ppm-8hr while engaged in moderate or greater exertion. This is primarily due to the larger range of 2002-2004 $4^{th}$ highest concentrations for Boston compared to Los Angeles, which allows for higher concentrations (and therefore exposures) in Boston.

The draft Exposure Analysis TSD presents additional exposure results, and describes an evaluation of APEX and an analysis of model sensitivity to selected model inputs.

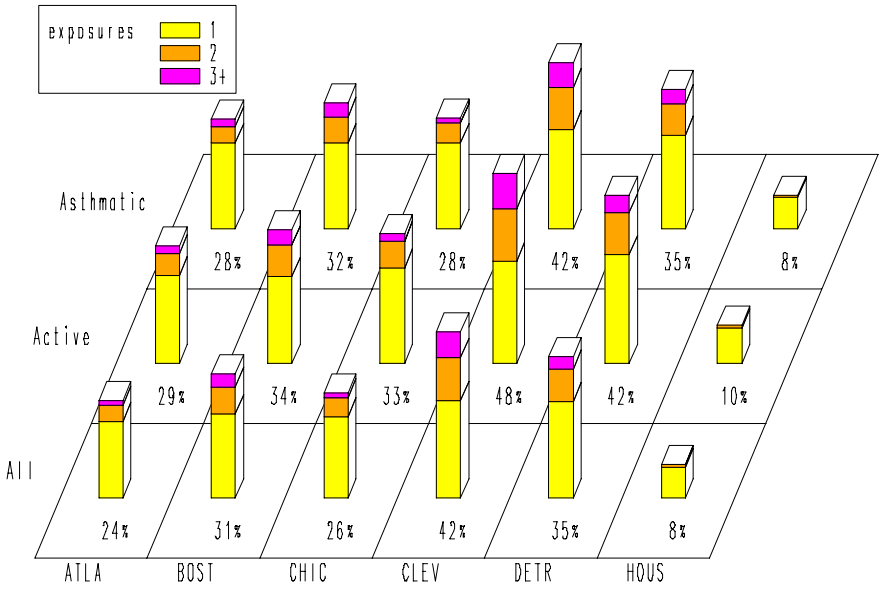



**Figure 4-2. Percent of persons with repeated 8-hr exposures > 0.06 ppm-8hr, for exposures concomitant with moderate or greater exertion, scenario 74/4, for three children groups (Atlanta, Boston, Chicago, Cleveland, Detroit, Houston)**

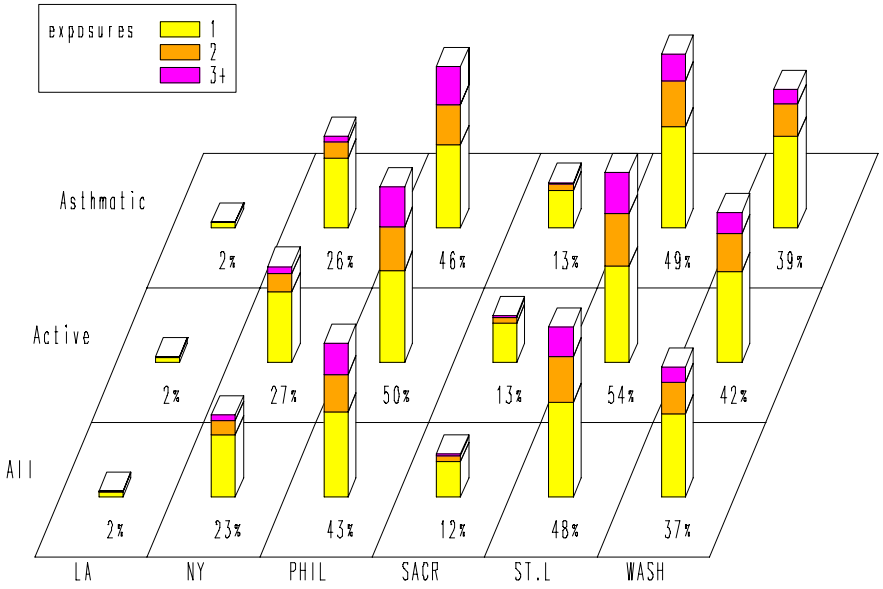



**Figure 4-3. Percent of persons with repeated 8-hr exposures > 0.06 ppm-8hr, for exposures with moderate or greater exertion, scenario 74/4, for three children population groups (Los Angeles, New York, Philadelphia, Sacramento, St. Louis, Washington)**

**Table 4-8. Counts of children (ages 5-18) with one or more 8-hr ozone exposures above 0.07 ppm-8hr, concomitant with moderate or greater exertion, based on 2002 air quality**

| Urban Area (CSA) | Children[1] | 64/4[2] | 70/4 | 74/4 | 80/4 | 84/4 |
|---|---|---|---|---|---|---|
| Atlanta | 908,283 | 0 | 7,352 | 26,681 | 78,830 | 138,785 |
| Boston | 1,054,501 | 9,238 | 50,192 | 94,288 | 190,290 | 263,244 |
| Chicago | 1,872,237 | 776 | 9,000 | 52,295 | 196,767 | 354,119 |
| Cleveland | 572,569 | 785 | 9,130 | 48,499 | 128,121 | 184,180 |
| Detroit | 1,066,088 | 0 | 5,446 | 43,301 | 176,863 | 285,784 |
| Houston | 1,054,811 | 160 | 2,809 | 8,105 | 32,017 | 66,603 |
| Los Angeles | 3,552,553 | 0 | 1,637 | 3,274 | 13,916 | 30,560 |
| New York | 3,976,040 | 3,916 | 24,205 | 97,888 | 321,073 | 580,566 |
| Philadelphia | 1,139,862 | 4,666 | 56,089 | 127,148 | 284,820 | 390,485 |
| Sacramento | 397,487 | 0 | 868 | 3,956 | 14,120 | 27,886 |
| St. Louis | 558,934 | 1,331 | 25,794 | 69,259 | 155,453 | 213,697 |
| Washington | 1,428,891 | 2,398 | 39,120 | 111,934 | 259,580 | 381,988 |

[1] The number of children who have at least one instance of moderate or greater exertion.
[2] This notation for alternative standards is defined in Table 4-6.

**Table 4-9. Counts of children (ages 5-18) with three or more 8-hr ozone exposures above 0.07 ppm-8hr, concomitant with moderate or greater exertion, based on 2002 air quality**

| Urban Area (CSA) | Children[1] | 64/4 | 70/4 | 74/4 | 80/4 | 84/4 |
|---|---|---|---|---|---|---|
| Atlanta | 908,283 | 0 | 0 | 0 | 227 | 2,956 |
| Boston | 1,054,501 | 0 | 286 | 1,143 | 6,191 | 15,810 |
| Chicago | 1,872,237 | 0 | 0 | 155 | 2,173 | 10,087 |
| Cleveland | 572,569 | 0 | 0 | 442 | 5,498 | 15,561 |
| Detroit | 1,066,088 | 0 | 0 | 0 | 2,321 | 11,963 |
| Houston | 1,054,811 | 0 | 0 | 0 | 0 | 0 |
| Los Angeles | 3,552,553 | 0 | 0 | 0 | 0 | 273 |
| New York | 3,976,040 | 0 | 356 | 1,068 | 3,916 | 19,578 |
| Philadelphia | 1,139,862 | 0 | 0 | 3,791 | 20,316 | 49,479 |
| Sacramento | 397,487 | 0 | 0 | 0 | 96 | 450 |
| St. Louis | 558,934 | 0 | 46 | 597 | 7,389 | 21,113 |
| Washington | 1,428,891 | 0 | 0 | 1,136 | 9,717 | 24,103 |

[1] The number of children who have at least one instance of moderate or greater exertion.

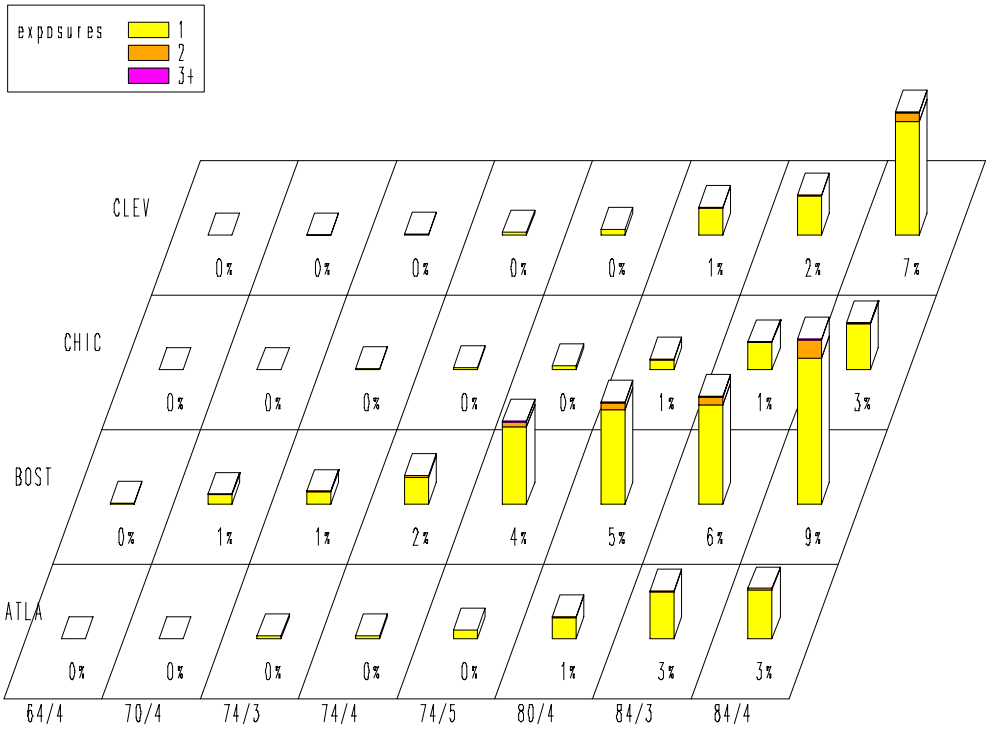



**Figure 4-4. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.08 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Atlanta, Boston, Chicago, Cleveland)**

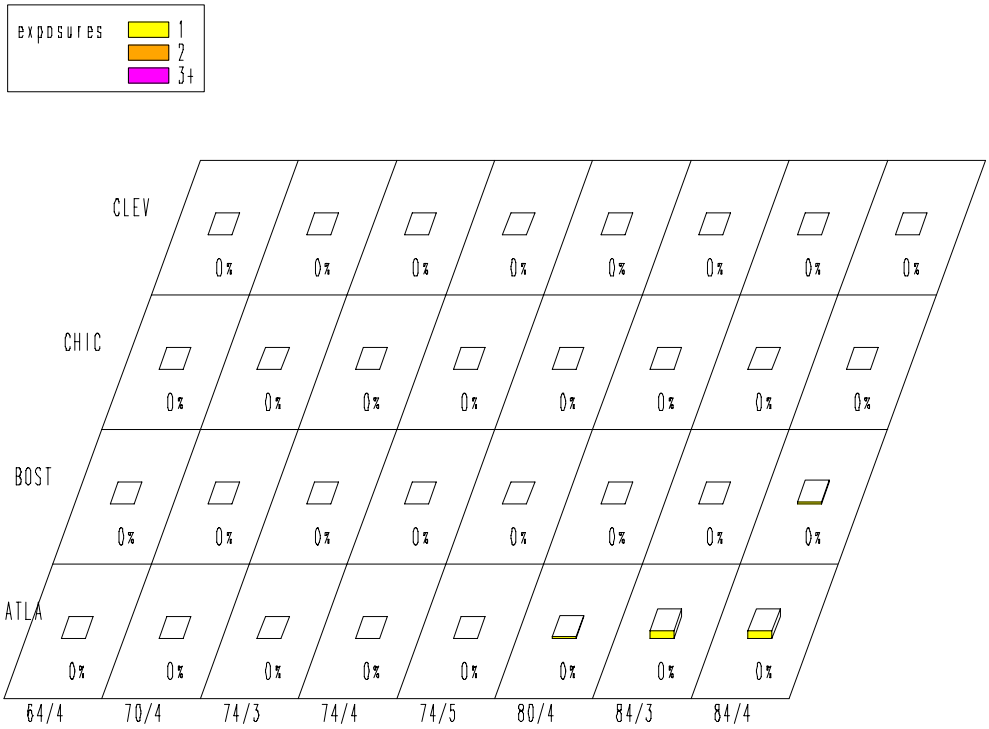



**Figure 4-5. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.08 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Atlanta, Boston, Chicago, Cleveland)**

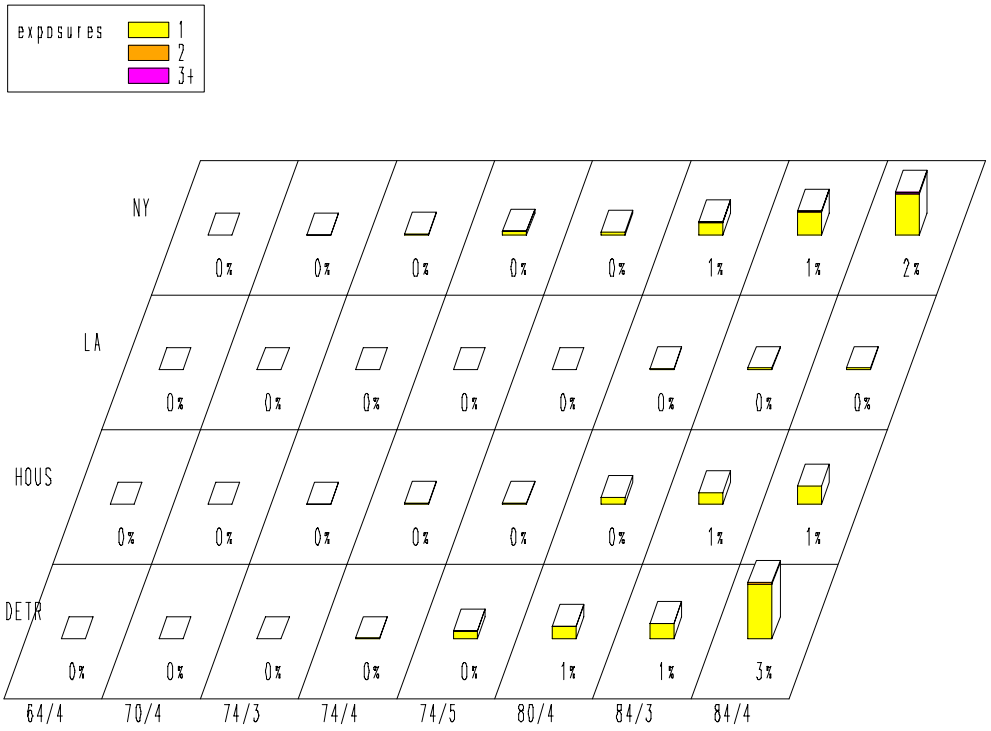



**Figure 4-6. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.08 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Detroit, Houston, Los Angeles, New York)**

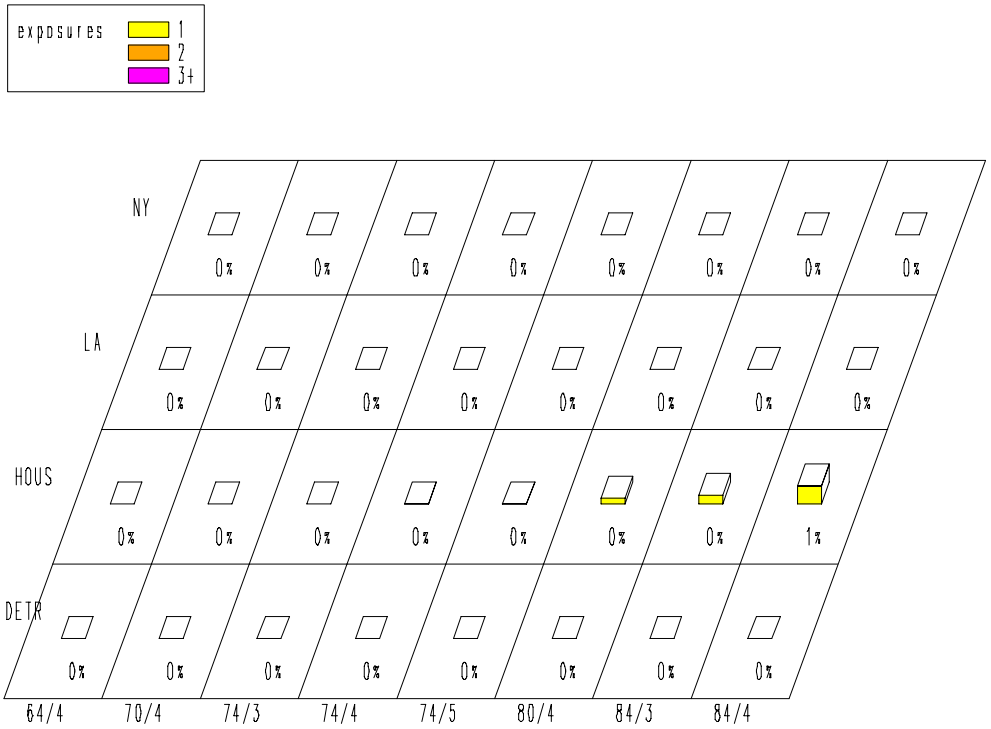



**Figure 4-7. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.08 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Detroit, Houston, Los Angeles, New York)**

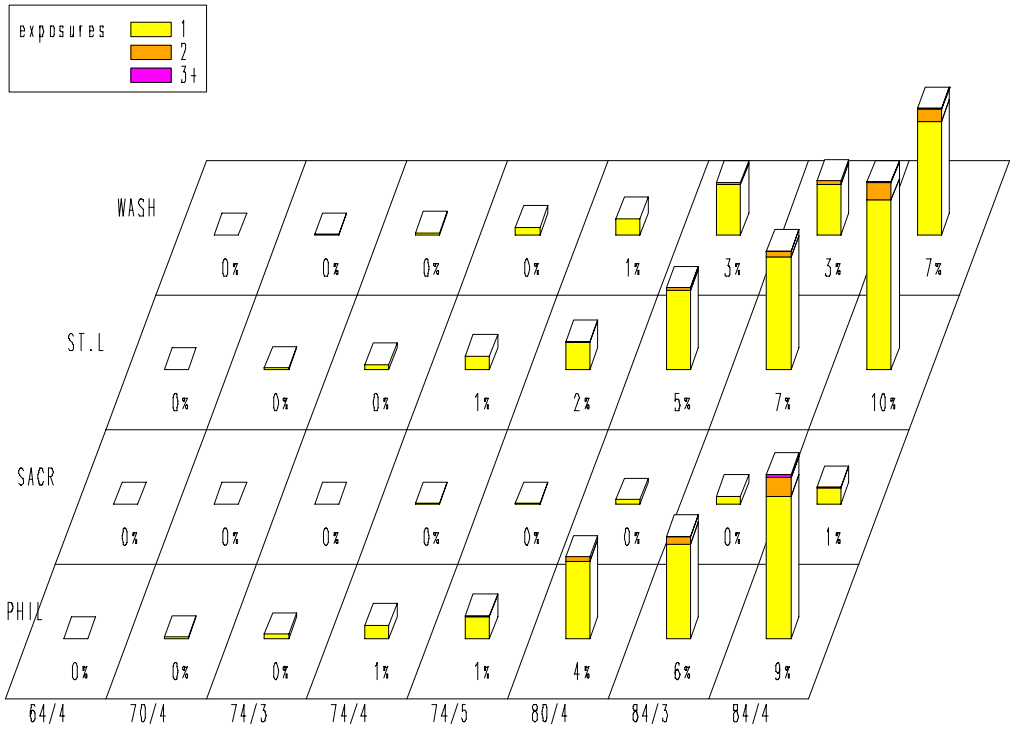



**Figure 4-8. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.08 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Philadelphia, Sacramento, St. Louis, Washington)**

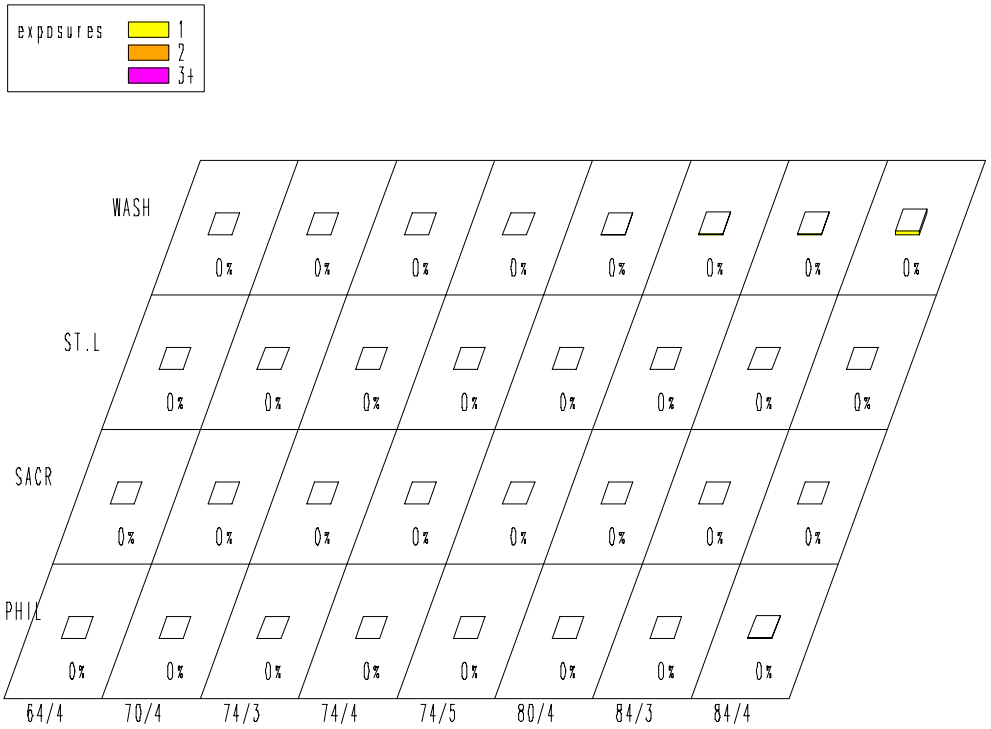



**Figure 4-9. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.08 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Philadelphia, Sacramento, St. Louis, Washington)**

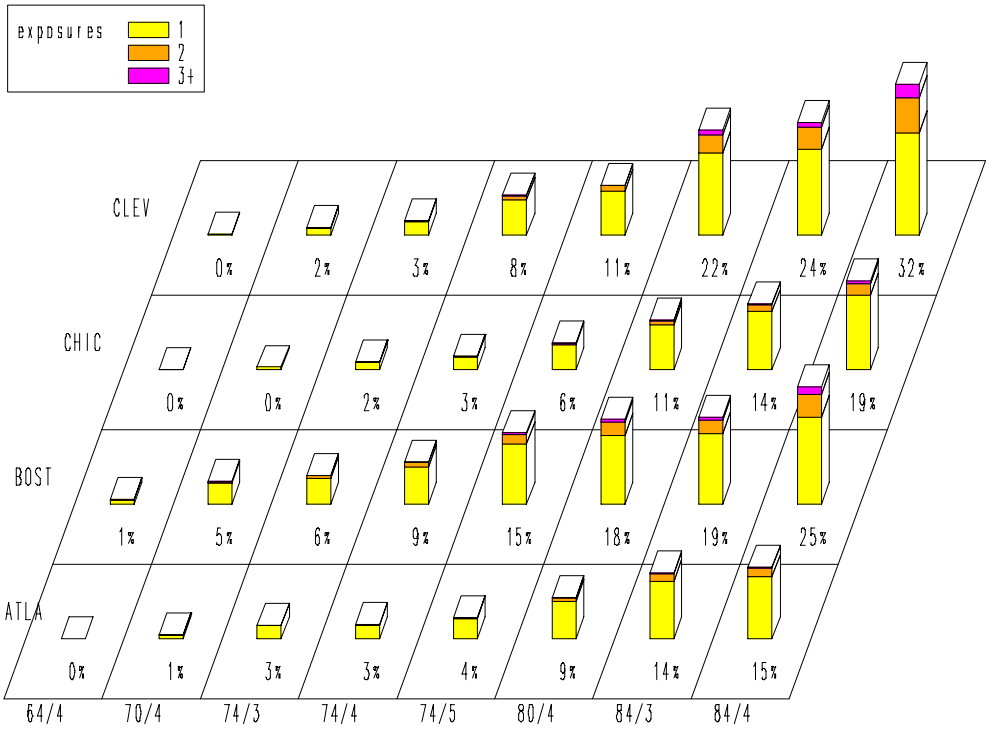



**Figure 4-10. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.07 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Atlanta, Boston, Chicago, Cleveland)**

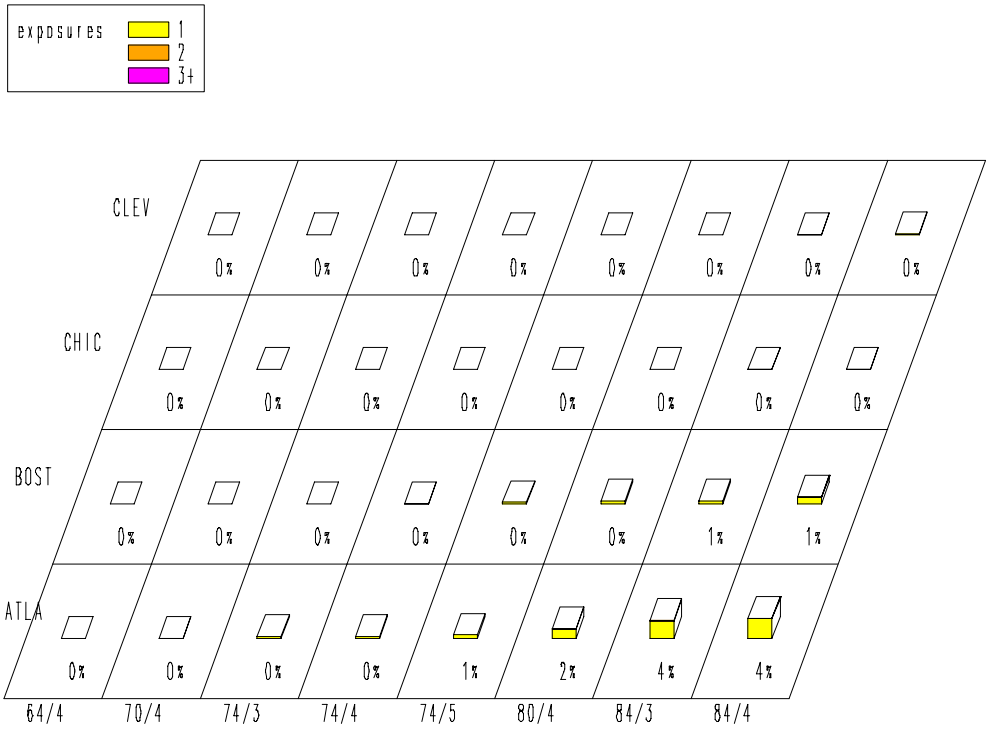



**Figure 4-11. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.07 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Atlanta, Boston, Chicago, Cleveland)**

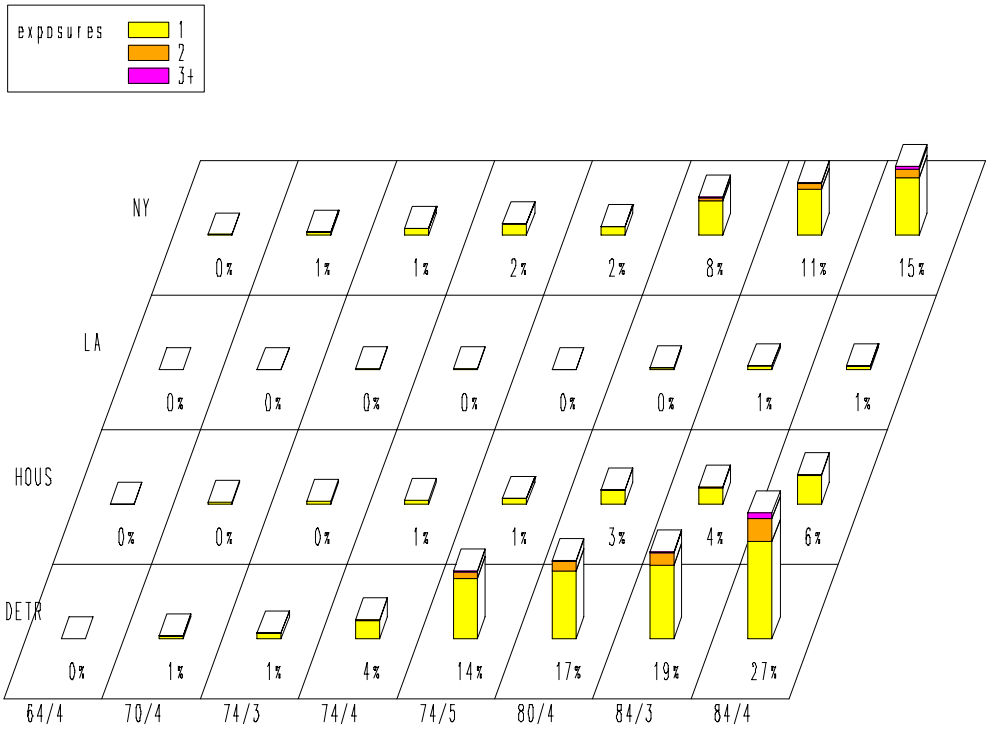



**Figure 4-12. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.07 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Detroit, Houston, Los Angeles, New York)**

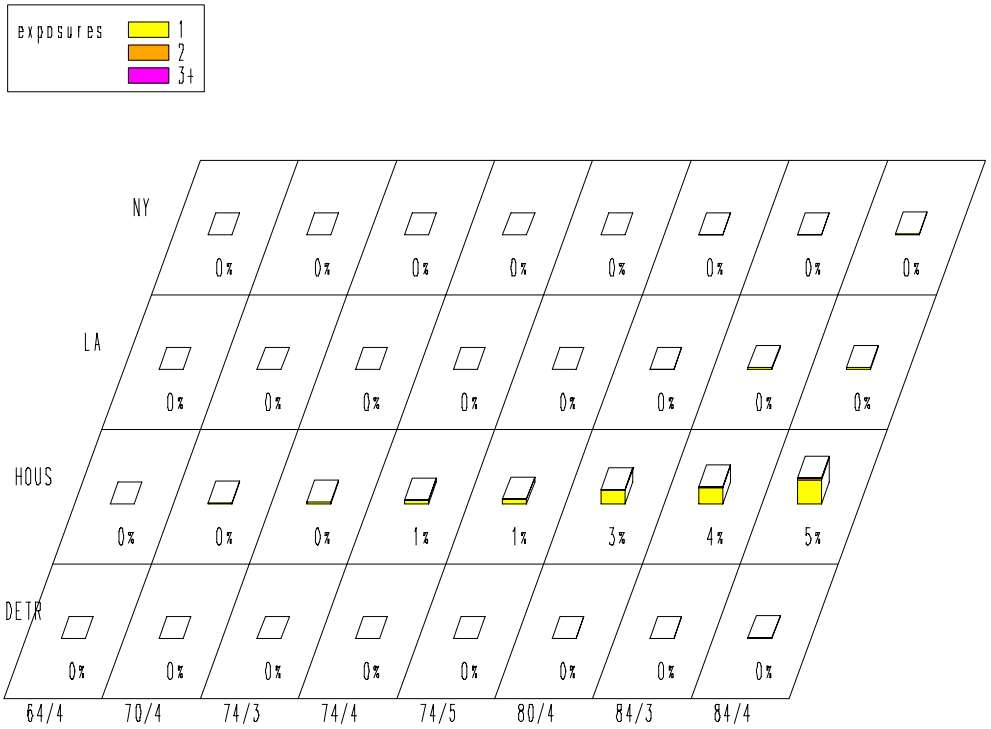



**Figure 4-13. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.07 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Detroit, Houston, Los Angeles, New York)**

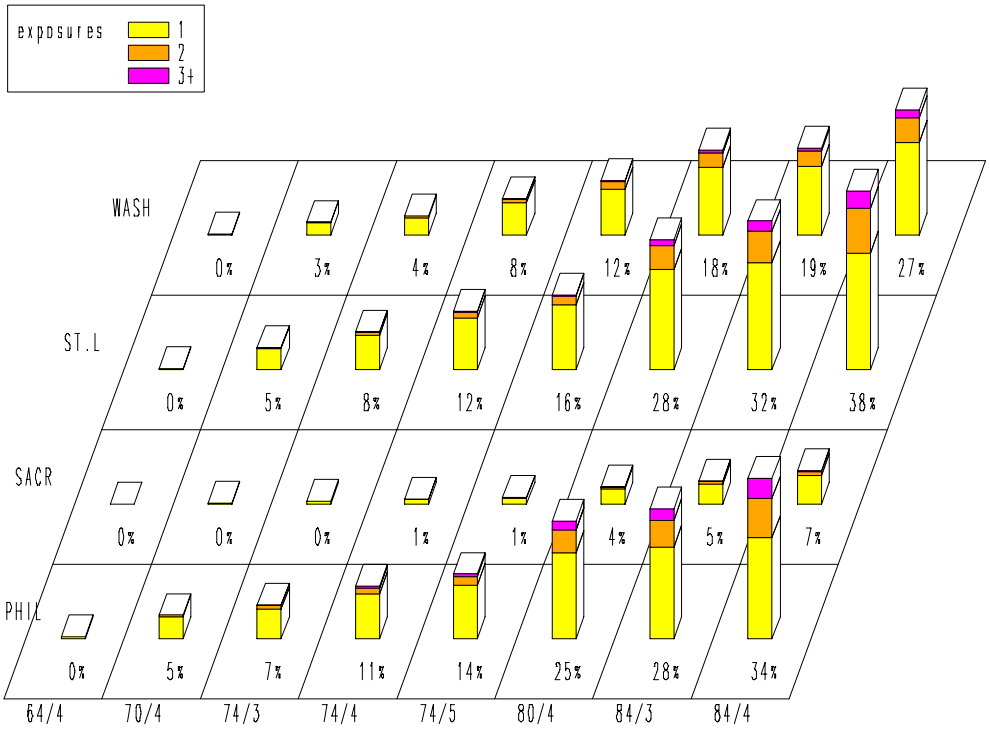



**Figure 4-14. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.07 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Philadelphia, Sacramento, St. Louis, Washington)**

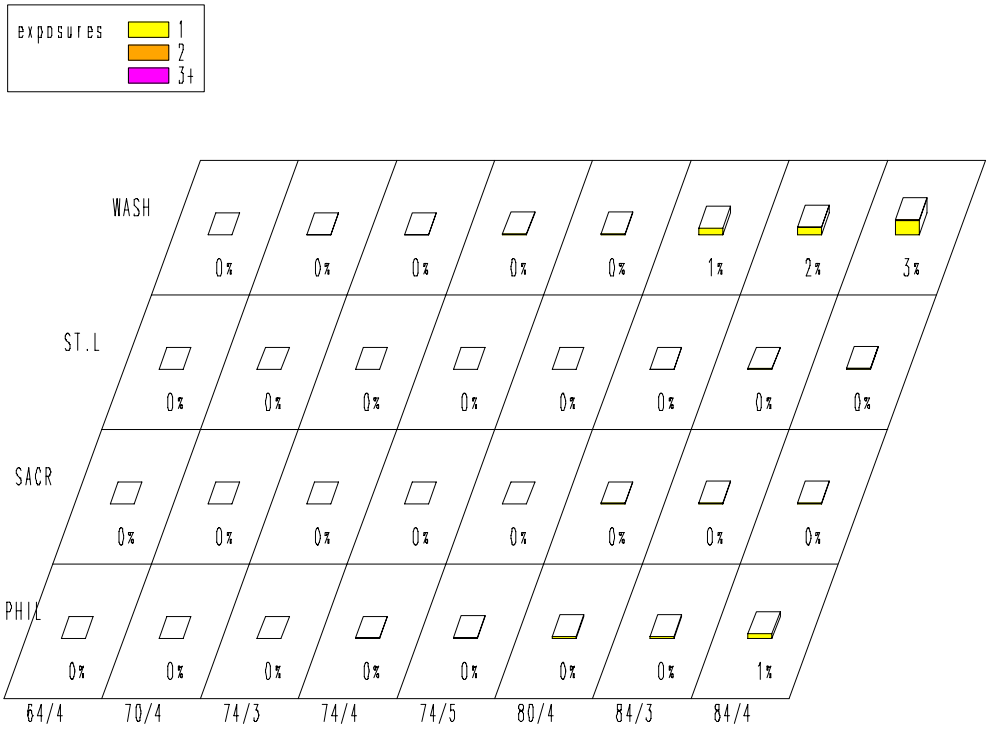



**Figure 4-15. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.07 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Philadelphia, Sacramento, St. Louis, Washington)**

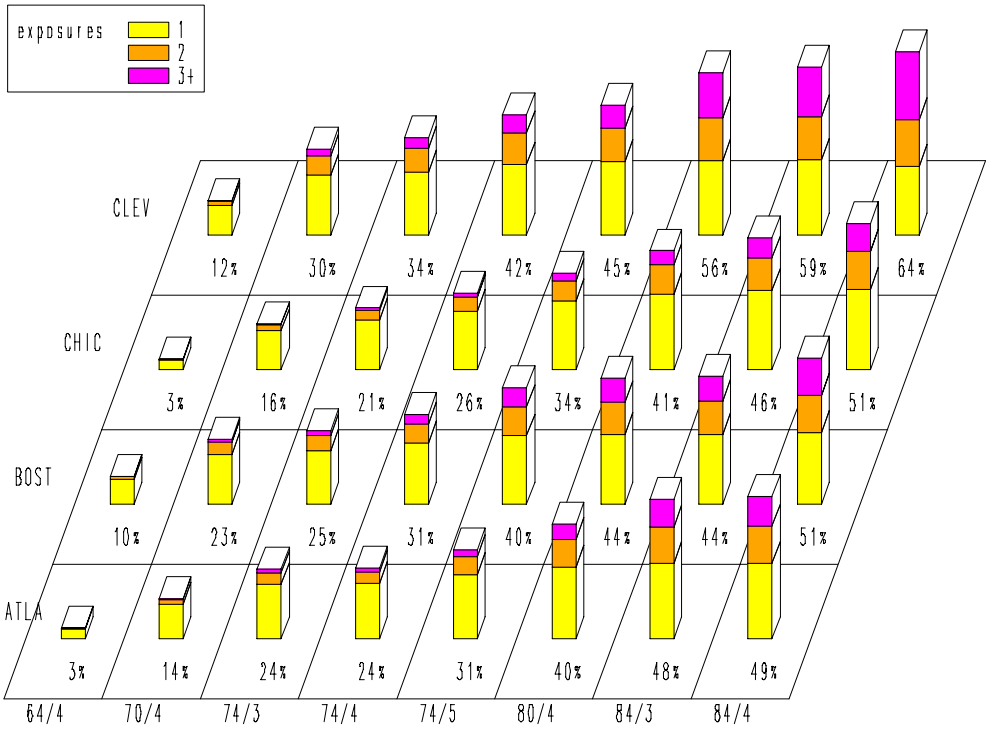



**Figure 4-16. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.06 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Atlanta, Boston, Chicago, Cleveland)**


**Figure 4-17. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.06 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Atlanta, Boston, Chicago, Cleveland)**

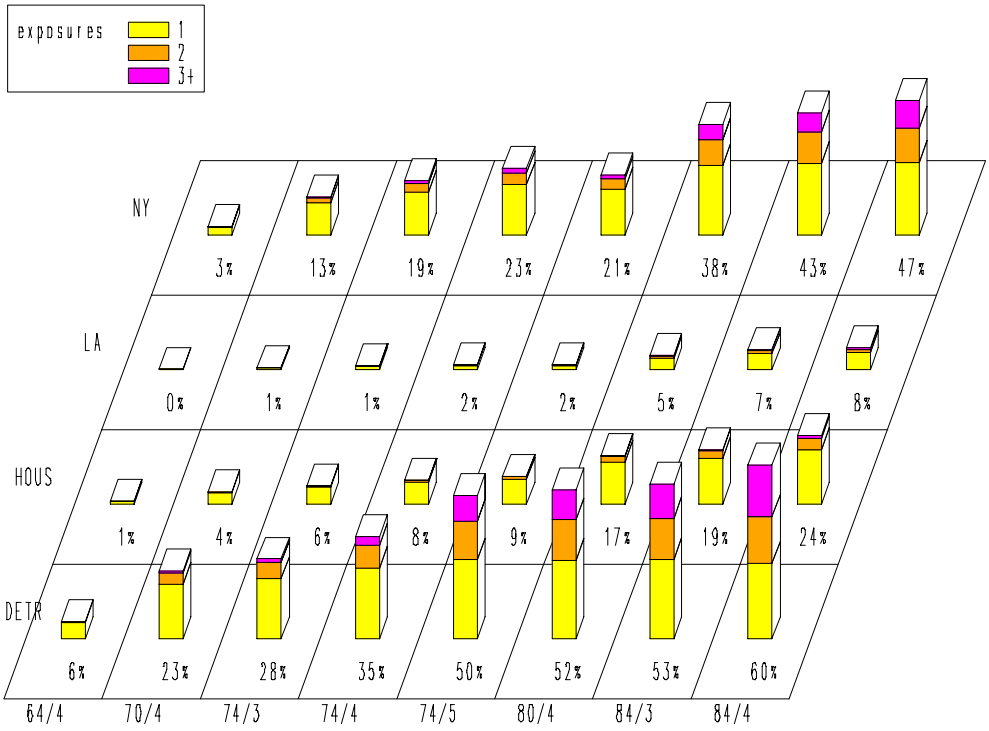



**Figure 4-18. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.06 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Detroit, Houston, Los Angeles, New York)**

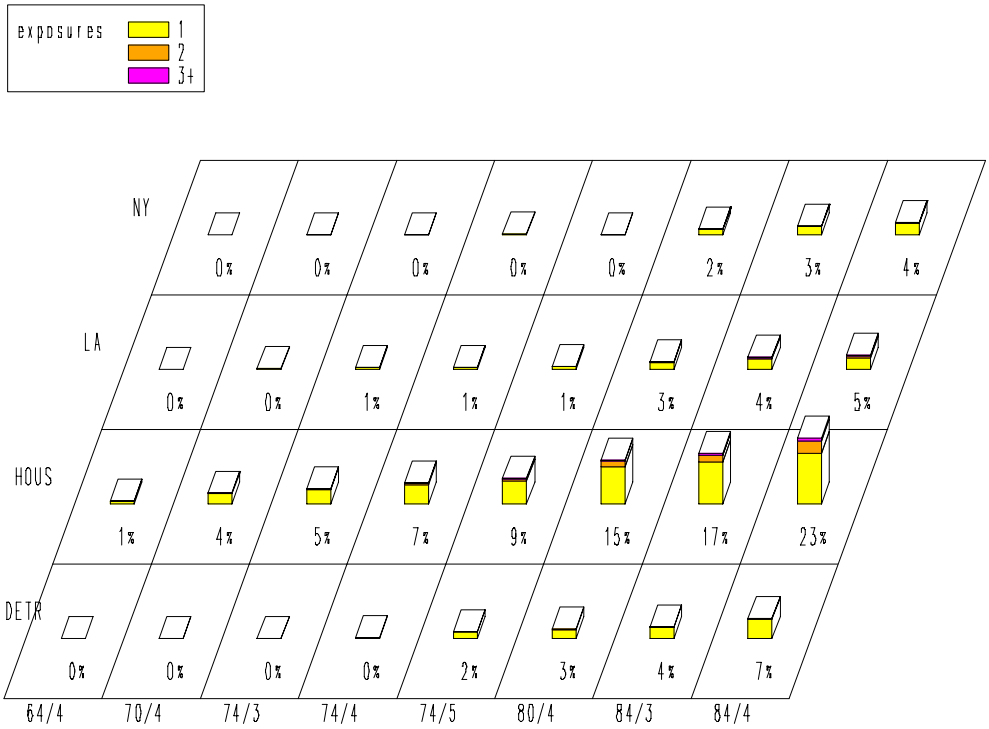



**Figure 4-19. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.06 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Detroit, Houston, Los Angeles, New York)**

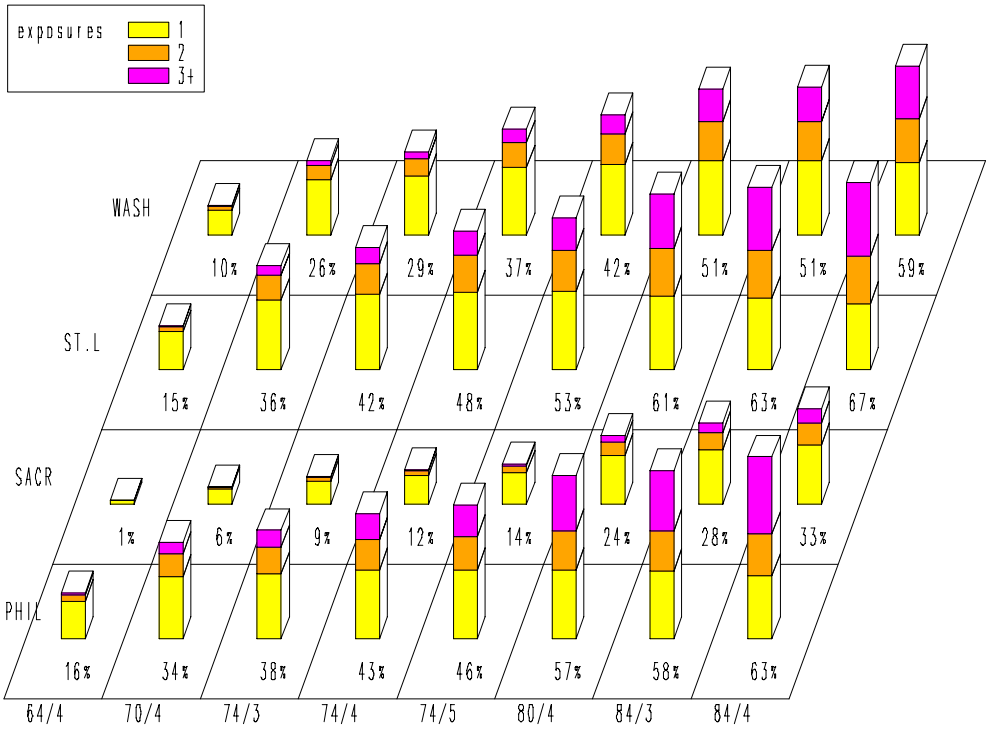



**Figure 4-20. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.06 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2002 air quality data (Philadelphia, Sacramento, St. Louis, Washington)**

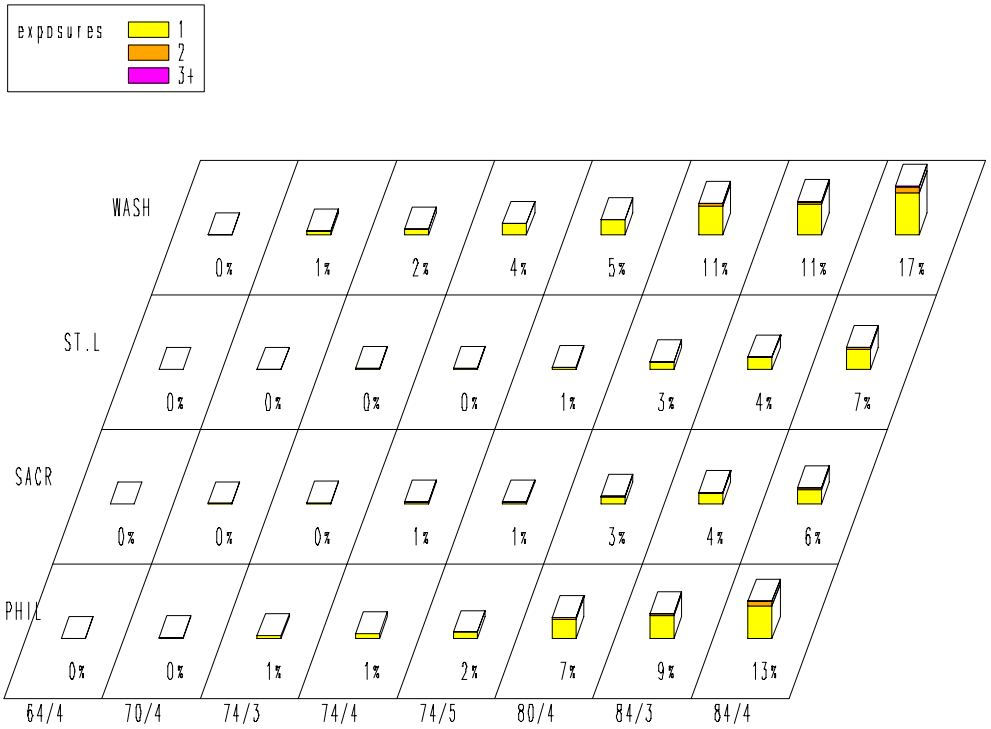



**Figure 4-21. Percent of children (ages 5-18) with repeated 8-hr ozone exposures > 0.06 ppm-8hr, for exposures concomitant with moderate or greater exertion, based on 2004 air quality data (Philadelphia, Sacramento, St. Louis, Washington)**

1

### 4.6.1 Comparison With Exposure Estimates From the Prior Review

The exposure models and the model inputs used in the current and previous (1997) reviews are very different. Table 4-10 lists the major differences between the current and previous reviews that are pertinent to this comparison. Table 4-11 compares exposure modeling results for Houston, and Table 4-12 compares exposure modeling results for six cities combined (Houston, Los Angeles, New York, Philadelphia, St. Louis, and Washington). The results from the previous (1997) review are taken from the memorandum "*Sensitivity of Exposure Estimates to Air Quality Adjustment Procedure*" (Johnson, 1997). Due to the several differences in what is being reported, the only relevant comparison is of the percent of modeled population. Table 4-10 gives the probable reasons for these differences, but we do not know which of these are most important.

**Table 4-10. Comparison of exposure modeling between the current and the 1997 reviews**

| | **Current** | **1997** | **Comments** |
|---|---|---|---|
| The exposure model | APEX | pNEM | These models and their inputs are very different. |
| Population modeled | Outdoor children ages 5-18. 2000 Census data. | Active children ages 5-18. 1990 Census data. | Outdoor children and active children are defined differently, but are expected to have some overlap. |
| Exertion levels reported | Moderate and greater (EVR ≥ 13 liters/min-$m^2$) | Moderate (EVR in range 13-27 liters/min-$m^2$) | The current range is larger than the 1997 range. |
| Period modeled | 2002, 2004 | 1990 for 4 cities, 1991 for 1 city, 1992 for 1 city | For most cities 2002 was a high-ozone year and 2004 a low-ozone year. The years for the 1997 modeling were selected to be the middle years with respect to ozone levels. |
| Cities modeled | 12 cities | 6 cities | We can compare results for Houston and for the group of 6 cities combined that were included in both the prior and current review. |
| Extent of urban areas modeled | CSAs | Smaller areas | |
| Extent of Houston area modeled | Houston-Baytown-Huntsville, TX CSA (Brazoria, Chambers, Fort Bend, Galveston, Harris, Liberty, Montgomery, Waller Counties) | All census units with centers within 15 km of 11 selected monitors (these lie within 5 counties) | A "census unit" is described as a "census tract or block numbering area" in Section 4.1 of the April 1996 outdoor children exposure modeling report.<br>The 1997 area is much smaller than the current area modeled. |
| Rollback method | Quadratic | Quadratic | The same method was used. |
| Modeled standard | 84/3 | 84/3 | This is the only standard for which we have results for both sets of analyses. |

**Table 4-11. Comparison of exposure modeling results for the 84/3 standard between the current and the 1997 reviews (Houston)[1]**

| | Current (2002 air quality) | Current (2004 air quality) | 1997 |
|---|---|---|---|
| Modeled population (active children for current, outdoor children for 1997) | 475,929 | 486,681 | 200,600 [2] |
| Number of persons exceeding 0.08 ppm, 8-hr exposures | 2,809 | 2,568 | 8,567 |
| Percent of modeled population | 0.6 | 0.5 | 4.27 |
| Number of person-days (occurrences) | 2,809 | 2,568 | 8,932 |

[1] Current counts are for active children at moderate or greater exertion levels, 1997 counts are for outdoor children at moderate exertion levels.
[2] A smaller geographic area was modeled in 1997.

**Table 4-12. Comparison of exposure modeling results for the 84/3 standard between the current and the 1997 reviews (Houston, Los Angeles, New York, Philadelphia, St. Louis, and Washington combined)[1]**

| | Current (2002 air quality) | Current (2004 air quality) | 1997 |
|---|---|---|---|
| Modeled population (active children for current, outdoor children for 1997) | 5.32 million | 5.35 million | 2.4 million [2] |
| Number of persons exceeding 0.08 ppm, 8-hr exposures | 108,000 | 2,800 | 55,496 |
| Percent of modeled population | 2.0 | 0.05 | 2.31 |
| Number of person-days (occurrences) | 116,400 | 2,800 | 62,720 |

[1] Current counts are for active children at moderate or greater exertion levels, 1997 counts are for outdoor children at moderate exertion levels.
[2] A smaller geographic area was modeled in 1997.

### 4.6.2 Summary of Sensitivity, Uncertainty, and Evaluation Analyses

#### 4.6.2.1 Sensitivity Analyses

We conducted analyses of the sensitivity of APEX model results to four of the model inputs: the activity data (CHAD), ozone decay rates, proximity factors, and air exchange rate. These were done for the Boston and Houston 2002 base cases. In this section we give some of the results of these analysis; additional sensitivity results can be found in the draft Exposure Analysis TSD.

***Activity Patterns***

Because many of the studies included in the CHAD database are not national in scope, nor do they necessarily correspond to the CSAs targeted here, it would be useful to know how similar the component studies are. Strong similarity would suggest that extrapolation of activity data gathered from one sample population to another population is appropriate. The most comprehensive individual study currently in CHAD is the National Human Activity Pattern Study (NHAPS) and we compared the exposure modeling results with corresponding results using only the NHAPS data. The California database in CHAD is relatively large and represents a very large population, and so we also compared the modeling results with corresponding results using California activity patterns only. Table 4-13 summarizes these results for children with 8-hr exposures above 0.07 ppm-8hr concomitant with moderate or greater exertion. The model results are sensitive to the activity data used, with biases ranging from -21 to +66 percent in this table.

**Table 4-13. Sensitivity to activity database: counts of children (ages 5-18) with any or three or more 8-hr ozone exposures above 0.07 ppm-8hr concomitant with moderate or greater exertion**

| Urban Area (CSA) | One or more exposures | | | Three or more exposures | | |
|---|---|---|---|---|---|---|
| | Base case | NHAPS only | CA only | Base case | NHAPS only | CA only |
| Boston (2002 base case) | 4,672 | 4,693 (+0%) | 4,400 (-6%) | 775 | 849 (+10) | 807 (+5%) |
| Houston (2002 base case) | 3,542 | 3,794 (+7%) | 3,130 (-12%) | 169 | 281 (+66%) | 133 (-21%) |

The version of APEX used for this analysis includes a new approach to construct long-term individual activity patterns, as described in section 2.3.3 and Appendix C in the draft Exposure Analysis TSD. To test the sensitivity of the APEX results to this approach we compared the base case exposure results with corresponding results where (a) the new approach was not implemented, and (b) the diversity statistic was set to 0.75 instead of 0.2 (this increases the repetitiveness of activities for each simulated individual). The results presented in Table

4-14 indicate that APEX is moderately sensitive to the method for longitudinal arrangement of activities.

**Table 4-14. Sensitivity to longitudinal activity pattern algorithm: counts of Boston (2002 base case) population groups with any or three or more 8-hr ozone exposures above 0.07 ppm-8hr concomitant with moderate or greater exertion**

| Population group | One or more exposures | | | Three or more exposures | | |
|---|---|---|---|---|---|---|
| | Base case | Simple re-sampling | Diversity = 0.75 | Base case | Simple re-sampling | Diversity = 0.75 |
| General population | 12,429 | 12,730 (+2%) | 11,568 (-6%) | 1,623 | 1,478 (-9%) | 1,782 (+10%) |
| Children (ages 5-18) | 4,672 | 4,817 (+3%) | 4,294 (-8%) | 775 | 740 (-5%) | 841 (+9%) |

***Ozone Decay Rates***

To test the sensitivity of the APEX predictions to the ozone decay rate distribution, we compared the base case results with corresponding results with the decay rate set uniformly to its $10^{th}$ percentile value and its 90th percentile value (a very large range). The results are presented in Table 4-15 for the number of children exposed to 8-hr average concentrations exceeding 0.07 ppm-8hr concomitant with moderate or greater exertion. Considering the range of decay rates used, the model results are only moderately sensitive to the decay rate distributions.

**Table 4-15. Sensitivity to ozone decay rate: counts of children (ages 5-18) with any or three or more 8-hr ozone exposures above 0.07 ppm-8hr concomitant with moderate or greater exertion**

| Urban Area (CSA) | One or more exposures | | | Three or more exposures | | |
|---|---|---|---|---|---|---|
| | rate=$90^{th}$ percentile | Base case | Rate=$10^{th}$ percentile | rate=$90^{th}$ percentile | Base case | Rate=$10^{th}$ percentile |
| Boston (2002 base case) | 3,714 (-21%) | 4,672 | 5,102 (+9%) | 333 (-57%) | 775 | 1,051 (+36%) |
| Houston (2002 base case) | 3,154 (-11%) | 3,542 | 3,734 (+5%) | 105 (-38%) | 169 | 182 (+8%) |

***Proximity Factors***

As done for the decay rates, we set the proximity factors uniformly to the $10^{th}$ percentile and 90th percentile values (a wide range) to test the sensitivity of the APEX predictions to the proximity factor distribution. These sensitivity results are given in Table 4-16, and are similar to the results for decay rates.

**Table 4-16. Sensitivity to proximity factor: counts of children (ages 5-18) with any or three or more 8-hr ozone exposures above 0.07 ppm-8hr concomitant with moderate or greater exertion**

| Urban Area (CSA) | One or more exposures | | | Three or more exposures | | |
|---|---|---|---|---|---|---|
| | Factor = 90th percentile | Base case | Factor = 10th percentile | Factor = 90th percentile | Base case | Factor = 10th percentile |
| Boston (2002 base case) | 4,428 (-5%) | 4,672 | 5,216 (+12%) | 646 (-17%) | 775 | 1,058 (+37%) |
| Houston (2002 base case) | 3,384 (-4%) | 3,542 | 4,034 (+14%) | 135 (-20%) | 169 | 244 (+44%) |

***Air Exchange Rates***

We set the AER distributions uniformly to the 10th percentile and 90th percentile values (again a wide range). Table 4-17 presents the results of these sensitivity simulations. It appears that the model is very sensitive to the input distributions of AERs.

**Table 4-17. Sensitivity to air exchange rate: counts of children (ages 5-18) with any or three or more 8-hr ozone exposures above 0.07 ppm concomitant with moderate or greater exertion**

| Urban Area (CSA) | One or more exposures | | | Three or more exposures | | |
|---|---|---|---|---|---|---|
| | Rate = 10th percentile | Base case | Rate = 90th percentile | Rate = 10th percentile | Base case | Rate = 90th percentile |
| Boston (2002 base case) | 3,363 (-28%) | 4,672 | 7,947 (+70%) | 252 (-67%) | 775 | 4,413 (+469%) |
| Houston (2002 base case) | 3,029 (-14%) | 3,542 | 8,130 (+130%) | 89 (-47%) | 169 | 3,274 (+1837%) |

### 4.6.2.2 Uncertainty Analyses

We are conducting an analysis of the uncertainties of the exposure modeling using a Monte Carlo method for propagating the uncertainties of model inputs through to uncertainties of the model results, as well as selected sensitivity analyses. See Langstaff (2006) for interim results and the plan for completing this assessment of uncertainties.

### 4.6.2.3 Model Evaluation

In order to evaluate the performance of APEX we compared APEX simulation results to personal $O_3$ concentration measurements taken from the Harvard Southern California Chronic Ozone Exposure Study (Xue et al. 2005, Geyh et al. 2000). Although this study of limited scope, and the measurements of ozone are averaged over 6 days, it is the only study we could find that measured enough personal exposures to $O_3$ to be useful for this evaluation and for which the data are available. In this study, children 7 to 12 years old were followed from June 1995 to May

1996. There are 160 subjects on which longitudinal $O_3$ concentrations have been made in at least 6 of the 12 months of the study period. Passive $O_3$ samplers were used to measure 6-day average personal $O_3$ concentrations, as well as indoor and outdoor concentrations at participants homes, for six days each month. The subjects resided in two separate areas of San Bernardino County: urban Upland CA, and the small mountain towns of Lake Arrowhead, Crestline, and Running Springs, CA.

For the APEX simulations we used hourly outdoor concentrations from fixed site monitors located in Upland and Crestline as inputs. The AERs used were those developed for Sacramento from measurements taken in the inland portions of the Los Angeles area: Sacramento, Riverside, and San Bernardino Counties. For each 6-day period for which personal measurements were available we simulated 10,000 subjects in the 7 – 12 age range in each of the two study areas. For each case the distribution of simulated 6-day average exposure concentrations was compared to the corresponding distribution of measured values. Comparisons were also made between the continuous measurements made inside the subjects' homes and the APEX indoor residential concentration estimates during the times of exposure, and between the $O_3$ concentrations measured outside the homes of the study subjects and those measured at the nearby fixed site monitors.

In general, APEX systematically underpredicts the measured values by 0.001 to 0.02 ppm (zero to 50 percent). Figure 4-22, comparing the population distributions of modeled and observed exposures for a 6-day period in Upland, is fairly typical of the comparisons performed. Additional results and analyses of the reasons for the underpredictions are presented in the draft Exposure Assessment TSD. Since this evaluation is based on 6-day average exposures, it is only of limited relevance for assessing the uncertainty of daily maximum 8-hr average exposures. However, it does indicate that APEX is not significantly overpredicting exposures and may be underpredicting exposures.

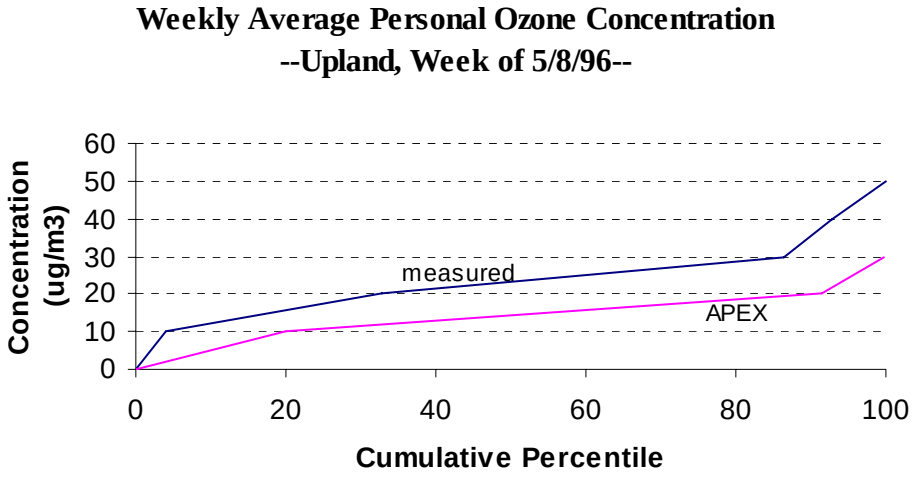



**Figure 4-22. Comparison of measured and modeled personal 6-day average exposures (children, ages 7-12)**

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# 5. CHARACTERIZATION OF HEALTH RISKS

## 5.1 INTRODUCTION

This chapter presents information regarding the results from an updated ozone ($O_3$) health risk assessment that builds upon the methodology used in the assessment conducted as part of the last $O_3$ NAAQS review. This updated assessment includes estimates of (1) risks of lung function decrements in school age children, respiratory symptoms in asthmatic children, respiratory – related hospital admissions, and respiratory, non-accidental, and cardiorespiratory mortality associated with recent ambient $O_3$ levels; and (2) risk reductions associated with just meeting the current and several alternative 8-hr $O_3$ NAAQS. The current risk assessment is more fully described and presented in a draft technical support document, *Ozone Health Risk Assessment for Selected Urban Areas* (Abt Associates, 2006a; henceforth referred to as the draft Risk Assessment Technical Support Document and cited as draft Risk Assessment TSD).

The goals of this $O_3$ risk assessment are: (1) to provide estimates of the potential magnitude of mortality and morbidity effects associated with current $O_3$ levels, and with meeting the current $O_3$ 8-hr NAAQS and alternative $O_3$ 8-hr standards, in specific urban areas; (2) to develop a better understanding of the influence of various inputs and assumptions on the risk estimates; and (3) to gain insights into the distribution of risks and patterns of risk reductions associated with meeting alternative $O_3$ standards. We recognize that while there are many sources of uncertainty and variability inherent in the inputs to this assessment which make the specific estimates uncertain, there is sufficient confidence in the direction and general magnitude of the estimates provided by the assessment, particularly with respect to relative differences between alternative potential standards, for the assessment to serve as a useful input to decisions on the adequacy of the $O_3$ standard. While some of these uncertainties have been addressed quantitatively in the form of estimated confidence ranges around central risk estimates, other uncertainties and the variability in key inputs are not reflected in these confidence ranges, but rather are addressed through separate sensitivity analyses or characterized qualitatively.

Following this introductory section, this chapter discusses the scope of the risk assessment, including selection of urban areas and health endpoints and the degree of confidence associated with the various health outcomes that have been associated with ambient $O_3$ exposures; components of the risk model; characterization of uncertainty and variability associated with the risk estimates; and key results from the assessment. The draft Risk Assessment TSD provides a more detailed discussion of the risk assessment methodology and includes additional risk estimates beyond those summarized herein.

### 5.1.1 Overview of Risk Assessment From Last Review

EPA conducted a health risk assessment that produced risk estimates for the number and percent of children and outdoor workers experiencing lung function and respiratory symptoms associated with the exposures estimated for 9 urban areas. This portion of the risk assessment was based on exposure-response relationships developed from analysis of data from several controlled human exposure studies which was combined with exposure estimates developed for children who spent more time outdoors and for outdoor workers. The risk assessment for the last review also included risk estimates for excess respiratory-related hospital admissions related to $O_3$ concentrations for New York City based on a concentration-response relationship reported in an epidemiological study (Thurston et al., 1992). Risk estimates for lung function decrements, respiratory symptoms, and hospital admissions were developed associated with recent air quality levels (referred to as "as is" air quality) and for just meeting the existing 1-hr standard and several alternative 8-hr standards. The methodological approach followed in conducting the last risk assessment and risk estimates resulting from that assessment are described in Chapter 6 of the 1996 Staff Paper (EPA, 1996b) and in several technical reports and publications (Whitfield et al., 1996; Whitfield, 1997; Whitfield et al., 1998).

In the 1997 review of the $O_3$ NAAQS, the risk estimates played a significant role in both the staff recommendations and in the proposed and final decisions to revise the $O_3$ standards. CASAC stated (Wolff, 1995) in its advice and recommendations to the Administrator on the $O_3$ Staff Paper that "EPA's risk assessments must play a central role in identifying an appropriate level," while also noting that "because of the myriad of assumptions that are made to estimate population exposure and risk, large uncertainties exist in these estimates." In the 1997 notice (62 FR 38856) announcing the decision to revise the $O_3$ standards EPA indicated that the Administrator considered the results of the exposure and risk analyses and key observations and conclusions from these analyses in putting effects considered to be adverse to individuals into a broader public health perspective and in making judgments about the level of a standard that would be requisite to protect public health with an adequate margin of safety.

### 5.1.2 Development of Approach for Current Risk Assessment

The health risk assessment described in this Chapter and in the draft Risk Assessment TSD builds upon the methodology and lessons learned from the risk assessment work conducted for the last review. The current risk assessment also is based on the information evaluated in the final CD. The general approach used in the current risk assessment was described in the draft Health Assessment Plan (EPA, 2005a), that was released to the CASAC and general public in April 2005 for review and comment and which was the subject of a consultation with the CASAC $O_3$ Panel on May 5, 2005. The approach used in the current risk assessment reflects

consideration of the comments offered by CASAC members and the public on the draft Health Assessment Plan, comments offered on the first draft Staff Paper and draft Risk Assessment TSD at and subsequent to a consultation with CASAC on December 8, 2005, and CASAC comments provided to the Agency in a June 5, 2006 letter (Henderson, 2006b).

The basic structure of the current risk assessment reflects the two different types of human studies on which the $O_3$ health risk assessment is based: controlled human exposure studies and epidemiological studies. Controlled human exposure studies involve volunteer subjects who are exposed while engaged in different exercise regimens to specified levels of $O_3$ under controlled conditions for specified amounts of time. For the current health risk assessment, we are using probabilistic exposure-response relationships based on analysis of individual data that describe the relationship between a measure of personal exposure to $O_3$ and measures of lung function recorded in the studies. The measure of personal exposure to ambient $O_3$ is typically some function of hourly exposures – e.g., 1-hr maximum or 8-hr maximum. Therefore, a risk assessment based on exposure-response relationships derived from controlled human exposure study data requires estimates of personal exposure to ambient $O_3$, typically on a 1-hr or multi-hour basis. Because data on personal hourly $O_3$ exposures are not available, estimates of personal exposures to varying ambient concentrations are derived through exposure modeling, as described in Chapter 4.

In contrast to the **exposure-response** relationships derived from controlled human exposure studies, epidemiological studies provide estimated **concentration-response** relationships based on data collected in real world settings. Ambient $O_3$ concentrations, measured as the average of monitor-specific measurements, using population-oriented monitors, are used as a surrogate measure of population exposure. Population health responses for $O_3$ include respiratory symptoms in asthmatic children, hospital admissions for respiratory illness, and premature mortality. As described more fully below, a risk assessment based on epidemiological studies typically requires baseline incidence rates and population data for the risk assessment locations.

The characteristics that are relevant to carrying out a risk assessment based on controlled human exposure studies versus one based on epidemiology studies evaluated in the CD can be summarized as follows:

- The relevant controlled human exposure studies in the CD provide data that can be used to estimate exposure-response functions, and therefore a risk assessment based on these studies requires as input (modeled) personal exposures to ambient $O_3$. The relevant epidemiological studies in the CD provide concentration-response functions, and therefore a risk assessment based on these studies requires as input (actual monitored or adjusted based on monitored) ambient $O_3$ concentrations, and personal exposures are not required as inputs to the assessment.

- Epidemiological studies are carried out in specific real world locations (e.g., specific urban areas). To minimize uncertainty, a risk assessment based on epidemiological studies has been performed for the locations in which the studies were carried out. Controlled human exposure studies, carried out in laboratory settings, are generally not specific to any particular real world location. A risk assessment based on controlled human exposure studies can therefore appropriately be carried out for any location for which there are adequate air quality and other data on which to base the modeling of personal exposures. There are, therefore, some locations for which a risk assessment based on controlled human exposure studies could appropriately be carried out but a risk assessment based on epidemiological studies would involve considerably greater uncertainty.
- The adequate modeling of hourly personal exposures associated with ambient concentrations for use with exposure-response relationships requires more complete ambient monitoring data than are necessary to estimate average ambient concentrations used to calculate risks based on concentration-response relationships. Therefore, there may be some locations in which an epidemiological studies-based risk assessment could appropriately be carried out, but a controlled human exposure studies-based risk assessment would involve considerably greater uncertainty.
- To derive estimates of risk from concentration-response relationships estimated in epidemiological studies, it is usually necessary to have estimates of the baseline incidences of the health effects involved. Such baseline incidence estimates are not needed in a controlled human exposure studies-based risk assessment.

The scope of the current $O_3$ risk assessment is described in the next section along with air quality considerations that are relevant to both parts of the risk assessment. Then, the methods for the two parts of the risk assessment – the part based on controlled human exposure studies and the part based on epidemiological and field studies – are discussed in sections 5.3.1 and 5.3.2 below, followed by presentation and discussion of the $O_3$ risk estimates in section 5.4. Both parts of the risk assessment were implemented within a new probabilistic version of TRIM.Risk, the component of EPA's Total Risk Integrated Methodology (TRIM) model that estimates human health risks.

## 5.2 SCOPE OF OZONE HEALTH RISK ASSESSMENT

The current $O_3$ health risk assessment estimates risks of various health effects associated with exposure to ambient $O_3$ in a number of urban areas selected to illustrate the public health impacts of this pollutant. The short-term exposure related health endpoints selected for the $O_3$ risk assessment, discussed in section 5.2.1, include those for which the CD concludes that the

evidence as a whole supports the general conclusion that $O_3$, acting alone and/or in combination with other components in the ambient air pollution mix is likely causal[1].

As discussed in section 3.7, we recognize that there are varying levels of confidence that various health effect endpoints are associated with $O_3$ at ambient levels. As discussed in section 3.7.5 there is clear evidence of a causal relationship between lung function decrements and $O_3$ exposures for school age children engaged in moderate exertion for 8-hours based on the numerous controlled human exposure studies and summer camp field studies conducted by various investigators over the last 30 years. We also judge that there is clear evidence of a causal relationship between increased respiratory symptoms in moderate to severe asthmatic children and $O_3$ exposures. There also is strong evidence of a causal relationship between increased respiratory-related hospital admissions and $O_3$ exposure during the warm $O_3$ season based on extensive and fairly consistent epidemiological studies as well as evidence from controlled human exposure studies reporting increased lung inflammation and airway responsiveness.

The CD concludes that there is strong evidence which is highly suggestive of a causal relationship between respiratory-related, non-accidental, and cardiorespiratory-related mortality and $O_3$ exposures during the warm $O_3$ season. Our judgment with respect to these health outcomes is based on the fairly consistent positive associations found between elevated warm $O_3$ season levels and these mortality outcomes even when the effect of PM is controlled for, and supporting evidence about potential mechanisms of effects on the cardiovascular system from animal toxicology, human clinical and epidemiological studies. There is certainly greater uncertainty about these outcomes than the other effects discussed above. We also recognize, as discussed in section 3.7.5, that for some of the effects observed in epidemiological studies, such as increased respiratory-related hospital admissions and non-accidental and cardiorespiratory mortality, $O_3$ may be serving as an indicator for reactive oxidant species in the overall photochemical oxidant mix and that these other constituents may be responsible in whole or part for the observed effects.

The current risk assessment includes risk estimates for 12 urban areas. The basis for selection of these areas is discussed below (section 5.2.2).

Another important aspect of the current risk assessment is that the risks estimated are only those associated with ambient $O_3$ concentrations exceeding estimated policy-relevant background levels (hereafter, referred to as "background" in this Chapter).[2] Risks associated

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[1] As discussed in 5.2.1, certain endpoints met this criteria of likely causality, but were not included in the risk assessment for other reasons, such as insufficient exposure-response data or lack of baseline incidence data.

[2] Policy relevant background is defined in section 2.7 of this Staff Paper and development of estimates for policy relevant background for use in the risk assessment are discussed in section 5.2.3.

with concentrations above this background are judged to be more relevant to policy decisions about the NAAQS than estimates that include risks potentially attributable to uncontrollable background concentrations.

### 5.2.1 Selection of Health Endpoint Categories

As noted above, in the last review a significant portion of the health risk assessment involved developing risk estimates for both lung function decrements ($\geq 10$, $\geq 15$, and $\geq 20\%$ changes in $FEV_1$) and respiratory symptoms in children (age 6 to 18 years old) who spend more time outdoors and outdoor workers with 1-hr exposures at moderate and heavy exertion and 8-hr exposures at moderate exertion. As discussed in section 3.3.1.2 and Chapter 6 of the CD, there is a significant body of controlled human exposure studies reporting lung function decrements and respiratory symptoms in adults associated with 1- and 6 to 8-hr exposures to $O_3$.

Consistent with the approach used in the last review, we judge that it is reasonable to estimate exposure-response relationships for lung function decrements associated with $O_3$ exposures in children 5-18 years old based on data from adult subjects (18-35 years old). As discussed in the 1996 Staff Paper and 1996 CD, findings from other chamber studies (McDonnell et al., 1985) for children 8-11 years old at a single exposure level and summer camp field studies in at least six different locations in the U.S. and Canada found lung function decrements in healthy children similar to those observed in healthy adults exposed to $O_3$ under controlled chamber conditions. The same approach is being used in the current assessment. In the prior risk assessment, staff focused on the risk estimates for lung function decrements associated with 1-hr heavy exertion, 1-hr moderate exertion, and 8-hr moderate exertion exposures in children age 5-18 years of age. Since the 8-hr moderate exertion exposure scenario in children who spend more time outdoors clearly resulted in the greatest health risks in terms of both the magnitude of the lung function decrements and the percent of the population estimated to experience these effects, and since no new information published since the last review suggests any changes that would impact this conclusion, we have included only the lung function decrements ($\geq 10$, 15, and 20% $FEV_1$) associated with 8-hr moderate exertion exposures in children and "active" children (age 5 to 18 years old) in the current risk assessment. As discussed in Chapter 4 of the draft Staff Paper, levels of physical activity were categorized by a daily Physical Activity Index (PAI). Children were characterized as active if their median daily PAI over the period modeled was 1.75 or higher, a level characterized by exercise physiologists as being "moderately active" or "active."

Although respiratory symptoms in healthy children were estimated in the last review, we have not included this endpoint in the current quantitative risk assessment. This is because several field studies conducted since the last review failed to find respiratory symptoms in field

studies examining responses in healthy children. The CD concludes that "collectively, these studies indicate that there is no consistent evidence of an association between $O_3$ and respiratory symptoms among healthy children" (CD, p. 7-55). Thus, we decided to limit this portion of the risk assessment to lung function decrements in children and to again base the exposure-response relationships on data obtained for 18-35 year old subjects

While a number of controlled human exposure studies have reported additional health endpoints associated with short-term exposures to $O_3$, including airway hyperresponsiveness, inflammation, and immune system effects, there is insufficient exposure-response data at different concentrations to develop quantitative risk estimates for these effects. These additional effects are discussed in Chapter 3, and it is important to recognize that the current quantitative risk assessment only presents a partial picture of the risks to public health associated with short-term $O_3$ exposures.

As discussed in the CD and Chapter 3, a significant number of epidemiological studies examining a variety of health effects associated with ambient $O_3$ concentrations in various locations throughout the U.S., Canada, Europe, and other regions of the world have been published since the last $O_3$ NAAQS review. Chapter 3 reviews the epidemiological evidence evaluated in Chapter 7 of the CD. In selecting health endpoints to be included in the current quantitative risk assessment, we have focused on health endpoints that are better understood in terms of health consequences (i.e., where there is greater consensus about the degree of response that should be considered as representing an adverse health effect in the population) and endpoint categories for which the weight of the evidence supports the inference of a likely causal relationship between $O_3$ and the effect category. Certain health endpoints met the criteria of likely causality, but were not included in the risk assessment for other reasons, such as insufficient exposure-response data or lack of baseline incidence data. Based on these considerations, the following endpoints associated with short-term exposures to $O_3$ during the "warm $O_3$ season" (April 1 to September 30) have been included:

- Respiratory symptoms in moderate/severe asthmatic children (ages 0 to 12);
- Hospital admissions for respiratory illness and asthma;
- Premature total non-accidental and cardiorespiratory mortality.

As discussed in section 3.3.1.2.1 of this Staff Paper, the CD also concludes that collectively, the results of epidemiological studies suggest that respiratory symptoms and increased medication use in asthmatic children are associated with acute exposure to $O_3$. These recent studies provide strong evidence that some asthmatic children are likely to experience $O_3$-related effects.

Large multi-city studies, as well as many studies from individual cities, have reported an association of $O_3$ concentrations with respiratory-related hospital admissions. Studies with data restricted to the summer or warm season, in general, indicated positive and robust associations between ambient $O_3$ concentrations and respiratory-related hospital admissions. With respect to acute $O_3$ effects on mortality, the CD concludes (p.7-175) that, "The majority of the studies suggest an elevated risk of all cause mortality associated with acute exposure to $O_3$, especially in the summer or warm season when $O_3$ levels are typically high."

As discussed in Chapter 7 of the CD and sections 3.3.1.1 and 3.3.1.2.1 of this Staff Paper, several additional health endpoints including ED visits for respiratory illness and increased school absences have been reported to be associated with short-term $O_3$ exposures. The current quantitative risk assessment does not include these additional health endpoints. Emergency department visits were excluded from the quantitative risk assessment because of the limited and less consistent database as well as the lack of baseline incidence data for ED visits. We also judge that the data reporting an association between short-term $O_3$ exposures and school absences is too limited to include in the current risk assessment.

### 5.2.2 Selection of Study Areas

The criteria and considerations that went into selection of urban areas for the $O_3$ risk assessment included the following:

- The overall set of urban locations should represent a range of geographic areas, urban population demographics, and climatology and be focused on areas that do not meet the current 8-hr $O_3$ NAAQS.
- The largest areas with major $O_3$ nonattainment problems should be included.
- There must be sufficient air quality data for a recent three year period.
- An area should be the same or close to the location where at least one concentration-response function for the health endpoints included in the assessment has been estimated by a study that satisfies the study selection criteria (see below). If the study was a hospital admissions study, then relatively recent location-specific baseline incidence data had to be available.
- Locations in which more health endpoints have been assessed were preferred to those with fewer.

Since the exposure-response functions for lung function decrements based on the controlled human exposure studies were based on controlled laboratory conditions, the location of these studies played no role in selecting urban locations for the risk assessment.

Based on the selection criteria and considerations listed above, the following urban areas were included in the risk assessment:

- Atlanta

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

As discussed in Chapter 4, for the purposes of estimating population exposure and the risk of lung function decrements associated with these population exposure estimates, the 12 urban areas have been defined based on consolidated statistical areas (CSAs). The population estimates for these 12 urban area CSAs are given in Table 4-9. About 40% of the total U.S. urban population resides in these 12 urban areas including 18.3 million school age children (ages 5 to 18). As discussed in Chapter 4, we estimate that roughly 8 million of these 18.3 million school age children would be considered "active children."

In contrast to the risk assessment for lung function decrements, for the risk estimates for premature mortality and excess hospital admissions, the urban areas have been defined to be generally consistent with the geographic boundaries used in the epidemiological studies which were the source of the concentration-response functions used in this risk assessment. In most cases the epidemiological studies only included the core urban county or a limited number of counties in one or more of the 12 urban areas. In addition, estimates of respiratory symptoms in asthmatic children were developed for one urban area (the Boston CSA).

### 5.2.3 Air Quality Considerations

Both the portion of the risk assessment based on controlled human exposure and the portion based on epidemiological studies include risk estimates for a recent year of air quality (labeled "as is" air quality in the draft Risk Assessment TSD) and for air quality adjusted so that it simulates just meeting the current 8-hr $O_3$ NAAQS based on a recent three-year period (2002-2004). This period was selected to represent the most recent air quality data for which complete data were available when the risk assessment was conducted.

In order to estimate health risks associated with just meeting the current and alternative 8-hr $O_3$ NAAQS, it is necessary to estimate the distribution of hourly $O_3$ concentrations that would occur under any given standard. Since compliance with the current $O_3$ standard is based on a 3-

year average, air quality data from 2002 to 2004 have been used to determine the amount of reduction in $O_3$ concentrations required to meet the current standard. Estimated design values[3] are used to determine the adjustment necessary to just meet the current 8-hr daily maximum standard. The amount of control has then been applied to each of two single years of data (2002 and 2004) to estimate risks for a single $O_3$ season or single warm $O_3$ season, depending on the health effect, in each of these individual years.

As described in section 4.5.6 and in more detail in Rizzo (2006), after considering several approaches, including proportional rollback and Weibull adjustment procedures, we concluded that the Quadratic air quality adjustment procedure generally best represented the pattern of reductions across the $O_3$ air quality distribution observed over the last decade. The Quadratic air quality adjustment procedure was applied in each of the 12 urban areas to the filled in 2002 and 2004 $O_3$ monitoring data, based on the 3-year period (2002-2004) $O_3$ design values, to generate new time series of hourly $O_3$ concentrations for 2002 and 2004 that reflect air quality levels that just meet the current 8-hr $O_3$ standard over this three year period.

We note that since compliance with the current standard is based on the 3-year average of the 4$^{th}$ daily maximum 8-hr values, the air quality distribution in each of the 3 years can and generally does vary. As a consequence, the risk estimates associated with air quality just meeting the current standard also will vary depending on the year chosen for the analysis. We include assessments involving adjustment of both 2002 and 2004 air quality data to illustrate the magnitude of this year-to-year variability in the risk estimates. The year 2002 generally had meteorology that was very conducive to producing $O_3$ over the eastern half of the U.S. and this resulted in the highest $O_3$ levels over the 2002-2004 time period in the vast majority of the 12 urban study areas. In contrast, 2004 was a year associated with an unusually cool and rainy summer in the eastern half of the U.S. and this contributed to the fact that the lowest $O_3$ levels over this same three-year period were observed in this year in most of the urban areas included in the assessment. The lower $O_3$ levels observed in 2004 also were lower, in part, as a result of reductions in $NO_x$ emissions associated with implementation of additional regional controls on large power plants in the eastern half of the U.S. Differences in meteorology were less evident in Texas and California and these latter areas also were not impacted by the recent additional

[3] A design value is a statistic that describes the air quality status of a given area relative to the level of the NAAQS. Design values are often based on multiple years of data, consistent with the specification of the NAAQS in Part 50 of the CFR. For example, for the current $O_3$ NAAQS, the 3-year averages of the annual 4$^{th}$ daily maximum 8-hr average concentration based on the maximum monitor within an urban area are the design values.

regional controls imposed on large power plants. Thus, its not surprising that the daily maximum 8-hr levels observed in Houston in 2004 were somewhat higher than those observed in 2002 and that 8-hr levels were similar in Los Angeles between these two years. The risk results for 2002 and 2004, thus, provide generally lower-end and upper-end estimates of the annual risks that can occur over a three-year period when alternative standards are just met.

As noted earlier, the risk estimates developed for both the recent air quality scenario and just meeting the current 8-hr standard represent risks associated with $O_3$ levels in excess of estimated background concentrations. The results of the global tropospheric $O_3$ model GEOS-CHEM have been used to estimate average background $O_3$ levels for different geographic regions across the U.S. These GEOS-CHEM simulations include a background simulation in which North American anthropogenic emissions of nitrogen oxides, non-methane volatile organic compounds, and carbon monoxide are set to zero, as described in Fiore et al. (2003). We estimated monthly background concentrations for each of the 12 urban areas based on the GEOS-CHEM simulations, including daily diurnal profiles which were fixed for each day of each month during the $O_3$ season (See Appendix 2-A of this Staff Paper for plots of these estimated background values).

## 5.3 COMPONENTS OF THE RISK MODEL

As noted above in section 5.1.2, there are two parts to the health risk assessment: one based on combining information from controlled human exposure studies with modeled population exposure and the other based on combining information from community epidemiological studies with either monitored or adjusted ambient concentrations levels. Section 5.3.1 below discusses the portion of the current risk assessment related to effects reported in controlled human exposure studies and section 5.3.2 below discusses the portion of the current risk assessment related to health effects reported in community epidemiological studies.

### 5.3.1 Assessment of Risk Based on Controlled Human Exposure Studies

#### 5.3.1.1 General Approach

The major components of the portion of the health risk assessment based on data from controlled human exposure studies are illustrated in Figure 5-1. As shown in Figure 5-1, under this portion of the risk assessment, exposure estimates for a number of different air quality scenarios (i.e, recent year of air quality, just meeting the current 8-hr standard, just meeting alternative standards, and background) are combined with probabilistic exposure-response relationships derived from the controlled human exposure studies to develop risk estimates

for recent air quality and just meeting the current and alternative standards in excess of background. As discussed above, the health effect included in this portion of the risk assessment is lung function decrement, as measured by $FEV_{1i}$ .in school aged children engaged in moderate exertion for 8 hours. The air quality and exposure analysis components that are integral to this portion of the risk assessment are discussed in greater detail in Chapter 4 and in the draft Exposure Assessment TSD.

Several risk measures were generated for this portion of the risk assessment. In addition to the estimates of the number of school age children and "active" children experiencing one or more occurrences of a lung function decrement $\geq$10, $\geq$15, and $\geq$20% in an $O_3$ season, risk estimates have been developed for the total number of occurrences of these lung function decrements in school age children and "active" school age children. The population sizes for children and "active" children for each of the 12 urban areas used in this part of the risk assessment are given in Table 4-3 of this Staff Paper.

A population risk estimate for a given lung function decrement (e.g., $\geq$20% change in $FEV_1$) is an estimate of the expected number of people who will experience that lung function decrement. Since we are interested in risk estimates associated with $O_3$ concentrations in excess of background concentrations, the following steps were taken to estimate the risk associated with recent conditions in excess of background: (1) expected risk given the personal exposures associated with recent ambient $O_3$ concentrations was estimated, (2) expected risk given the personal exposures associated with estimated background ambient $O_3$ concentrations was estimated, and (3) the latter was subtracted from the former. As shown in Equation 5-1 below, the population risk is then calculated by multiplying the resulting expected risk by the number of people in the relevant population. Because response rates are calculated for 21 fractiles, estimated population risks are similarly fractile-specific.

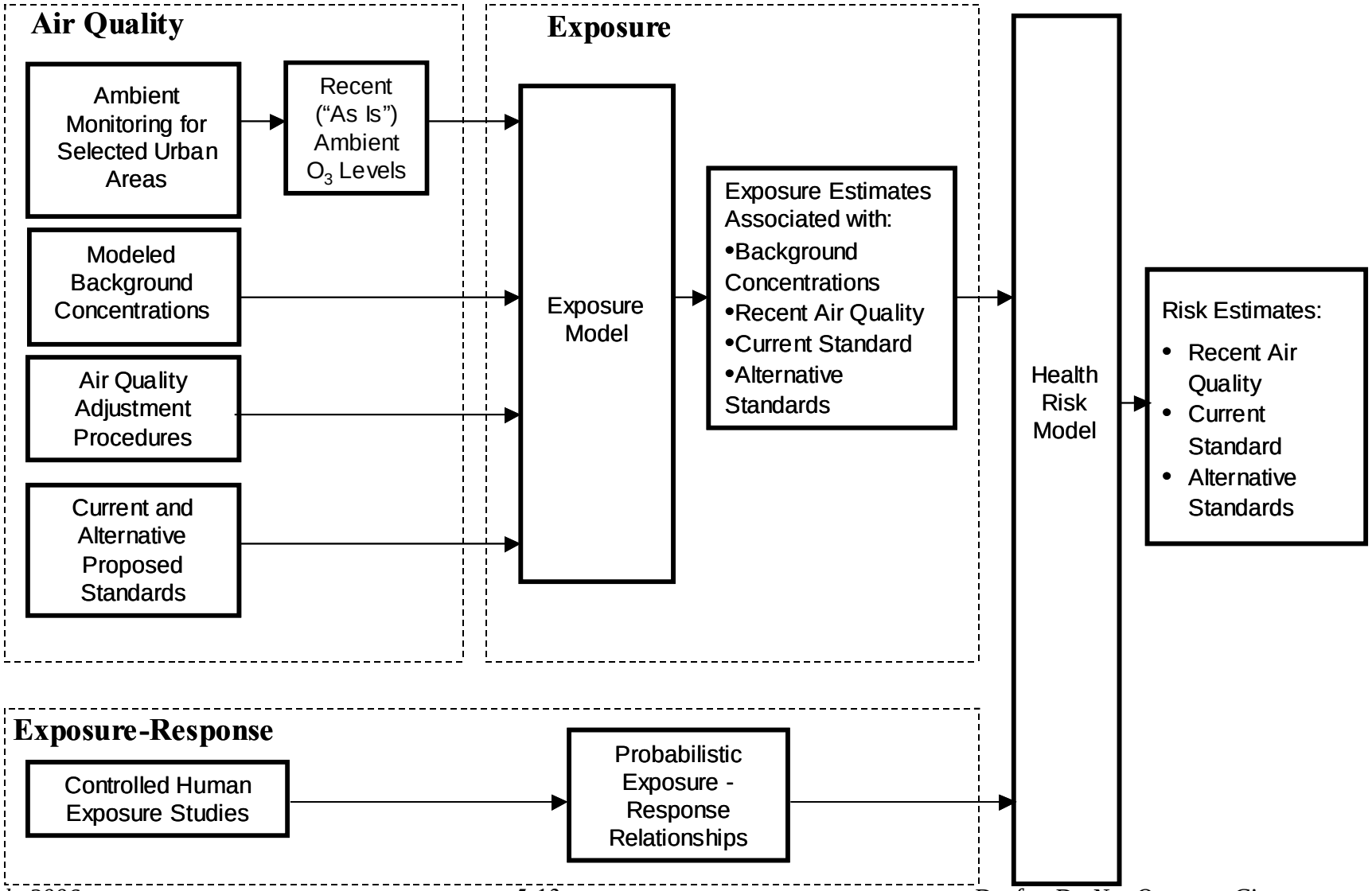
The risk (i.e., expected fractional response rate) for the $k^{th}$ fractile, $R_k$ is:

$$R_k = \sum_{j=1}^{N} P_j \; x \; (RR_k \mid e_j) \quad - \quad \sum_{i=1}^{N_b} P_i^b \; x \; (RR_k \mid e_i^b) \quad \text{(Equation 5-1)}$$

where:

$e_j$ = (the midpoint of) the jth category of personal exposure to $O_3$, given recent ambient $O_3$ concentrations;

**Figure 5-1. Major Components of Ozone Health Risk Assessment Based on Controlled Human Exposure Studies**



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

$P_j$ = the fraction of the population having personal exposures to $O_3$ concentration of $e_j$ ppm, given recent ambient $O_3$ concentrations;

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

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

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

$N$ = number of intervals (categories) of $O_3$ personal exposure concentration, given recent ambient $O_3$ concentrations; and

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

For example, if the median expected response rate for recent ambient concentrations is 0.065 (i.e., the median expected fraction of the population responding is 6.5%) and the median expected response rate for background ambient concentrations is 0.001 (i.e., the median expected fraction of the population responding is 0.1%), then the median expected response rate associated with recent ambient concentrations above background concentrations is 0.065 – 0.001 = 0.064. If there are 300,000 people in the relevant population, then the population risk is 0.064 x 300,000 = 19,200.

#### 5.3.1.2 Exposure Estimates

Exposure estimates used in this portion of the risk assessment were obtained from running TRIM.Expo for each of the 12 urban areas for the various air quality scenarios (i.e., for 2004 and 2002 air quality representing recent years, for 2004 and 2002 air quality adjusted to just meet the current and several potential alternative 8-hr standards, and for air quality levels representing background based on estimates from the GEOS-CHEM model). Chapter 4 and the draft Exposure Assessment TSD (EPA, 2006d) provide additional details about the inputs and methodology used to estimate population exposure in the 12 urban areas. Exposure estimates for

all and "active" school age children (ages 5 to 18) were separately combined with probabilistic exposure-response relationships for lung function decrements associated with 8-hr exposure while engaged in moderate exertion. Children were characterized as active if their median daily physical activity index (see section 4.4.3) over the period modeled was 1.75 or higher, a level characterized by exercise physiologists as being "moderately active" or "active." Individuals engaged in activities that resulted in an average equivalent ventilation rate (EVR) for the 8-hr period at or above 13 l/min-$m^2$ were included in the exposure estimates for 8-hr moderate or greater exertion. This range was selected to match the EVR for the group of subjects in the controlled human exposure studies that were the basis for the exposure-response relationships used in this portion of the risk assessment.

#### 5.3.1.3 Exposure-Response Functions

A similar methodology to that developed in the prior risk assessment has been used to estimate probabilistic exposure-response relationships for lung function decrements in school age children and "active" school age children associated with 8-hr moderate exertion exposures. Building on the prior assessment, a combined data set including the data from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) studies used previously and the more recent data from Adams (2002, 2003, 2006) have been used to estimate exposure-response relationships for 8-hr exposures under moderate exertion. The previously used studies were all conducted in EPA's facility in Chapel Hill, while the Adams studies were conducted at the University of California at Davis. Data from these controlled human exposure studies were corrected for the effect of exercise in clean air to remove any systematic bias that might be present in the data attributable to an exercise effect. Generally, this correction for exercise in clean air was small relative to the total effects measures in the $O_3$-exposed cases. After we made corrections for the effect of exercise in clean air, we averaged individual responses to the same $O_3$ concentration under different exposure protocols within the same study. For example, in Adams (2006) subjects were exposed to $O_3$ concentrations of 0.08 ppm in a square-wave pattern in Protocol 2 and in a triangular pattern in Protocol 3, and we used the average of the responses for each subject in estimating the exposure-response relationship used in the risk assessment. The rationale for averaging the responses is that there are a multitude of patterns of exposure in the real world, thus it seems sensible to include all of the data rather than rely on data for any single pattern. However, averaging an individual's responses across the various protocols may lead to an underestimation of the fraction of the population experiencing a specified response in lung function decrement. EPA is exploring alternative approaches to better reflect all of the individual subject data that do not involve averaging the responses across the various protocols.

For the risk assessment conducted during the last $O_3$ NAAQS review, there were data for only 3 exposure levels (0.08, 0.10, and 0.12 ppm) and a linear exposure-response relationship was estimated for use in the risk assessment. With the addition of data from three more recent Adams' studies that included 0.04, 0.06, and/or 0.08 ppm, 6.6 hour exposures, the combined data set appears to be more S-shaped and, therefore, we used nonlinear regression techniques to fit a 3-parameter logistic function to the data for each of the three measures of lung function decrement.[4,5] Figures 5-2a,b,c shows both the linear exposure-response functions used previously and the new 3-parameter.logistic exposure-response functions used in the current risk assessment for changes in $FEV_1 \geq 10\%$, $\geq 15\%$ and $\geq 20\%$. of the draft Risk Assessment TSD. These figures also show the currently available combined data points for which the 3-parameter logistic functions were fit. We note that the fraction of the population experiencing $FEV_1 \geq 15\%$ and $\geq 20\%$ associated with 0.08 ppm $O_3$ exposures is lower in the three Adams'studies compared to the combined data set based on the studies by Folinsbee et al. (1991), Horstmann et al. (1990), and McDonell et al. (1991). For example, the fraction of the population experiencing $FEV_1$ decrements $\geq$15% associated with 0.08 ppm $O_3$ exposures was 3.3, 6.7, and 16.7% in the three Adams studies compared to 18.3% in the combined data set from the Chapel Hill studies. The 0.08 ppm level is the only common level tested in both sets of studies. This observed difference may be due to differences in sensitivity of the subjects tested, random variability due to the relatively small number of subjects tested, and/or possibly greater attenuation of response for subjects living in or near Davis, California (where the Adams studies were conducted) compared to subjects living in or near Chapel Hill, NC (where the other studies were conducted). Adams notes in his studies that they were conducted over a 6-month period when the 0.09 ppm, 1-hr California standard was not exceeded in the area where his subjects resided. The difference in observed responses between these two sets of studies is an additional uncertainty that should be considered.

#### 5.3.1.4 Characterizing Uncertainty and Variability

An important issue associated with any population health risk assessment is the characterization of uncertainty and variability. *Uncertainty* refers to the lack of knowledge regarding both the actual values of model input variables (parameter uncertainty) and the

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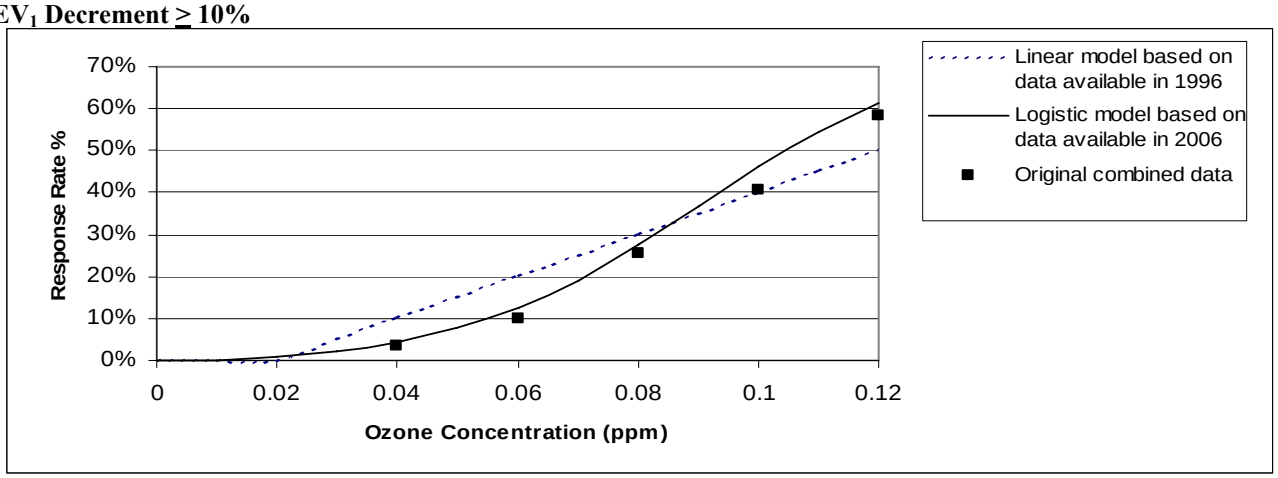
[4] As noted in Whitfield et al., 1996, the response data point associated with 0.12 ppm for the response measure $FEV_1 \geq 15\%$ appeared to be inconsistent with the other data points (see Whitfield et al., 1996, Table 10, footnote c). Because of this, we estimated the probability of a response of $FEV_1 \geq 15\%$ at an $O_3$ concentration of 0.12 ppm by interpolating between the $FEV_1 \geq 10\%$ and $FEV_1 \geq 20\%$ response rates at that $O_3$ concentration.

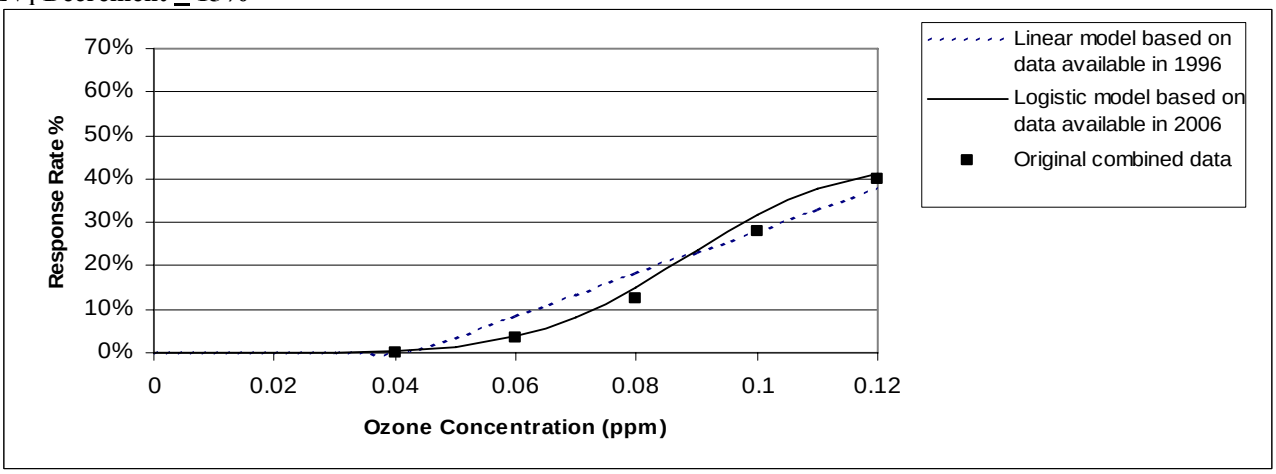
[5] The 3-parameter logistic function is a special case of the 4-parameter logistic, in which the function is forced to go through the origin, so that the probability of response to 0.00 ppm is 0.

**Figure 5-2a, b, c. Probabilistic Exposure-Response Relationships for $FEV_1$ Decrement ≥ 10%, ≥ 15%, and ≥ 20% for 8-Hour Exposures Under Moderate Exertion**

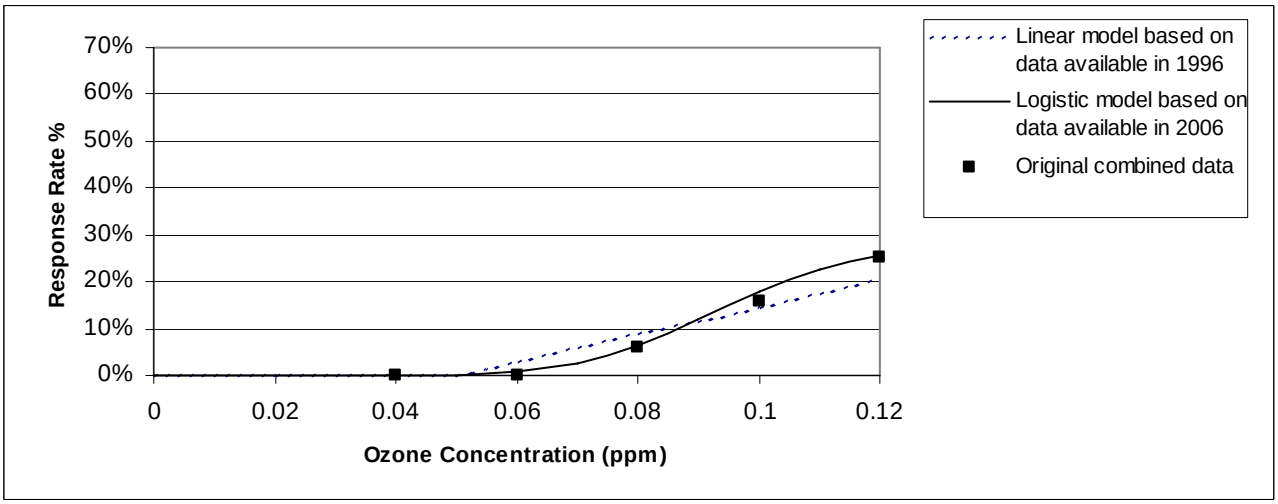
**a) $FEV_1$ Decrement ≥ 10%**




**b) $FEV_1$ Decrement ≥ 15%**




**c) $FEV_1$ Decrement ≥ 20%**



physical systems or relationships (model uncertainty – e.g., the shapes of 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, the statistical uncertainty surrounding the estimated $O_3$ coefficients in the exposure-response functions is reflected in the credible intervals provided for the risk estimates in this chapter and in the draft Risk Assessment TSD.

A Bayesian approach was used to characterize uncertainty attributable to sampling error based on sample size considerations. In this approach, for any given $O_3$ concentration, we specify a prior probability distribution describing our prior beliefs about the probability that the rate of response to exposure to that $O_3$ concentration will fall in any specified range. Given this prior distribution and the actual data – a sample size, N (the number of subjects exposed to the specified $O_3$ concentration), and a number of responders, X – the Bayesian approach calculates a posterior distribution, which provides a description of the uncertainty about the response rate corresponding to the specified $O_3$ concentration. If the prior distribution is a Beta distribution with parameters $\alpha$ and $\beta$, the posterior distribution is also a Beta distribution, but with parameters $(\alpha+X)$ and $(\beta+N-X)$. For prior distributions we used diffuse Beta distributions, in which $\alpha = \beta = 0$.[6] The resulting posterior distributions are therefore Beta distributions with parameters X and (N-X).

We have actual samples (and therefore actual sample sizes and numbers of responders), however, for only five $O_3$ concentrations – 0.04, 0.06, 0.08, 0.10, and 0.12 ppm. Therefore a true Bayesian approach can be carried out for only these five $O_3$ concentrations. As an alternative, we approximated this approach by setting N=30 (the smallest of the five sample sizes) for all $O_3$ concentrations and calculating X for any given $O_3$ concentration as the number of responders (out of 30 subjects) predicted by the estimated logistic exposure-response function. For example, the estimated logistic exposure-response function for response defined as $\Delta FEV_1 \geq 10\%$ predicts a probability of response to 0.05 ppm $O_3$ to be 0.067475. The predicted number of responders to 0.05 ppm $O_3$ is thus 0.067475 x 30 = 2.024. Applying the inverse Beta function with parameters X = 2.024 and (N-X) = (30 – 2.024), the predicted response rate associated with any percentile of the posterior distribution for an $O_3$ concentration of 0.05 ppm can be calculated. The 1st percentile response rate is 0.005, the 2.5th percentile response rate is 0.034, the 50th percentile response rate is 0.058, and so forth.

[6] The use of a diffuse prior distribution allows the data to determine the shape of the posterior distribution.

Because we don't actually have samples for every possible $O_3$ concentration, there is no perfect method to characterize the uncertainty associated with sampling error for the entire logistic exposure-response function. By using the smallest of the actual five sample sizes, we maximize the estimated uncertainty associated with sample size considerations. Because other sources of uncertainty about the exposure-response function cannot easily be quantified, we believe this conservative approach to be reasonable. Figures 5-3a, b, and c show the resulting $2.5^{th}$ percentile, $50^{th}$ percentile (median), and $97.5^{th}$ percentile curves for the three lung function response definitions.

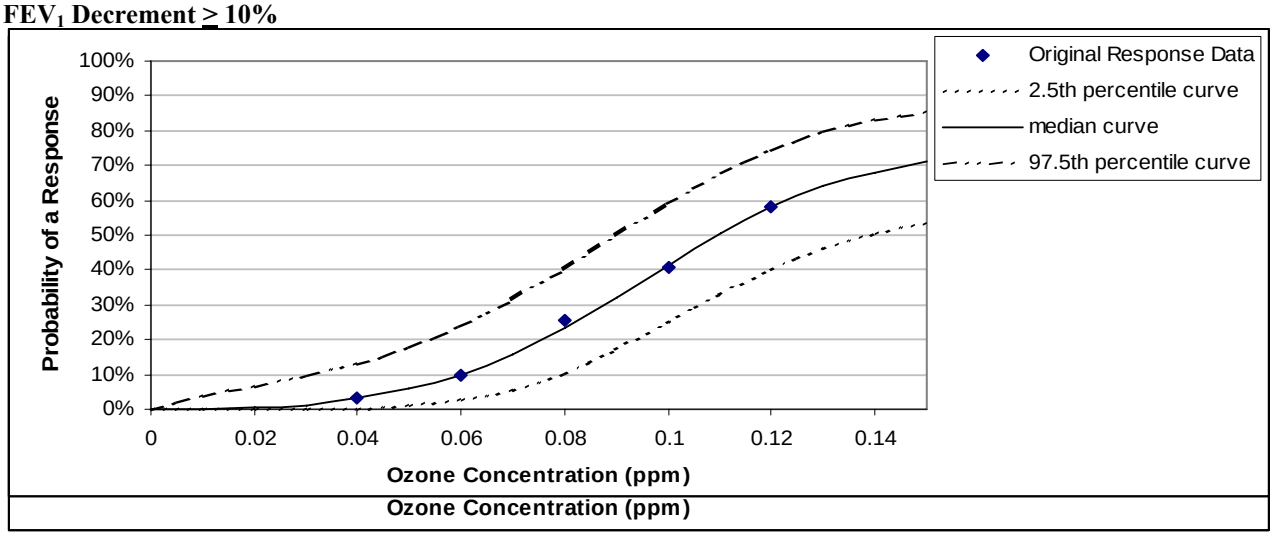
In addition to uncertainties arising from sample size considerations, there are other uncertainties associated with the use of the exposure-response relationships for lung function responses. For example, while we have used the combined data set for the current risk assessment, as it represents the best available data, we believe that the observed differences in response between the Adams studies and the Chapel Hill studies contribute to additional uncertainty about the exact shape of the exposure-response relationship, especially for levels at or below 0.08 ppm. Additional uncertainties with respect to the estimated exposure-response relationships are briefly summarized below.[7] These additional uncertainties include:

- Length of exposure. The 8-hr moderate exertion risk estimates are based on a combined data set from three controlled human exposure studies conducted using 6.6-hr exposures. The use of these data to estimate responses associated with an 8-hr exposure are reasonable, in our judgment, because lung function response appears to level off after exposure for 4 to 6 hours. It is unlikely that the exposure-response relationships would have been appreciably different had the studies been conducted over an 8-hr period.
- Extrapolation of exposure-response relationships. It was necessary to estimate responses at $O_3$ levels below the lowest exposure levels used in the controlled human studies (i.e., 0.04 ppm) down to background levels.
- Reproducibility of $O_3$-induced responses. The risk assessment assumed that the $O_3$-induced responses for individuals are reproducible. This assumption is supported by the evaluation in the CD (see section AX6.4) which cites studies by McDonnell et al. (1985b) and Hazucha et al. (2003) as showing significant reproducibility of response. The CD also notes that Hazucha et al. (2003) similarly observed generally reproducible $O_3$-induced lung function responses in a controlled human exposure study
- Age and lung function response. As in the prior review, exposure-response relationships based on controlled human exposure studies involving 18-35 year old subjects were used in the risk assessment to estimate responses for school age children

[7] Additional uncertainties with respect to the exposure inputs to the risk assessment are described in Chapter 4 of this draft Staff Paper, in the draft Exposure Assessment TSD, and in Langstaff (2006).

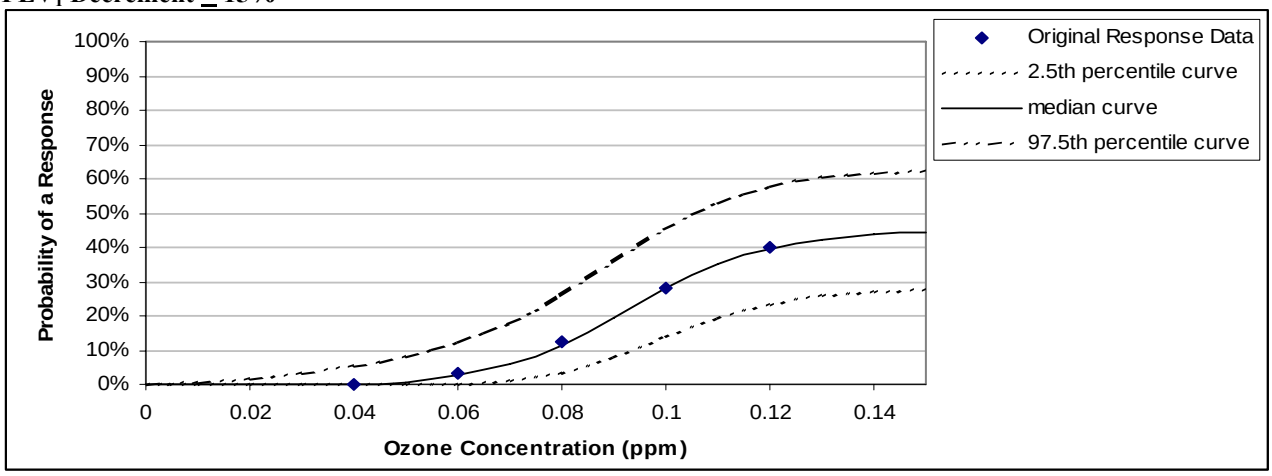
**Figure 5-3a, b, c. Probabilistic Exposure-Response Relationships for $FEV_1$ Decrement ≥ 10%, ≥ 15%, and ≥ 20% for 8-Hour Exposures Under Moderate Exertion**

**a) $FEV_1$ Decrement ≥ 10%**

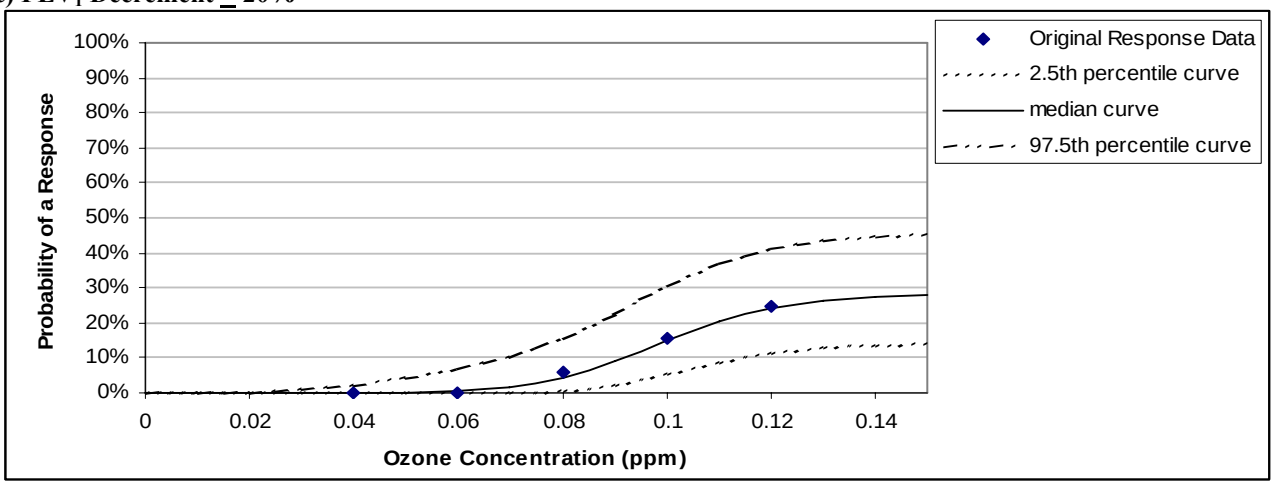


Ozone Concentration (ppm)

**b) $FEV_1$ Decrement ≥ 15%**




**c) $FEV_1$ Decrement ≥ 20%**



(ages 5-18). This approach is supported by evaluation in the CD (see section AX6.4) which cites the findings of McDonnell et al. (1985a) who reported that children 8-11 years old experienced $FEV_1$ responses similar to those observed in adults 18-35 years old when both groups were exposed to concentrations of 0.12 ppm at an EVR of 35 $L/min/m^2$. . In addition, a number of summer camp studies of school age children exposed in outdoor environments in the Northeast also showed $O_3$-induced lung function changes similar to those observed in controlled human exposure studies.

- Exposure history. The risk assessment assumed that the $O_3$-induced response on any given day is independent of previous $O_3$ exposures. As discussed in Chapter 3 and in the CD, $O_3$-induced responses can be enhanced on the second day of exposure or attenuated after more than 2 consecutive days of exposure. The possible impact of recent exposure history on the risk estimates is an additional source of uncertainty that is not quantified in this assessment. We note that the three Adams' studies which were conducted in Davis, California reported a smaller fraction of the subjects experiencing $FEV_1$ decrements $\geq$15 and 20% associated with $O_3$ exposures to 0.08 ppm for 6.6 hours than the Folinsbee/Horstman/McDonnell studies conducted in Chapel Hill, NC at this same level and exposure period. While Adams indicates in each of these studies that $O_3$ levels did not exceed the 0.09 ppm, 1-hr California standard, we do not know whether the exposures outside the chamber played any role in the differences observed between these two sets of studies or whether the differences might reflect differential sensitivity among the pools of subjects tested.

- Interaction between $O_3$ and other pollutants. Because the controlled human exposure studies used in the risk assessment involved only $O_3$ exposures, it was assumed that estimates of $O_3$-induced health responses would not be affected by the presence of other pollutants (e.g., $SO_2$, $PM_{2.5}$, etc). Some evidence exists that other pollutants may enhance the respiratory effects associated with exposure to $O_3$, but the evidence is not consistent across studies.

*Variability* refers to the heterogeneity in a population or variable of interest that is inherent and cannot be reduced through further research. The current controlled human exposure studies portion of the risk assessment incorporates some of the variability in key inputs to the analysis by using location-specific inputs for the exposure analysis (e.g., location-specific population data, air exchange rates, air quality and temperature data). Although spatial variability in these key inputs across all U.S. locations has not been fully characterized, variability across the selected locations is embedded in the analysis by using, to the extent possible, inputs specific to each urban area. Temporal variability is more difficult to address, because the risk assessment focuses on some unspecified time in the future. 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 the most current inputs available – for example, year 2004 and 2002 air quality data for all of the urban locations, and the most recent available population data (from the 2000 Census). However, future changes in inputs have not been predicted (e.g., future population levels).

### 5.3.2 Assessment of Risk Based on Epidemiological Studies

As discussed above, the current quantitative risk assessment based on epidemiological studies includes risk estimates for respiratory symptoms in moderate to severe asthmatic children, respiratory-related hospital admissions, and total non-accidental and cardiorespiratory mortality associated with short-term $O_3$ exposures in selected urban locations in the U.S. The methods used in this portion of the risk assessment are described below.

#### 5.3.2.1 General Approach

In order to estimate the incidence of a particular health effect associated with recent conditions in a specific county or set of counties attributable to ambient $O_3$ exposures in excess of background, as well as the change in incidence of the health effect in that county or set of counties corresponding to a given change in $O_3$ levels resulting from just meeting the current or alternative 8-hr $O_3$ standards, the following three elements are required:

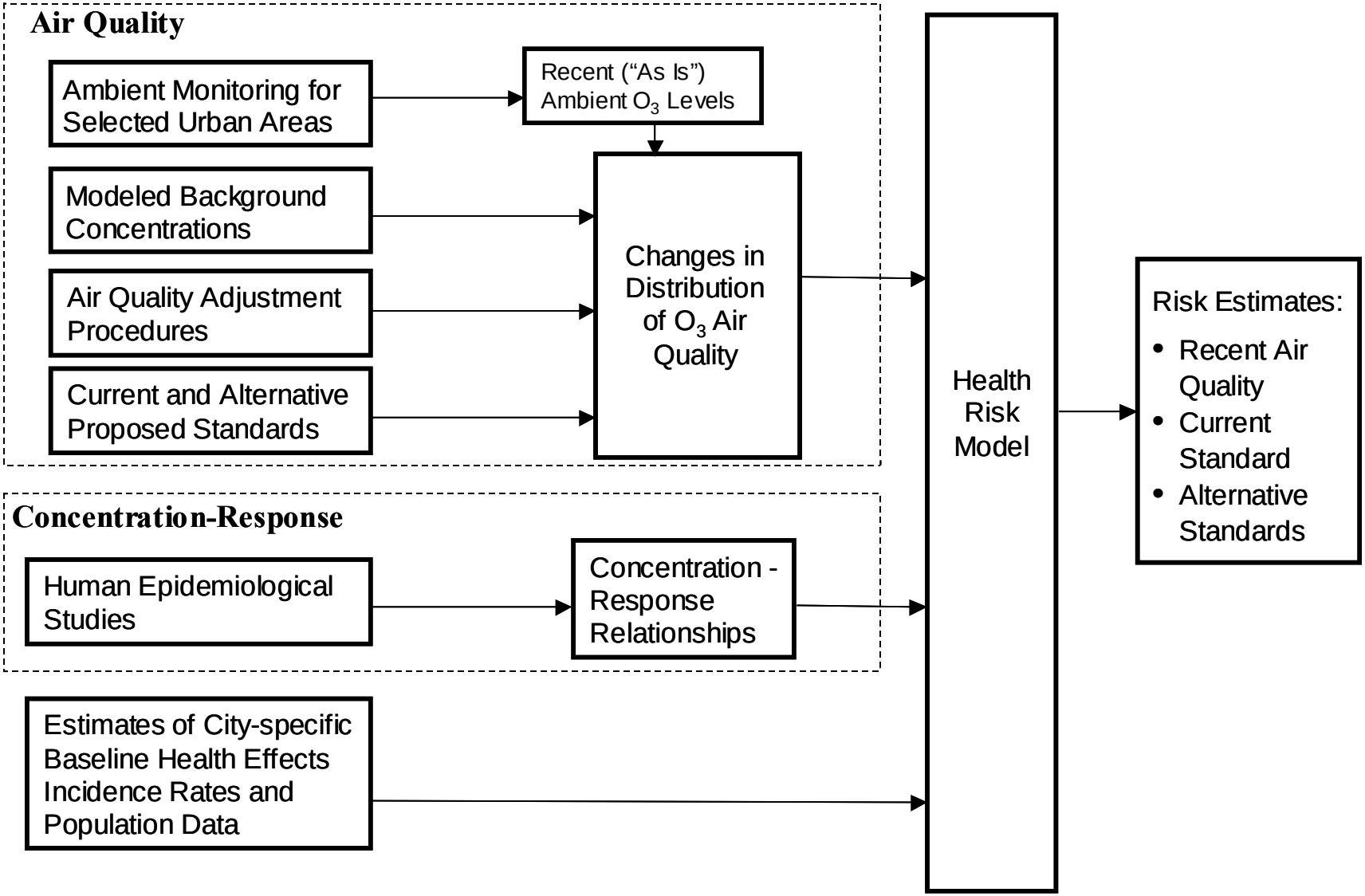
- **Air quality information** including: (1) recent air quality data for $O_3$ from population-oriented monitors in the assessment location, (2) estimates of background $O_3$ concentrations appropriate to this location, and (3) recent concentrations adjusted to reflect patterns of air quality estimated to occur when the area just meets the specified standards. (These air quality inputs are discussed in more detail in section 4.5.6)
- **Concentration-response function(s)** which provide an estimate of the relationship between the health endpoint of interest and ambient $O_3$ concentrations, preferably derived in the assessment location, as use of functions estimated in other increases uncertainty.
- **Seasonal baseline health effects incidence rate and population**. The baseline incidence rate provides an estimate of the incidence rate in the assessment location corresponding to recent $O_3$ levels in that location

Figure 5-3 provides a broad schematic depicting the role of these components in this part of the risk assessment. Each of the key components (i.e., air quality information, estimated concentration-response functions, and baseline incidence and population data) 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 $O_3$ levels. Although some epidemiological studies have estimated linear or logistic concentration-response functions, by far the most common form is the exponential (or log-linear) form:

$$y = Be^{\beta x}, \qquad \text{(Equation 5-2)}$$

**Figure 5-3. Major Components of Ozone Health Risk Assessment Based on Epidemiological Studies**



where x is the ambient $O_3$ level, y is the incidence of the health endpoint of interest at $O_3$ level x, β is the coefficient of ambient $O_3$ concentration, and B is the incidence at x=0, i.e., when there is no ambient $O_3$. The relationship between a specified ambient $O_3$ level, $x_0$, for example, and the incidence of a given health endpoint associated with that level (denoted as $y_0$) is then

$$y_0 = Be^{\beta x_0}. \qquad \text{(Equation 5-3)}$$

Because the log-linear form of concentration-response function (equation (5-2)) is by far the most common form, we use this form to illustrate the derivation of the "health impact function" used in this portion of the risk assessment.

The difference in health effects incidence, $\Delta y = y_0 - y$, from $y_0$ to the baseline incidence rate, y, corresponding to a given difference in ambient $O_3$ levels, $\Delta x = x_0 - x$, can be derived by dividing equation (5-3) by equation (5-2), which yields:

$$\Delta y = y[e^{\beta \Delta x} - 1]. \qquad \text{(Equation 5-4)}$$

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 mortality at ambient $O_3$ level $x_0$ relative to the risk of mortality at ambient $O_3$ level x, for example, may be characterized by the ratio of the two mortality rates: the mortality rate among individuals when the ambient $O_3$ level is $x_0$ and the mortality rate among (otherwise identical) individuals when the ambient $O_3$ level is x. This is the RR for mortality associated with the difference between the two ambient $O_3$ levels, $x_0$ and x. Given a concentration-response function of the form shown in equation (5-1) and a particular difference in ambient $O_3$ levels, Δx, the RR associated with that difference in ambient $O_3$, 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 $O_3$ levels, Δx, can then be calculated based on this $RR_{\Delta x}$:

$$\Delta y = y[RR_{\Delta x} - 1]. \qquad \text{(Equation 5-5)}$$

Equations (5-4) and (5-5) are simply alternative ways of expressing the relationship between a given difference in ambient $O_3$ levels, Δx, 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 ambient $O_3$ health risk.

#### 5.3.2.2 Air Quality Considerations

As illustrated in Figure 5-3, and noted earlier, air quality information required to conduct the $O_3$ risk assessment includes: (1) recent air quality data for $O_3$ from suitable monitors for each selected location, (2) estimates of background concentrations for each selected location, and (3) air quality adjustment procedures to modify the recent data to reflect changes in the distribution of hourly $O_3$ air quality estimated to occur when an area just meets a given $O_3$ standard. We retrieved $O_3$ ambient air quality data for the years 2002 through 2004 from EPA's Air Quality System (AQS).

To estimate the change in incidence of a health effect associated with a change in $O_3$ concentrations from recent levels to background levels in an assessment location, two time series of $O_3$ concentrations are needed for that location: (1) hourly $O_3$ concentrations from a recent year for the period April 1 through September 30, and (2) hourly background $O_3$ concentrations for the same time period. In order to be consistent with the approach generally used in the epidemiological studies that estimated $O_3$ concentration-response functions, the (spatial) average ambient $O_3$ concentration on each hour for which measured data are available is deemed most appropriate for the risk assessment. A composite monitor data set was created for each assessment location based on averaging each hourly value from all monitors eligible for comparison with the current standard for each hour of the day. Table 4-6 provides a summary of the design values for the 12 urban study areas. Appendix 5A.1 to this Chapter provides more detailed information on ambient $O_3$ concentrations for these locations.

Different exposure metrics have been used in epidemiological $O_3$ studies, including the 24-hr average and the daily 1-hr and 8-hr maximum. Therefore, daily changes at the composite monitor in the $O_3$ exposure metric appropriate to a given concentration-response function were calculated for use in the risk assessment (see Tables 5A-13 and 5A-14, Appendix 5A.1 for summary statistics for the composite monitor $O_3$ concentrations in the 12 urban locations for 2002 and 2004). For example, if a concentration-response function related daily mortality to daily 1-hr maximum $O_3$ concentrations, the daily changes in 1-hr maximum $O_3$ concentrations at the composite monitor were calculated. In the first part of the epidemiology-based risk assessment, in which risks associated with the recent levels of $O_3$ above background levels were estimated, this required the following steps:

- Using the monitor-specific input streams of hourly $O_3$ concentrations from a recent year, calculate a stream of hourly $O_3$ concentrations at the composite monitor. The recent $O_3$ concentration at the composite monitor for a given hour on a given day is the average of the monitor-specific $O_3$ concentrations for that hour on that day.

- Using this stream of hourly $O_3$ concentrations from a recent year at the composite monitor, calculate the 1-hr maximum $O_3$ concentration for each day at the composite monitor.
- Using the monitor-specific input streams of hourly background $O_3$ concentrations, calculate a stream of hourly background $O_3$ concentrations at the composite monitor.
- Using this stream of background hourly $O_3$ concentrations at the composite monitor, calculate the 1-hr maximum background $O_3$ concentration for each day at the composite monitor.
- For each day, calculate $\Delta x$ = (the 1-hr maximum $O_3$ concentration for that day at the composite monitor) - (the 1-hr maximum background $O_3$ concentration for that day at the composite monitor).

The calculations for the second part of the epidemiology-based risk assessment, in which risks associated with estimated $O_3$ levels that just meet the current and potential alternative 8-hr standards above background levels were estimated, were done analogously. For this case the series of monitor-specific adjusted hourly concentrations were used rather than the series of monitor-specific recent monitored hourly concentrations. Similarly, calculations for concentration-response functions that used a different exposure metric (e.g., the 8-hr daily maximum or 24-hr average) were done analogously, using the exposure metric appropriate to the concentration-response function.

#### 5.3.2.3 Concentration-Response Functions

As indicated in Figure 5-3, another key component in the risk model based on epidemiological studies is the set of concentration-response functions which provide estimates of the relationships between each health endpoint of interest and ambient concentrations. As discussed above, the health endpoints that have been included in the $O_3$ risk assessment include respiratory symptoms in moderate-to-severe asthmatic children, respiratory-related hospital admissions, and premature mortality associated with short-term exposures. For those health endpoints, the assessment includes all estimates of response magnitude from studies judged suitable for inclusion in this assessment, including those which are not statistically significant. Effect estimates that are not statistically significant are used from studies judged suitable for inclusion in this assessment to avoid introducing bias into the estimate of the magnitude of the effect. Table 5-1 summarizes the studies included in this part of the risk assessment for each of the urban locations.

Studies often report more than one estimated concentration-response function for the same location and health endpoint. Sometimes models including different sets of co-pollutants are estimated in a study; sometimes different lags are estimated. In some cases, two or more studies estimated a concentration-response function for $O_3$ and the same health endpoint in the

same location (this is the case, for example, with $O_3$ and mortality associated with short-term exposures). For some health endpoints, there are studies that estimated multi-city $O_3$ concentration-response functions, while other studies estimated single-city functions.

All else being equal, a concentration-response function estimated in the assessment location is preferable to a function estimated elsewhere, since it avoids uncertainties related to potential differences due to geographic location. That is why the urban areas selected this part of the $O_3$ risk assessment are, generally, those locations in which concentration-response functions have been estimated. There are several advantages, however, to using estimates from multi-city studies versus studies carried out in single cities. These advantages include, but are not limited to: (1) more precise effect estimates due to larger data sets, (2) greater consistency in data handling and model specification that can eliminate city- to-city variation due to study design, and (3) less likelihood of publication bias or exclusion of reporting of negative or nonsignificant findings. Multi-city studies are applicable to a variety of settings, since they estimate a central tendency across multiple locations. When they are estimating a single concentration-response function based on several cities, multi-city studies also tend to have more statistical power and provide effect estimates with relatively greater precision than single city studies due to larger sample sizes, reducing the uncertainty around the estimated coefficient. Because single-city and multi-city studies have different advantages, where both are available for a given location, risk estimates have been developed for both functions.

As discussed in the CD and section 3.3.2.1 of this draft Staff Paper, $O_3$ epidemiological studies have reported relationships based on single pollutant models and/or multi-pollutant models (i.e., where PM, nitrogen dioxide, sulfur dioxide, or carbon monoxide were entered into the health effects model along with $O_3$. To the extent that any of the co-pollutants present in the ambient air may have contributed to the health effects attributed to $O_3$ in single pollutant models, risks attributed to $O_3$ might be overestimated where concentration-response functions are based on single pollutant models. However, if co-pollutants are highly correlated with $O_3$, their inclusion in an $O_3$ health effects model can lead to misleading conclusions in identifying a specific causal pollutant. When collinearity exists, inclusion of multiple pollutants in models often produces unstable and statistically insignificant effect estimates for both $O_3$ and the co-pollutants. Given that single and multi-pollutant models each have both potential advantages and disadvantages, with neither type clearly preferable over the other in all cases, we report risk estimates based on both single- and multi-pollutant models where both are available.

Epidemiological studies have reported effect estimates associated with varying lag periods, but for the reasons discussed in the CD and summarized in section 3.4.5 above the CD focuses on effect estimates from models using 0- or 1-day lag periods, with some consideration of multi-day lag effects (CD, p. 7-11). For quantitative assessments, we conclude that it is

**Table 5-1. Locations and Health Endpoints Included in the $O_3$ Risk Assessment Based on Epidemiological Studies***

| Urban Area | Premature Mortality | Hospital Admissions for Respiratory Illnesses | Respiratory Symptoms in Asthmatic Children |
|---|---|---|---|
| Atlanta | Bell et al. (2004)<br>Bell et al. (2004) – 95 cities<br>Huang et al. (2004)*<br>Huang et al. (2004) – 19 cities* | | |
| Boston | Bell et al. (2004) – 95 cities | | Gent et al. (2003) |
| Chicago | Bell et al. (2004) – 95 cities<br>Huang et al. (2004)*<br>Huang et al. (2004) – 19 cities*<br>Schwartz (2004)<br>Schwartz (2004) – 14 cities | | |
| Cleveland | Bell et al. (2004)<br>Bell et al. (2004) – 95 cities<br>Huang et al. (2004)*<br>Huang et al. (2004) – 19 cities* | Schwartz et al. (1996) | |
| Detroit | Bell et al. (2004)<br>Bell et al. (2004) – 95 cities<br>Huang et al. (2004)*<br>Huang et al. (2004) – 19 cities*<br>Schwartz (2004)<br>Schwartz (2004) – 14 cities<br>Ito (2003) | Ito (2003) | |
| Houston | Bell et al. (2004)<br>Bell et al. (2004) – 95 cities<br>Huang et al. (2004)*<br>Huang et al. (2004) – 19 cities*<br>Schwartz (2004)<br>Schwartz (2004) – 14 cities | | |
| Los Angeles | Bell et al. (2004)<br>Bell et al. (2004) – 95 cities<br>Huang et al. (2004)*<br>Huang et al. (2004) – 19 cities* | Linn et al. (2000) | |
| New York | Bell et al. (2004) – 95 cities<br>Huang et al. (2004)*<br>Huang et al. (2004) – 19 cities* | Thurston et al. (1992) | |
| Philadelphia | Bell et al. (2004) – 95 cities<br>Huang et al. (2004) *<br>Huang et al. (2004) – 19 cities*<br>Moolgavkar et al. (1995) | | |
| Sacramento | Bell et al. (2004)<br>Bell et al. (2004) – 95 cities | | |
| St. Louis | Bell et al. (2004)<br>Bell et al. (2004) – 95 cities | | |
| Washington, D.C. | Bell et al. (2004) – 95 cities | | |

*This study estimated concentration-response functions for cardiorespiratory mortality.

appropriate to use results from lag period analyses consistent with those reported in the CD, focusing on single day lag periods of 0-1 days for associations with mortality or respiratory hospitalization, depending on availability of results (CD, p. 8-59). If the effect of $O_3$ on health outcomes persists over several days, distributed lag model results can provide more accurate effect estimates for quantitative assessment than an effect estimate for a single lag period (CD, p. 7-10). Therefore, we have used distributed lag models when they are available. Where only single day lags are available we have focused on single day lag periods of 0-1 days for associations with mortality or respiratory hospitalization, depending on availability of effect estimates (CD, p. 8-59).

In summary:

- if a single-city concentration-response function was estimated in a risk assessment location and a multi-city function which includes that location was also available for the same health endpoint, both functions were included for that location in the risk assessment;
- risk estimates based on both single- and multi-pollutant models were used when both were available;
- distributed lag models were used, when available; when a study reported several single lag models for a health effect, the initial selection of the appropriate lag structure for the health effect was based on the overall assessment in the CD, considering all studies reporting concentration-response functions for that health effect.

The locations, health endpoints, studies, and concentration-response functions included in that portion of the risk assessment based on epidemiological studies are summarized in Tables 5B-1 through 5B-12 in Appendix 5B.1.

#### 5.3.2.4 Baseline Health Effects Incidence and Population Estimates

As illustrated in Equation 5-4, the most common health risk model based on epidemiological studies expresses the reduction in health risk ($\Delta y$) associated with a given reduction in $O_3$ concentrations ($\Delta x$) as a percentage of the baseline incidence (y). To accurately assess the impact of changes in $O_3$ air quality on health risk in the selected urban areas, information on the baseline incidence of health effects in each location is therefore needed. For this assessment, baseline incidence is the incidence under recent air quality conditions. Population sizes, for both total population and various age ranges used in the risk assessment were obtained for the year 2000 (U.S. Census) and are summarized in Table 5-2. Where possible, county-specific incidence or incidence rates have been used in the assessment. County specific mortality incidences were available for the year 2002 from CDC Wonder (CDC, 2005), an interface for public health data dissemination provided by the Centers for Disease Control (CDC). The baseline mortality rates for each risk assessment location are provided

in Table 5-3 and are expressed as a rate per 100,000 population.

County-specific rates for respiratory hospital discharges, and various subcategories (e.g., asthma, pneumonia) have been obtained, where possible, from state, local, and regional health departments and hospital planning commissions for each of the risk assessment locations.[8] Baseline hospitalization rates used in each risk assessment location are summarized in Table 5-4 and are expressed as a rate per 100,000 relevant population.

Baseline rates of symptoms among asthmatic children who used maintenance medications in the Boston area were estimated by using the median rates of the respiratory symptoms reported in Table 3 of Gent et al. (2003). Each symptom rate, the percentage of days on which the symptom occurred, was calculated for each subject by dividing the number of days of the symptom by the number of days of participation in the study and then multiplying by 100. Median symptom rates among maintenance medication users for wheeze, chest tightness, and shortness of breath were 2.8%, 1.2%, and 1.5% of days, respectively.

#### 5.3.2.5 Characterizing Uncertainty and Variability

Section 5.3.1.4 previously defined what is meant by *uncertainty* and *variability* in the context of this risk assessment. For the portion of the risk assessment based on epidemiological studies, the statistical uncertainty surrounding the estimated $O_{.3}$ coefficients in the reported concentration-response functions is reflected in the confidence or credible intervals provided for the risk estimates in this chapter and in the draft Risk Assessment TSD. Additional uncertainties have been addressed quantitatively through sensitivity analyses and/or have been discussed throughout section 5.3.

With respect to variability within this portion of the risk assessment, there may be variability among concentration-response functions describing the relation between $O_3$ and mortality across urban areas. This variability may be due to differences in population (e.g., age distribution), population activities that affect exposure to $O_3$ (e.g., use of air conditioning), levels and composition of co-pollutants, and/or other factors that vary across urban areas.

[8] The data were annual hospital discharge data, which were used as a proxy for hospital admissions. Hospital discharges are issued to all people who are admitted to the hospital, including those who die in the hospital. Use of the annual or seasonal discharge rate is based on the assumption that the admissions at the end of the year (or season) that carry over to the beginning of the next year (or season), and are therefore not included in the discharge data, are offset by the admissions in the previous year (or season) that carry over to the beginning of the current year (or season).

**Table 5-2. Relevant Population Sizes for $O_3$ Risk Assessment Locations***

| City | Counties | Population (in millions)* | | | |
|---|---|---|---|---|---|
| | | Total | Ages ≥30 | Ages ≥ 65 | Children, Ages ≤ 12, with asthma** |
| **Atlanta** | Fulton, DeKalb | 1.5 | --- | --- | --- |
| **Boston** | Suffolk | 0.7 | --- | --- | |
| **Boston** | Essex, Middlesex, Norfolk, Suffolk, Worcester | --- | --- | --- | 0.025 |
| **Chicago** | Cook | 5.4 | --- | --- | --- |
| **Cleveland** | Cuyahoga | 1.4 | --- | 0.2 | |
| **Detroit** | Wayne | 2.1 | --- | --- | --- |
| **Houston** | Harris | 3.4 | --- | --- | --- |
| **Los Angeles** | Los Angeles | 9.5 | --- | --- | --- |
| **Los Angeles** | Los Angeles, Riverside, San Bernardino, Orange | --- | 8.4 | --- | --- |
| **New York** | Bronx, Kings, Queens, New York, Richmond, Westchester | 8.9 | --- | --- | --- |
| **New York** | Bronx, Kings, Queens, New York, Richmond | 8.0 | --- | --- | --- |
| **Philadelphia** | Philadelphia | 1.5 | --- | --- | --- |
| **Sacramento** | Sacramento | 1.2 | --- | --- | --- |
| **St. Louis** | St. Louis City | 0.3 | --- | --- | --- |
| **Washington, D.C.** | Washington, D.C. | 0.6 | --- | --- | --- |

* Total population and age-specific population estimates taken from the 2000 U.S. Census. Populations are rounded to the nearest 0.1 million. The urban areas given in this table are those considered in the studies used in the $O_3$ risk assessment, with the exception of the larger Boston area, which is the CSA for Boston (since the study that estimated a concentration-respone function for asthma among children was conducted in Springfield, MA and CT).

** Population derived as follows: The populations of children <5 and 5 - 12 in the counties listed were multiplied by corresponding percents of children [in each age group] in New England with "current asthma" -- 5.1% and 10.7% for the two age groups, respectively (see "The Burden of Asthma in New England." Asthma Regional Council. March 2006. Table S-2. www.asthmaregionalcouncil.org ). These estimated numbers of asthmatic children were then multiplied by the estimated percent of asthmatic children using maintenance medications (40%) (obtained via email 4-05-06 from Jeanne Moorman) and the results were summed.

**Table 5-3. Baseline Mortality Rates (per 100,000 Population) Used in the $O_3$ Risk Assessment***

| City | Counties | Type of Mortality (ICD-9 Codes) | | |
|---|---|---|---|---|
| | | Non-accidental (<800) | Cardiorespiratory (390-448; 490-496; 487; 480-486; 507) | Respiratory (460-519) |
| **Atlanta** | Fulton, DeKalb | 623 | 131 | --- |
| **Boston** | Suffolk | 736 | --- | --- |
| **Chicago** | Cook | 781 | 189 | --- |
| **Cleveland** | Cuyahoga | 1,058 | 268 | --- |
| **Detroit** | Wayne | 913 | 234 | 76 |
| **Houston** | Harris | 533 | 123 | --- |
| **Los Angeles** | Los Angeles | 569 | 155 | --- |
| **New York** | Bronx, Kings, Queens, New York, Richmond, Westchester | 704 | 199 | --- |
| **Philadelphia** | Philadelphia | 1,057 | 242 | --- |
| **Sacramento** | Sacramento | 686 | --- | --- |
| **St. Louis** | St. Louis City | 1147 | --- | --- |
| **Washington, D.C.** | Washington, D.C. | 942 | --- | --- |
| **National** | --- | 790 | 196 | 80 |

* Data for the year 2002 from United States Department of Health and Human Services (US DHHS), Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS), Compressed Mortality File (CMF) compiled from CMF 1968-1988, Series 20, No. 2A 2000, CMF 1989-1998, Series 20, No. 2E 2003 and CMF 1999-2002, Series 20, No. 2H 2004 on CDC WONDER On-line Database. See http://wonder.cdc.gov/.

**Table 5-4. Baseline Rates for Hospital Admissions Used in the $O_3$ Risk Assessment**

| Relevant Population | Rate per 100,000 Relevant Population* | | | |
|---|---|---|---|---|
| | Los Angeles[1] | New York[2] | Detroit[3] | Cleveland[4] |
| | Ages 30+ | All Ages | Ages 65+ | Ages 65+ |
| **Admissions for:** | | | | |
| Pulmonary illness (DRG Codes 75 – 101) – spring | 208 | --- | --- | --- |
| Pulmonary illness (DRG Codes 75 – 101) – summer | 174 | --- | --- | --- |
| Respiratory illness (ICD codes 466, 480-486, 490, 491, 492, 493) | --- | 800 | --- | --- |
| Asthma (ICD code 493) | --- | 327 | --- | --- |
| Pneumonia (ICD codes 480-486) | --- | --- | 2,068 | --- |
| Respiratory illness ((ICD codes 460-519) | --- | --- | --- | 3,632 |

[1] Rates of unscheduled hospital admissions were calculated from patient discharge data for 1999, obtained from California's Office of Statewide Health Planning and Development, which also provided records of hospital admissions for the study by Linn et al. (2000).
[2] Rates of unscheduled hospital admissions were calculated from patient discharge data for 2001, obtained from the New York Statewide Planning and Research Cooperative.
[3] Rates were calculated from hospitalization data for Wayne County for the year 2000, obtained from the Michigan Health and Hospital Association in April 2002.
[4] Based on mean daily hospital admissions for ages 65+ for ICD-9 codes 460-519 -- Table 1 in Schwartz et al. (1996).

The current risk assessment incorporates some of the variability in key inputs to the analysis by using location-specific inputs (e.g., location-specific concentration-response functions, baseline incidence rates, and air quality data). Although spatial variability in these key inputs across all U.S. locations has not been fully characterized, variability across the selected locations is imbedded in the analysis by using, to the extent possible, inputs specific to each urban area. Temporal variability is more difficult to address, because the risk assessment focuses on some unspecified time in the future. 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, years 2002 and 2004 air quality data for all of the urban locations, and recent mortality baseline incidence rates (from 2002). However, future changes in inputs have not been predicted (e.g., future population levels or possible changes in baseline incidence rates).

A number of important sources of uncertainty were addressed where possible. Section 4.1.9 in the draft Risk Assessment TSD 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 epidemiological portion of the risk assessment and how they are dealt with or considered in the risk assessment:

- Causality. There is uncertainty about whether each of the estimated associations between $O_3$ indicators and the various health endpoints included in this risk assessment actually reflect a causal relationship. Our judgment, as discussed in more detail in Chapter 3 (section 3.7.5), is that for the health effects included in the risk assessment (i.e, increased respiratory symptoms in moderate to severe asthmatic children, increased respiratory-related hospital admissions, total non-accidental mortality, and cardiorespiratory mortality) we judge that there is, at a minimum, a likely causal relationship with either short-term $O_3$ exposure itself or with $O_3$ serving as an indicator for itself and other components of the photochemical oxidant mix, especially during the warm $O_3$ season.

- Empirically estimated concentration-response relationships. In estimating the concentration-response relationships, there are uncertainties: (1) surrounding estimates of $O_3$ coefficients in concentration-response functions used in the assessment, (2) concerning the specification of the concentration-response model (including the shape of the relationship) and whether or not a population threshold or non-linear relationship exists within the range of concentrations examined in the studies , (3) related to the extent to which concentration-response relationships derived from studies in a given location and time when $O_3$ levels were higher or behavior and/or housing conditions were different provide accurate representations of the relationships for the same locations with lower air quality distributions and different behavior and/or housing conditions, and (4) concerning the possible role of co-pollutants which also may have varied between the time of the studies and the current assessment period. The approach taken to characterize uncertainties in the concentration-response functions

arising from sample size considerations is discussed below. With respect to the shape of the function and whether or not a population threshold may exist, as discussed in Chapter 3, the CD concludes (section 8.5, p.8-44) that "the limited evidence suggests that if there is a threshold level in $O_3$ health effects, it is likely near the lower limit of ambient $O_3$ concentrations in the United States." As discussed in Chapter 3 and in the CD (CD, p.7-175), results from recent large U.S. multi-city time-series studies and meta-analyses also show effect estimates that are consistent across studies and robust to control for potential confounders.

- Adequacy of ambient $O_3$ monitors as surrogate for population exposure. The extent to which there are differences in the relationship between spatial variation in ambient $O_3$ concentrations and ambient exposures in the original epidemiology studies compared to more recent ambient $O_3$ data introduces additional uncertainty in the risk estimates. As discussed in the CD, Section 3.9, using ambient concentrations to determine exposure generally overestimates true personal $O_3$ exposures by approximately 2- to 4-fold in available studies, resulting in biased descriptions of underlying concentration-response relationships and attenuated risk estimates. The implication is that the effects being estimated occur at fairly low exposures and the potency of $O_3$ is greater than these effects estimates indicate. Thus, the risk estimates presented here may underestimate the overall impact of $O_3$ exposures on mortality and hospital admissions.

- Adjustment of air quality distributions to simulate just meeting the current standard. The shape of the distribution of hourly $O_3$ concentrations that would result upon just meeting the current or alternative 8-hr standards is unknown. Based on an analysis of historical data, we believe that the Quadratic air quality adjustment procedure provides reasonable estimates of the shape of the distribution; however, there is greater uncertainty for those urban areas that have air quality well above the current standard (e.g., Los Angeles, Houston). As noted previously, there is considerable year to year variability in $O_3$ concentrations over a three-year period in many of the urban areas examined. This leads to substantial year-to-year variability in risk estimates associated with $O_3$ concentrations when air quality is simulated to just meet the current and potential alternative standards.

- Estimated background concentrations for each location. The calculation of risk associated with recent air quality in excess of background requires as an input estimates of background concentrations for each location throughout the period of the assessment. The estimated background concentrations have been obtained from runs of the GEOS-CHEM global model (see section 2.7) and introduce some uncertainty into the risk estimates for both the recent air quality scenario and the just meeting the current 8-hr standard, both of which are calculated as risk in excess of background.

- Baseline incidence rates and population data. There are uncertainties related to: (1) the extent to which baseline incidence rates, age distributions, and other relevant demographic variables that impact the risk estimates vary for the year(s) when the actual epidemiological studies were conducted, the recent year of air quality used in this assessment, and some unspecified future year when air quality is adjusted to simulate just meeting the current or alternative standards and (2) the use of annual or seasonal incidence rate data to develop daily health effects incidence data. Spatial

variability in baseline incidence and population data is taken into account by use of city-specific data in most cases.

One of the most critical elements in the risk assessment is the concentration-response relationships used in the assessment. The uncertainty resulting from the statistical uncertainty associated with the estimate of the $O_3$ coefficient in the concentration-response function was characterized either by confidence intervals or by Bayesian credible intervals around the corresponding point estimates of risk. Confidence and credible intervals express the range within which the true risk is likely to fall if the only uncertainty surrounding the $O_3$ coefficient involved sample size considerations. Other uncertainties, such as differences in study location, time period, and model uncertainties are not represented by the confidence or credible intervals presented.

Two large scale multi-city mortality studies, Bell et al. (2004) and Huang et al. (2004), reported both multi-location and single-location concentration-response functions, using a Bayesian two-stage hierarchical model. In these cases, the single-location estimates can be adjusted to make more efficient use of the data from all locations. The resulting "shrinkage" estimates are so called because they "shrink" the location-specific estimates towards the overall mean estimate (the mean of the posterior distribution of the multi-location concentration-response function coefficient). The greater the uncertainty about the estimate of the location-specific coefficient relative to the estimate of between-study heterogeneity, the more the location-specific estimate is "pulled in" towards the overall mean estimate. Bell et al. (2004) calculated these shrinkage estimates, which were presented in Figure 2 of that paper. These location-specific shrinkage estimates, and their adjusted standard errors were provided by the study authors and were used in the risk assessment.

The location-specific estimates reported in Table 1 of Huang et al. (2004) are not "shrinkage" estimates. However, the study authors provided the posterior distribution for the heterogeneity parameter, $\tau$, for their distributed lag model, shown in Figure 4(b) of their paper. Given this posterior distribution, and the original location-specific estimates presented in Table 1 of their paper, we calculated location-specific "shrinkage" estimates using a Bayesian method described in DuMouchel (1994) (see section 5B.3 in Appendix 5B of this Staff Paper). As with the shrinkage estimates presented in Bell et al. (2004), the resulting Bayesian shrinkage estimates use the data from all of the locations considered in the study more efficiently than do the original location-specific estimates. The calculation of these shrinkage estimates is thus one way to address the relatively large uncertainty surrounding estimates of coefficients in location-specific concentration-response functions.

With respect to model form, most of the epidemiological studies estimated $O_3$ coefficients using log-linear models. However, there still is substantial uncertainty about the correct

functional form of the relationship between $O_3$ and various health endpoints, especially at the low end of the range of observed concentrations. While there are likely biological thresholds in individuals for specific health responses, as discussed in section 3.4.6 available studies have found little evidence for population thresholds. For example, in a recent study, Bell et al. (2006), applied several statistical models to data on air pollution, weather, and mortality for the 98 NMMAPS communities to evaluate whether a threshold level exists for premature mortality. The results suggested that even low levels of tropospheric $O_3$, well below 0.08 ppm, are associated with premature mortality. However, as discussed in section 3.4.6 and in the CD, the use of ambient $O_3$ concentrations may obscure the presence of thresholds in epidemiological studies (CD p. 7-158). In those studies that provide suggestive evidence of thresholds, the potential thresholds are at low concentrations (CD, p. 7-159).

The CD finds that no definitive conclusion can be reached with regard to the existence of thresholds in epidemiological studies (CD, p. 8-44). We recognize, however, the possibility that thresholds for individuals may exist for reported associations at fairly low levels within the range of air quality observed in the studies, but not be detectable as population thresholds in epidemiological analyses. Based on the CD's conclusions, we judge that there is insufficient evidence to support use of potential threshold levels in the quantitative risk assessment, but we do recognize there is increasing uncertainty about the concentration-response relationship at lower concentrations that is not captured by the characterization of the statistical uncertainty due to sampling error. Therefore, as discussed later in this Chapter, the risk estimates for premature mortality, respiratory symptoms in moderate to severe asthmatic children, and respiratory-related hospital admissions associated with exposure to $O_3$ must be considered in the light of uncertainties about whether or not these $O_3$-related effects occur in the population at very low concentrations.

Several recent meta-analyses (Bell et al. 2005; Levy et al., 2005; and Ito et al., 2005) have addressed the impact of various factors on estimates of mortality associated with short-term exposures to $O_3$. We reviewed these meta-analyses for additional information that might be used to assist in characterizing the uncertainties associated with concentration-response functions for this health outcome. As discussed in Chapter 3, the CD observes common findings across all three analyses, in that all reported that effect estimates were larger in warm season analyses, reanalysis of results using default GAM criteria did not change the effect estimates, and there was no strong evidence of confounding by PM (CD, p. 7-97). Bell et al. (2005) and Ito et al. (2005) both provided suggestive evidence of publication bias, but $O_3$-mortality associations remained after accounting for that potential bias. The results from these meta-analyses, as well as several single- and multiple-city studies, also indicate that copollutants generally do not appear to substantially confound the association between $O_3$ and mortality.

As discussed in Chapter 3, while concluding that $O_3$-health associations are found to be generally consistent, the recent $O_3$-mortality meta-analyses indicate that some heterogeneity exists across studies (CD, pp. 7-96 – 7-97). The CD discusses a number of factors that could result in heterogeneity in associations between different geographic areas, focusing particularly on variables that can affect exposure to ambient $O_3$. For example, the use of air conditioning can reduce ambient exposures during the warm season, while increased outdoor activity can increase exposure.

## 5.4 OZONE RISK ESTIMATES

We present risk estimates associated with several air quality scenarios, including two recent years of air quality as represented by 2002 and 2004 monitoring data in section 5.4.1. In Section 5.4.2 we summarize risk estimates associated with air quality adjusted to simulate just meeting the current and several potential alternative 8-hr standards. In Section 5.4.3 we discuss and compare the risk estimates developed for the current review with the risk estimates developed for the prior $O_3$ NAAQS review completed in July 1997. Finally, in section 5.4.4 we present key observations from the health risk assessment.

### 5.4.1 Recent Air Quality

In the prior risk assessment, risks for lung function decrements associated with 1-hr heavy exertion, 1-hr moderate exertion, and 8-hr moderate exertion exposures were estimated. Since the 8-hr moderate exertion exposure scenario for children clearly resulted in the greatest health risks in terms of lung function decrements, we have chosen to include only the 8-hr moderate exertion exposures in the current risk assessment for this health endpoint. Thus, the risk estimates presented here are most useful for making relative comparisons across alternative air quality scenarios and do not represent the total risks for lung function decrements in children or other groups within the general population associated with any of the air quality scenarios. Thus, some outdoor workers and adults engaged in moderate exertion over multi-hour periods (e.g., 6-8 hr exposures) also would be expected to experience similar lung function decrements. However, the percentage of each of these other subpopulations expected to experience these effects is expected to be smaller than children or "active" children who tend to spend more hours outdoors while active based on the exposure analyses conducted during the prior review.

Tables 5-5 and 5-6 display the risk estimates for "active" school age children (ages 5-18) associated with 2004 and 2002 $O_3$ concentrations for three different levels ($\geq$ 10, 15 and $\geq$ 20%) of lung function decrement responses for the 12 urban areas Similar estimates for $\geq$ 10, 15, and 20% decrement in lung function for all school age children can be found in the draft Risk Assessment TSD. These two tables also include risk estimates associated with air quality

adjusted to simulate just meeting the current 0.08 ppm, 8-hr standard, which will be discussed further in section 5.4.2. All estimates in both tables reflect responses associated with exposure to $O_3$ in excess of exposures associated with background $O_3$ concentrations. Table 5-5 shows the number and percent of "active" children estimated to have at least 1 lung function response during the $O_3$ season. Table 5-6 displays the total number of occurrences for the specified lung function responses during the $O_3$ season. As illustrated by the estimates shown in these two tables, a child may experience multiple occurrences of a lung function response during the $O_3$ season. For example, in Atlanta the median estimate is that 15,000 "active" school age children experienced an $FEV_1$ decrement $\geq$ 15% during the $O_3$ season with a median estimate of 48,000 occurrences of this same response in this population for 2004 air quality data. Thus, for this example on average each child is estimated to have over 3 occurrences of this lung function response during the $O_3$ season.

As shown in Table 5-5, across the 12 urban areas, the ranges in median estimates of the percent of "active" school age children estimated to experience at least one $FEV_1$ decrement $\geq$ 15% during the $O_3$ season are 1.2-6.5% for 2004 and 5.3-10.4% for 2002. The ranges in median estimates of the percent of "active" school age children estimated to experience at least one $FEV_1$ decrement $\geq$ 20% during the $O_3$ season across these same 12 urban areas is 0.2-2.3% for 2004 and 1.8-4.4% for 2002.

In terms of total occurrences of $FEV_1$ decrement $\geq$ 15% during the $O_3$ season, Table 5-6 shows a range of median estimates from 14,000 to over 500,000 responses in 2004 and from 37,000 to over 500,000 responses in 2002 for "active" school age children across the 12 urban areas associated with $O_3$ concentrations. For $FEV_1$ decrement $\geq$ 20% during the $O_3$ season, Table 5-6 shows a range of median estimates from 1,000 to 95,000 in 2004 and from 7,000 to over 130,000 across the 12 urban areas for total occurrences in "active" school age children.

Both Tables 5-5 and 5-6 also include 95% confidence intervals for the lung function decrement risk estimates based on sample size considerations. These confidence intervals only represent part of the uncertainty associated with these risk estimates. Additional uncertainties are summarized in section 5.3.2.5 and should be kept in mind as one considers the risk estimates in these tables.

The risk estimates associated with 2004 and 2002 $O_3$ concentrations for morbidity health endpoints based on epidemiological studies are shown in Tables 5-7 and 5-8 for respiratory symptoms in moderate to severe asthmatic children for the Boston urban area and in Tables 5-9 and 5-10 for excess hospital admissions for total respiratory illness and asthma (which is a subset of total respiratory illness admissions) for the New York City urban area. Additional hospital admission estimates for three other locations are provided in the draft Risk Assessment TSD. All

**Table 5-5. Comparison of Number and Percent of Active School Age Children Estimated to Experience Lung Function Responses Associated with 8-Hour Ozone Exposure While Engaged in Moderate Exertion for Location Specific $O_3$ Seasons***

| Location | Health Outcome | Active Children (Ages 5-18) Having at Least 1 Lung Function Response Associated with 8-Hour O3 Exposure Under Moderate Exertion** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Recent Air Quality (2004) | | Just Meeting Current 8-Hour Standard (based on adjusting 2004 air quality) | | Recent Air Quality (2002) | | Just Meeting Current 8-Hour Standard (based on adjusting 2002 air quality) | |
| | | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent |
| Atlanta | FEV1>=10% | 44 (15 - 73) | 9.8% (3.3% - 16.2%) | 32 (9 - 57) | 7.2% (2% - 12.7%) | 62 (25 - 94) | 13.8% (5.7% - 21.1%) | 45 (16 - 74) | 10.2% (3.5% - 16.6%) |
| | FEV1>=15% | 15 (3 - 47) | 3.4% (0.6% - 10.5%) | 9 (1 - 35) | 2% (0.2% - 7.9%) | 27 (7 - 65) | 6% (1.5% - 14.6%) | 16 (3 - 49) | 3.6% (0.6% - 10.9%) |
| | FEV1>=20% | 4 (0 - 30) | 0.9% (0.1% - 6.7%) | 2 (0 - 23) | 0.4% (0% - 5.1%) | 9 (1 - 42) | 2.1% (0.3% - 9.4%) | 4 (0 - 31) | 1% (0.1% - 7%) |
| Boston | FEV1>=10% | 34 (9 - 59) | 7% (2% - 12.4%) | 24 (5 - 46) | 5% (1.1% - 9.5%) | 72 (33 - 108) | 15.2% (6.9% - 22.7%) | 53 (20 - 84) | 11.1% (4.3% - 17.7%) |
| | FEV1>=15% | 9 (1 - 37) | 2% (0.2% - 7.7%) | 5 (0 - 28) | 1.1% (0.1% - 5.8%) | 35 (12 - 77) | 7.4% (2.4% - 16.2%) | 21 (5 - 57) | 4.5% (1.1% - 12%) |
| | FEV1>=20% | 2 (0 - 23) | 0.4% (0% - 4.9%) | 1 (0 - 17) | 0.1% (0% - 3.6%) | 14 (3 - 50) | 3% (0.7% - 10.6%) | 7 (1 - 36) | 1.5% (0.2% - 7.6%) |
| Chicago | FEV1>=10% | 48 (11 - 89) | 5.5% (1.2% - 10.2%) | 33 (5 - 65) | 3.7% (0.6% - 7.4%) | 125 (54 - 190) | 14.8% (6.3% - 22.3%) | 89 (32 - 145) | 10.5% (3.7% - 17%) |
| | FEV1>=15% | 10 (1 - 54) | 1.2% (0.1% - 6.2%) | 5 (0 - 39) | 0.6% (0% - 4.4%) | 58 (16 - 133) | 6.8% (1.9% - 15.7%) | 33 (6 - 95) | 3.9% (0.7% - 11.2%) |
| | FEV1>=20% | 1 (0 - 35) | 0.2% (0% - 3.9%) | 0 (0 - 24) | 0% (0% - 2.8%) | 21 (3 - 86) | 2.5% (0.4% - 10.1%) | 9 (1 - 61) | 1.1% (0.1% - 7.2%) |
| Cleveland | FEV1>=10% | 17 (5 - 31) | 6.9% (1.9% - 12.2%) | 11 (2 - 22) | 4.5% (0.9% - 8.7%) | 45 (21 - 65) | 18.3% (8.7% - 26.6%) | 30 (12 - 48) | 12.4% (4.8% - 19.6%) |
| | FEV1>=15% | 5 (0 - 19) | 1.9% (0.2% - 7.6%) | 2 (0 - 13) | 0.8% (0% - 5.2%) | 23 (8 - 48) | 9.5% (3.2% - 19.5%) | 12 (3 - 32) | 5.1% (1.1% - 13.3%) |
| | FEV1>=20% | 1 (0 - 12) | 0.4% (0% - 4.8%) | 0 (0 - 8) | 0.1% (0% - 3.3%) | 10 (2 - 31) | 3.9% (0.8% - 12.7%) | 4 (0 - 21) | 1.6% (0.1% - 8.4%) |

| Location | Health Outcome | Active Children (Ages 5-18) Having at Least 1 Lung Function Response Associated with 8-Hour O3 Exposure Under Moderate Exertion** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Recent Air Quality (2004) | | Just Meeting Current 8-Hour Standard (based on adjusting 2004 air quality) | | Recent Air Quality (2002) | | Just Meeting Current 8-Hour Standard (based on adjusting 2002 air quality) | |
| | | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent |
| **Detroit** | FEV1>=10% | 33 (9 - 59) | 6.7% (1.8% - 11.9%) | 24 (5 - 46) | 4.9% (1% - 9.3%) | 74 (32 - 111) | 15.4% (6.7% - 23.2%) | 55 (21 - 89) | 11.6% (4.3% - 18.5%) |
| | FEV1>=15% | 9 (1 - 37) | 1.7% (0.1% - 7.4%) | 5 (0 - 28) | 1% (0% - 5.6%) | 34 (10 - 79) | 7.2% (2% - 16.4%) | 21 (4 - 59) | 4.5% (0.8% - 12.3%) |
| | FEV1>=20% | 2 (0 - 23) | 0.3% (0% - 4.7%) | 1 (0 - 18) | 0.1% (0% - 3.5%) | 13 (2 - 50) | 2.6% (0.3% - 10.5%) | 6 (0 - 38) | 1.3% (0.1% - 7.8%) |
| **Houston** | FEV1>=10% | 59 (24 - 91) | 12.2% (4.9% - 18.7%) | 34 (10 - 58) | 6.9% (2% - 11.9%) | 58 (24 - 89) | 12.3% (5% - 18.7%) | 34 (10 - 57) | 7.1% (2.1% - 12%) |
| | FEV1>=15% | 25 (6 - 62) | 5.2% (1.3% - 12.8%) | 10 (1 - 37) | 2% (0.2% - 7.5%) | 25 (7 - 61) | 5.3% (1.4% - 12.9%) | 10 (1 - 36) | 2.1% (0.3% - 7.6%) |
| | FEV1>=20% | 9 (1 - 41) | 1.8% (0.3% - 8.3%) | 2 (0 - 24) | 0.4% (0% - 4.8%) | 9 (1 - 40) | 1.8% (0.3% - 8.4%) | 2 (0 - 23) | 0.5% (0% - 4.9%) |
| **Los Angeles** | FEV1>=10% | 223 (99 - 323) | 13.8% (6.1% - 20%) | 62 (15 - 110) | 3.8% (0.9% - 6.8%) | 225 (103 - 324) | 13.8% (6.3% - 19.9%) | 63 (16 - 110) | 3.9% (1% - 6.8%) |
| | FEV1>=15% | 105 (28 - 229) | 6.5% (1.7% - 14.1%) | 14 (0 - 67) | 0.9% (0% - 4.1%) | 110 (32 - 232) | 6.7% (1.9% - 14.2%) | 15 (1 - 67) | 0.9% (0% - 4.1%) |
| | FEV1>=20% | 37 (6 - 150) | 2.3% (0.3% - 9.2%) | 1 (0 - 44) | 0.1% (0% - 2.7%) | 41 (7 - 153) | 2.5% (0.5% - 9.4%) | 2 (0 - 45) | 0.1% (0% - 2.7%) |
| **New York** | FEV1>=10% | 148 (45 - 255) | 8.1% (2.4% - 13.9%) | 82 (16 - 160) | 4.5% (0.9% - 8.7%) | 312 (144 - 459) | 17.3% (8% - 25.4%) | 178 (60 - 296) | 9.9% (3.3% - 16.3%) |
| | FEV1>=15% | 45 (6 - 162) | 2.5% (0.3% - 8.8%) | 15 (0 - 96) | 0.8% (0% - 5.2%) | 155 (50 - 331) | 8.6% (2.8% - 18.3%) | 62 (10 - 192) | 3.4% (0.6% - 10.6%) |
| | FEV1>=20% | 11 (1 - 103) | 0.6% (0% - 5.6%) | 1 (0 - 60) | 0.1% (0% - 3.3%) | 62 (12 - 216) | 3.4% (0.7% - 11.9%) | 16 (1 - 122) | 0.9% (0.1% - 6.8%) |
| **Philadelphia** | FEV1>=10% | 49 (16 - 82) | 9.2% (3% - 15.4%) | 32 (8 - 58) | 5.9% (1.4% - 10.9%) | 104 (51 - 149) | 19.5% (9.5% - 27.9%) | 70 (28 - 108) | 13.1% (5.2% - 20.4%) |
| | FEV1>=15% | 16 (2 - 53) | 3% (0.4% - 9.9%) | 7 (0 - 35) | 1.4% (0.1% - 6.6%) | 55 (20 - 110) | 10.4% (3.7% - 20.7%) | 29 (7 - 74) | 5.5% (1.3% - 13.9%) |

| Location | Health Outcome | Active Children (Ages 5-18) Having at Least 1 Lung Function Response Associated with 8-Hour O3 Exposure Under Moderate Exertion** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Recent Air Quality (2004) | | Just Meeting Current 8-Hour Standard (based on adjusting 2004 air quality) | | Recent Air Quality (2002) | | Just Meeting Current 8-Hour Standard (based on adjusting 2002 air quality) | |
| | | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent |
| | FEV1>=20% | 4 (0 - 34) | 0.7% (0% - 6.3%) | 1 (0 - 23) | 0.2% (0% - 4.2%) | 23 (5 - 72) | 4.4% (1% - 13.6%) | 10 (1 - 47) | 1.8% (0.2% - 8.9%) |
| Sacramento | FEV1>=10% | 12 (4 - 19) | 7.9% (2.8% - 12.5%) | 6 (2 - 10) | 4% (1% - 6.9%) | 20 (9 - 29) | 13.2% (5.9% - 19.2%) | 11 (4 - 17) | 7.2% (2.4% - 11.5%) |
| | FEV1>=15% | 4 (1 - 12) | 2.9% (0.4% - 8.1%) | 1 (0 - 6) | 1% (0% - 4.2%) | 9 (2 - 21) | 6.3% (1.7% - 13.6%) | 4 (0 - 11) | 2.5% (0.3% - 7.4%) |
| | FEV1>=20% | 1 (0 - 8) | 0.7% (0% - 5.3%) | 0 (0 - 4) | 0.1% (0% - 2.8%) | 3 (0 - 13) | 2.2% (0.3% - 8.9%) | 1 (0 - 7) | 0.5% (0% - 4.8%) |
| St. Louis | FEV1>=10% | 18 (5 - 33) | 6.6% (1.7% - 11.8%) | 15 (3 - 28) | 5.4% (1.2% - 10%) | 44 (20 - 64) | 16.2% (7.3% - 24%) | 36 (15 - 55) | 13.4% (5.4% - 20.7%) |
| | FEV1>=15% | 5 (0 - 20) | 1.7% (0.1% - 7.2%) | 3 (0 - 17) | 1.1% (0% - 6.1%) | 21 (6 - 46) | 7.8% (2.4% - 17.2%) | 15 (4 - 38) | 5.8% (1.4% - 14.2%) |
| | FEV1>=20% | 1 (0 - 13) | 0.3% (0% - 4.6%) | 0 (0 - 11) | 0.1% (0% - 3.9%) | 8 (1 - 30) | 3% (0.5% - 11.1%) | 5 (1 - 24) | 1.9% (0.2% - 9.1%) |
| Washington, D.C. | FEV1>=10% | 68 (24 - 111) | 9.9% (3.5% - 16.2%) | 44 (12 - 79) | 6.4% (1.7% - 11.5%) | 121 (57 - 177) | 17.8% (8.3% - 26%) | 82 (31 - 130) | 12.1% (4.6% - 19.1%) |
| | FEV1>=15% | 24 (5 - 73) | 3.6% (0.7% - 10.6%) | 11 (1 - 49) | 1.7% (0.1% - 7.1%) | 61 (20 - 129) | 9% (3% - 18.9%) | 33 (7 - 88) | 4.8% (1% - 12.8%) |
| | FEV1>=20% | 7 (1 - 47) | 1% (0.1% - 6.8%) | 2 (0 - 31) | 0.3% (0% - 4.5%) | 25 (5 - 84) | 3.7% (0.8% - 12.3%) | 10 (1 - 56) | 1.5% (0.1% - 8.2%) |

*Risks are estimated for exposures in excess of policy relevant background.

**Numbers are median (0.5 fractile) numbers of children. Numbers in parentheses below the median are 95% confidence intervals based on statistical uncertainty surrounding the O3 coefficient. Numbers are rounded to the nearest 1000. Percents are rounded to the nearest tenth.

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**Table 5-6. Comparison of Number and Percent of Occurrences of Lung Function Responses Among Active School Age Children Associated with 8-Hour O3 Exposure While Engaged in Moderate Exertion for Location Specific O3 Seasons***

| Location | Health Outcome | Occurrences of Lung Function Response Associated with 8-Hour O3 Exposure Among Active Children (Ages 5-18) While Engaged in Moderate Exertion** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Recent Air Quality (2004) | | Just Meeting Current 8-Hour Standard (based on adjusting 2004 air quality) | | Recent Air Quality (2002) | | Just Meeting Current 8-Hour Standard (based on adjusting 2002 air quality) | |
| | | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent |
| **Atlanta** | FEV1>=10% | 439 (53 - 1389) | 1.1% (0.1% - 3.5%) | 333 (31 - 1143) | 0.8% (0.1% - 2.9%) | 527 (91 - 1457) | 1.3% (0.2% - 3.7%) | 404 (55 - 1203) | 1% (0.1% - 3%) |
| | FEV1>=15% | 48 (3 - 732) | 0.1% (0% - 1.8%) | 27 (1 - 592) | 0.1% (0% - 1.5%) | 88 (11 - 800) | 0.2% (0% - 2%) | 51 (4 - 647) | 0.1% (0% - 1.6%) |
| | FEV1>=20% | 7 (0 - 320) | 0% (0% - 0.8%) | 2 (0 - 244) | 0% (0% - 0.6%) | 18 (2 - 380) | 0% (0% - 1%) | 8 (0 - 293) | 0% (0% - 0.7%) |
| **Boston** | FEV1>=10% | 272 (27 - 934) | 0.9% (0.1% - 3.1%) | 205 (15 - 767) | 0.7% (0% - 2.6%) | 488 (94 - 1357) | 1.6% (0.3% - 4.6%) | 378 (57 - 1146) | 1.3% (0.2% - 3.9%) |
| | FEV1>=15% | 24 (1 - 485) | 0.1% (0% - 1.6%) | 12 (0 - 391) | 0% (0% - 1.3%) | 93 (18 - 747) | 0.3% (0.1% - 2.5%) | 55 (7 - 614) | 0.2% (0% - 2.1%) |
| | FEV1>=20% | 3 (0 - 198) | 0% (0% - 0.7%) | 1 (0 - 149) | 0% (0% - 0.5%) | 25 (4 - 350) | 0.1% (0% - 1.2%) | 11 (1 - 272) | 0% (0% - 0.9%) |
| **Chicago** | FEV1>=10% | 453 (35 - 1536) | 0.8% (0.1% - 2.8%) | 319 (16 - 1181) | 0.6% (0% - 2.1%) | 889 (171 - 2315) | 1.7% (0.3% - 4.4%) | 662 (97 - 1881) | 1.2% (0.2% - 3.5%) |
| | FEV1>=15% | 29 (1 - 811) | 0.1% (0% - 1.5%) | 13 (0 - 615) | 0% (0% - 1.1%) | 168 (25 - 1304) | 0.3% (0% - 2.5%) | 92 (8 - 1033) | 0.2% (0% - 2%) |
| | FEV1>=20% | 2 (0 - 334) | 0% (0% - 0.6%) | 0 (0 - 235) | 0% (0% - 0.4%) | 39 (4 - 638) | 0.1% (0% - 1.2%) | 15 (1 - 480) | 0% (0% - 0.9%) |
| **Cleveland** | FEV1>=10% | 166 (16 - 548) | 0.9% (0.1% - 3%) | 115 (7 - 420) | 0.6% (0% - 2.3%) | 353 (79 - 890) | 2% (0.5% - 5.1%) | 254 (42 - 712) | 1.5% (0.2% - 4.1%) |
| | FEV1>=15% | 14 (1 - 290) | 0.1% (0% - 1.6%) | 6 (0 - 218) | 0% (0% - 1.2%) | 80 (15 - 506) | 0.5% (0.1% - 2.9%) | 40 (5 - 391) | 0.2% (0% - 2.3%) |
| | FEV1>=20% | 1 (0 - 122) | 0% (0% - 0.7%) | 0 (0 - 84) | 0% (0% - 0.5%) | 22 (3 - 252) | 0.1% (0% - 1.5%) | 8 (0 - 183) | 0% (0% - 1.1%) |

| Location | Health Outcome | Occurrences of Lung Function Response Associated with 8-Hour O3 Exposure Among Active Children (Ages 5-18) While Engaged in Moderate Exertion** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Recent Air Quality (2004) | | Just Meeting Current 8-Hour Standard (based on adjusting 2004 air quality) | | Recent Air Quality (2002) | | Just Meeting Current 8-Hour Standard (based on adjusting 2002 air quality) | |
| | | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent |
| **Detroit** | FEV1>=10% | 288 (26 - 978) | 0.9% (0.1% - 3.1%) | 219 (14 - 805) | 0.7% (0% - 2.5%) | 556 (111 - 1456) | 1.8% (0.4% - 4.8%) | 433 (69 - 1227) | 1.4% (0.2% - 4.1%) |
| | FEV1>=15% | 23 (1 - 513) | 0.1% (0% - 1.6%) | 12 (0 - 416) | 0% (0% - 1.3%) | 110 (17 - 815) | 0.4% (0.1% - 2.7%) | 66 (6 - 670) | 0.2% (0% - 2.2%) |
| | FEV1>=20% | 2 (0 - 211) | 0% (0% - 0.7%) | 1 (0 - 160) | 0% (0% - 0.5%) | 26 (2 - 397) | 0.1% (0% - 1.3%) | 12 (0 - 312) | 0% (0% - 1%) |
| **Houston** | FEV1>=10% | 449 (75 - 1037) | 0.7% (0.1% - 1.7%) | 266 (31 - 602) | 0.4% (0% - 1%) | 389 (68 - 870) | 0.7% (0.1% - 1.5%) | 227 (28 - 475) | 0.4% (0% - 0.8%) |
| | FEV1>=15% | 72 (9 - 620) | 0.1% (0% - 1%) | 27 (1 - 374) | 0% (0% - 0.6%) | 66 (9 - 529) | 0.1% (0% - 0.9%) | 25 (1 - 307) | 0% (0% - 0.5%) |
| | FEV1>=20% | 14 (2 - 332) | 0% (0% - 0.5%) | 3 (0 - 202) | 0% (0% - 0.3%) | 14 (2 - 287) | 0% (0% - 0.5%) | 3 (0 - 172) | 0% (0% - 0.3%) |
| **Los Angeles** | FEV1>=10% | 3093 (525 - 7966) | 1.5% (0.2% - 3.7%) | 1106 (73 - 3598) | 0.5% (0% - 1.7%) | 2811 (482 - 7212) | 1.3% (0.2% - 3.3%) | 997 (70 - 3105) | 0.5% (0% - 1.4%) |
| | FEV1>=15% | 503 (56 - 4496) | 0.2% (0% - 2.1%) | 58 (1 - 1948) | 0% (0% - 0.9%) | 465 (62 - 4100) | 0.2% (0% - 1.9%) | 57 (1 - 1718) | 0% (0% - 0.8%) |
| | FEV1>=20% | 95 (8 - 2247) | 0% (0% - 1.1%) | 2 (0 - 826) | 0% (0% - 0.4%) | 97 (10 - 2046) | 0% (0% - 0.9%) | 3 (0 - 745) | 0% (0% - 0.3%) |
| **New York** | FEV1>=10% | 1288 (137 - 4116) | 1.1% (0.1% - 3.5%) | 795 (48 - 2939) | 0.7% (0% - 2.5%) | 2487 (521 - 6315) | 2.1% (0.4% - 5.4%) | 1587 (212 - 4682) | 1.4% (0.2% - 4%) |
| | FEV1>=15% | 124 (8 - 2191) | 0.1% (0% - 1.9%) | 38 (1 - 1521) | 0% (0% - 1.3%) | 519 (90 - 3580) | 0.4% (0.1% - 3.1%) | 197 (15 - 2539) | 0.2% (0% - 2.2%) |
| | FEV1>=20% | 16 (1 - 941) | 0% (0% - 0.8%) | 2 (0 - 583) | 0% (0% - 0.5%) | 131 (16 - 1779) | 0.1% (0% - 1.5%) | 29 (1 - 1154) | 0% (0% - 1%) |
| **Philadelphia** | FEV1>=10% | 481 (59 - 1419) | 1.2% (0.1% - 3.6%) | 331 (27 - 1085) | 0.8% (0.1% - 2.8%) | 900 (206 - 2159) | 2.3% (0.5% - 5.4%) | 641 (108 - 1710) | 1.6% (0.3% - 4.3%) |

| Location | Health Outcome | Occurrences of Lung Function Response Associated with 8-Hour O3 Exposure Among Active Children (Ages 5-18) While Engaged in Moderate Exertion** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Recent Air Quality (2004) | | Just Meeting Current 8-Hour Standard (based on adjusting 2004 air quality) | | Recent Air Quality (2002) | | Just Meeting Current 8-Hour Standard (based on adjusting 2002 air quality) | |
| | | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent | Number (1000s) | Percent |
| | FEV1>=15% | 53 (3 - 774) | 0.1% (0% - 2%) | 23 (1 - 581) | 0.1% (0% - 1.5%) | 207 (40 - 1252) | 0.5% (0.1% - 3.2%) | 104 (12 - 957) | 0.3% (0% - 2.4%) |
| | FEV1>=20% | 7 (0 - 352) | 0% (0% - 0.9%) | 2 (0 - 244) | 0% (0% - 0.6%) | 56 (8 - 643) | 0.1% (0% - 1.6%) | 20 (1 - 463) | 0.1% (0% - 1.2%) |
| **Sacramento** | FEV1>=10% | 165 (20 - 486) | 0.9% (0.1% - 2.8%) | 94 (7 - 315) | 0.5% (0% - 1.8%) | 229 (38 - 623) | 1.3% (0.2% - 3.6%) | 140 (15 - 436) | 0.8% (0.1% - 2.5%) |
| | FEV1>=15% | 18 (1 - 263) | 0.1% (0% - 1.5%) | 5 (0 - 166) | 0% (0% - 0.9%) | 37 (4 - 342) | 0.2% (0% - 2%) | 14 (1 - 232) | 0.1% (0% - 1.3%) |
| | FEV1>=20% | 2 (0 - 122) | 0% (0% - 0.7%) | 0 (0 - 70) | 0% (0% - 0.4%) | 7 (1 - 166) | 0% (0% - 1%) | 1 (0 - 103) | 0% (0% - 0.6%) |
| **St. Louis** | FEV1>=10% | 184 (17 - 591) | 0.9% (0.1% - 2.8%) | 150 (12 - 507) | 0.7% (0.1% - 2.4%) | 335 (69 - 845) | 1.7% (0.4% - 4.3%) | 282 (50 - 744) | 1.4% (0.3% - 3.8%) |
| | FEV1>=15% | 15 (0 - 313) | 0.1% (0% - 1.5%) | 10 (0 - 267) | 0% (0% - 1.3%) | 69 (11 - 479) | 0.4% (0.1% - 2.4%) | 49 (6 - 416) | 0.3% (0% - 2.1%) |
| | FEV1>=20% | 1 (0 - 135) | 0% (0% - 0.6%) | 1 (0 - 111) | 0% (0% - 0.5%) | 17 (2 - 240) | 0.1% (0% - 1.2%) | 10 (1 - 203) | 0.1% (0% - 1%) |
| **Washington, D.C.** | FEV1>=10% | 562 (71 - 1758) | 1.1% (0.1% - 3.5%) | 394 (34 - 1374) | 0.8% (0.1% - 2.7%) | 983 (205 - 2541) | 1.9% (0.4% - 5%) | 712 (110 - 2044) | 1.4% (0.2% - 4%) |
| | FEV1>=15% | 66 (6 - 933) | 0.1% (0% - 1.8%) | 29 (1 - 711) | 0.1% (0% - 1.4%) | 204 (36 - 1425) | 0.4% (0.1% - 2.8%) | 105 (11 - 1109) | 0.2% (0% - 2.2%) |
| | FEV1>=20% | 10 (1 - 409) | 0% (0% - 0.8%) | 3 (0 - 288) | 0% (0% - 0.6%) | 52 (7 - 704) | 0.1% (0% - 1.4%) | 19 (1 - 515) | 0% (0% - 1%) |

*Risks are estimated for exposures in excess of policy relevant background.

**Numbers are median (0.5 fractile) numbers of occurrences. Numbers in parentheses below the median are 95% confidence intervals based on statistical uncertainty surrounding the O3 coefficient. Numbers are rounded to the nearest 1000. Percents are rounded to the nearest tenth.

results are for health risks associated with short-term exposures to $O_3$ concentrations in excess of background levels from April through September for 2004 and 2002, respectively.

As discussed previously, risk estimates were developed for several respiratory symptoms in asthmatic children ages 0 to 12 who use maintenance medications based on the concentration-response functions provided in Gent et al. (2003). These estimates were only developed for the Boston urban area which was near the location of the original epidemiological study. Tables 5-7 and 5-8 show risk estimates for three different respiratory symptoms (i.e., chest tightness, shortness of breath, and wheeze) for the Boston area associated with $O_3$ levels above background for April through September of 2004 and 2002, respectively. The risk estimates are expressed in terms of cases, cases per 100,000 relevant population, and percent of total incidence

Tables 5-9 and 5-10 show risk estimates of unscheduled hospital admissions for respiratory illness in the New York City area associated with $O_3$ levels above background for April through September of 2004 and 2002, respectively. The risk estimates are expressed in terms of cases, cases per 100,000 relevant population, and percent of total incidence.

Tables 5-11 and 5-12 show risk estimates for non-accidental mortality associated with $O_3$ levels above background for April through September of 2004 and 2002, respectively. Similar tables for cardiorespiratory mortality are included in the draft Risk Assessment TSD. The risk estimates are presented in terms of estimated incidence, incidence per 100,000 relevant population, and percent of total incidence.

Bell et al. (2004) reported both multi-location and single-location concentration-response functions in a variety of locations, using a Bayesian two-stage hierarchical model. In these cases, the single-location estimates can be adjusted to make more efficient use of the data from all locations. The resulting "shrinkage" estimates are so called because they "shrink" the location-specific estimates towards the overall mean estimate (the mean of the posterior distribution of the multi-location concentration-response function coefficient). The greater the uncertainty about the estimate of the location-specific coefficient relative to the estimate of between-study heterogeneity, the more the location-specific estimate is "pulled in" towards the overall mean estimate. Bell et al. (2004) calculated these shrinkage estimates, which were presented in Figure 2 of that paper. These location-specific shrinkage estimates, and their adjusted standard errors were provided to us by the study authors and were used in the risk assessment. Thus, where available, risk estimates are included in Tables 5-11 and 5-12 based on both single-city and multi-city functions. The ranges shown in these tables are based either on the 95 percent confidence intervals around those estimates (if the coefficients were estimated using classical statistical techniques) or on the 95 percent credible intervals (if the coefficients were estimated using Bayesian statistical techniques).

**Table 5-7. Estimated Respiratory Symptoms Associated with Recent (April - September, 2004) $O_3$ Concentrations Above Background in Boston, MA**

| Health Effects* | Study | Ages | Lag | Exposure Metric | Other Pollutants in Model | Health Effects Associated with $O_3$ Above Policy Relevant Background Levels** | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 1-day lag | 1 hr max. | none | 5300 (800 - 9200) | 20700 (3300 - 36300) | 9.4% (1.5% - 16.5%) |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 0-day lag | 1 hr max. | PM2.5 | 8400 (3800 - 12400) | 33100 (14900 - 49100) | 15.1% (6.8% - 22.3%) |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 1-day lag | 1 hr max. | PM2.5 | 7700 (3000 - 11800) | 30400 (11800 - 46800) | 13.8% (5.4% - 21.3%) |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 1-day lag | 8 hr max. | none | 5400 (1700 - 8700) | 21400 (6900 - 34500) | 9.7% (3.1% - 15.7%) |
| Respiratory symptoms among asthmatic medication-users -- shortness of breath | Gent et al. (2003) | 0 - 12 | 1-day lag | 1 hr max. | none | 5700 (700 - 10200) | 22500 (2700 - 40200) | 8.2% (1% - 14.7%) |
| Respiratory symptoms among asthmatic medication-users -- shortness of breath | Gent et al. (2003) | 0 - 12 | 1-day lag | 8 hr max. | none | 6300 (1200 - 10800) | 24700 (4800 - 42500) | 9% (1.8% - 15.5%) |
| Respiratory symptoms among asthmatic medication-users -- wheeze | Gent et al. (2003) | 0 - 12 | 0-day lag | 1 hr max. | PM2.5 | 15400 (5500 - 24200) | 60800 (21800 - 95600) | 11.9% (4.3% - 18.7%) |

*Health effects are associated with short-term exposures to $O_3$.

**Incidence was quantified down to estimated policy relevant background levels. Incidences of respiratory symptom-days and respiratory symptom-days per 100,000 relevant population are rounded to the nearest 100. Percents are rounded to the nearest tenth.

Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient.

**Table 5-8. Estimated Respiratory Symptoms Associated with Recent (April - September, 2002) $O_3$ Concentrations Above Background in Boston, MA**

| Health Effects* | Study | Ages | Lag | Exposure Metric | Other Pollutants in Model | Health Effects Associated with $O_3$ Above Policy Relevant Background Levels** | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 1-day lag | 1 hr max. | none | 6900 (1100 - 11800) | 27200 (4500 - 46600) | 12.4% (2% - 21.2%) |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 0-day lag | 1 hr max. | PM2.5 | 10800 (5000 - 15700) | 42700 (19700 - 62100) | 19.5% (9% - 28.3%) |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 1-day lag | 1 hr max. | PM2.5 | 10000 (4000 - 15000) | 39400 (15700 - 59400) | 17.9% (7.1% - 27%) |
| Respiratory symptoms among asthmatic medication-users -- chest tightness | Gent et al. (2003) | 0 - 12 | 1-day lag | 8 hr max. | none | 7200 (2400 - 11400) | 28400 (9300 - 44900) | 12.9% (4.2% - 20.5%) |
| Respiratory symptoms among asthmatic medication-users -- shortness of breath | Gent et al. (2003) | 0 - 12 | 1-day lag | 1 hr max. | none | 7500 (900 - 13200) | 29500 (3700 - 52000) | 10.8% (1.3% - 19%) |
| Respiratory symptoms among asthmatic medication-users -- shortness of breath | Gent et al. (2003) | 0 - 12 | 1-day lag | 8 hr max. | none | 8300 (1700 - 14000) | 32800 (6600 - 55300) | 11.9% (2.4% - 20.2%) |
| Respiratory symptoms among asthmatic medication-users -- wheeze | Gent et al. (2003) | 0 - 12 | 0-day lag | 1 hr max. | PM2.5 | 20100 (7400 - 31000) | 79200 (29000 - 122300) | 15.5% (5.7% - 23.9%) |

*Health effects are associated with short-term exposures to $O_3$.

**Incidence was quantified down to estimated policy relevant background levels. Incidences of respiratory symptom-days and respiratory symptom-days per 100,000 relevant population are rounded to the nearest 100. Percents are rounded to the nearest tenth.

Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient.

We observe from Tables 5-11 and 5-12 that estimates of $O_3$-related non-accidental mortality reported by Schwartz (2004) for Chicago, Detroit, and Houston, based on both single city and multi-city concentration-response functions, tend to be higher than other estimates for these locations. This is mainly due to the use of the 1-hr maximum $O_3$ concentration in Schwartz (2004), rather than the 24-hr average, as the exposure metric. The changes from recent (2004 or 2002)) 1-hr maximum to background 1-hr maximum $O_3$ concentrations were generally larger in the assessment locations than the corresponding changes from recent 24-hr average to background 24-hr average $O_3$ concentrations. For example, for 2004 air quality the estimated $O_3$-related (non-accidental) mortality in Detroit based on Bell et al. (2004), which used a 24-hr average indicator, ranged from 0.2% (based on 95 city model) to 0.4% of total incidence (based on single-city model). In contrast, the estimated $O_3$-related (non-accidental) mortality in Detroit based on Schwartz (2004), which used a 1-hr maximum $O_3$ concentration as the indicator, ranged from 0.7% (based on 14 city model) to 1.4% (based on single-city model).

Figures 5-4a and b show the estimated annual percent of non-accidental mortality associated with short-term exposure to $O_3$ concentrations within specified ranges for the warm $O_3$ season (April 1 to September 30) in two recent years. While the current $O_3$ standard is expressed in terms of an 8-hr daily maximum inidicator, the large multicity non-accidental (Bell et al. (2004) and cardiorespiratory (Huang et al. (2004) mortality studies reported concentration-response relationships for 24-hr average $O_3$ levels. Thus, the intervals shown in this figure are for 24-hr average concentrations. To provide some perspective on the 24-hr intervals shown, scatter plots comparing 8-hr daily maximum concentrations at the highest monitor with the average of the 24-hr average over all monitors within an urban area were developed and are included in Appendix 5A.2. These scatter plots show that 8-hr daily maximum concentrations on average are roughly twice the observed 24-hr average levels, although there is considerable variability in this relationship from day-to-day within an urban area. There also is some variability in this relationship between 8-hr daily maximum and 24-hr average levels across the 12 urban areas.

As shown in Figure 5-4a, in 2004, all $O_3$-related non-accidental mortality was associated with $O_3$ concentrations less than 0.06 ppm, 24 hr average, and most of that was associated with $O_3$ concentrations less than 0.04 ppm, 24-hr average. As shown in Figure 5-4b, in 2002, all $O_3$-related non-accidental mortality was associated with $O_3$ concentrations less than 0.08 ppm, 24-hr average and the great majority was associated with $O_3$ concentrations less than 0.06 ppm, 24-hr average. The results for cardiorespiratory mortality follow a similar pattern and are included in the draft Risk Assessment TSD.

**Table 5-9. Estimated Hospital Admissions Associated with Recent (April - September, 2004) $O_3$ Concentrations in NY, NY****

| Health Effects* | Study | Ages | Lag | Exposure Metric | Other Pollutants in Model | Health Effects Associated with $O_3$ Above Policy Relevant Background Levels* | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| Hospital admissions (unscheduled), respiratory illness | Thurston et al. (1992)*** | all | 3-day lag | 1 hr max. | none | 447 (108 - 786) | 5.6 (1.4 - 9.8) | 1.3% (0.3% - 2.2%) |
| Hospital admissions (unscheduled), asthma | Thurston et al. (1992)*** | all | 1-day lag | 1 hr max. | none | 382 (81 - 683) | 4.8 (1 - 8.5) | 2.9% (0.6% - 5.2%) |

*Incidences are rounded to the nearest whole number; incidences per 100,000 relevant population and percents are rounded to the nearest tenth.
**New York in this study is defined as the five boroughs of New York City.

Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient.

**Table 5-10. Estimated Hospital Admissions Associated with Recent (April - September, 2002) $O_3$ Concentrations in NY, NY****

| Health Effects | Study | Ages | Lag | Exposure Metric | Other Pollutants in Model | Health Effects Associated with $O_3$ Above Policy Relevant Background Levels* | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| Hospital admissions (unscheduled), respiratory illness | Thurston et al. (1992)*** | all | 3-day lag | 1 hr max. | none | 608 (147 - 1068) | 7.6 (1.8 - 13.3) | 1.7% (0.4% - 3%) |
| Hospital admissions (unscheduled), asthma | Thurston et al. (1992)*** | all | 1-day lag | 1 hr max. | none | 519 (110 - 928) | 6.5 (1.4 - 11.6) | 4% (0.8% - 7.1%) |

*Incidences are rounded to the nearest whole number; incidences per 100,000 relevant population and percents are rounded to the nearest tenth.
**New York in this study is defined as the five boroughs of New York City.

Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient.

**Table 5-11. Estimated Non-Accidental Mortality Associated with Recent (April - September, 2004) Ozone Concentrations**

| Location | Study | Lag | Exposure Metric | Non-Accidental Mortality Associated with $O_3$ Above Policy Relevant Background Levels** | | |
|---|---|---|---|---|---|---|
| | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| **Atlanta** | Bell et al. (2004) | distributed lag | 24 hr avg. | 6 (-26 - 38) | 0.4 (-1.8 - 2.6) | 0.1% (-0.6% - 0.8%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 12 (4 - 20) | 0.8 (0.3 - 1.4) | 0.3% (0.1% - 0.4%) |
| **Boston** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 7 (2 - 12) | 1.0 (0.3 - 1.7) | 0.3% (0.1% - 0.5%) |
| **Chicago** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 49 (16 - 81) | 0.9 (0.3 - 1.5) | 0.2% (0.1% - 0.4%) |
| | Schwartz (2004) | 0-day lag | 1 hr max. | 394 (125 - 658) | 7.3 (2.3 - 12.2) | 1.9% (0.6% - 3.1%) |
| | Schwartz -- 14 US Cities (2004) | 0-day lag | 1 hr max. | 148 (46 - 250) | 2.8 (0.9 - 4.6) | 0.7% (0.2% - 1.2%) |
| **Cleveland** | Bell et al. (2004) | distributed lag | 24 hr avg. | 27 (-17 - 69) | 1.9 (-1.2 - 5) | 0.4% (-0.2% - 0.9%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 17 (6 - 28) | 1.2 (0.4 - 2) | 0.2% (0.1% - 0.4%) |
| **Detroit** | Bell et al. (2004) | distributed lag | 24 hr avg. | 33 (-11 - 76) | 1.6 (-0.5 - 3.7) | 0.4% (-0.1% - 0.8%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 17 (6 - 28) | 0.8 (0.3 - 1.4) | 0.2% (0.1% - 0.3%) |
| | Schwartz (2004) | 0-day lag | 1 hr max. | 128 (-21 - 274) | 6.2 (-1 - 13.3) | 1.4% (-0.2% - 2.9%) |
| | Schwartz -- 14 US Cities (2004) | 0-day lag | 1 hr max. | 70 (22 - 117) | 3.4 (1.1 - 5.7) | 0.7% (0.2% - 1.2%) |
| | Ito (2003) | 0-day lag | 24 hr avg. | 40 (-37 - 116) | 2.0 (-1.8 - 5.6) | 0.4% (-0.4% - 1.2%) |
| **Houston** | Bell et al. (2004) | distributed lag | 24 hr avg. | 35 (2 - 67) | 1.0 (0.1 - 2) | 0.4% (0% - 0.7%) |

| Location | Study | Lag | Exposure Metric | Non-Accidental Mortality Associated with $O_3$ Above Policy Relevant Background Levels** | | |
|---|---|---|---|---|---|---|
| | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 17 (6 - 28) | 0.5 (0.2 - 0.8) | 0.2% (0.1% - 0.3%) |
| | Schwartz (2004) | 0-day lag | 1 hr max. | 93 (9 - 176) | 2.7 (0.3 - 5.2) | 1% (0.1% - 1.9%) |
| | Schwartz -- 14 US Cities (2004) | 0-day lag | 1 hr max. | 78 (24 - 130) | 2.3 (0.7 - 3.8) | 0.9% (0.3% - 1.4%) |
| **Los Angeles** | Bell et al. (2004) | distributed lag | 24 hr avg. | 62 (-149 - 271) | 0.6 (-1.6 - 2.8) | 0.2% (-0.5% - 1%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 133 (45 - 221) | 1.4 (0.5 - 2.3) | 0.5% (0.2% - 0.8%) |
| **New York** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 60 (20 - 100) | 0.7 (0.2 - 1.1) | 0.2% (0.1% - 0.3%) |
| **Philadelphia** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 23 (8 - 38) | 1.5 (0.5 - 2.5) | 0.3% (0.1% - 0.5%) |
| | Moolgavkar et al. (1995) | 1-day lag | 24 hr avg. | 82 (52 - 112) | 5.4 (3.4 - 7.4) | 1% (0.6% - 1.4%) |
| **Sacramento** | Bell et al. (2004) | distributed lag | 24 hr avg. | 12 (-36 - 59) | 1.0 (-3 - 4.8) | 0.3% (-0.9% - 1.4%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 18 (6 - 29) | 1.4 (0.5 - 2.4) | 0.4% (0.1% - 0.7%) |
| **St Louis** | Bell et al. (2004) | distributed lag | 24 hr avg. | 3 (-6 - 13) | 1.0 (-1.7 - 3.6) | 0.2% (-0.3% - 0.6%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 3 (1 - 5) | 0.9 (0.3 - 1.5) | 0.2% (0.1% - 0.3%) |
| **Washington, D.C.** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 8 (3 - 14) | 1.5 (0.5 - 2.4) | 0.3% (0.1% - 0.5%) |

*All results are for mortality (among all ages) associated with short-term exposures to $O_3$. All results are based on single-pollutant models.

***IIncidence was quantified down to estimated policy relevant background levels. Incidences are rounded to the nearest whole number; incidences per 100,000 relevant population and percents are rounded to the nearest tenth.

Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient.

**Table 5-12. Estimated Non-Accidental Mortality Associated with Recent (April - September, 2002) $O_3$ Concentrations**

| Location | Study | Lag | Exposure Metric | Non-Accidental Mortality Associated with $O_3$ Above Policy Relevant | | |
|---|---|---|---|---|---|---|
| | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| Atlanta | Bell et al. (2004) | distributed lag | 24 hr avg. | 9 (-37 - 54) | 0.6 (-2.5 - 3.6) | 0.2% (-0.8% - 1.2%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 17 (6 - 29) | 1.2 (0.4 - 1.9) | 0.4% (0.1% - 0.6%) |
| Boston | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 10 (3 - 17) | 1.5 (0.5 - 2.5) | 0.4% (0.1% - 0.7%) |
| Chicago | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 69 (23 - 115) | 1.3 (0.4 - 2.1) | 0.3% (0.1% - 0.5%) |
| | Schwartz (2004) | 0-day lag | 1 hr max. | 505 (161 - 840) | 9.4 (3 - 15.6) | 2.4% (0.8% - 4%) |
| | Schwartz -- 14 US Cities (2004) | 0-day lag | 1 hr max. | 191 (60 - 321) | 3.6 (1.1 - 6) | 0.9% (0.3% - 1.5%) |
| Cleveland | Bell et al. (2004) | distributed lag | 24 hr avg. | 61 (-38 - 157) | 4.3 (-2.7 - 11.3) | 0.8% (-0.5% - 2.1%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 38 (13 - 64) | 2.8 (0.9 - 4.6) | 0.5% (0.2% - 0.9%) |
| Detroit | Bell et al. (2004) | distributed lag | 24 hr avg. | 57 (-18 - 131) | 2.8 (-0.9 - 6.3) | 0.6% (-0.2% - 1.4%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 29 (10 - 48) | 1.4 (0.5 - 2.3) | 0.3% (0.1% - 0.5%) |
| | Schwartz (2004) | 0-day lag | 1 hr max. | 181 (-30 - 385) | 8.8 (-1.4 - 18.7) | 1.9% (-0.3% - 4.1%) |
| | Schwartz -- 14 US Cities (2004) | 0-day lag | 1 hr max. | 99 (31 - 165) | 4.8 (1.5 - 8) | 1% (0.3% - 1.8%) |
| | Ito (2003) | 0-day lag | 24 hr avg. | 69 (-64 - 198) | 3.4 (-3.1 - 9.6) | 0.7% (-0.7% - 2.1%) |
| Houston | Bell et al. (2004) | distributed lag | 24 hr avg. | 29 (2 - 57) | 0.9 (0.1 - 1.7) | 0.3% (0% - 0.6%) |

| Location | Study | Lag | Exposure Metric | Non-Accidental Mortality Associated with $O_3$ Above Policy Relevant | | |
|---|---|---|---|---|---|---|
| | | | | Incidence | Incidence per 100,000 Relevant Population | Percent of Total Incidence |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 14 (5 - 24) | 0.4 (0.1 - 0.7) | 0.2% (0.1% - 0.3%) |
| | Schwartz (2004) | 0-day lag | 1 hr max. | 85 (8 - 161) | 2.5 (0.2 - 4.7) | 0.9% (0.1% - 1.8%) |
| | Schwartz -- 14 US Cities (2004) | 0-day lag | 1 hr max. | 71 (22 - 119) | 2.1 (0.7 - 3.5) | 0.8% (0.2% - 1.3%) |
| **Los Angeles** | Bell et al. (2004) | distributed lag | 24 hr avg. | 51 (-124 - 224) | 0.5 (-1.3 - 2.4) | 0.2% (-0.5% - 0.8%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 110 (37 - 184) | 1.2 (0.4 - 1.9) | 0.4% (0.1% - 0.7%) |
| **New York** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 105 (35 - 174) | 1.2 (0.4 - 2) | 0.3% (0.1% - 0.6%) |
| **Philadelphia** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 37 (12 - 62) | 2.4 (0.8 - 4.1) | 0.5% (0.2% - 0.8%) |
| | Moolgavkar et al. (1995) | 1-day lag | 24 hr avg. | 132 (83 - 180) | 8.7 (5.5 - 11.9) | 1.6% (1% - 2.2%) |
| **Sacramento** | Bell et al. (2004) | distributed lag | 24 hr avg. | 16 (-48 - 78) | 1.3 (-3.9 - 6.4) | 0.4% (-1.1% - 1.9%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 23 (8 - 39) | 1.9 (0.6 - 3.2) | 0.6% (0.2% - 0.9%) |
| **St Louis** | Bell et al. (2004) | distributed lag | 24 hr avg. | 6 (-11 - 23) | 1.9 (-3.1 - 6.7) | 0.3% (-0.5% - 1.2%) |
| | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 6 (2 - 10) | 1.7 (0.6 - 2.8) | 0.3% (0.1% - 0.5%) |
| **Washington, D.C.** | Bell et al. -- 95 US Cities (2004) | distributed lag | 24 hr avg. | 15 (5 - 25) | 2.6 (0.9 - 4.4) | 0.6% (0.2% - 0.9%) |

*All results are for mortality (among all ages) associated with short-term exposures to $O_3$. All results are based on single-pollutant models.

**Incidence was quantified down to estimated policy relevant background levels. Incidences are rounded to the nearest whole number; incidences per 100,000 relevant population and percents are rounded to the nearest tenth.

Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient.

1

**Figure 5-4. Estimated Annual Percent of Non-Accidental Mortality Associated with Short-Term Exposure to Recent $O_3$ Concentratons Above Background for the Period April – September (Based on Bell et al., 2004) – Total and Contribution of 24-Hour $O_3$ Ranges**

**Figure 5-4a. Based on 2004 Air Quality**

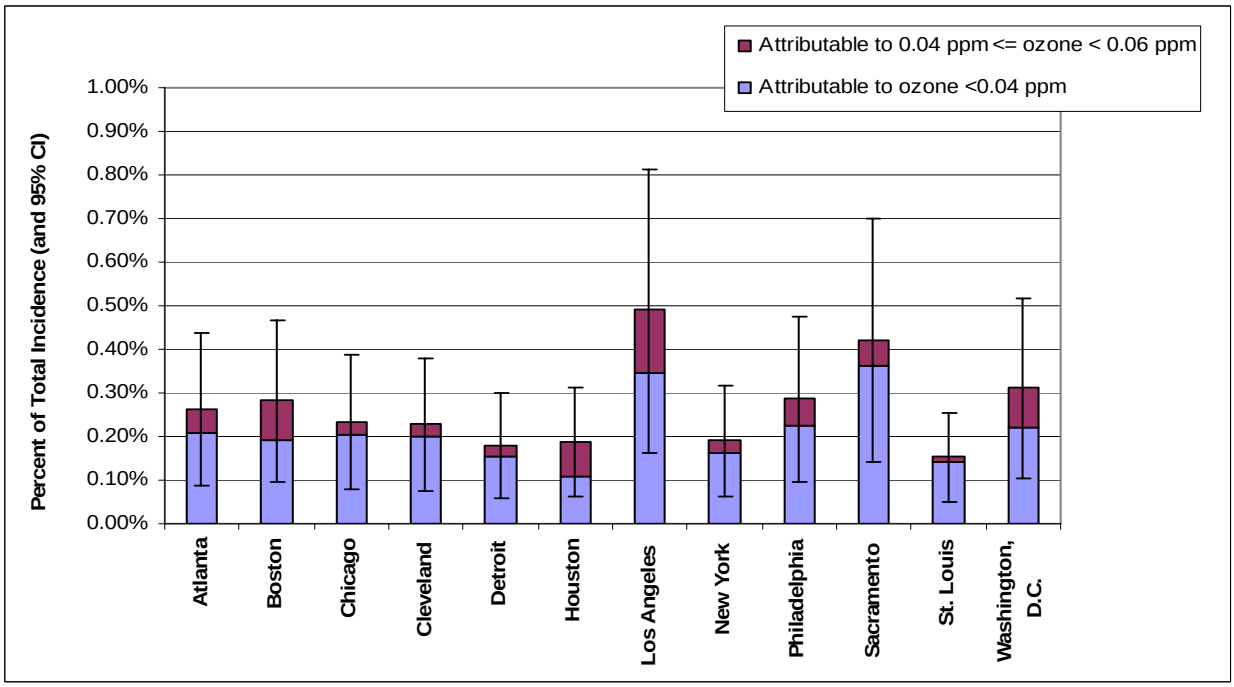
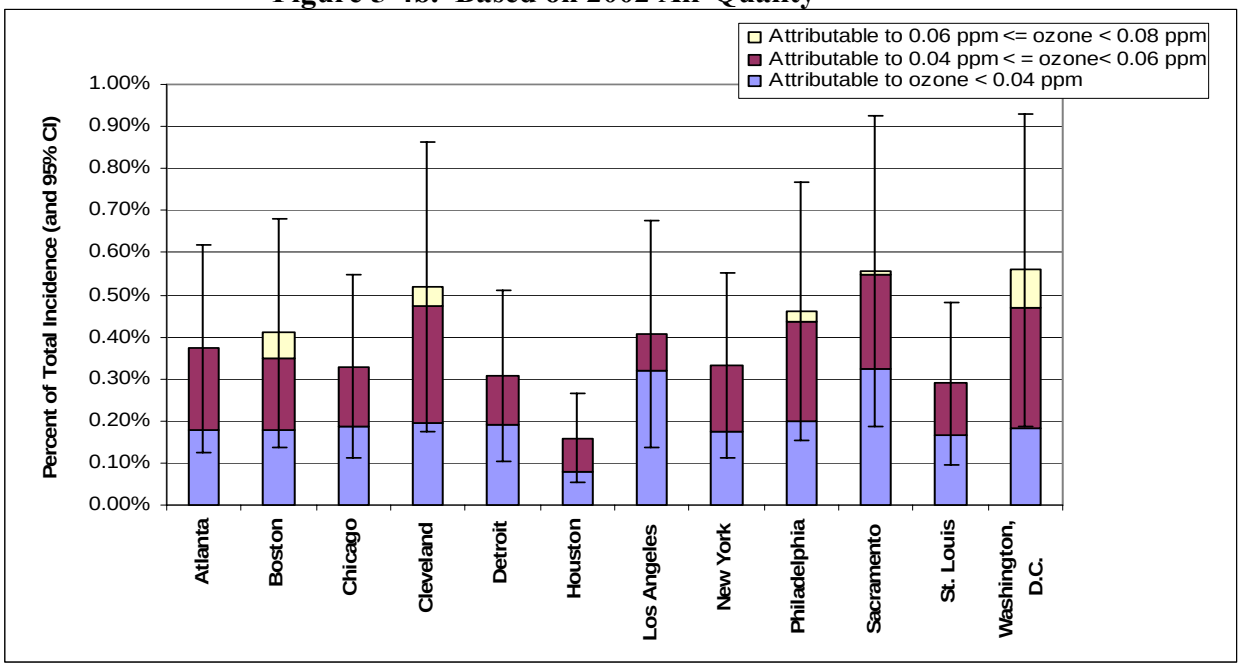



**Figure 5-4b. Based on 2002 Air Quality**



### 5.4.2 Just Meeting Current and Alternative Ozone Standards

As described in Chapter 4 and briefly in section 5.3.2.2, the risk estimates described in this section represent the risks for two separate $O_3$ seasons based on adjusting the $O_3$ levels observed in 2004 or 2002 to simulate $O_3$ levels associated with just meeting the current 0.08 ppm standard and several potential alternative 8-hr standards, using the 3-year design value from the 2002-2004 time period. To facilitate comparison of risk estimates across the 12 urban areas, figures used in this section present summaries of the risk estimates for the current and potential alternative 8-hr daily maximum standards using the current average 4$^{th}$ daily maximum 8-hr average form of the standard. Risk estimates for three additional alternative 8-hr standards (0.084 ppm, using an average 3$^{rd}$ daily maximum 8-hr average and 0.074 ppm using an average 3$^{rd}$ daily maximum 8-hr average form) are included in the tables in the draft Risk Assessment TSD. Because we had to simulate the profiles of $O_3$ concentrations that just meet the current and alternative 8-hour daily maximum $O_3$ standards in each location, there is additional uncertainty surrounding estimates of the reduced incidence associated with $O_3$ concentrations that just meet these $O_3$ standards.

This section first discusses the risk estimates for lung function responses, which are based on exposure-response relationships derived from controlled human exposure studies, and then risk estimates are explored for respiratory symptoms in asthmatic children, respiratory-related hospital admissions, and premature mortality which are based on concentration-response relationships obtained from epidemiological studies.

The risk estimates for lung function responses are for the $O_3$ season, which is all year in 3 of the study areas (Houston, Los Angeles, and Sacramento) and which is generally 6-7 months long in the other 9 urban study areas (e.g., April to September or October). The risk estimates for lung function responses in "active" school age children (ages 5 to 18) for just meeting the current 8-hr standard for 12 urban areas are summarized in Tables 5-5 and 5-6 presented in the previous section. Additional risk estimates for all school age children are presented in the draft Risk Assessment TSD.

In terms of total occurrences of $FEV_1$ decrement $\geq$ 15% during the $O_3$ season, Table 5-6 shows a range of median estimates from 5,000 to nearly 60,000 responses during the $O_3$ season for "active" school age children based on adjusting 2004 air quality data to just meeting the current 8-hour standard and from 14,000 to nearly 200,000 responses across the 12 urban areas associated with adjusting 2002 $O_3$ concentrations to just meeting the current 8-hour standard. For $FEV_1$ decrement $\geq$ 20% during the $O_3$ season, Table 5-6 shows a range of median estimates for "active" school age children across the 12 urban areas from 0 to 3,000 responses and from

1,000 to 29,000 responses based on adjusting 2004 and 2002 air quality data, respectively, to just meeting the current 8-hour standard.

Figures 5-5 shows the median estimates of the percent of "active" school age children estimated to experience at least one $FEV_1$ decrement $\geq$ 15% during the $O_3$ season across the 12 urban areas for recent air quality (2004) and upon just meeting the current and several alternative 8-hr standards. Figure 5C-1 in Appendix 5C of this Staff Paper shows a similar figure based on 2002 air quality data. For just meeting the current 8-hr standard the ranges of median estimates across the 12 urban areas are 0.6-2% based on adjusting 2004 air quality data and 0.9-5.8% based on adjusting 2002 air quality data. The ranges in median estimates of the percent of "active" school age children estimated to experience at least one $FEV_1$ decrement $\geq$ 20% during the $O_3$ season across these same 12 urban areas are 0-0.4% and 0.1-1.9%, based on adjusting 2004 and 2002 air quality data, respectively.

As an illustration, the median estimate for the number of "active" school age children estimated to experience $FEV_1$ decrements $\geq$ 15% under the current standard ranges from 2,000 to 15,000 children per urban area across the 12 urban areas and this would be reduced to a range of 0 to 3,000 children under the most stringent alternative standard examined (i.e., 0,06 ppm,) $4^{th}$ daily 8-hr maximum) Somewhat higher estimates are observed based on adjusting 2002 air quality to just meet the current and alternative 8-hr standards (see Table 5C-3 in the Appendix). By comparing the estimated number of occurrences shown in Tables 5C-1 and 5C-3 with the number of "active" children estimated to experience 1 or more responses shown in Tables 5C-5 and 5C-6, one can get an estimate of the average number of occurrences of a given response in an $O_3$ season. For example, for Atlanta it is estimated that 9,000 "active" children would have an $FEV_1$ decrement $\geq$ 15% and that there would be 27,000 occurrences of this response in this same population when 2004 air quality is adjusted to just meet the current 8-hr standard. Thus, on average it is estimated that there would be 3 occurrences per $O_3$ season per responding child for air quality just meeting the current 8-hr standard in this urban area. We recognize that some children in the population might have only 1 or 2 occurrences and some might have more than 3 per $O_3$ season.

Figure 5-6a and b shows the 95% confidence intervals for the lung function risk estimates for each of the 12 urban areas using the $FEV_1$ decrement $\geq$ 15% health response for recent $O_3$ levels (2004) and for 2004 air quality adjusted to just meet the current and alternative 8-hr average $4^{th}$ daily maximum standards. A comparable figure (Figure 5C-2a,b) using 2002 air quality and adjusting 2002 air quality to just meet the current and alternative 8-hr standards is included in Appendix 5C.

**Figure 5-5. Percent of Active Children (Ages 5-18) Engaged in Moderate Exertion Estimated to Experience At Least One Lung Function Response (Decrement in $FEV_1 \geq 15\%$) Associated with Exposure to $O_3$ Concentrations That Just Meet the Current and Alternative Average 4th Daily Maximum 8-Hour Standards, for Location-Specific $O_3$ Seasons (Based on Adjusting 2004 Air Quality)**

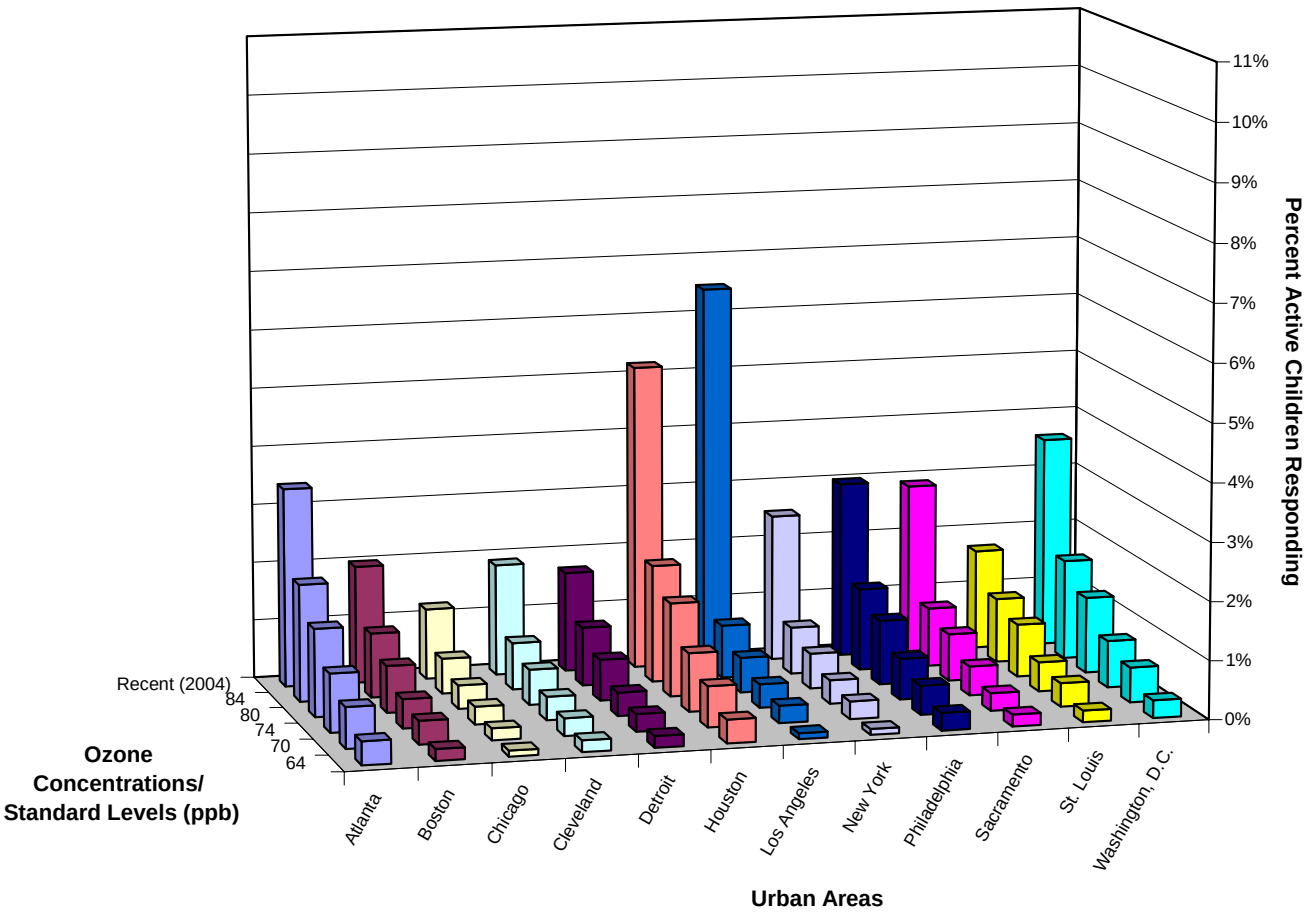


Figure 5-7 summarizes respiratory symptom response risk estimates associated with $O_3$ exposures during the April to September period for moderate/severe asthmatic children ages 0 to 12 in the Boston urban area based on the concentration-response relationships reported in Gent et al. (2003) for 2004 air quality and the current and alternative 8-hr standards based on adjusting 2004 air quality data. Figure 5C-3 (Appendix 5C) presents comparable estimates associated with 2002 air quality and just meeting the current and alternative 8-hr standards based on adjusting 2002 air quality data. These figures includes risk estimates for chest tightness based on single pollutant models and models that included $PM_{2.5}$. Two additional symptom endpoints, shortness of breath and wheeze are included in the tables in the draft Risk Assessment TSD and show similar patterns as the risk estimates for chest tightness.

The median estimated number of days involving chest tightness (using the concentration-response relationship with only $O_3$ in the model) ranges from 4,500 (based on adjusting 2004 air quality) to 6,100 (based on adjusting 2002 air quality) upon meeting the current 8-hr standard and these are reduced to 3,100 (based on adjusting 2004 air quality) to 4,600 days upon meeting the most stringent alternative examined (0.064 ppm, 4$^{th}$ daily maximum 8-hr average). These same ranges correspond to 8 to 11% of total incidence of chest tightness upon meeting the current 8-hr standard and to about 5.5 to 8% of total incidence of chest tightness upon meeting a 0.064 ppm, 4$^{th}$ daily maximum 8-hr average standard. As shown in Tables 5C-7 and 5C-9 (Appendix 5C), the symptom with the greatest incidence is wheeze and is based on an $O_3$ concentration-response relationship that included $PM_{2.5}$ in the model. These median estimates range from about 13,000 days with wheeze (based on adjusting 2004 air quality) to nearly 18,000 days (based on adjusting 2002 air quality) upon meeting the current 8-hr standard and these estimates are reduced to 9,000 (based on adjusting 2004 air quality) to about 13,000 (based on adjusting 2002 air quality) upon meeting a 0.064 ppm, 4$^{th}$ daily maximum 8-hr average standard. Confidence intervals, based on statistical uncertainty reflecting sample size considerations for incidence and percent of total incidence are shown in Tables 5C-7 through 5C-10 (Appendix 5C) based on adjusting 2004 and 2002 air quality.

Figure 5-8 summarizes unscheduled hospital admission risk estimates for respiratory illness and asthma in New York City associated with short-term exposures to $O_3$ concentrations in excess of background levels from April through September under recent air quality and when the current and alternative 8-hr standards are just met based on adjusting 2004 and 2002 air quality data, respectively. For total respiratory illness, Figure 5-8 shows about 4.6 cases per 100,000 relevant population, which represents 1% of total incidence or 366 cases when 2004 $O_3$ levels are adjusted to just meet the current 8-hr standard. For asthma-related hospital admissions, which are a subset of total respiratory illness admissions, the estimates are about 3.9 cases per 100,000 relevant population, which represents about 2.4% of total incidence or 313

**Figure 5-6a. Percent of Active Children (Ages 5-18) Engaged in Moderate Exertion Estimated to Experience At Least One Lung Function Response ($FEV_1$ decrement ≥ 15 %) Associated with Exposure to Recent (2004) $O_3$ Levels and Levels That Just Meet Alternative Average 4th Daily Maximum 8-Hour Standards, for Location-Specific $O_3$ Seasons**

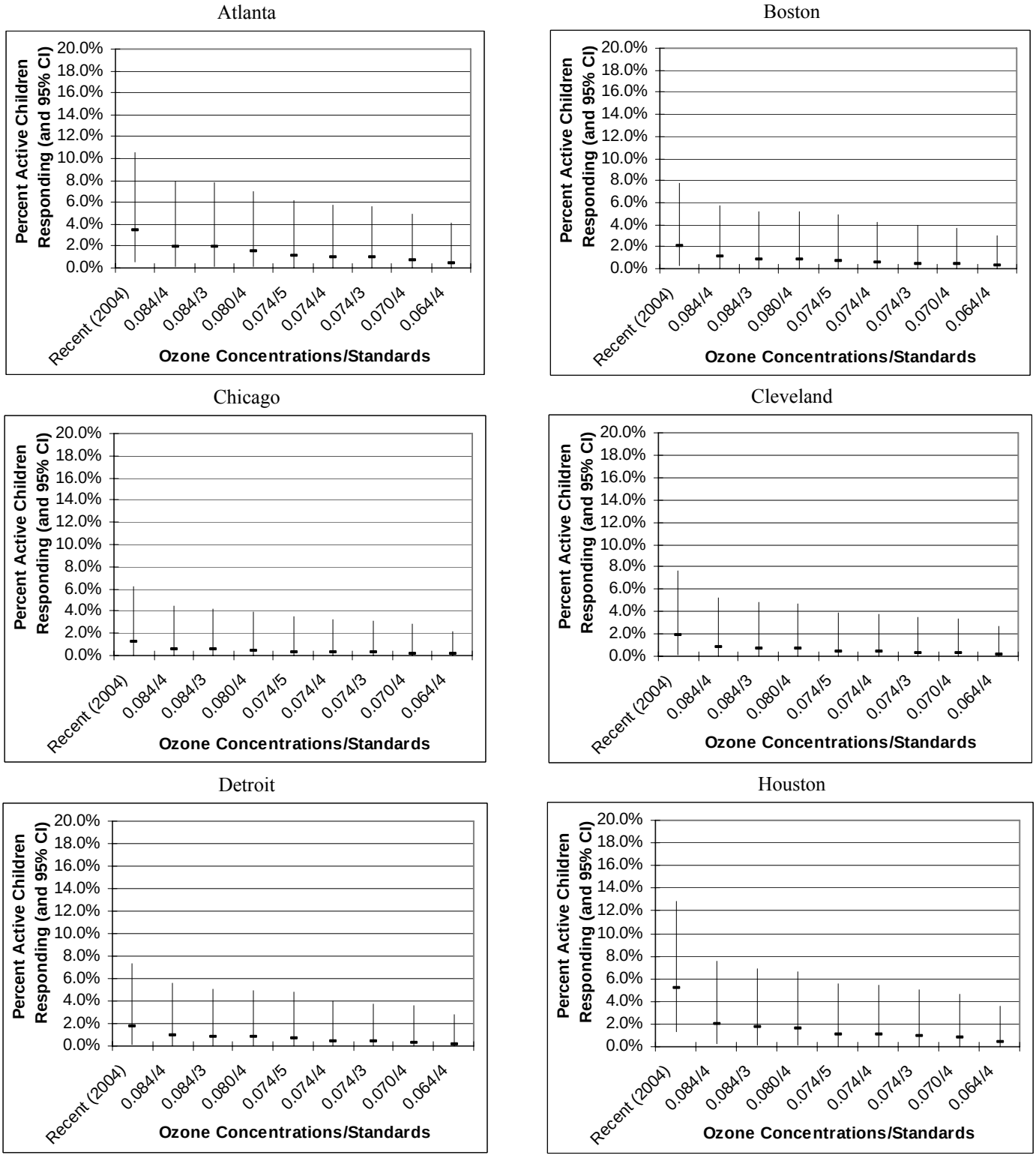
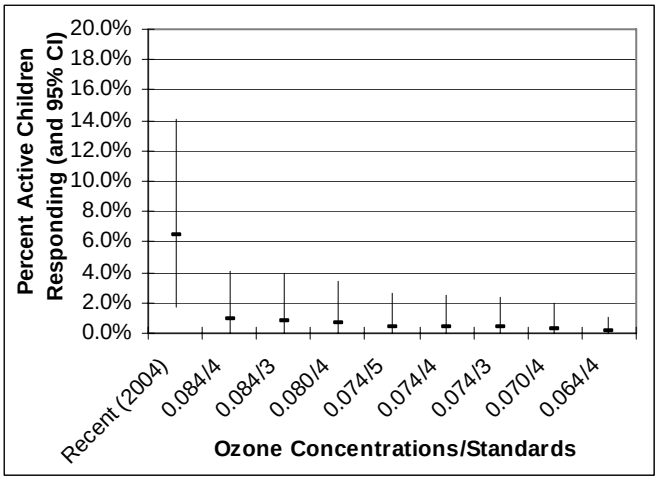
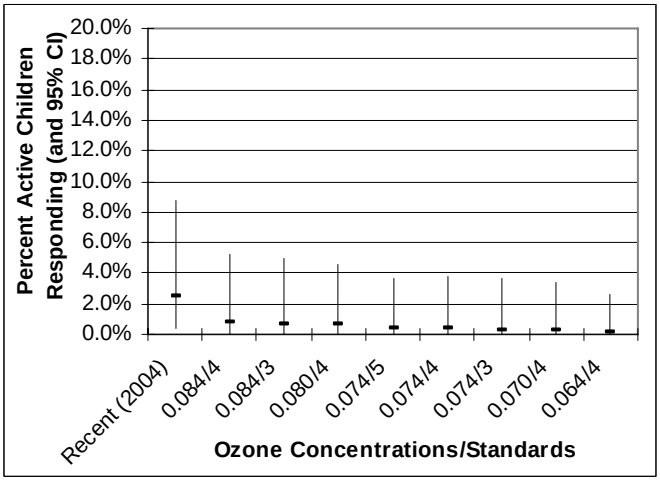


**Figure 5-6b. Percent of Active Children (Ages 5-18) Engaged in Moderate Exertion Estimated to Experience At Least One Lung Function Response ($FEV_1$ decrement ≥ 15 %) Associated with Exposure to Recent (2004) $O_3$ Levels and Levels That Just Meet Alternative Average 4th Daily Maximum 8-Hour Standards, for Location-Specific $O_3$ Seasons (cont'd)**

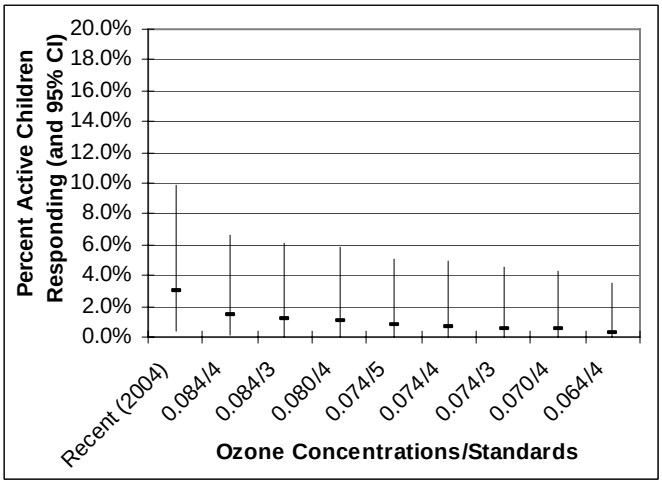
Los Angeles



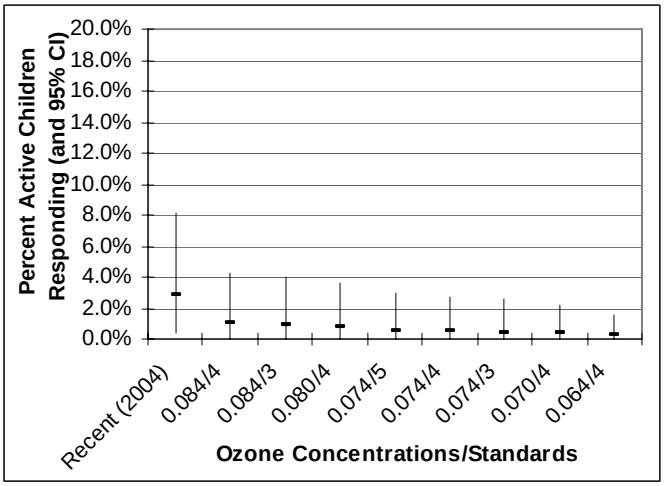

New York



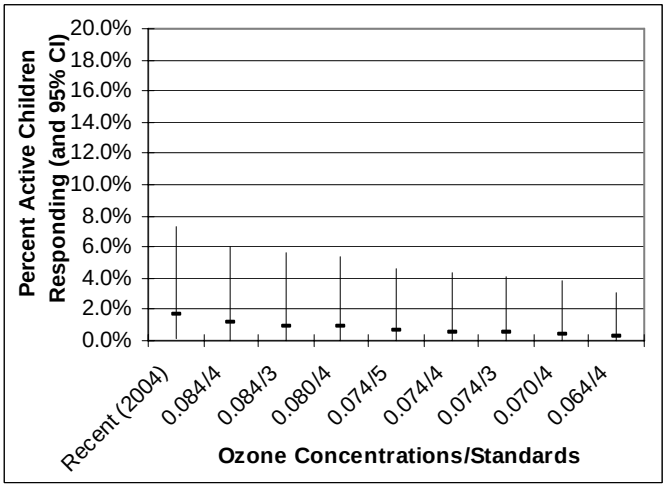

Philadelphia




Sacramento




St. Louis




Washington, D.C.

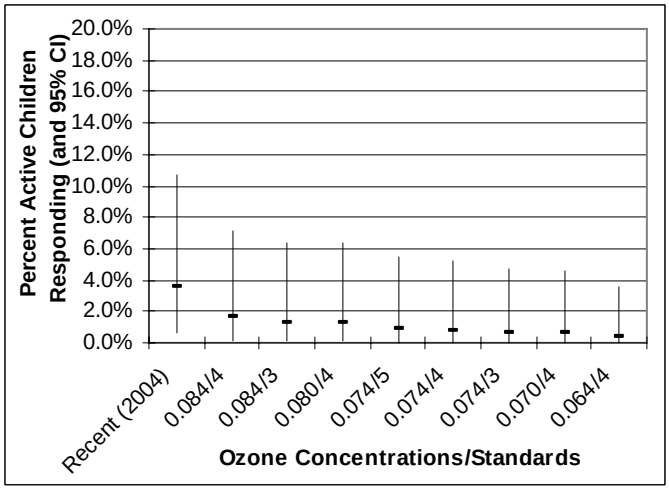
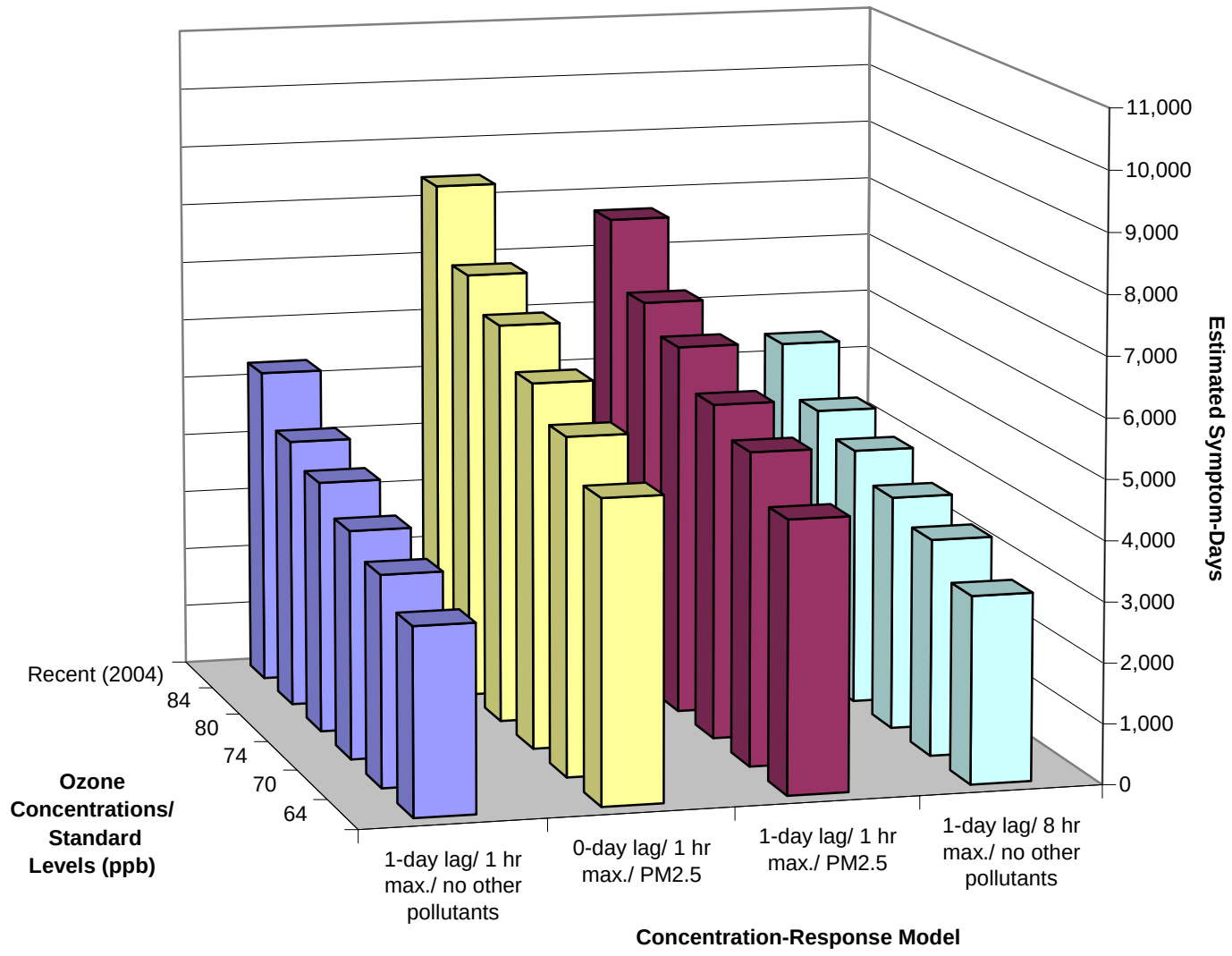


**Figure 5-7. Estimated Symptom-Days for Chest Tightness Among Moderate/Severe Asthmatic Children (Ages 0 – 12) in Boston Associated with Recent (April-September 2004) $O_3$ Levels and with Levels Just Meeting Alternative Average 4th Daily Maximum 8-Hour Ozone Standards***

(Based on Gent et al., 2003)




*95% confidence intervals associated with these risk estimates are provided in Table 5C-5 of the Appendix.

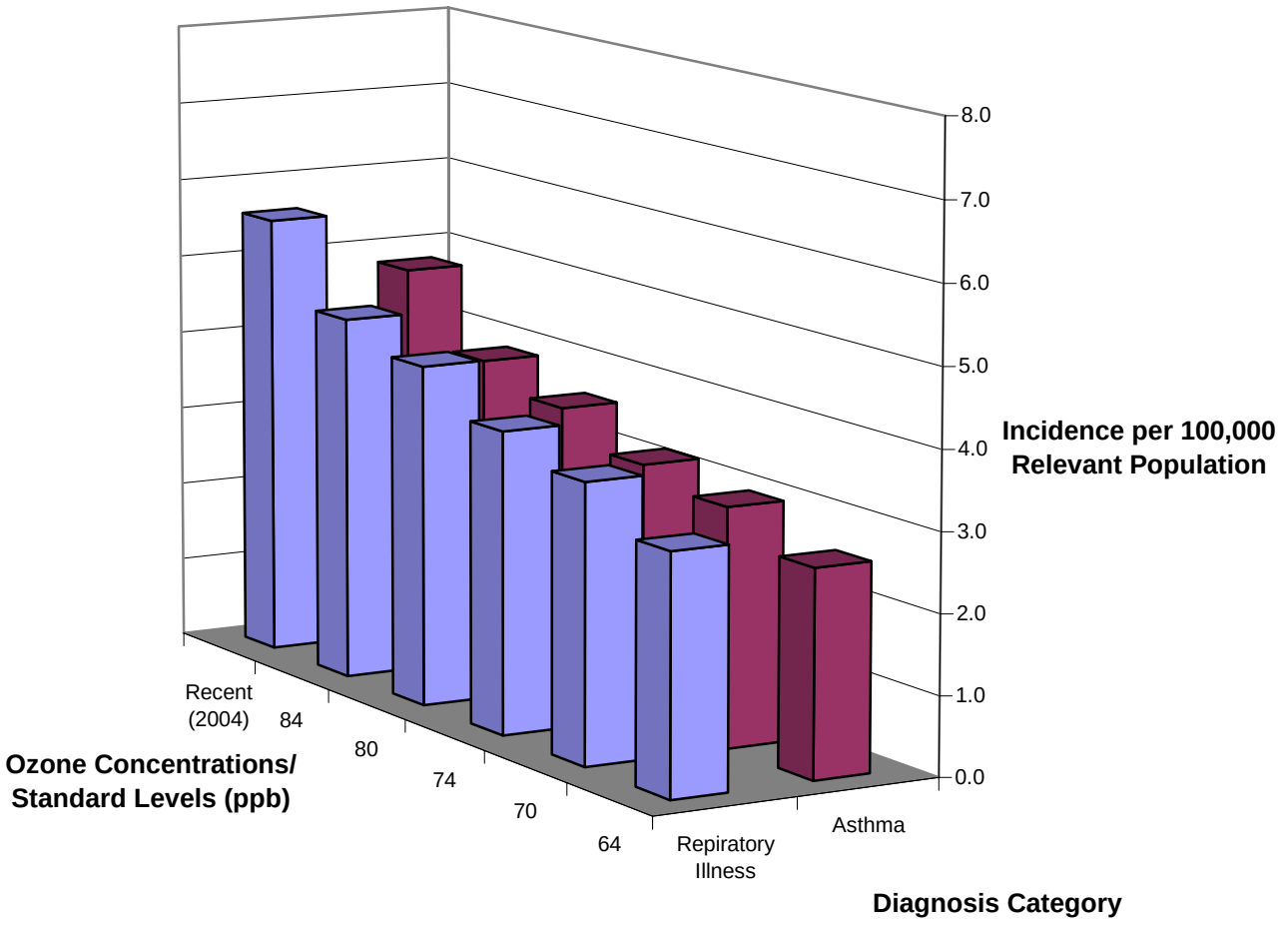
cases for this same air quality scenario. For increasingly more stringent alternative 8-hr standards, Figure 5-8 shows a gradual reduction in the cases per 100,000 relevant population from 4.6 cases per 100,000 upon just meeting the current 8-hr standard to about 3.0 cases per 100,000 under the most stringent 8-hr standard (i.e., 0.064 ppm, average 4$^{th}$ daily maximum) analyzed. The comparable estimates based on adjusting 2002 air quality are shown in Figure 5C-4 (Appendix 5C) and are somewhat higher, but show a similar pattern of gradual reduction. Confidence intervals, based on statistical uncertainty reflecting sample size considerations for incidence, incidence per 100,000 relevant population, and percent of total incidence are shown in Tables 5C-11 and 5C-12 (Appendix 5C) based on adjusting 2004 and 2002 air quality data to just meet the current and potential alternative standards.

Additional respiratory-related hospital admission estimates for three other locations are provided in the draft Risk Assessment TSD. We note that the concentration-response functions for each of these locations examined different outcomes in different age groups (e.g., > age 30 in Los Angeles, >age 64 in Cleveland and Detroit, vs. all ages in New York City), making comparison of the risk estimates across the areas very difficult. For hospital admissions in Detroit, none of the estimates were statistically significant and the median estimates were negative for 0- and 1-day lags and small but positive for 2- and 3-day lags for COPD-related and pneumonia hospital admissions.

Figure 5-9 summarizes the results of the assessment of the reduced non-accidental mortality risks associated with $O_3$ concentrations above background that just meet the current and several potential alternative 8-hr daily maximum standards across the 12 urban areas for air quality adjusted based on 2004 air quality data. The risk estimates in this figure are based on the 95-city function reported in Bell et al. (2004) for non-accidental mortality. Additional risk estimates for cardiorespiratory mortality are included in the draft Risk Assessment TSD for 8 of the 12 urban areas. Also, Figure 5C-5 (Appendix 5C) shows comparable risk estimates based on adjusting 2002 air quality data. Figure 5-9 shows the annual median risk estimates for recent air quality and for just meeting alternative 8-hr standards based on the $O_3$ coefficients estimated in the studies. Ranges reflecting the statistical uncertainty, taking into account sample size considerations, based either on the 95 percent confidence intervals around those estimates (if the coefficients were estimated using classical statistical techniques) or on the 95 percent credible intervals (if the coefficients were estimated using Bayesian statistical techniques) are presented in Tables 5C-13 through 5C-16 (Appendix 5C) and in the draft Risk Assessment TSD.

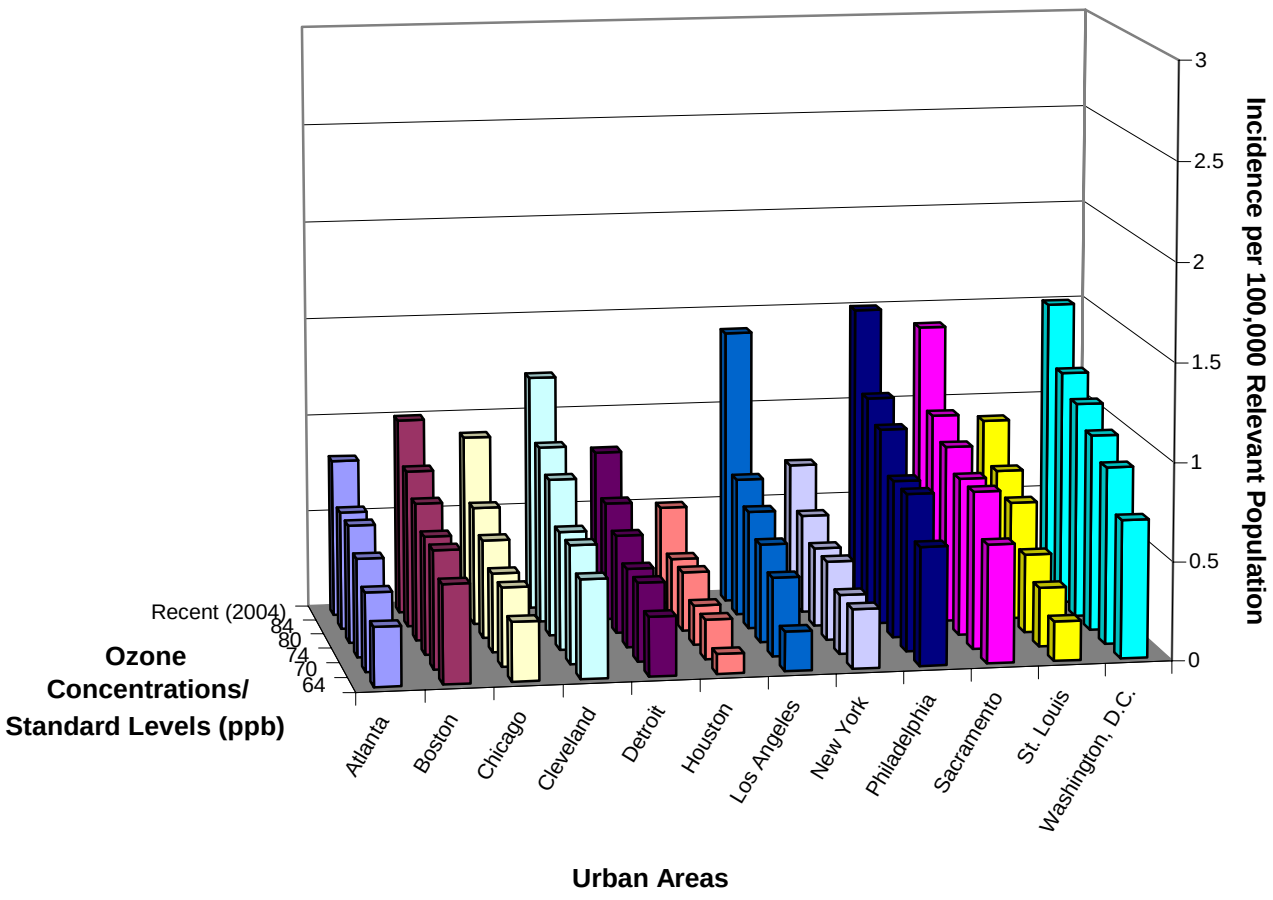
**Figure 5-8. Estimated Incidence of (Unscheduled) Respiratory Hospital Admissions per 100,000 Relevant Population in New York Associated with Recent (April – September, 2004) $O_3$ Levels and with $O_3$ Levels Just Meeting Alternative Average 4$^{th}$ Daily Maximum 8-Hour Standards**

**(based on Thurston et al., 1992)**




***95% confidence intervals associated with these risk estimates are provided in Table 5C-7 of Appendix 5C.**

**Figure 5-9. Estimated Incidence of Non-Accidental Mortality per 100,000 Relevant Population Associated with Recent Air Quality (2004) and with Just Meeting Alternative Average 4th Daily Maximum 8-Hour Ozone Standards (Using Bell et al., 2004 – 95 U.S. Cities Function), Based on 2004 Ozone Concentrations**




*95% confidence intervals associated with these risk estimates are provided in Table 5C-13 of Appendix 5C and Figure 5-10a,b
.

Figures 5-10a and b show the median estimates and 95% credible intervals for each of the 12 urban areas for non-accidental mortality based on the 95-cities concentration-response function in Bell et al. (2004). Figure 5C-6a,b (Appendix 5C) present the comparable figure for 2002 air quality and just meeting alternative standards based on adjusting 2002 air quality data. For example, Figure 5-10a shows a median risk estimate associated with just meeting the current 8-hr standard for non-accidental mortality in Atlanta is around 0.2% of total incidence and the 95% credible interval is < 0.1% to about 0.3% of total incidence. While the 95% credible intervals get progressively smaller as one considers more stringent standards, as discussed previously these credible intervals do not consider overall model uncertainty (e.g., whether or not the shape of the concentration-response relationship is best represented by a log linear relationship versus a more sigmoidal shape, particularly at lower $O_3$ concentration levels).

The results in this portion of the risk assessment across the 12 urban areas follow the same patterns as the results discussed in section 5.4.1 for risks associated with recent year $O_3$ concentrations, because they are largely driven by the same concentration-response function coefficient estimates and confidence or credible intervals. While there is a noticeable reduction in the median risk estimates in some of the urban areas between that associated with a recent year of air quality and just meeting the current 8-hr standard, the reductions associated with progressively more stringent alternative 8-hr standards are more modest. The range of median estimates associated with O3 upon just meeting the current standard is 0.3 to 1.2 cases per hundred thousand relevant population across the 12 urban areas and this range is reduced to 0.2 to 0.7 cases per 100,000 relevant population upon just meeting the most stringent alternative standard analyzed (0.064 ppm, average 4$^{th}$ daily maximum 8-hr average) We also note that the risk estimates expressed in terms of incidence per 100,000 population are noticeably smaller for Houston based on both 2002 and 2004 air quality data and for Los Angeles based on 2002 air quality, especially upon just meeting the current or alternative 8-hr standards than the other urban areas. The risk estimates are notably higher in most of the urban areas for 2002 air quality data and air quality data simulated to just meet the current and alternative standards based on adjusting 2002 data.

As shown in Table 5C-9 and 5C-10 in the Appendix to this Chapter, estimated $O_3$-related (non-accidental) mortality reported by Schwartz (2004) for Chicago, Detroit, and Houston, based on both the single-city and the multi-city concentration-response functions, tend to be higher than the Bell et al. (2004) estimates in those locations in large part because Schwartz used the 1-hr maximum $O_3$ concentration, rather than the 24-hr average, as the exposure metric. The changes from 1-hr maximum $O_3$ concentrations that just meet the current 8-hr $O_3$ standard to

**Figure 5-10a. Annual Warm Season (April to September) Estimated $O_3$-Related Non-Accidental Mortality Associated with Recent (2004) $O_3$ Levels and Levels Just Meeting Alternative 8-hr $O_3$ Standards (Using Bell et al., 2004 – 95 U.S. Cities Function**

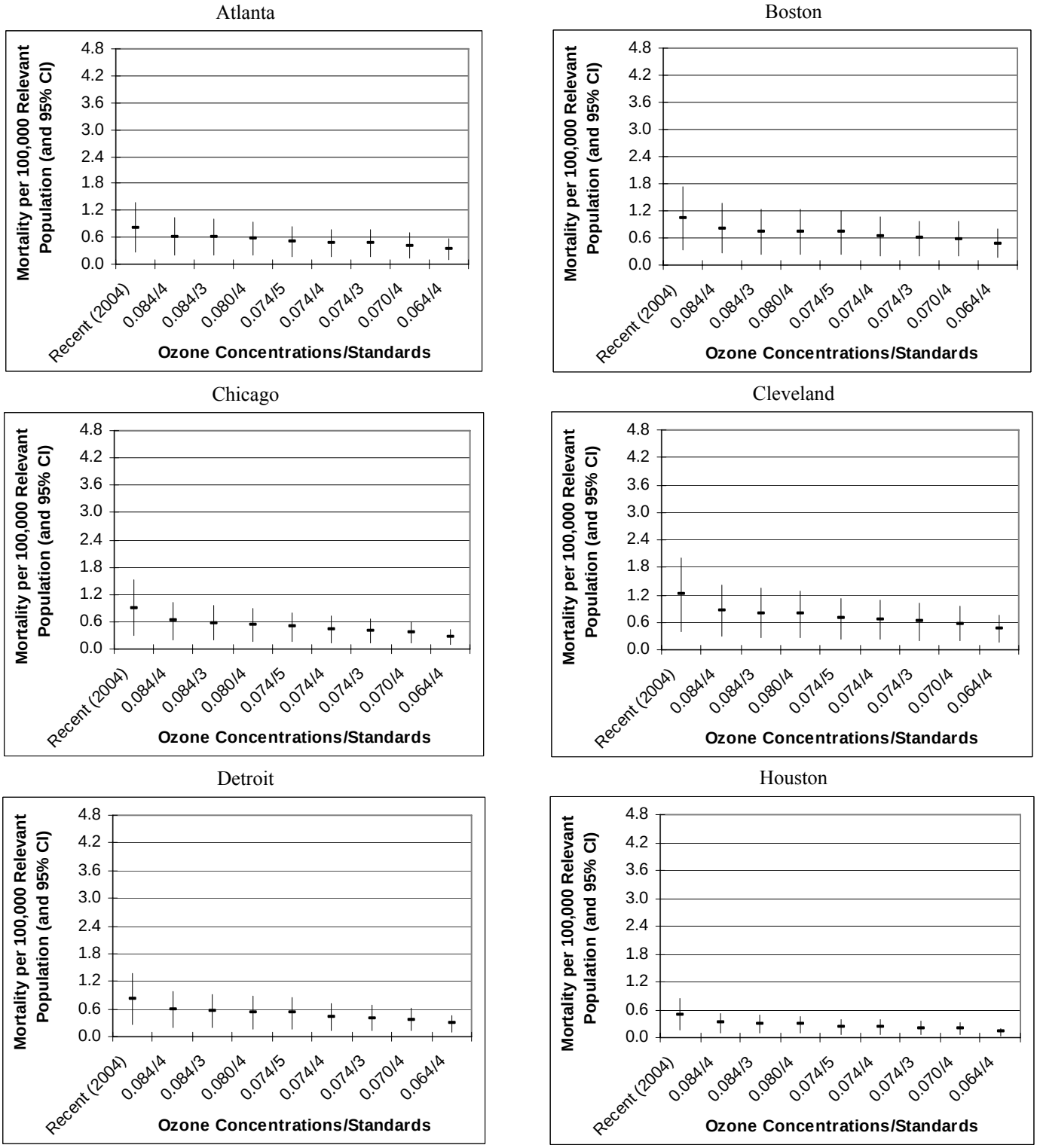
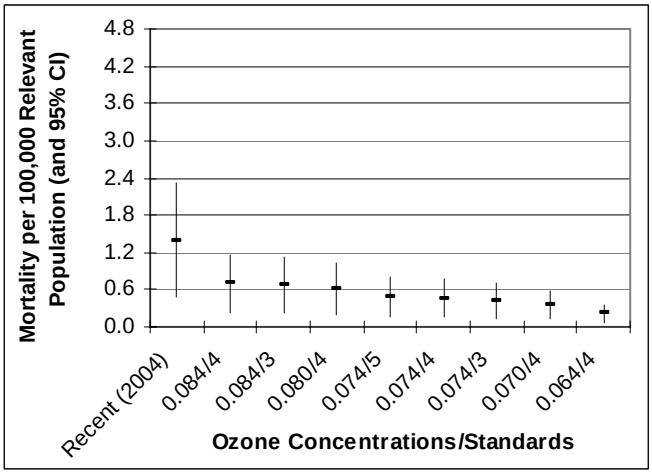
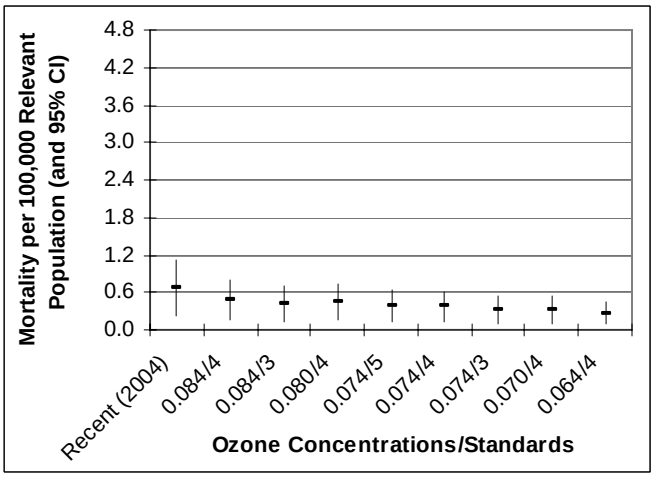


**Figure 5-10b. Annual Warm Season (April to September) Estimated $O_3$-Related Non-Accidental Mortality Associated with Recent (2004) $O_3$ Levels and Levels Just Meeting Alternative 8-hr $O_3$ Standards (Using Bell et al., 2004 – 95 U.S. Cities Function)**

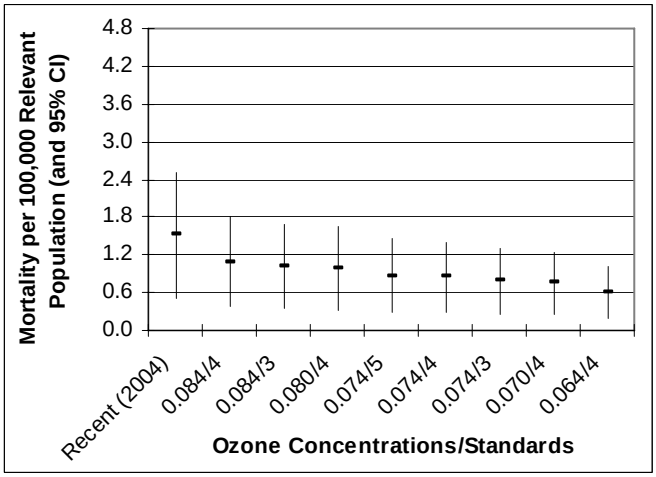
Los Angeles



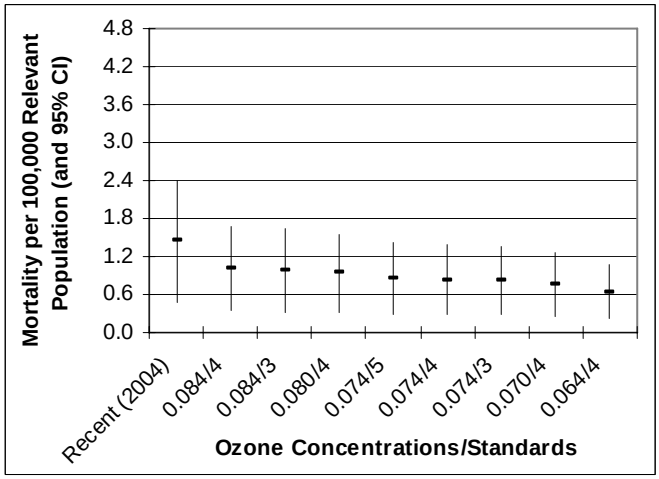

New York



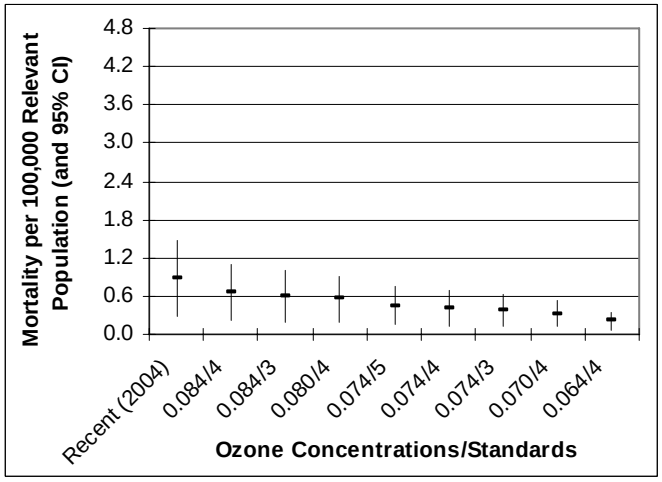

Philadelphia



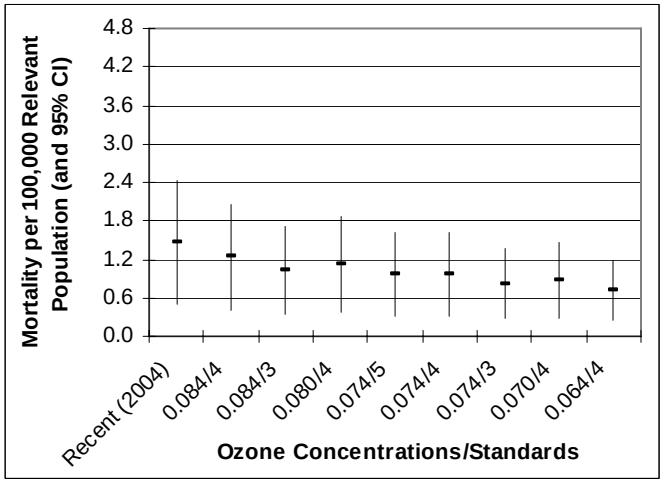

Sacramento




St. Louis




Washington, D.C.



background 1-hr maximum $O_3$ concentrations were generally larger in these assessment locations than the corresponding changes using the 24-hr average metric.

Figure 5-11a and b shows the estimated annual percent of non-accidental mortality mortality associated with short-term exposure to $O_3$ concentrations that just meet the current 8-hour daily maximum standard that fall within specified ranges. The pattern of results is similar to the pattern seen for recent year $O_3$ concentrations discussed in section 5.4.1. Using simulated $O_3$ concentrations that just meet the current 8-hour standard based on 2004 air quality data, all $O_3$-related non-accidental mortality was associated with $O_3$ concentrations less than 0.06 ppm, 24-hr average and most of that was associated with $O_3$ concentrations less than 0.04 ppm, 24-hr average. Using simulated $O_3$ concentrations that just meet the current 8-hour standard based on 2002 air quality data, all $O_3$-related non-accidental mortality was associated with $O_3$ concentrations less than 0.08 ppm, 24-hr average and the great majority was associated with $O_3$ concentrations less than 0.06 ppm, 24-hr average. The results for cardiorespiratory mortality follow a similar pattern. As discussed in section 5.4.1, scatter plots comparing 8-hr daily maximum concentrations at the highest monitor with the average of the 24-hr average over all monitors within an urban area were developed and are included in Appendix 5A.2 to provide some perspective on the 24-hr intervals shown. These scatter plots show that 8-hr daily maximum concentrations on average are roughly twice the observed 24-hr average levels, although there is considerable variability in this relationship from day-to-day within an urban area. There also is some variability in this relationship between 8-hr daily maximum and 24-hr average levels across the 12 urban areas.

### 5.4.3 Comparison with Risk Estimates from Prior Review

As noted in section 5.1.1, EPA conducted a health risk assessment during the prior $O_3$ NAAQS review. For two of the health endpoints, lung function ($FEV_1$) decrements and respiratory-related and asthma hospital admissions it is possible to do some limited comparison between the estimates generated for the current review and previous estimates. The other two health endpoints included in the current risk assessment, respiratory symptoms in moderate/severe asthmatic children and non-accidental and cardiorespiratory mortality are based on more recent scientific studies and, were not included in the prior review.

The lung function risk estimates developed for the current and prior review are based on exposure distributions generated by running $O_3$ exposure models and exposure-response relationships developed using the available controlled human exposure studies data. There have been significant changes in the exposure model between the prior and current review. As

**Figure 5-11. Estimated Annual Percent of Non-Accidental Mortality Associated with Short-Term Exposure to $O_3$ Above Policy Relevant Background for the Period April – September When the Current 8-Hour Standard is Just Met (Based on Bell et al., 2004) – Total and Contribution of 24-Hour $O_3$ Ranges**

**Figure 5-11a. Based on Adjusting 2004 Air Quality Data**

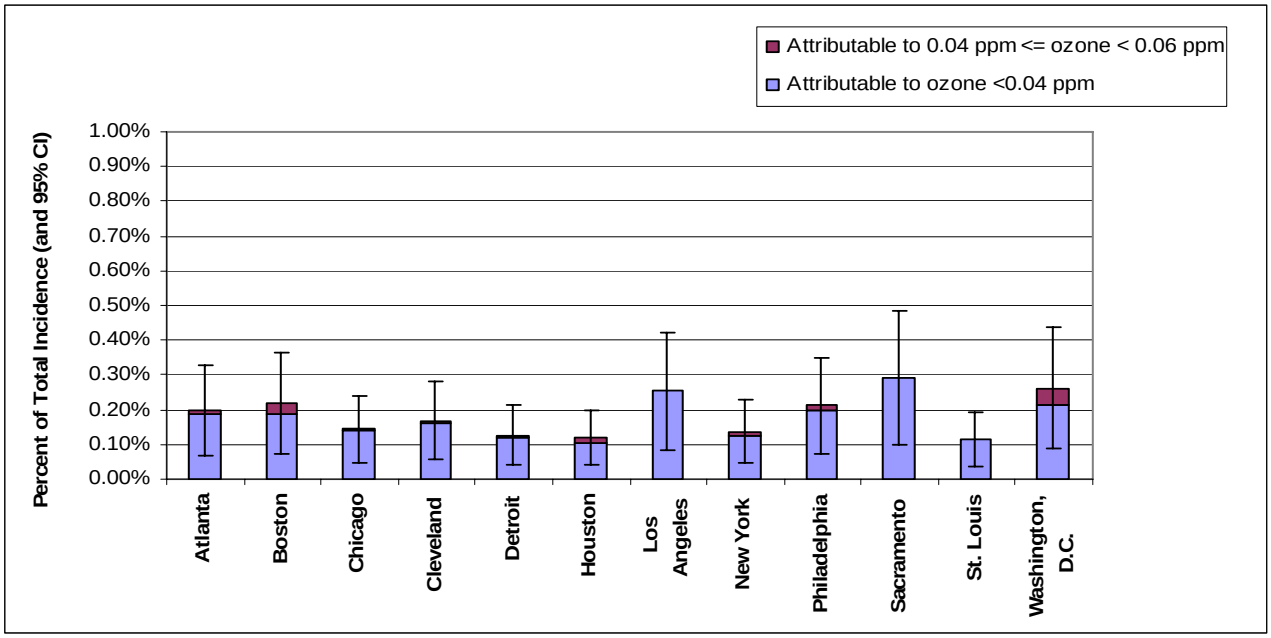
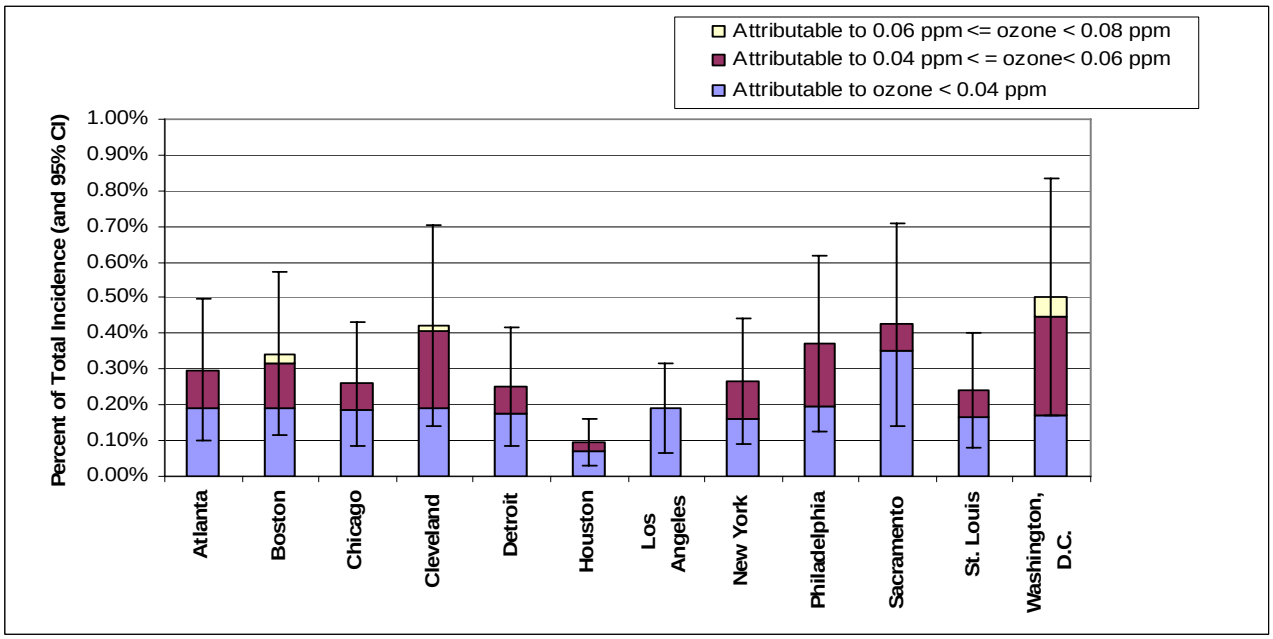



**Figure 5-11b. Based on Adjusting 2002 Air Quality Data**



discussed in Chapter 4, the estimated 8-hr exposures for children engaged in moderate exertion associated with just meeting the current 8-hr standard from the new analysis range from being roughly similar (using the estimates based on adjusting 2002 air quality data) to significantly lower than (using the estimates based on adjusting 2004 air quality data) the most comparable exposure estimates developed during the prior review.

For the 6 urban areas included in both the current and prior assessments, the median risk estimates for lung function response, using $FEV_1$ decrements $\geq$ 15% as an example, are considerably lower in the current risk assessment associated with just meeting the current 8-hr standard than in the assessment conducted for the prior review. The main reason for the lower risk estimates is the change in the shape of the exposure-response relationship from a linear relationship to one that is sigmoidal or s-shaped. During the prior review we only had data available for 3 exposure levels (0.08, 0.10, and 0.12 ppm) for 6.6 hour exposures under moderate exertion. With the addition of more recent data including observations at 0.04 and 0.06 ppm, as well as providing additional data at 0.08 ppm, a 3-parameter logistic function provides a very good fit to the available data. As one can see from Figure 5-12, there is a considerable difference in the estimated fraction of the population that is expected to have $FEV_1$ decrements $\geq$15% between the two exposure-response relationships and this difference has the effect of significantly lowering the risk estimates relative to the estimates provided during the prior review. For example, comparing the aggregate estimates for 6 urban areas (Houston, Los Angeles, New York, Philadelphia, St. Louis, and Washington, DC.) using the quadratic air quality adjustment procedure for "outdoor" children resulted in a median estimate of about 5.6% experiencing 1 or more $FEV_1$ decrements $\geq$15% associated with meeting the current 8-hr, average 4$^{th}$ daily max standard. This contrasts with about 3% of "active" children estimated to have this same response associated with meeting the current 8-hr standard in the current risk assessment. We note that the definitions of "outdoor" and "active" children are not the same; "outdoor" children represented about 47% of 6 to 13 year olds and 31% of 14 to 18 year olds in the prior assessment compared to "active" children representing about 50% of 5 to 18 year olds in the current assessment. The fact that a lower range of background values is used based on the predictions from the GEOS-CHEM model (see discussion in section 2.7) in the current review (i.e., background ranges from 0.015 to 0.035 ppm) compared to a fixed 0.04 ppm value used in the prior review would tend to increase the estimated risk in excess of background. The influence of changing the shape of the exposure-response relationship has a greater overall impact than the change in estimated background levels, and thus, we observe lower risk estimates for this health endpoint in the current assessment.

We note that the current estimates for $O_3$-related hospital admissions for respiratory illness and asthma for New York City are higher than the estimates in the risk assessment

conducted during the prior $O_3$ NAAQS review. Both the prior and current assessments used the same concentration-response functions for these health outcomes. The main reason for higher estimates in the current assessment is the use of a single value of 0.04 ppm for background in the prior review which is higher than the current modeled values for background in the current assessment which are in the range of about 0.015 to 0.035 ppm. Thus, under the current risk assessment $O_3$ levels above background but below 0.04 ppm are contributing additional estimated cases that were not included in the assessment for the prior $O_3$ NAAQS review.

### 5.4.4 Key Observations

In considering the quantitative estimates from the risk assessment the limitations and uncertainties associated with the risk estimates discussed in section 5.3.1.4 for lung function decrements and section 5.3.2.5 for respiratory symptoms, hospital admissions, and pre-mature mortality should be kept in mind. It is also important to consider the degree of confidence about the extent to which $O_3$ is causally related to each of the effects for which risk estimates were produced (see section 3.7.5). For example, there is clear and convincing evidence of causality for lung function decrements in healthy children under moderate exertion for 8-hr average $O_3$ exposures. We also judge that there is strong evidence for a causal relationship between respiratory symptoms in asthmatic children and $O_3$ exposures and between hospital admissions for respiratory causes and ambient $O_3$ exposures. In contrast, there is greater uncertainty and somewhat less confidence about the relationship between $O_3$ and non-accidental and cardiorespiratory mortality, although the CD's overall evaluation is that it is highly suggestive that this relationship exists.

***Recent $O_3$ Air Quality Levels***

Section 5.4.1 has presented risk estimates associated with two recent years of air quality as represented by 2002 and 2004 monitoring data. Presented below are key observations resulting from this part of the risk assessment.

- The ranges in median estimates of the number of "active" school age children (ages 5-18) estimated to experience at least one $FEV_1$ decrement $\geq$ 15% due to 8-hr $O_3$ exposures during the $O_3$ season across the 12 urban areas are 4,000 to 105,000 (based on 2004 air quality) and 9,000 to 155,000 (based on 2002 air quality). In terms of percent of this population the ranges in median estimates are 1.2 to 6.5% (based on 2004 air quality) and 5.3 to 10.4% (based on 2002 air quality). In terms of estimated occurrences of this same response the ranges in median estimates are 15,000 to about 500,000 (based on 2004 air quality) and 37,000 to about 470,00 (based on 2002 air quality). The average number of occurrences per "active" child in an $O_3$ season ranged from about 2.5 to 5 (based on 2004 air quality) and from about 2 to 4 (based on 2002 air quality).

- Estimates for increased respiratory symptoms (i.e., chest tightness, shortness of breath, and wheeze) in asthmatic children (ages 0-12) who used maintenance medications were

only developed for the Boston urban area. The ranges in median estimates of symptom days for these three health outcomes are about 5,000 to 15,000 (based on 2004 air quality) and about 7,000 to 20,000 (based on 2002 air quality). In terms of percent of total incidence for these three health outcomes the ranges in median estimates are about 8 to 14% (based on 2004 air quality) and about 11 to 20% (based on 2002 air quality).

- Estimates for respiratory-related hospital admissions (e.g,, asthma-related) were developed for three urban areas (New York, Los Angeles, and Detroit). The median estimates for New York are about 380 (based on 2004 air quality) and about 520 (based on 2002 air quality) $O_3$-related excess hospital admissions for asthma. For 2004 and 2002 air quality, these estimates represent about 3 and 4%, respectively, of total incidence.

- The risk assessment included a variety of estimates based on single- and multi-city studies for non-accidental and cardiorespiratory mortality. Since the median estimates from single-city and multi-city studies and models were generally of similar magnitude, with a few notable exceptions, we have focused on the estimates based on the multi-city studies to compare risk estimates across the 12 urban areas. The median estimates for incidence for non-accidental mortality (based on Bell et al., 2004 – 95 cities concentration-response function) range from about 3 to 130 (based on 2004 air quality) which is about 0.2 to 0.4% of total incidence. These same estimates based on 2002 air quality range from about 10 to 110 which is about 0.2 to 0.6% of total Estimates of $O_3$-related non-accidental mortality reported by Schwartz (2004) for Chicago, Detroit, and Houston, based on both single city and multi-city concentration-response functions, are somewhat higher than other estimates for these locations. This is mainly due to the use of the 1-hr maximum $O_3$ concentration in Schwartz (2004), rather than the 24-hr average, as the exposure metric.

- Examining the contribution of various $O_3$ ranges to these non-accidental mortality estimates, we found all of the mortality was associated with 24-hr average concentrations less than 0.06 ppm and most of it was associated with concentrations less than 0.04 ppm for 2004 air quality. For 2002, all of the $O_3$-related non-accidental mortality was associated with 24-hr average concentrations less than 0.08 ppm and the great majority was associated with concentrations less than 0.06 ppm. Based on an examination of $O_3$ air quality relationships between 24-hr average concentrations average over the urban monitors in an urban area on a given day and the daily maximum 8-hr average on the corresponding day, we note that the 8-hr daily maximum concentrations are on average about twice the 24-hr average level. So, for example, a range of 0.04 to 0.06 ppm, 24-hr average corresponds with roughly daily maximum 8-hr levels in the range 0.08 to 0.12 ppm measured at the highest fixed-site monitor within an urban area.

***Meeting the Current and Alternative 8-hr Standards***

Section 5.4.2 has presented risk estimates associated with just meeting the current and several potential alternative 8-hr standards based on adjusting 2004 and 2002 monitoring data

using design values for the 2002-2004 time period. Presented below are key observations resulting from this part of the risk assessment.

- In comparing risk estimates for alternative standards, uncertainties in quantifying the health risks associated ambient $O_3$ concentrations would be expected to remain relatively constant in different models. Thus, we have greater confidence in relative comparisons in risk estimates between alternative standards than in the absolute magnitude of risk estimates associated with any particular standard.

- Significant year-to-year variability in O3 concentrations combined with the use of a 3-year design value to determine the amount of air quality adjustment to be applied to each year analyzed, results in significant year-to-year variability in the annual health risk estimates associated with just meeting the current and potential alternative 8-hr standards.

- The ranges in median estimates of the number of "active" school age children (ages 5-18) estimated to experience at least one $FEV_1$ decrement $\geq$ 15% due to 8-hr $O_3$ exposures during the $O_3$ season across the 12 urban areas are 1,000 to 15,000 (based on adjusting 2004 air quality to just meet the current 8-hr standard) and 4,000 to 62,000 (based on adjusting 2002 air quality). In terms of percent of this population the ranges in median estimates are 0.6 to 2% (based on adjusting 2004 air quality to just meet the current 8-hr standard) and 2.1 to 5.8% (based on 2002 air quality). In terms of estimated occurrences of this same response the ranges in median estimates are 5,000 to about 58,000 (based on adjusting 2004 air quality to just meet the current 8-hr standard) and 14,000 to nearly 200,000 (based on 2002 air quality). The average number of occurrences per "active" child in an $O_3$ season ranged from about 2.5 to 5 (based on adjusting 2004 air quality to just meet the current 8-hr standard) and from about 2.5 to 4 (based on 2002 air quality).

- Estimates for increased respiratory symptoms (i.e., chest tightness, shortness of breath, and wheeze) in moderate/severe asthmatic children (ages 0-12) were only developed for the Boston urban area. The median estimated number of days involving chest tightness (using the concentration-response relationship with only $O_3$ in the model) ranges from 4,500 (based on adjusting 2004 air quality) to 6,100 (based on adjusting 2002 air quality) upon meeting the current 8-hr standard and these are reduced to 3,100 (based on adjusting 2004 air quality) to 4,600 days upon meeting the most stringent alternative examined (0.064 ppm, $4^{th}$ daily maximum 8-hr average). These same ranges correspond to 8 to 11% of total incidence of chest tightness upon meeting the current 8-hr standard and to about 5.5 to 8% of total incidence of chest tightness upon meeting a 0.064 ppm, $4^{th}$ daily maximum 8-hr average standard. Similar patterns of reduction were observed for each of the reported respiratory symptoms.

- Estimates for respiratory-related hospital admissions (e.g,, respiratory illness, asthma-related) were developed for three urban locations (New York City, Los Angeles, and Detroit). For asthma-related admissions in New York City the estimates are about 3.9

cases per 100,000 relevant population, which represents about 2.4% of total incidence or 313 cases upon just meeting the current standard based on adjusting 2004 air quality data. For increasingly more stringent alternative 8-hr standards, a gradual reduction in the cases per 100,000 relevant population is observed from 3.9 cases per 100,000 upon just meeting the current 8-hr standard to about 2.6 cases per 100,000 under the most stringent 8-hr standard (i.e., 0.064 ppm, average 4$^{th}$ daily maximum) analyzed. Based on adjusting 2002 air quality data, asthma-related admissions in New York City are about 5.5 cases per 100,000 relevant population, which represents about 3.3% of total incidence or 438 cases upon just meeting the current standard. For increasingly more stringent alternative 8-hr standards, a gradual reduction is observed from 5.5 cases per 100,000 (3.3% of total incidence) upon just meeting the current 8-hr standard to about 3.9 cases per 100,000 (2.4% of total incidence).

- Based on the median estimates for incidence for non-accidental mortality (based on Bell et al., 2004 – 95 cities concentration-response function), meeting the most stringent standard shown (0.064 ppm, 4$^{th}$ daily maximum) is estimated to reduce mortality by 55 percent of what it would be associated with just meeting the current standard (based on adjusting 2004 air quality data). Adjusting 2002 air quality data to just meet the 0.064 ppm, standard results in a 40 percent reduction in non-accidental mortality relative to just meeting the current 8-hr standard . The patterns for cardiorespiratory mortality are similar. The aggregate $O_3$-related cardiorespiratory mortality at the most stringent standard shown is estimated to be about 57 percent of what it would be at the current standard, using simulated $O_3$ concentrations that just meet the current and alternative 8-hour standards based on 2004 air quality data. Using 2002 air quality data, the corresponding result is about 42 percent.

- Much of the contribution to the risk estimates for non-accidental and cardiorespiratory mortality upon just meeting the current 8-hr standard is associated with 24-hr $O_3$ concentrations between background and 0.04 ppm. Based on examining relationships between 24-hr concentrations and 8-hr daily maximum concentrations, 8-hr daily maximum levels associated with these 24-hr levels are generally about twice as high.

***Uncertainty and Variability***

- There is noticeable variability in estimated $O_3$-related incidence of morbidity and mortality across the 12 urban areas analyzed for both recent years of air quality and for air quality adjusted to simulate just meeting the current and several potential alternative 8-hr standards. This variability is likely due to differences in air quality distributions, differences in exposure related to many factors including varying activity patterns and air exchange rates, differences in baseline incidence rates, and differences in susceptible populations and the age distribution across the 12 urban areas. For the lung function part of the risk assessment, spatial variability in air quality and population exposure inputs has been included in the assessment by use of a location specific exposure analysis and location specific input data to that analysis. For the epidemiology-based health endpoints, spatial variability in key inputs has been embedded in the analysis by use of

location specific inputs (e.g., air quality, population data, baseline incidence data, concentration-response relationships).

- The most important uncertainty is the extent to which the associations between O3 and the health endpoints included in the assessment actually reflect causal relationships. For lung function decrements, respiratory symptoms in moderate to severe asthmatic children, and respiratory-related hospital admissions there is clear and very strong evidence supporting the judgment that the relationships are causal. With respect to non-accidental and cardiorespiratory mortality, there is greater uncertainty, with the CD concluding that the overall body of evidence is highly suggestive that $O_3$ directly or indirectly contributes to nonaccidental and cardiopulmonary-related mortality (CD, p. 8-78).

- Statistical uncertainty in the exposure-response relationships associated with sampling error has been characterized in the lung function part of the risk assessment. Other important uncertainties in the exposure-response relationship for the lung function health outcomes include:

    - uncertainty associated with extrapolation of the exposure-response relationship to levels below 0.04 ppm, the lowest tested level in controlled human exposure studies;
    - uncertainty due to use of 6.6-hr data for subjects engaged in moderate exertion to estimate response associated with 8-hr exposures under moderate or greater exertion;
    - uncertainty about whether O3-induced responses are reproducible, although this is generally supported by other controlled human exposure studies showing significant reproducibility of response;
    - uncertainty introduced by use of exposure-response relationships based on 18 to 35 year old subjects to represent the relationship for school age children age 5 to 18, although the use of adult data is supported by a study testing 8 to 11 year olds and observations from a number of summer camp field studies of school age children which found comparable responses to those observed in adults;
    - uncertainty in the estimated exposure-response relationship due to assumption that response on any given day is independent of previous O3 exposure; and
    - uncertainty in the estimated exposure-response due to assumption that the response would not be affected by the presence of other co-pollutants.

- Uncertainties related to estimating the concentration-response relationships for the epidemiological-based part of the risk assessment include:

    - statistical uncertainty due to sampling error which is characterized in the assessment;
    - model uncertainty (i.e., uncertainty about the shape and magnitude of the concentration-response relationship taking into account lags, other pollutants, etc.); and

- uncertainty about whether a concentration-response function provides an accurate representation of the relationship in the location of interest because of a) the possible role of associated co-pollutants, b) variations in the relationship of total ambient exposure to ambient monitoring in different location, and c) differences in population characteristics and population behavior patterns across locations or over time in the same location.

- Uncertainties related to the air quality data affect both the controlled human exposure studies-based and epidemiological studies-based parts of the risk assessment and include:
  - uncertainties associated with the air quality adjustment procedure that was used to simulate just meeting the current and alternative 8-hr standards; and
  - uncertainties about estimated background concentrations for each location.

Our judgment based on sensitivity analyses conducted during the prior review of alternative air quality adjustment approaches, is that the choice of adjustment procedure has only a modest impact on the risk estimates. With respect to the uncertainties about estimated background concentrations, as discussed in section 2.7, based on EPA's assessment of the validity of the GEOS-Chem model, the CD states "in conclusion, we estimate that the PRB ozone values reported by Fiore et al. (2003) for afternoon surface air over the United States are likely 10 ppbv too high in the southeast in summer, and accurate within 5 ppbv in other regions and seasons." Thus, uncertainty about background concentrations also is likely to have only a modest impact on the risk estimates developed during the current review.

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# 6. STAFF CONCLUSIONS ON PRIMARY $O_3$ NAAQS

## 6.1 INTRODUCTION

This chapter presents staff conclusions and identifies options that the staff believes are appropriate for the Administrator to consider in deciding whether the existing primary $O_3$ standard should be revised and, if so, what revised standard is appropriate. The current primary $O_3$ standard is an 8-hr standard set at a level of 0.08 ppm to provide protection to the public, especially children and other at-risk populations, against a wide range of $O_3$-induced effects. Our conclusions on this standard and our identification of options for consideration are based on the assessment and integrative synthesis of information presented in the CD and on staff analyses and evaluations presented in Chapters 2 through 5 herein.

In identifying options for the Administrator's consideration, we note that the final decision on retaining or revising the current $O_3$ standard is largely a public health policy judgment. A final decision should draw upon scientific information and analyses about health effects, population exposure and risks, as well as judgments about the appropriate response to the range of uncertainties that are inherent in the scientific evidence and analyses. Our approach to these judgments, discussed more fully below, is based on a recognition that the available health effects evidence generally reflects a continuum consisting of ambient levels at which scientists generally agree that health effects are likely to occur through lower levels at which the likelihood and magnitude of the response become increasingly uncertain.

This approach is consistent with the requirements of the NAAQS provisions of the Act and with how EPA and the courts have historically interpreted the Act. These provisions require the Administrator to establish primary standards that, in the Administrator's judgment, are requisite to protect public health with an adequate margin of safety. In so doing, the Administrator seeks to establish standards that are neither more nor less stringent than necessary for this purpose. The Act does not require that primary standards be set at a zero-risk level but rather at a level that avoids unacceptable risks to public health, including the health of sensitive groups.

## 6.2 APPROACH

To evaluate whether it is appropriate to consider retaining the current primary $O_3$ standard, or whether consideration of revisions is appropriate, we adopted an approach in this review that builds upon the general approach used in the last review and reflects the broader body of evidence now available. The 1997 final decision notice (62 FR 38856) outlined the key factors considered in selecting the elements of a standard for $O_3$ (judged to be the most

appropriate indicator for photochemical oxidants): the averaging time; the $O_3$ concentration (i.e., level); and the form (i.e., the air quality statistic to be used as a basis for determining compliance with the standard). Decisions on these elements were based on an integration of information on acute and chronic health effects associated with exposure to ambient $O_3$; expert judgment on the adversity of such effects on individuals; and policy judgments as to when the standard is requisite to protect public health with an adequate margin of safety, which were informed by air quality analysis and quantitative exposure and risk assessments when possible, as well as qualitative assessment of impacts that could not be quantified.

As in the last review, in developing conclusions and identifying options for the $O_3$ standard in this review, staff has taken into account both evidence-based and quantitative exposure- and risk-based considerations. Evidence-based considerations include the assessment of evidence from controlled human exposure, animal toxicological, field, and epidemiological studies for a variety of health endpoints. For those endpoints based on epidemiological studies, we have placed greater weight on associations with health endpoints that the CD has judged to be likely causal based on an integrative synthesis of the entire body of evidence, including not only all available epidemiological evidence but also evidence from animal toxicological and controlled human exposure studies. Less weight has been given to evidence of associations that were judged to be only suggestive of possible causal relationships. For the purpose of evaluating the level of the $O_3$ standard in this review, we have placed greater weight on U.S. and Canadian studies, taking into account the extent to which such studies have reported statistically significant associations. This is because findings of U.S. and Canadian studies are more directly applicable for quantitative considerations in this review as studies conducted in other countries may well reflect quite different populations, exposure characteristics, and air pollution mixtures.

Staff's consideration of quantitative exposure- and risk-based information draws from the results of the exposure and risk assessments conducted for as many as twelve urban areas in the U.S. (discussed in Chapters 4 and 5). More specifically, we have considered estimates of the magnitude of $O_3$-related exposures and risks associated with recent air quality levels, as well as the exposure and risk reductions likely to be associated with just meeting the current 8-hr primary $O_3$ NAAQS and potential alternative 8-hr standards. We recognize the considerable uncertainties inherent in such estimates, which are discussed in Chapters 4 and 5 in part by providing where possible some sense of the direction and/or magnitude of the uncertainties which should be taken into account as one considers these estimates.

In this review, a series of general questions frames our approach to reaching conclusions and identifying options for consideration by the Administrator, based on the available information, as to whether consideration should be given to retaining or revising the current

primary $O_3$ standard. Our review of the adequacy of the current standard begins in section 6.3.1 below by addressing questions such as the following:

- To what extent does newly available information reinforce or call into question evidence of associations with effects identified in the last review?
- To what extent has evidence of new effects and/or sensitive populations become available since the last review?
- To what extent have important uncertainties identified in the last review been reduced and have new uncertainties emerged?
- To what extent does newly available information reinforce or call into question any of the basic elements of the current standards?

To the extent that the available information suggests that revision of the current standard may be appropriate to consider, we also address whether the currently available information supports consideration of a standard that is either more or less protective by addressing the following questions:

- Is there evidence that associations, especially likely causal associations, extend to air quality levels that are as low as or lower than had previously been observed, and what are the important uncertainties associated with that evidence?
- Are exposures of concern and health risks estimated to occur in areas that meet the current standard; are they important from a public health perspective; and what are the important uncertainties associated with the estimated risks?

To the extent that there is support for consideration of a revised standard, we then identify ranges of standards (in terms of an indicator, averaging time, level, and form in sections 6.3.2 through 6.3.5 below, respectively) that would reflect a range of alternative public health policy judgments, based on the currently available information, as to the degree of protection that is requisite to protect public health with an adequate margin of safety. In so doing, staff addresses the following questions:

- Does the evidence provide support for considering a different $O_3$ indicator?
- Does the evidence provide support for considering different averaging times?
- What ranges of levels and forms of alternative standards are supported by the evidence, and what are the uncertainties and limitations in that evidence?
- To what extent do specific levels and forms of alternative standards reduce the estimated exposures of concern and risks attributable to $O_3$, and what are the uncertainties associated with the estimated exposure and risk reductions?

Following a summary of staff conclusions and the identification of options on alternative standards for the Administrator to consider (section 6.3.6), this chapter concludes with a discussion of key uncertainties and recommendations for additional research related to setting a primary $O_3$ standard (section 6.4).

## 6.3 PRIMARY $O_3$ STANDARD

As an introduction to our consideration of the adequacy of the current $O_3$ standard and potential options for alternative standards, it is useful to summarize the key factors that formed the basis of the decision in the last review to revise the averaging time, level, and form of the then current 1-hr standard. In the last review, the key factor in deciding to revise the averaging time of the primary standard was evidence from human controlled human exposure studies of healthy young adult subjects exposed for 1 to 8 hr to $O_3$. The best documented health endpoints in these studies were decrements in forced expiratory volume in 1 second ($FEV_1$), also known as lung function decrements, and respiratory symptoms, such as cough and chest pain on deep inspiration. For short-term exposures of 1 to 3 hr, group mean $FEV_1$ decrements were statistically significant for $O_3$ concentrations only at and above 0.12 ppm, and only when subjects engaged in very heavy exertion. By contrast, prolonged exposures of 6 to 8 hr produced statistically significant $FEV_1$ decrements at the lowest $O_3$ concentrations evaluated in those studies, 0.08 ppm, even when experimental subjects were engaged in more realistic intermittent moderate exertion levels. The health significance of this newer evidence led to the conclusion in the 1997 final decision that the 8-hr averaging time is more directly associated with health effects of concern at lower $O_3$ concentrations than is the 1-hr averaging time.

Based on the available evidence of $O_3$-related health effects, the following factors were of particular importance in the last review in informing the selection of the level and form of a new 8-hr standard: (1) quantitative estimates of $O_3$-related risks to active children in terms of transient and reversible respiratory effects judged to be adverse, including moderate to large decreases in lung function and moderate to severe pain on deep inspiration, and the uncertainty and variability in such estimates; (2) consideration of both the estimated percentages, total numbers of children, and number of times they were likely to experience such effects; (3) epidemiological evidence of associations between ambient $O_3$ and increased respiratory hospital admissions, and quantitative estimates of percentages and total numbers of asthma-related admissions in one example urban area that were judged to be indicative of a pyramid of much larger effects, including respiratory-related hospital admissions, emergency department (ED) visits, doctor visits, and asthma attacks and related increased medication use; (4) quantitative estimates of the number of "exposures of concern" (defined as exposures $\geq$ 0.08 ppm for 6 to 8 hr) that active children are likely to experience, and the uncertainty and variability in such

estimates; (5) the judgment that such exposures are an important indicator of public health impacts of $O_3$-related effects for which information is too limited to develop quantitative risk estimates, including increased nonspecific bronchial responsiveness (e.g., related to aggravation of asthma), decreased pulmonary defense mechanisms (suggestive of increased susceptibility to respiratory infection), and indicators of pulmonary inflammation (related to potential aggravation of chronic bronchitis or long-term damage to the lungs); (6) the broader public health perspective of the number of people living in areas that would breathe cleaner air as a result of the revised standard; (7) consideration of the relative seriousness of various health effects and the relative degree of certainty in both the likelihood that people will experience various health effects and their medical significance; (8) the relationship of a standard level to estimated "background" levels associated with nonanthropogenic sources of $O_3$; and (9) CASAC advice and recommendations. Additional factors that were considered in selecting the form of the standard included the public health implications of the expected number of times in an $O_3$ season that the standard level might be exceeded in an area that is in attainment with the standard and the year-to-year stability of the air quality statistic, so as to avoid disruptions to ongoing control programs which could interrupt public health protections.

In reaching a final decision in the last review, the Administrator was mindful that $O_3$ exhibits a continuum of effects, such that there is no discernible threshold above which public health protection requires that no exposures be allowed or below which all risks to public health can be avoided. The final decision reflected a recognition that important uncertainties remained, for example with regard to interpreting the role of other pollutants co-occurring with $O_3$ in observed associations, understanding biological mechanisms of $O_3$-related health effects, and estimating human exposures and quantitative risks to at-risk populations for these health effects.

### 6.3.1 Adequacy of Current $O_3$ Standard

Overall, the new evidence available in this review generally supports and builds further upon key health-related conclusions drawn in the previous review. New human clinical studies provide information about lung function responses to prolonged exposures at $O_3$ levels at and below 0.08 ppm. There is an expanded body of evidence about the mechanisms of respiratory effects, including important new evidence about increased susceptibility of people with asthma and limited new evidence about plausible mechanisms by which $O_3$ exposure could induce effects on the cardiovascular system. In this review, there is additional epidemiologic evidence supporting associations between $O_3$ exposure and respiratory symptoms in asthmatic children, ED visits and hospital admissions for respiratory causes, and new evidence that links $O_3$ exposure to premature mortality.

As discussed in Chapter 3, the CD concludes that, based on the extensive body of human clinical, toxicological, and epidemiological evidence, there is a causal relationship between short-term $O_3$ exposure and a range of respiratory morbidity effects, including: lung function decrements, increased respiratory symptoms, airway inflammation, and increased airway responsiveness. Aggregate population time-series studies provide evidence that ambient $O_3$ concentrations are positively and robustly associated with respiratory-related hospitalizations and ED visits during the warm season. The CD concludes that the overall body of evidence supports a causal relationship between acute ambient $O_3$ exposures and these respiratory morbidity outcomes (CD, p. 8-77). Based on the evidence from animal toxicology, human clinical, and epidemiological studies, the CD concludes that a generally limited body of evidence provides considerable plausibility for mechanisms and is highly suggestive that $O_3$ can directly or indirectly contribute to cardiovascular-related morbidity but that much needs to be done to more fully substantiate links between ambient $O_3$ exposures and adverse cardiovascular outcomes (CD, p. 8-77). The CD also finds that results from U.S. multi-city time-series studies, along with a number of single-city studies and meta-analyses, provide relatively strong evidence for associations between short-term $O_3$ exposure and all-cause mortality, even after adjustment for the influence of season and PM (CD, p. 8-78).

In considering this evidence as a basis for evaluating the adequacy of the current $O_3$ standard and for identifying alternative standard options for consideration, we recognize that important uncertainties remain. For example, as discussed above in section 3.4, we note that inherent limitations in time-series epidemiological studies raise questions about the utility of such evidence to inform judgments about a NAAQS for an individual pollutant such as $O_3$ within a mix of highly correlated pollutants, such as the mix of photochemical oxidants. We also recognize that the available epidemiological evidence neither supports nor refutes the existence of thresholds at the population level for effects such as increased hospital admissions and premature mortality. While there are limitations in epidemiological studies that make discerning thresholds in populations difficult, including low data density in the lower concentration ranges, the possible influence of exposure measurement error, and interindividual differences in susceptibility to $O_3$-related effects in populations, the CD concludes that there is limited controlled human exposure and epidemiological evidence to suggest that if a population threshold level does exist, it is likely near the lower limit of ambient $O_3$ concentrations in the U.S. (CD, p. 8-44).

Based on the above considerations and findings from the CD, while being mindful of important remaining uncertainties, staff concludes that the newly available information generally reinforces our judgments about causal relationships between $O_3$ exposure and respiratory effects observed in the last review and broadens the evidence of $O_3$-related associations to include

additional respiratory-related endpoints, newly identified cardiovascular-related health endpoints, and mortality. Newly available evidence also has identified increased susceptibility in people with asthma. While recognizing that important uncertainties and research questions remain, we also conclude that progress has been made since the last review in advancing our understanding of potential mechanisms by which ambient $O_3$, alone and in combination with other pollutants, is causally linked to a range of respiratory- and cardiovascular-related health endpoints. Thus, staff generally finds support in the available evidence, including the direction of the evidence developed since the last review, for consideration of an $O_3$ standard that is at least as protective as the current standard and does not find support for consideration of an $O_3$ standard that is less protective than the current standard. The available evidence is discussed in greater detail below, as are exposure- and risk-based considerations, followed by discussion of consideration of standards that would provide more protection than the current standard.

#### 6.3.1.1 Evidence-based Considerations

In looking more specifically at the controlled human exposure and epidemiological evidence summarized in Chapter 3 and Appendix 3B, staff has focused on studies that examined associations between $O_3$ and health effects for which the CD judges associations with $O_3$ to be causal or likely causal, with a focus on effects in the warm season, as discussed above. In considering the epidemiological evidence, we note that it is difficult to consistently characterize relevant air quality statistics from the studies so as to examine the extent to which there is evidence of effects in areas that likely would not have met the current standard or in areas that likely would have met the current standard.[1] These difficulties arise in particular in panel studies of lung function or respiratory symptoms in which the study periods were often shorter than a complete $O_3$ season; Appendix 3B includes $98^{th}$ and $99^{th}$ percentile values as a way to approximate the fourth-highest value for studies with differing study periods. Difficulties also arise as well in all studies in which the air quality data were averaged across multiple monitors in a study area (as are reported in Appendix 3B), since an area's attainment status is in essence determined by the monitor measuring the highest $O_3$ concentrations in an area, not averaged across monitors. For studies with relatively low air quality values that are based on averaging across multiple monitors, we have further explored the available air quality data so as to help inform a comparison with the level of the current standard, as discussed below.

*Lung Function, Respiratory Symptoms, and Other Respiratory Effects*

Health effects for which the CD continues to find clear evidence of causal associations with short-term $O_3$ exposures include lung function decrements, respiratory symptoms, and

[1] Determining attainment with the current standard is based on the 3-year average of the annual (over an $O_3$ season) fourth-highest daily maximum 8-hr average $O_3$ concentration at each monitor in an area.

pulmonary inflammation. In the last review, these $O_3$-induced effects were demonstrated with statistical significance down to the lowest level tested in controlled human exposure studies at that time (i.e., 0.08 ppm). As discussed in Chapter 3 (section 3.3.1.1.1), in two new controlled human exposure studies, healthy adult volunteers were exposed to 6.6-hr average $O_3$ levels down to lower levels (i.e., 0.04 and 0.06 ppm) while engaged in moderate exertion. These studies did not find statistically significant changes in group mean $FEV_1$ decrements at these lower levels; however, when corrected for the effects of exercise in clean air a small percentage (7%) of healthy adult subjects experienced moderate lung function decrements ($\geq$ 10% $FEV_1$) with exposure to 0.06 and 0.04 ppm $O_3$.

Newer information indicates that people with asthma have somewhat larger decreases in lung function in response to $O_3$ relative to healthy individuals and that lung function responses in people with asthma appear to be affected by baseline lung function (i.e., responses increase with increasing disease severity, CD, p. 8-80). As discussed in the CD (Chapter 6, sections 6.8 and 6.9; Chapter 8, sections 8.7 and 8.8) this newer information expands our understanding of the physiological basis for increased sensitivity in people with asthma and other airway diseases, recognizing that people with asthma present a different response profile for cellular, molecular, and biochemical responses than people who do not have asthma. New evidence indicates that some people with asthma have increased occurrence and duration of nonspecific airway responsiveness, which is an increased bronchoconstrictive response to airway irritants. Controlled-human exposure studies also indicate that some people with allergic asthma and rhinitis have increased airway responsiveness to allergens following $O_3$ exposure. Exposures to $O_3$ exacerbated lung function decrements in people with pre-existing allergic airway disease, with and without asthma. Ozone-induced exacerbation of airway responsiveness persists longer and attenuates more slowly than $O_3$-induced lung function decrements and respiratory symptom responses and can have important clinical implications for asthmatics. Newly available human exposure studies suggest that some people with asthma also have increased inflammatory responses, relative to non-asthmatic subjects, and that this inflammation may take longer to resolve. The new data on airway responsiveness, inflammation, and various molecular markers of inflammation and bronchoconstriction indicate that people with asthma and allergic rhinitis (with or without asthma) comprise susceptible groups for $O_3$-induced adverse effects. This body of evidence qualitatively informs our evaluation of the adequacy of the current $O_3$ standard in that it indicates that human clinical and epidemiologic panel studies of lung function decrements and respiratory symptoms that evaluate only healthy, non-asthmatic subjects may underestimate the effects of $O_3$ exposure on asthmatics and other susceptible populations.

In addition to the experimental evidence of lung function decrements, respiratory symptoms, and other respiratory effects in healthy and asthmatic populations discussed above,

epidemiologic studies have reported associations of lung function decrements and respiratory symptoms in several locations (Appendix 3B; also Figure 3-4 for respiratory symptoms). As discussed in Chapter 3, two large U.S. studies (the National Cooperative Inner-City Asthma Study (NCICAS), Mortimer et al., 2002; Gent et al., 2003), as well as several smaller U.S. and international studies, have reported fairly robust associations between ambient $O_3$ concentrations and measures of lung function and daily symptoms (e.g., chest tightness, wheeze, shortness of breath) in children with moderate to severe asthma and between $O_3$ and increased asthma medication use. The NCICAS reported statistically significant increases in incidence of $\geq$10% declines in morning lung function and respiratory symptoms in asthmatic children for multi-day lags in 8-hr average $O_3$ concentrations in single pollutant models. For various co-pollutant models, the $O_3$ effect was attenuated, but there was still a positive association. Gent et al. (2003) included asthmatic children in the area of southern New England and reported associations between various respiratory symptoms and both daily 1-hr max and 8-hr max $O_3$ levels for asthmatics who used maintenance medications and would be considered moderate to severe asthmatics, while not finding an association for mild asthmatics, defined as not using maintenance medication. In this study, effects of $O_3$, but not $PM_{2.5}$, remained statistically significant and even increased in magnitude in two-pollutant models (CD, p.7-53). The CD concludes that overall the multi-city NCICAS, Gent et al. (2003) and several other single-city studies indicate a fairly robust positive association between ambient $O_3$ concentrations and increased respiratory symptoms in asthmatics. We recognize, however, that uncertainties remain with regard to the relative contribution of $O_3$ and other co-pollutants, some of which show moderate correlations during the summer time, for the effects observed in asthmatic individuals.

In considering the large number of single-city epidemiological studies reporting lung function or respiratory symptoms in healthy or asthmatic populations (Appendix 3B), we note that most such studies that reported positive and often statistically significant associations in the warm season were conducted in areas with relevant air quality statistics that are indicative of areas that likely would not have met the current standard (e.g., Gent et al., 2003; Ostro et al., 2001; Neas et al., 1995; Delfino et al, 1998; Linn et al., 1996; Korrick et al., 1998). In considering the large multi-city NCICAS (Mortimer et al., 2002), we first note that while the 98$^{th}$ percentile 8-hr daily maximum $O_3$ concentrations at the highest monitor in each of the study areas ranged from 0.084 ppm to >0.10 ppm, the authors indicate that less than 5 percent of the days in the eight areas had 8-hr daily $O_3$ concentrations exceeding 80 ppb. The authors also observed that when days with 8-hr average $O_3$ levels greater than 80 ppb were excluded, similar effect estimates were seen. There also are some other studies in which the relevant air quality statistics provide some indication that lung function and respiratory symptom effects may be occurring in areas that likely would have met the current standard (e.g., Naeher et al., 1999; Ross

et al., 2002; Brauer et al., 1996). We note that this last group of studies reported associations that were often but not always statistically significant, and that Brauer et al. (1996) was an outdoor worker study of berry pickers with exposure patterns that would not be typical of the general population.

*Respiratory Hospital Admissions and Emergency Department Visits*

At the time of the last review, many time-series studies indicated positive associations between ambient $O_3$ and increased respiratory hospital admissions and emergency room visits, providing strong evidence for a relationship between $O_3$ exposure and increased exacerbations of preexisting lung disease at $O_3$ levels below the level of the then current 1-hr standard. Analyses of data from studies conducted in the northeastern U.S. indicated that $O_3$ air pollution was associated with summertime respiratory hospital admissions (CD, section 8.4.4).

Since the last review, new epidemiological studies have evaluated the association between short-term exposures to $O_3$ and unscheduled hospital admissions for respiratory causes (CD, section 7.3.3). Large multi-city studies, as well as many studies from individual cities have reported positive and often statistically significant $O_3$ associations with total respiratory hospitalizations as well as asthma- and COPD-related hospitalizations, especially in studies analyzing the $O_3$ effect during the summer or warm season. Analyses using multipollutant regression models suggest that copollutants generally do not confound the association between $O_3$ and respiratory hospitalizations, and that the $O_3$ effect estimates were generally robust to PM adjustment in all-year and warm-season only data (CD, p. 7-79; Figure 7-12). The CD concludes that the evidence supports a causal relationship between acute $O_3$ exposures and increased respiratory-related hospitalizations during the warm season (CD, p. 8-77).

In looking specifically at U.S. and Canadian respiratory hospitalization studies that reported positive and often statistically significant associations (and that either did not use GAM or were reanalyzed to address GAM-related problems), we note that many such studies were conducted in areas that likely would not have met the current $O_3$ standard, with most providing only all-year effect estimates, and with Schwartz et al. (1996) reporting a statistically significant association in the warm season. Of the studies that provide some indication that $O_3$-related respiratory hospitalizations may be occurring in areas that likely would have met the current standard, we note that some are all-year studies (e.g., Sheppard et al., 2003; Yang et al., 2003), whereas others reported statistically significant warm-season associations (e.g., Burnett et al., 1997a, in 16 Canadian cities; and Burnett et al., 1997b, 2001, in Toronto). In further examining the relevant air quality statistics in the 16 Canadian cities study (Burnett et al., 1997a), we observe that while the aggregated 98$^{th}$ percentile $O_3$ concentration was calculated as 47 ppb (Appendix 3B), the fourth-highest values at the highest monitors in each of the cities ranged from approximately 35 to 110 ppb, making it difficult to determine the extent to which the

reported association can be attributed to effects occurring in areas that likely would have met the current U.S. standard. We also further examined the relevant air quality statistics in the Burnett et al. (1997b, 2001) studies in Toronto. We observed that in one of those studies (Burnett et al., 2001) the fourth-highest values at the highest monitor ranged from approximately 80 to 150 ppb across the years of the study (from 1980 to 1994). In the other study (Burnett et al., 1997b) the calculated $98^{th}$ percentile values averaged across the several monitors used in the study ranged from 62 to 64 ppb in each of the three years of the study (Appendix 3B), but individual monitor data were not available for further examination. Based on these observations, we find it difficult to judge the extent to which these studies provide evidence of an association with respiratory-related hospitalizations in areas that likely would have met the current standard.

Emergency department visits for respiratory causes have been the focus of a number of new studies that have examined visits related to asthma, COPD, bronchitis, pneumonia, and other upper and lower respiratory infections, such as influenza, with asthma visits typically dominating the daily incidence counts (CD, section 7.3.2). Among studies with adequate controls for seasonal patterns, many reported at least one significant positive association involving $O_3$. However, inconsistencies were observed which were at least partially attributable to differences in model specifications and analysis approach among various studies. In general, $O_3$ effect estimates from summer-only analyses tended to be positive and larger compared to results from cool season or all year analyses. Almost all of the studies that reported statistically significant effect estimates had calculated $98^{th}$ percentile $O_3$ concentrations (Appendix 3B), averaged across monitors, that are indicative of areas that likely would not have met the current standard. The notable exception was a study in Montreal (Delfino et al., 1997) that reported statistically significant warm-season associations with $O_3$ and ED visits in a population of older adults with a calculated $98^{th}$ percentile value, averaged across several monitors, of approximately 60 ppb (and for which individual monitor data were not available for further examination), although the CD raises questions about the plausibility of this result due to the low $O_3$ concentrations and inconsistent results across years and age groups. The CD concluded that analyses stratified by season generally supported a positive association between $O_3$ concentrations and ED visits for asthma in the warm season. These studies provide evidence of effects in areas that likely would not have met the current standard but do not address the likelihood of effects occurring in areas that likely would have met the current standard.

*Mortality*

The 1996 CD concluded that an association between daily mortality and $O_3$ concentration for areas with high $O_3$ levels (e.g., Los Angeles) was suggested. However, due to a very limited number of studies available at that time, there was insufficient evidence to conclude that the

observed association was likely causal, and thus the possibility that $O_3$ exposure may be associated with mortality was not relied upon in the 1997 decision on the $O_3$ primary standard.

Since the last review, newly available large multi-city studies designed specifically to examine the effect of $O_3$ and other pollutants on mortality have provided much more robust and credible information. New data are also available from several single-city studies conducted world-wide, as well as from several meta-analyses that have combined information from multiple studies. The majority of these studies suggest that there is an elevated risk of total non-accidental mortality associated with acute exposure to $O_3$, especially in the summer or warm season when $O_3$ levels are typically high, with somewhat larger effect estimate sizes for associations with cardiovascular mortality (CD, p. 7-175). The CD finds that the results from U.S. multi-city time-series studies, along with the meta-analyses, provide relatively strong evidence for associations between short-term $O_3$ exposure and all-cause mortality even after adjustment for the influence of season and PM (CD, p. 8-78). The results of these analyses indicate that copollutants generally do not appear to substantially confound the association between $O_3$ and mortality (CD, p. 7-103; Figures 7-22 and 7-23). The multi-city mortality studies generally included a large number of cities that are not in attainment with the current $O_3$ standard. Most all single-city studies that show statistically significant associations with mortality had calculated $98^{th}$ percentile $O_3$ concentrations (Appendix 3B) that are indicative of $O_3$ levels that likely would not have met the current standard. The notable exception was a study in Vancouver (Vedal et al., 2003) that reported a statistically significant warm-season association with $O_3$ and total non-accidental mortality with a calculated $98^{th}$ percentile value, averaged across many monitors, of approximately 53 ppb. Upon further examination, the relevant air quality statistics for each individual monitor in this study ranged from 57 to 59 ppb. This study provides evidence of an $O_3$-related mortality association in the warm season that extends below the level of the current standard. Another study done in Vancouver over a much longer time period (Villeneuve et al., 2003) did not provide evidence of $O_3$-related mortality associations, but only all-year results were presented which may be more likely confounded by other pollutants than the warm-season results in Vedal et al. (2003).

#### 6.3.1.2 Exposure- and Risk-based Considerations

In addition to the evidence-based considerations, staff has also considered the extent to which exposures and health risks estimated to occur upon attainment of the current $O_3$ standard may be judged to be important from a public health perspective, taking into account key uncertainties associated with the estimated exposures and risks. In so doing, we note that the exposure analysis and risk assessment discussed in Chapters 4 and 5, respectively, identify a number of uncertainties, as highlighted below.

With respect to the exposure analysis, the exposure modeling approach represents variability in ambient $O_3$ levels, demographic characteristics, physiological attributes, activity patterns, and factors affecting microenvironmental concentrations. In our judgment the most important uncertainties affecting the exposure estimates are related to the modeling of activity patterns over an $O_3$ season, modeling micro-scale variations in ambient concentrations (e.g., near roadways), and modeling air exchange rates in microenvironments. Another important uncertainty that does not directly affect estimates of exposure, but affects the characterization of how many exposures are associated with moderate or greater exertion, is the characterization of energy expenditure (i.e., measured in terms of METS) for children engaged in various activities. As discussed in section 4.3.4.7, the uncertainty in METS values carries over to the uncertainty of the modeled ventilation rates, which are important since they are used to classify exposures of potentially greater risk. An ongoing uncertainty analysis of the exposure model is described in a draft staff memorandum (Langstaff, 2006).

With respect to the lung function part of the health risk assessment, key uncertainties include uncertainties in the exposure estimates for children engaged in moderate or greater exertion (noted above) and uncertainties associated with the shape of the exposure-response relationship, especially at levels below 0.08 ppm, 8-hr average, where only limited data are available down to 0.04 ppm and there is an absence of data below 0.04 ppm. With respect to the part of the health risk assessment based on effects reported in epidemiological studies, the most important uncertainty is the extent to which the associations between $O_3$ and the health endpoints included in the assessment actually reflect causal relationships, especially with regard to the relationship between $O_3$ and mortality. Other important uncertainties for this part of the risk assessment include uncertainties (1) surrounding estimates of $O_3$ coefficients in concentration-response functions used in the assessment, (2) concerning the specification of the concentration-response model (including the shape of the relationship) and whether or not a population threshold or non-linear relationship exists within the range of concentrations examined in the studies, (3) related to the extent to which concentration-response relationships derived from studies in a given location and time when $O_3$ levels were higher or behavior and/or housing conditions were different provide accurate representations of the relationships for the same locations with lower air quality distributions and different behavior and/or housing conditions, and (4) concerning the possible role of co-pollutants which also may have varied between the time of the studies and the current assessment period. For both parts of the risk assessment, statistical uncertainty due to sampling error has been characterized.

This section focuses first on the results of the exposure assessment and then on the results of the risk assessment. As described in Chapter 4, for this review estimates of exposures have been calculated for people of all ages, school age children (ages 5-18), "active" school age

children,[2] and asthmatic school age children in 12 urban areas across the U.S. In this draft Staff Paper we focus particularly on the exposure estimates for all, active, and asthmatic school age children since these groups are particularly at risk for experiencing $O_3$-related health effects due to the greater amount of time spent outdoors during the $O_3$ season engaged in relatively high levels of physical activity. As discussed in Chapter 4, we estimated exposures and risks for two recent years (2004 and 2002) from the most recent 3-year period for which data were available at the time of the analyses. Among the 3 years (2002-2004) used to determine the amount of adjustment required to simulate just meeting the current standard, 2002 was a year with generally poorer air quality and provides a generally more upper-end estimate of exposures and risks.

For this exposure analysis, an "exposure of concern" was defined the same way as it was in the last review, i.e., an 8-hr average exposure $\geq$ 0.08 ppm $O_3$ while engaged in intermittent moderate or greater exertion levels (62 FR 38860). Estimating exposures of concern is important because it provides an indication of the potential magnitude of incidence of health outcomes, such as cases of pulmonary inflammation or increased airway responsiveness, that have been demonstrated to occur at levels as low as 0.08 ppm, but which were not quantified in the current risk assessment due to lack of adequate information on the overall exposure-response relationship.

Exposure results are displayed in tables in Appendix 4A for daily maximum 8-hr average exposures $\geq$ 0.08 ppm $O_3$, in 12 urban areas across the U.S., for several scenarios (i.e., recent air quality (2002 and 2004) and just meeting the current 0.08 ppm, 8-hr primary standard based on adjusting 2004 and 2002 air quality using the three year period 2002-2004 to determine the amount of adjustment needed), at moderate or greater exertion levels for the general population, and for all, "active," and asthmatic school age (5-18) children. Drawing from Appendix 4A, exposure estimates for 4 scenarios (i.e., recent air quality and just meeting the current standard, based on adjusting 2002 and 2004 air quality) aggregated across 12 urban areas are shown in Table 6-1. The exposure estimates are for the number and percent of people exposed, in each of the groups, and the number of person-days (occurrences) of exposure, with daily 8-hr maximum average exposures above 0.08 ppm while at moderate or greater exertion.

As shown in Table 6-1, the patterns of exposures in terms of percentages of the population exceeding a given exposure level are very similar for the general population and for

[2]As indicated in section 4.4.3 above, "active" school age children were defined as those with a physical activity index $\geq$ 1.75.

**Table 6-1. Summary of Estimates of Number of People Exposed and Number of Occurrences at Moderate Exertion Associated with 8-Hour Daily Maximum Ozone Concentrations ≥ 0.08 ppm for 12 Urban Areas in the U.S.**

| Air Quality Scenario | Ozone Exposure Level and Exertion Category | General Population (88.5 million people) | | All Children (5-18) (18.1 million children) | | Active Children (5-18) (8.0 million children) | | Asthmatic Children (5-18) (2.8 million children) | |
|---|---|---|---|---|---|---|---|---|---|
| | | Persons[1] (% of pop.) | Person Days[1] [% from recent] | Persons[1] (% of pop.) | Person Days[1] [% from recent] | Persons[1] (% of pop.) | Person Days[1] [% from recent] | Persons[1] (% of pop.) | Person Days[1] [% from recent] |
| Recent Air Quality (2004) | ≥ 0.08 ppm, moderate exertion[2] | 2000 (2%) | 2520 | 780 (4%) | 1000 | 370 (4%) | 460 (4%) | 110 (4%) | 150 |
| Just Meeting Current 8-hr Standard | ≥ 0.08 ppm, moderate exertion[2] | 50 (0.1%) | 50 [98% reduction] | 20 (0.1%) | 20 [98% reduction] | 10 (0.1%) | 10 [98% reduction] | 3 (0.1%) | 3 [98% reduction] |
| Recent Air Quality (2002) | ≥ 0.08 ppm, moderate exertion[2] | 9010 (11%) | 11670 | 3660 (20%) | 4930 | 1890 (20%) | 2580 | 570 (20%) | 760 |
| Just Meeting Current 8-hr Standard | ≥ 0.08 ppm, moderate exertion[2] | 1550 (2%) | 1670 [86% reduction] | 600 (3%) | 660 [87% reduction] | 330 (3%) | 360 [86% reduction] | 100 (3%) | 110 [86% reduction] |

[1]Estimates for persons and person days are in thousands and numbers greater than 10,000 were rounded to the nearest 10,000. Estimates for persons and person days less than 10,000 were rounded to the nearest thousand. Percentages greater than or equal to 1 are rounded to the nearest percent and percentages less than one are rounded to the nearest tenth.

[2]Moderate exertion is defined as having an 8-hr average equivalent ventilation rate (EVR) in the range 13-27 l-min/$m^2$.

all, "active," and asthmatic school age (5-18) children. Figures 4-2 and 4-3 also show that the pattern of exposures is similar for all, "active", and asthmatic school age children on a relative percentage basis. Thus, in the discussion below we focus on the patterns observed for all school age children, which includes active and asthmatic children, with the recognition that these exposure patterns apply to these other subpopulations.

For recent years, almost 800,000 (4% of all school age children for the 12 urban areas) to nearly 3.7 million children (20% of all school age children for the 12 urban areas), for 2004 and 2002 air quality, respectively, are estimated to experience one or more exposures of concern. When air quality is adjusted to simulate just meeting the 8-hr standard, the number of children exposed drops substantially. Depending on which year is adjusted, approximately 20,000 children (0.1% of all school age children) for 2004 and 600,000 (3% of all school age children) for 2002 air quality are estimated to experience one or more exposures of concern. These results suggest substantial reductions (97% based on 2004 air quality and 84% based on 2002 air quality) in the estimated number of children estimated to experience one or more 8-hr average exposures above 0.08 ppm when the current 8-hr $O_3$ standard is just met.

A comparison of the number of children exposed with the number of occurrences indicates that very few children are likely to be exposed more than one time during the $O_3$ season to 8-hr exposures of concern while engaged in moderate exertion. This is particularly the case when the current 8-hr standard is met. For example, under the 2004 air quality scenario, there are an estimated 1.0 million person days of 8-hr, moderate exertion exposures of concern experienced by about 800,000 school age children. When 2004 air quality is adjusted to just meet the current 8-hr standard, there are an estimated 50,000 person days of 8-hr, moderate exertion exposures of concern experienced by about 50,000 school age children, which means that there are very few occasions where there are multiple occurrences of exposures of concern.

The exposure estimates discussed above reflect variability in the various inputs that influence population exposure, but do not characterize the uncertainties in the estimates. Sensitivity analyses have been conducted which have varied key inputs to the exposure model (e.g., AER's, activity pattern data used in the model, parameters for the algorithms used to construct the sequence of activity patterns over a season) and are described in the Exposure Analysis TSD. As described above, we are in the process of using a Monte Carlo approach to produce quantitative estimates of the uncertainty of the model results, based on estimates of the uncertainties of the model inputs, the results of which will be included in the final Staff Paper.

Turning to risk-based considerations, as discussed in Chapter 5, risk estimates have been calculated and are discussed below for lung function decrements in school age children and active school age children, respiratory symptoms (i.e., chest tightness, shortness of breath, wheeze) in

moderate to severe asthmatic children, respiratory-related hospital admissions, and non-accidental and cardiorespiratory mortality.

Tables 5-5 and 5-6 in Chapter 5 display risk estimates for "active" school age children (ages 5-18) for two different levels of lung function decrement responses for the 12 urban areas. As with the exposure estimates, the risk estimates are associated with two years of recent air quality (i.e., 2002, 2004) and air quality based on adjusting these same two years (i.e., 2002, 20004) to simulate just meeting the current 0.08 ppm, 8-hr $O_3$ standard based on the three-year design value using the period 2002 to 2004. All estimates in both tables reflect responses associated with exposure to $O_3$ in excess of exposures associated with policy relevant background $O_3$ concentrations. Table 5-5 shows the number and percent of active school age children estimated to have at least one lung function response (i.e., $FEV_1$ decrement $\geq$ 10, 15, and 20%) during the $O_3$ season. Table 5-6 displays the total number of occurrences for the specified lung function responses during the $O_3$ season. Since very similar patterns are observed between the risk estimates for "active" children and all school age children, we will discuss the estimates for all children in this Chapter since this is the more inclusive population that is at risk for experiencing lung function decrements. Table 6-2 draws upon for the risk estimates for all school age children contained in the draft Risk Assessment TSD and provides the number of children estimated to experience one or more occurrences of the specified health outcome and the number of total days of occurrences, aggregated across all 12 urban areas.

As discussed in greater detail in section 3.6.3, $FEV_1$ decrements $\geq$ 10 but <20% have been judged to represent moderate levels of functional responses for active healthy people and would likely interfere with normal activity for relatively few sensitive individuals. However, for persons with lung disease, such as asthma, lung function decrements at the lower end of the moderate range (i.e., $FEV_1$ decrements $\geq$ 10%) would likely interfere with normal activity for many individuals and would likely result in additional and more frequent use of medication. We also note that new evidence described above indicates that children with asthma are more likely to have lung function and symptomatic responses, and have bigger responses, from $O_3$ exposure than children who do not have asthma. Studies discussed in section 3.3.1.1 that show increased lung function responses, inflammation, and increased airway responsiveness in asthmatics indicate that the risk estimates for lung function decrements derived from controlled exposures of healthy adult volunteers likely underestimate the percent of asthmatic school age children that would experience $\geq$ 15% decrements in $FEV_1$. In the last review, we used a $\geq$ 15% decrease in $FEV_1$ as a benchmark for a moderate lung function responses, because it is the middle of the range judged to represent moderate functional responses (ranging from $\geq$ 10% to < 20%). However, in light of the more recent evidence noted above, we have considered not only the risk estimates for $\geq$ 15% decrements in $FEV_1$ but also for the lower end of the moderate range, a $\geq$ 10% decrement in $FEV_1$, as a benchmark for asthmatic children.

**Table 6-2. Summary of Number and Percent of All School Age Children Estimated to Experience Lung Function Responses and the Number of Occurrences[1] Associated with 8-Hour Ozone Exposures While Engaged in Moderate Exertion[2] for 2004 and 2002 Air Quality and Just Meeting the Current 8-Hour Standard**

| Air Quality Scenario | $FEV_1 \geq 10\%$ | | $FEV_1 \geq 15\%$ | | $FEV_1 \geq 20\%$ | |
|---|---|---|---|---|---|---|
| | Children (in thousands and % of population in parentheses) [1] | Occurrencess (thousands)[1] [% reduction from recent] | Children (in thousands and % of population in parentheses)[1] | Occurrencess (thousands)[1] [% reduction from recent] | Children (in thousands and % of population in parentheses)[1] | Occurrencess (thousands)[1] [% reduction from recent] |
| Recent Air Quality (2004) | 1550 (9%) | 15690 | 550 (3%) | 1890 | 160 (0.9%) | 310 |
| Just Meeting Current 8-hr Standard | 820 (5%) | 8630 [45% reduction] | 170 (0.9%) | 480 [75% reduction] | 20 (0.1%) | 30 [85% reduction] |
| Recent Air Quality (2002) | 2620 (14%) | 22060 | 1240 (7%) | 4060 | 470 (3%) | 960 |
| Just Meeting Current 8-hr Standard | 1550 (9%) | 13550 [39% reduction] | 550 (3%) | 1630 [60% reduction] | 150 (1%) | 260 [73% reduction] |

[1]Estimates for persons and person days greater than 10,000 were rounded to the nearest 10,000. Estimates for persons and person days less than 10,000 were rounded to the nearest thousand. Percentages less than 1 are rounded to the nearest tenth, percentages greater than or equal to 1 are rounded to the nearest percent.

[2]Moderate exertion is defined as having an 8-hr average EVR ≥ 13 l-min/$m^2$.

As shown in Table 6-2, for two recent years (2004 and 2002), from 550,000 to over 1.2 million school age children are estimated to experience 1 or more moderate lung function responses (≥ 15% reduction in $FEV_1$) in the 12 urban areas combined. Similar to the exposure estimates discussed above, when air quality is adjusted to simulate just meeting the current 8-hr standard, there are significant reductions in estimated health outcomes. Depending on which year is adjusted to just meet the current 8-hr standard, about 170,000 children (0.9% of all school age children) for 2004 and 550,000 children (3% of all school age children) for 2002 are estimated to experience moderate (≥ 15% reduction in $FEV_1$) lung function responses in these 12 urban areas combined upon just meeting the current standard.

Among all school age children, these estimates indicate that the percent of children likely to experience one or more moderate or greater lung function decrements (≥ 15% $FEV_1$ decrement) drops by about 56% and 70% when the current standard is just met based on adjusting a year with generally poorer (2002) and generally better (2004) air quality, respectively. Using the more precautionary definition of moderate lung function decrements (≥ 10% $FEV_1$ decrement) the percent drops to about 40% and 50% when the current standard is just met for the two different years. Among active children, the reduction in percent of children likely to experience one or more moderate or greater lung function decrements is similar. Among all school age children, these estimates indicate that meeting the current 8-hr primary standard will result in a 60% and 75% reduction in the number of occurrences of moderate or greater lung function decrements (≥ 15% $FEV_1$ decrement) based on adjusting a year with generally poorer and generally better air quality, respectively. Using the more precautionary definition of moderate lung function decrements (≥ 10% $FEV_1$ decrement) the number of occurrences drops by about 39% to 45% when the current standard is just met. Among active children, and likely among asthmatic children, the reductions in occurrences would be about the same.

These estimates also indicate that there are substantial differences in the natural fluctuation of air quality levels from year to year. This can result in significant variability in the number of children affected by moderate or greater lung function decrements and the number of occurrences they experience during a 3-year period that is adjusted to just meet the current 8-hr standard. As shown in Table 6-2, the number of children affected, and the number of occurrences, can increase by more than 100% for a year with generally poorer air quality compared to a year with better air quality, within a three year period.

Several other aspects of the risk information presented are important to consider. The first is that there is some degree of consistency in the estimated population risk across the 12 urban areas, as indicated by the percent of the population estimated to be affected, which

describes the risk normalized across the urban areas with very different population sizes. In Table 6-2, the percent of all children likely to experience one or more moderate or greater lung function responses (≥ 15% reduction in $FEV_1$) under recent air quality and when air quality just meets the current 8-hr standard are 3% and 0.9% (based on 2004 air quality) respectively. The range across the 12 urban areas, from Tables 3-5 and 3-17 in the draft Risk Assessment TSD is 1.1% to 4.7% under recent (2004) air quality, and about 0.5% to 1.8 % when air quality is adjusted to just meet the current 8-hr standard based on that year. The pattern across the 12 urban areas is similar for the risk estimates based on 2002 air quality.

It is also important to note that many of these children will experience repeated occurrences of moderate or greater lung function responses. These results indicate that each of these children is likely to experience about 3 occurrences of moderate or greater lung function responses, on average, during an $O_3$ season.[3] However, based on the distribution of exposures estimated from the 1997 review, the more likely distribution will be that many children will experience one or just a few moderate or greater lung function responses, while a smaller number of children will experience large numbers of such responses. This range of estimated number of occurrences (i.e., from one to many, with a mean of approximately 3) of moderate or greater lung function decrements in an $O_3$ season is important in considering the implications for the health status of individuals likely to experience these effects. Moderate or greater lung function decrements are transient and reversible, so the extent to which such effects are considered to be adverse to the health status of the individual depends not only on the severity and duration of the effect, but also on the frequency with which an individual experiences such effects throughout an $O_3$ season (62 FR 38864).

Using the more precautionary definition of moderate lung function decrements, many more of these children are estimated to experience repeated occurrences of moderate or greater lung function responses. The results in Table 6-2 indicate that each of these children is likely to experience about 9 occurrences of moderate or greater lung function responses, on average, during an $O_3$ season. As discussed above, the more likely distribution is that many children will experience one or only a few occurrences of moderate or greater lung function decrements (≥ 10% decrement in $FEV_1$), while some may experience a very large number, based on these estimates. Recognizing that nationally over 14% of school age children have asthma, these numbers raise concern about the potential number of children with asthma who could experience a large number of occurrences of moderate or greater lung function decrements (≥ 10% decrement in $FEV_1$) even with air quality just meeting the current 8-hr standard.

[3]This number is estimated for example for all children, by dividing the estimated number of children into the estimated number of occurrences, resulting in an average of about 3 occurrences per child.

Risk estimates were developed for several respiratory symptoms (i.e., chest tightness, shortness of breath, and wheeze) in children age 0 to 12 with moderate to severe asthma (as defined by the use of maintenance asthma medications), living in the Boston area. About 40% of the children with asthma in the Boston area are estimated to be on controller medications and would be considered moderate-to-severe asthmatics.[4] In this population of 25,000 children with moderate-to-severe asthma, as shown in Tables 5-7 and 5-8, the estimated incidence of symptom days of chest tightness (across 4 models reflecting 2 different lags and $O_3$ alone vs. inclusion of $PM_{2.5}$ in the model) ranges from 5,300 to 8,400 based on a year with better (2004) air quality, and from almost 6,900 to 10,800 based on a year (2002) with poorer air quality.

As indicated by Figure 5-7, the current standard, and each of the alternative standards, reduces the incidence of symptom days for chest tightness by relatively small and consistent amounts across the 4 models specified. Risk estimates for the other symptom endpoints, shortness of breath and wheeze, show similar patterns as the risk estimates for chest tightness. The reduction of risks across the 4 models for chest tightness is shown in Table 6-3. Averaging the median estimates of symptom days indicates that just meeting the current 8-hr standard is estimated to reduce the total number of symptom days for chest tightness in children with moderate to severe asthma by 15% (from 6,700 to 5,700) based on a year (2004) with generally better air quality and 11% (8,700 to 7,700) based on a year (2002) with generally poorer air quality. The current standard clearly does not reduce the incidence of symptom days in children with moderate to severe asthma in Boston to the same degree that the standard reduces the occurrences of moderate or greater lung function decrements in all school age children and active school age children in the 12 urban areas, as discussed above.

Looking at percent of total incidence of symptom days, even after the current 8-hr standard is met, in a year with generally better air quality among children with moderate to severe asthma in the Boston area, as many as one symptom day in 8 is estimated to be attributable to $O_3$ exposure. In a year with generally poorer air quality, as many as one symptom day in 6 is estimated to be attributable to $O_3$ exposure. These results support the human clinical and epidemiological evidence that people with asthma are more likely to experience effects of $O_3$ exposure than the general population, and provide evidence that the current 8-hr $O_3$ standard is not as protective for children with moderate to severe asthma in the Boston area as it is for all school age children and all active school age children in the 12 urban areas evaluated.

[4]The estimated percent of asthmatic children using maintenance medications (40%) was obtained via email 4-05-06 from Jeanne Moorman, CDC).

**Table 6-3 Risks of Respiratory Symptom Days for Chest Tightness Associated with Recent (2004, 2002) Air Quality and Just Meets the Current Standard Based on Adjusting 2004 and 2002 Air Quality in Moderate to Severe Asthmatic Children in Boston, MA**

| Respiratory Symptoms in Asthmatic Children on Controller Meds | Year | Average Risks of Chest Tightness Associated with Air Quality (range of median estimates)[1,2] [reduction from recent air quality] | |
|---|---|---|---|
| | | Recent Air Quality | Just Meets 0.08 ppm |
| Incidence | 2004 | 6,700 (5,300 - 8,400) | 5,700 [15% reduction] (4,500 - 7,200) |
| | 2002 | 8,700 (6,900 - 10,800) | 7,700 [11% reduction] (6,100 - 9,600) |
| Incidence per 100,000 | 2004 | 26,400 (20,700 - 33,100) | 22,600 (17,700 - 28,400) |
| | 2002 | 34,400 (27,200 - 42,700) | 35,600 (24,100 - 38,100) |
| Percent of Total Incidence | 2004 | 9.4% - 15.1% | 8% - 12.9% |
| | 2002 | 12.4% - 19.5% | 11% - 17.3% |

[1]Incidence rounded to nearest 100.
[2]Range of median estimates across models using lag 0 and lag 1 day and $O_3$ only and including $PM_{2.5}$ in the model.

For unscheduled hospital admissions, risk estimates for the New York City area associated with $O_3$ levels above background for the period from April to September are shown in Table 6-4 for recent air quality (2002, 2004), and for just meeting the current 8-hr standard based on adjusting those years. The current 8-hr standard reduces the incidence of respiratory-related hospital admissions by about 18% in a year with better air quality (2004) and about 16% in a year with poorer air quality (2002). The incidence of asthma-related hospital admissions (which are a subset of total respiratory hospital admissions) were reduced by about the same amount in each of the two scenarios. This results in an incidence per 100,000 of 4.6 to 6.4 for respiratory related hospital admissions, and 3.9 to 5.5 for asthma-related hospital admissions, based on two air quality years, after the current standard is met.

Table 6-5 summarizes risk estimates for non-accidental mortality in 12 urban areas associated with $O_3$ levels above background for the period from April to September based on the 95-city function reported in Bell et al. (2004) for non-accidental mortality. This table includes

**Table 6-4 Risks of Respiratory- and Asthma-related Hospital Admissions Associated with Recent (2004, 2002) Air Quality and Air Quality Adjusted to Just Meets Current Standard Based on Adjusting 2004 and 2002 Air Quality in New York City, NY**

| Unscheduled Hospital Admissions | Air Quality Scenario | Incidence[1] (Range)[2] | | Incidence per 100,000 (Range)[2] | | Percent Total Incidence (Range)[2] | |
|---|---|---|---|---|---|---|---|
| | | 2004 | 2002 | 2004 | 2002 | 2004 | 2002 |
| Respiratory | Recent | 450 (110 – 790) | 610 (150 – 1070) | 5.6 (1.4 - 9.8) | 7.6 (1.8 - 13.3) | 1.3% (0.3 - 2.2%) | 1.7% (0.4 - 3%) |
| | Just Meets 0.08 ppm | 370 (90 - 640) [18 % reduction] | 510 (120 – 900) [16% reduction] | 4.6 (1.1 - 8) | 6.4 (1.5 - 11.3) | 1% (0.3 - 1.8%) | 1.5% (0.4 - 2.6%) |
| Asthma (subset of respiratory) | Recent | 380 (80 – 680) | 520 (110 – 930) | 4.8 (1 - 8.5) | 6.5 (1.4 - 11.6) | 2.9% (0.6 - 5.2%) | 4% (0.8 - 7.1%) |
| | Just Meets 0.08 ppm | 310 (70 - 560) [18% reduction] | 440 (90 - 780) [16% reduction] | 3.9 (0.8 - 7) | 5.5 (1.2 - 9.8) | 2.4% (0.5 - 4.3%) | 3.3% (0.7 - 6%) |

[1]Incidence rounded to the nearest 10.
[2]Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient

**Table 6-5. Risks of Non-accidental Mortality Associated with Recent (2004, 2002) Air Quality and Air Quality Adjusted to Just Meets Current Standard Based on Adjusting 2004 and 2002 Air Quality**

| Location | Air Quality Scenario | Estimated Risk of Non-accidental Mortality[1,2] | | | | | |
|---|---|---|---|---|---|---|---|
| | | Incidence (range)[3] | | Incidence per 100,000 (range)[3] | | Percent of Total Incidence (range)[3] | |
| | | 2004 | 2002 | 2004 | 2002 | 2004 | 2002 |
| Atlanta | Recent | 12 (4 - 20) | 17 (6 - 29) | 0.8 (0.3 - 1.4) | 1.2 (0.4 - 1.9) | 0.3% (0.1 - 0.4%) | 0.4% (0.1 - 0.6%) |
| | Just Meets 0.08 ppm | 9 (3 - 15) | 14 (5 - 23) | 0.6 (0.2 - 1) | 0.9 (0.3 - 1.6) | 0.2% (0.1 - 0.3%) | 0.3% (0.1 - 0.5%) |
| Boston | Recent | 7 (2 - 12) | 10 (3 - 17) | 1.0 (0.3 - 1.7) | 1.5 (0.5 - 2.5) | 0.3% (0.1 - 0.5%) | 0.4% (0.1 - 0.7%) |
| | Just Meets 0.08 ppm | 6 (2 - 9) | 9 (3 - 15) | 0.8 (0.3 - 1.4) | 1.3 (0.4 - 2.1) | 0.2% (0.1 - 0.4%) | 0.3% (0.1 - 0.6%) |
| Chicago | Recent | 49 (16 - 81) | 69 (23 - 115) | 0.9 (0.3 - 1.5) | 1.3 (0.4 - 2.1) | 0.2% (0.1 - 0.4%) | 0.3% (0.1 - 0.5%) |
| | Just Meets 0.08 ppm | 33 (11 - 55) | 55 (18 - 91) | 0.6 (0.2 - 1) | 1 (0.3 - 1.7) | 0.2% (0.1 - 0.3%) | 0.3% (0.1 - 0.4%) |
| Cleveland | Recent | 17 (6 - 28) | 38 (13 - 64) | 1.2 (0.4 - 2) | 2.8 (0.9 - 4.6) | 0.2% (0.1 - 0.4%) | 0.5% (0.2 - 0.9%) |
| | Just Meets 0.08 ppm | 12 (4 - 20) | 31 (10 - 52) | 0.9 (0.3 - 1.4) | 2.2 (0.8 - 3.7) | 0.2% (0.1 - 0.3%) | 0.4% (0.1 - 0.7%) |
| Detroit | Recent | 17 (6 - 28) | 29 (10 - 48) | 0.8 (0.3 - 1.4) | 1.4 (0.5 - 2.3) | 0.2% (0.1 - 0.3%) | 0.3% (0.1 - 0.5%) |
| | Just Meets 0.08 ppm | 12 (4 - 20) | 24 (8 - 39) | 0.6 (0.2 - 1) | 1.1 (0.4 - 1.9) | 0.1% (0 - 0.2%) | 0.3% (0.1 - 0.4%) |
| Houston | Recent | 17 (6- 28) | 14 (5 - 24) | 0.5 (0.2 - 0.8) | 0.4 (0.1 - 0.7) | 0.2% (0.1 - 0.3%) | 0.2% (0.1 - 0.3%) |
| | Just Meets 0.08 ppm | 11 (4 - 18) | 9 (3 - 15) | 0.3 (0.1 - 0.5) | 0.3 (0.1 - 0.4) | 0.1% (0% - 0.2%) | 0.1% (0% - 0.2%) |

| Location | Air Quality Scenario | Estimated Risk of Non-accidental Mortality[1,2] | | | | | |
|---|---|---|---|---|---|---|---|
| | | Incidence (range)[3] | | Incidence per 100,000 (range)[3] | | Percent of Total Incidence (range)[3] | |
| | | 2004 | 2002 | 2004 | 2002 | 2004 | 2002 |
| Los Angeles | Recent | 133 (45 - 221) | 110 (37 - 184) | 1.4 (0.5 - 2.3) | 1.2 (0.4 - 1.9) | 0.5% (0.2 - 0.8%) | 0.4% (0.1 - 0.7%) |
| | Just Meets 0.08 ppm | 67 (22 - 111) | 52 (17 - 86) | 0.7 (0.2 - 1.2) | 0.5 (0.2 - 0.9) | 0.2% (0.1 - 0.4%) | 0.2% (0.1 - 0.3%) |
| New York | Recent | 60 (20 - 100) | 105 (35 - 174) | 0.7 (0.2 - 1.1) | 1.2 (0.4 - 2) | 0.2% (0.1 - 0.3%) | 0.3% (0.1 - 0.6%) |
| | Just Meets 0.08 ppm | 43 (15 - 72) | 84 (28 - 139) | 0.5 (0.2 - 0.8) | 0.9 (0.3 - 1.6) | 0.2% (0.1 - 0.3%) | 0.3% (0.1 - 0.4%) |
| Philadelphia | Recent | 23 (8 - 38) | 37 (12 - 62) | 1.5 (0.5 - 2.5) | 2.4 (0.8 - 4.1) | 0.3% (0.1 - 0.5%) | 0.5% (0.2 - 0.8%) |
| | Just Meets 0.08 ppm | 17 (6 - 28) | 30 (10 - 50) | 1.1 (0.4 - 1.8) | 2 (0.7 - 3.3) | 0.2% (0.1 - 0.3%) | 0.4% (0.1 - 0.6%) |
| Sacramento | Recent | 18 (6 - 29) | 23 (8 - 39) | 1.4 (0.5 - 2.4) | 1.9 (0.6 - 3.2) | 0.4% (0.1 - 0.7%) | 0.6% (0.2 - 0.9%) |
| | Just Meets 0.08 ppm | 12 (4 - 21) | 18 (6 - 30) | 1 (0.3 - 1.7) | 1.5 (0.5 - 2.4) | 0.3% (0.1 - 0.5%) | 0.4% (0.1 - 0.7%) |
| St. Louis | Recent | 3 (1 - 5) | 6 (2 - 10) | 0.9 (0.3 - 1.5) | 1.7 (0.6 - 2.8) | 0.2% (0.1 - 0.3%) | 0.3% (0.1 - 0.5%) |
| | Just meets 0.08 ppm | 2 (1 - 4) | 5 (2 - 8) | 0.7 (0.2 - 1.1) | 1.4 (0.5 - 2.3) | 0.1% (0%- 0.2%) | 0.2% (0.1% - 0.4%) |
| Washington, DC | Recent | 8 (3 - 14) | 15 (5 - 25) | 1.5 (0.5 - 2.4) | 2.6 (0.9 - 4.4) | 0.3% (0.1 - 0.5%) | 0.6% (0.2 - 0.9%) |
| | Just Meets 0.08 ppm | 7 (2 - 12) | 14 (5 - 23) | 1.2 (0.4 - 2.1) | 2.4 (0.8 - 3.9) | 0.3% (0.1 - 0.4%) | 0.5% (0.2 - 0.8%) |

[1]All results are for mortality (among all ages) associated with short-term exposures to $O_3$. All results are based on single-pollutant model from Bell et al. (2004) 95-cities model.

[2]Incidence was quantified down to estimated policy relevant background levels. Incidences are rounded to the nearest whole number; incidences per 100,000 relevant population and percents are rounded to the nearest tenth.

[3] Note: Numbers in parentheses are 95% confidence or credible intervals based on statistical uncertainty surrounding the $O_3$ coefficient.

risks for two recent years of air quality (2002 and 2004) and risks associated with just meeting the current 8-hr standard over a recent 3-year period (2002-2004).[5] We chose to present the multi-city function risk estimates here because they are available for all 12 urban areas, while single-city estimates are only available for 7 of the 12 urban areas. In comparing estimates between recent air quality and just meeting the current standard, similar patterns are seen in terms of relative reductions regardless of whether single- or multi-city functions are used. Additional risk estimates for cardiorespiratory mortality are included in the draft Risk Assessment TSD for 8 of the 12 urban areas based on Huang et al. (2005). Across the 12 urban areas, the estimates of mortality incidence per 100,000 relevant population range from 0.5 to 1.5 (for 2004) and from 0.4 to 2.6 (for 2002). Meeting the current standard results in a reduction of the incidence per 100,000 to a range of 0.3 to 1.2 based on adjusting 2004 air quality and a range of 0.3 to 2.4 based on adjusting 2002 air quality. Estimates for cardiorespiratory mortality show similar patterns (Tables 5-8, 5-11).

#### 6.3.1.3 Summary

As discussed above, we have considered new evidence from controlled human exposure and epidemiologic studies as well as estimates of $O_3$-related exposures of concern and risks upon meeting the current standard in many urban areas across the U.S., together with associated uncertainties. Staff finds support in this information, including the direction of the evidence and exposure and risk estimates developed since the last review, for consideration of an $O_3$ standard that is at least as protective as the current standard, and does not find support for consideration of an $O_3$ standard that is any less protective.

Evidence of a range of respiratory-related morbidity effects seen in the last review has been strengthened, both through controlled human exposure studies as well as through many new panel and epidemiological studies. In addition, new evidence identifies people with asthma as an important susceptible population for which estimates of respiratory effects in the general population may underestimate the magnitude or importance of the effect. New evidence about mechanisms of toxicity helps to explain the biological plausibility of $O_3$-induced respiratory effects and is beginning to suggest mechanisms that may link $O_3$ exposure to cardiovascular effects.

We also note some new direct evidence of transient and reversible lung function effects in some individuals at exposure levels below the level of the current standard. In addition, there

[5]The information presented in Table 6-5 is based on Tables 5-10 and 5-11 in this draft Staff Paper which summarize the risk estimates for non-accidental mortality in 12 urban areas for recent air quality (2002, 2004) and Tables 5C-13 to 5C-16 in Appendix 5C of this draft Staff Paper and Tables 4-15 and 4-18 of the draft Risk Assessment TSD which present risk estimates for just meeting the current 8-hr standard based on adjusting the 3-year period (2002-2004).

is now epidemiological evidence in which the relevant air quality statistics provide some limited indication that lung function and respiratory symptom effects, as well as mortality effects, may be occurring in areas that likely would have met the current standard. These views reflect a scientifically cautious approach to interpreting the available time-series epidemiological studies, in that we recognize important limitations in such studies with regard to the extent to which they provide evidence of $O_3$-specific associations, especially in studies that examined all-year associations. We also note the difficulties in attempting to directly compare relevant $O_3$ air quality information from epidemiological studies to reach conclusions about the likelihood that observed effects would occur in areas that likely would have met the current standard.

With regard to estimates of risks of health effects in sensitive populations likely to remain upon attaining the current standard, we note that some such estimates related to relatively less serious lung function effects are now appreciably lower than in the last review, whereas risk estimates related to more serious effects, hospital admissions, are as high or higher than previously estimated. In addition, unlike in the last review, we now have evidence that supports estimating risks for respiratory symptoms in asthmatic children and $O_3$-related mortality. We recognize that some might generally view the much lower risk estimates of lung function effects as a basis for considering a less protective standard. However, when considered in context with current estimates of the risks of more serious effects and the importance of the new evidence on $O_3$-related effects for people with asthma, we conclude that the available evidence provides a stronger basis for an $O_3$ standard that is at least as protective as the current standard and that consideration of a less protective standard is not warranted.

More specifically, we note that meeting the current $O_3$ standard substantially reduces estimates of exposures of concern relative to those associated with recent air quality levels in many U.S. cities, which provides some perspective on the magnitude of the incidence of inflammation or increased airway responsiveness in the population. Meeting the current $O_3$ standard also substantially reduces the estimates for risk of moderate lung function decrements ($\geq$ 15% $FEV_1$ decrement) in children, respiratory symptom days in children with moderate to severe asthma, respiratory-related hospital admissions, and non-accidental and cardiorespiratory mortality. While the current standard also reduces the estimated risk of moderate lung function decrements in children using the more precautionary benchmark ($\geq$ 10% $FEV_1$ decrements) of more relevance for asthmatic children, the reduction is not as large, with about 5% to 9% of all school age children, and likely a similar percentage of children with asthma, estimated to experience one or more occurrences of moderate lung function decrements when the current standard is met. Moreover, in this case, the estimated number of occurrences per child is on average nine per ozone season, with several occurrences of moderate lung function decrements per $O_3$ season generally considered to be an adverse effect, especially for children with asthma.

We also recognize that even when the current standard is met over a three-year period, air quality can vary considerably, as evidenced by relatively large differences between risk estimates based on 2004 and 2002 air quality. We believe it is appropriate to consider this yearly variation in air quality allowed by the current standard in judging the extent to which impacts on members of sensitive groups in a year with relatively poorer air quality remains of concern from a public health perspective.

Staff recognizes that the exposure- and risk-based information can be considered both from the perspective of whether the risks estimated to remain upon attaining the current standard are important from a public health perspective and/or from the perspective of whether additional reductions in risk estimated to be associated with alternative, more protective standards are important. Judgments about the importance of the estimates of exposures and risks need to take into account the important uncertainties associated with such estimates. Recognizing that such public health policy judgments are ultimately decisions left to the Administrator, we conclude that the entire body of evidence and information could support the view that the level of public health protection afforded by the current standard protects the public health with an adequate margin or safety, whereas it could also support the view that additional protection is warranted. These alternative judgments would reflect differing views as to the relative weight to place on the evidence and the exposure- and risk-based information and on the associated uncertainties, as well as differing public health policy judgments.

Taking into account the above considerations, staff concludes that the body of information that is now available supports consideration of either retaining the current standard or revising the standard within the range of alternatives addressed in our exposure and risk assessments so as to afford greater public health. The following sections on indicator, averaging time, level, and form are intended to help inform consideration of this range of alternatives.

### 6.3.2 Indicator

In the last review EPA focused on a standard for $O_3$ as the most appropriate surrogate for ambient photochemical oxidants. Staff believes that conclusion remains valid today. It is generally recognized that control of ambient $O_3$ levels provides the best means of controlling photochemical oxidants of potential health concern. Further, among the photochemical oxidants, the acute exposure chamber, panel and field epidemiological human health database provides evidence only for $O_3$ at levels of photochemical oxidants commonly reported in the ambient air, in part because few other photochemical oxidants are measured. However, recent investigations on copollutant interactions have used simulated urban photochemical oxidant mixes. These investigations suggest the need for similar studies to help in understanding the biological basis for effects observed in epidemiologic studies that are associated with air pollutant mixtures,

where $O_3$ is used as the surrogate for the mix of photochemical oxidants. Meeting the $O_3$ standard can be expected to provide some degree of protection against potential health effects that may be independently associated with other photochemical oxidants but which are not discernable from currently available studies indexed by $O_3$ alone. Since the precursor emissions that lead to the formation of $O_3$ generally also lead to the formation of other photochemical oxidants, measures leading to reductions in population exposures to $O_3$ can generally be expected to lead to reductions in population exposures to other photochemical oxidants.

### 6.3.3 Averaging Time

#### 6.3.3.1 Short-Term and Prolonged (1 to 8 Hours)

The current 8-hr averaging time for the primary $O_3$ NAAQS was set in 1997. The decision to revise the averaging time of the primary standard from 1 to 8 hr was supported by the following key observations and conclusions (62 FR 38861):

(1) The 1-hr averaging time of the previous NAAQS was originally selected on the basis of health effects associated with short-term (i.e., 1- to 3-hr) exposures.

(2) Substantial health effects information was available for the 1997 review that demonstrated associations between a wide range of health effects (e.g., moderate to large lung function decrements, moderate to severe symptoms and pulmonary inflammation) and prolonged (i.e., 6- to 8-hr) exposures below the level of the NAAQS.

(3) Results of the quantitative risk analyses showed that reductions in risks from both short-term and prolonged exposures could be achieved through a primary standard with an averaging period of either 1 or 8 hr.

(4) The 8-hr averaging time is more directly associated with health effects of concern at lower $O_3$ concentrations than the 1-hr averaging time. It was thus the consensus of CASAC "that an 8-hour standard was more appropriate for a human health-based standard than a 1-hour standard." (Wolff, 1995)

In looking at the new information that is discussed in section 7.6.2 of the CD, epidemiological studies have used various averaging periods for $O_3$ concentrations, most commonly 1-hr, 8-hr and 24-hr averages. As described more specifically below, in general the results presented from U.S. and Canadian studies (Appendix 3B) show no consistent difference for various averaging times in different studies.

Only a few studies presented results for different $O_3$ averaging periods using the same data set. Two of the recent multi-city mortality studies reported associations for multiple averaging times (Bell et al., 2004; Gryparis et al., 2004). Both reported that the effect estimates for different averaging times were not statistically different, though the effect estimates for associations with 1-hr daily maximum $O_3$ concentrations were somewhat larger than those for

longer averaging times, especially 24-hr average $O_3$. In addition, Gent et al., (2003) reported that associations for 1-hr and 8-hr average $O_3$ with respiratory symptoms were not significantly different.

Among the single-city epidemiological studies, Peters et al. (2001) reported positive, but not statistically significant associations between $O_3$ and the incidence of myocardial infarction (CD, p. 7-55); this study differs from most since the short-term $O_3$ concentration used was the time period preceding the health event, not the highest daily short-term average concentration. The effect estimate for the association with $O_3$ averaged over 2 hr prior to the myocardial infarction was substantially larger than that reported for an association with 24-hr average $O_3$ (Peters et al., 2001). The CD reports results for a number of single-city results that generally reported effect estimate sizes that were larger when comparing 1-hr or 8-hr daily maximum $O_3$ concentrations with the 24-hr concentration, but the results did not differ statistically (CD, p. 7-120).

The CD observes that the various $O_3$ average concentrations were generally very highly correlated with one another, so it is not surprising that effect estimates would be similar. The CD concludes that the epidemiological study results were generally comparable for the three $O_3$ averaging times (CD, p. 7-120). Because the 8-hr averaging time continues to be more directly associated with health effects of concern from controlled human exposure studies at lower concentrations than do shorter averaging periods, staff concludes that it is appropriate for the Administrator to consider continuing to base the primary standard on 8-hr average $O_3$ concentrations for protection of public health against the effects of short-term or prolonged $O_3$ exposures.

#### 6.3.3.2 Long-Term

During the last review, there was a large animal toxicological database for consideration that provided clear evidence of associations between long-term (e.g., from several months to years) exposures and lung tissue damage, with additional evidence of reduced lung elasticity and accelerated loss of lung function. However, there was no corresponding evidence for humans, and the state of the science had not progressed sufficiently to allow quantitative extrapolation of the animal study findings to humans. For these reasons, consideration of a separate long-term primary $O_3$ standard was not judged to be appropriate at that time, recognizing that the 8-hr standard would act to limit long-term exposures as well as short-term and prolonged exposures.

In the current review, long-term animal toxicological studies continue to support the relationship between $O_3$ exposure and structural alterations in several regions of the respiratory tract and identify the CAR as the most affected region. In addition, animal toxicological studies that utilized exposure regimens to simulate seasonal exposure patterns also report increased lung

injury compared to conventional long-term, stable exposures. (CD, p. 8-85) Collectively, the evidence from animal studies strongly suggest that $O_3$ is capable of damaging the distal airways and proximal alveoli, resulting in lung tissue remodeling leading to apparently irreversible changes. Compromised pulmonary function and structural changes due to persistent inflammation may exacerbate the progression and development of chronic lung disease (CD, p. 8-70). Recent epidemiologic studies observed that reduced lung function growth in children was associated with seasonal exposure to $O_3$; however, cohort studies investigating the effect of annual or multiyear $O_3$ exposure observed little clear evidence for impacts of longer-term, relatively low-level $O_3$ exposure on lung function development in children.

Collectively, the epidemiologic studies are inconclusive, but suggestive of respiratory health effects from long-term $O_3$ exposure. While there continues to be evidence of structural changes in the respiratory tract in animal studies, with some very weak support from epidemiologic studies in children, it is highly uncertain as to what long-term patterns of exposure or $O_3$ concentrations in humans may be required to produce the morphological changes found in the animal studies and it is not currently possible to characterize the possible magnitude or severity of any such effects occurring in humans in response to ambient $O_3$ exposures at levels observed in the U.S. For these reasons, staff concludes that it would not be appropriate at this time to consider setting a primary $O_3$ standard with a long-term averaging time for the purpose of protecting against potential effects of long-term $O_3$ exposure. To the extent that meeting an 8-hr $O_3$ standard in some cases is expected to result in lower long-term average concentrations, the 8-hr standard would provide some protection against effects that may be associated with long-term $O_3$ exposures.

### 6.3.4 Level

In considering retaining the level of the primary $O_3$ standard as well as alternative levels that would afford greater public health protection than the current standard, we have taken into account both evidence-based considerations and exposure- and risk-based considerations, generally discussed above in section 6.3.1.1 and 6.3.1.2., and additional exposure- and risk-based considerations discussed below. The following discussion focuses on the evidence supporting a view that it would be appropriate to consider revising the standard to provide more protection. Section 6.3.1 includes discussion of the view that it would be appropriate to consider retaining the current standard.

We first observe that while the evidence discussed above provides a basis for considering alternative levels below the current standard, it does not provide a clear quantitative basis for identifying any specific range of alternative levels as being appropriate for consideration. The few epidemiological studies that provide some indication that $O_3$-related health effects (e.g., lung

function effects, respiratory symptoms, mortality) may be occurring in areas that likely would have met the current U.S. standard do not directly provide a clear quantitative signal that would inform judgments about specific alternative standard levels. However, as in the last review, we believe that the available evidence on specific health endpoints is indicative of a broader pyramid of effects that cannot be quantitatively estimated at this time, but that nonetheless are important to consider in reaching a judgment as to the level of a standard that protects public health with an adequate margin of safety. This pyramid of effects in part builds upon evidence of lung function and symptomatic effects in asthmatics, which are generally associated with increased medication use, visits for medical care in physician offices and EDs, as well as missed school and work days. We also note that the susceptible population for such effects is likely to extend beyond the population of people with asthma to include people with allergic rhinitis who do not have asthma, which would substantially increase the size of the susceptible populations that are quantified in the CD (Chapter 8).

With respect to the exposure estimates, we have examined the estimated reductions in exposures of concern (i.e., 8-hr exposures at or above 0.08 ppm while engaged in moderate exertion) associated with potential alternative 8-hr standards for the general population and for all, active, and asthmatic school age children. Based on the exposure estimates summarized in the tables in Appendix 4A, we observe that lowering the level of the 8-hr standard to 0.07 ppm, $4^{th}$ daily max (the 74/4 scenario) is estimated to reduce the number of individuals in each of these populations from experiencing exposures of concern by 90 to 100% relative to just meeting the current 8-hr standard. Lowering the standard level to 0.06 ppm, $4^{th}$ daily max (the 64/4 scenario) is estimated to reduce the number of individuals from experiencing exposures of concern by 99.9 to 100%. Retaining the current standard level, but specifying the standard in terms of 80 ppb (i.e., the 80/4 scenario) rather than the current 0.08 ppm (i.e., the 84/4 scenario) is estimated to reduce the number of individuals in each of these populations from experiencing exposures of concern by about 55 to 60% across the three population groups based on adjusting 2002 air quality and by about 75% across these population groups based on adjusting 2004 air quality. Reductions in total person days of exposures of concern shows similar patterns to those described above.

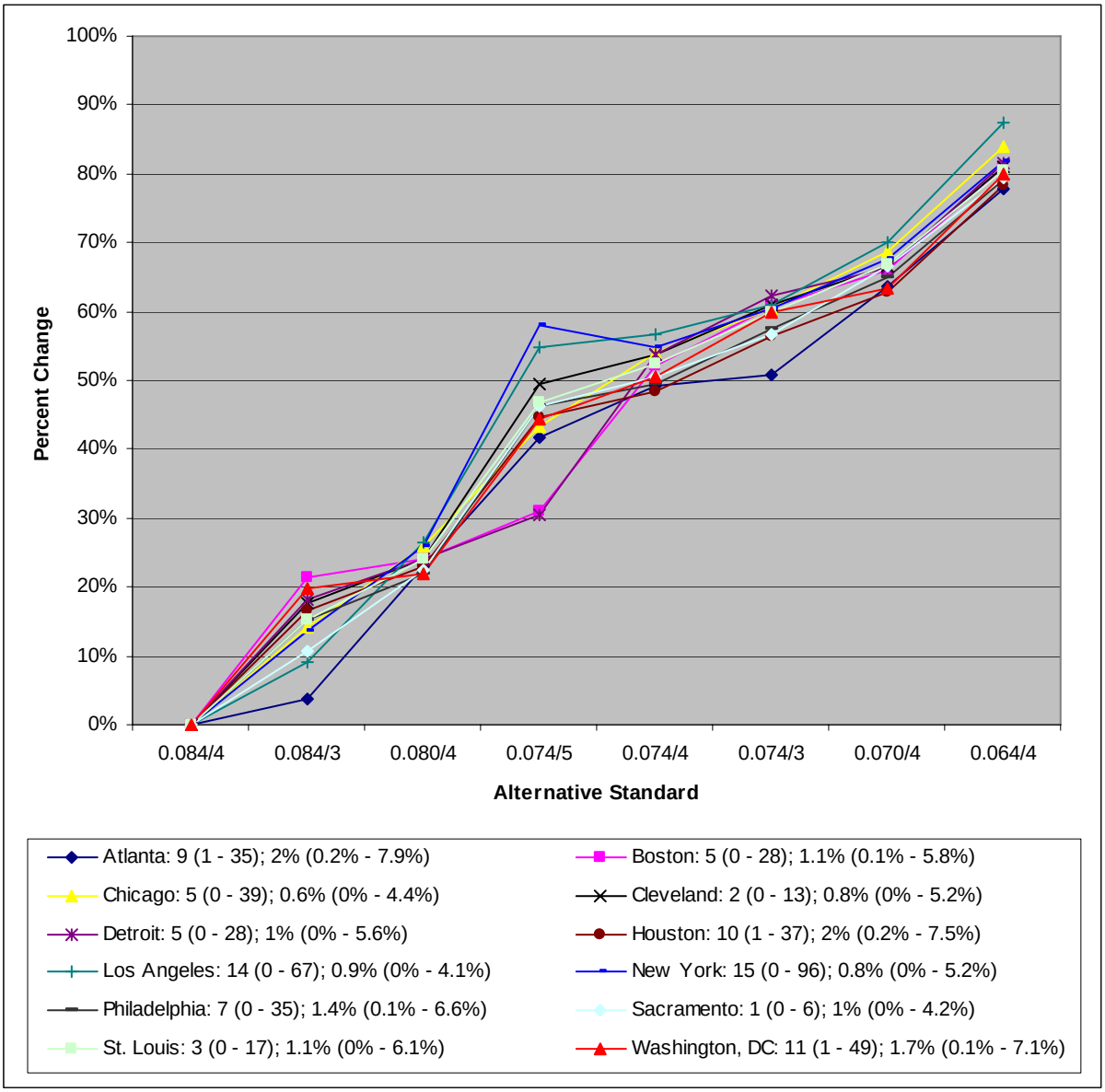
Turning to the estimates from the risk assessment, Figures 6-1 through 6-6 show the percent reduction in risk estimates, from the current 8-hr standard to alternative standards with varying levels and with varying forms (as discussed in the next section) that are assessed in this draft Staff Paper. Figures 6-1 and 6-2 show the percent reduction in risk estimates in the numbers of active school age children experiencing at least one decrement in $FEV_1 \geq 15\%$ in each of the 12 urban areas for 2004 and 2002, and Figures 6-3 and 6-4 show the percent reduction in the estimated number of active school age children experiencing at least one

decrement in $FEV_1 \geq 10\%$ (the more precautionary definition of moderate lung function decrements) in those same 12 urban areas for 2004 and 2002. Figures 6-5 and 6-6 show the percent reduction in risk estimates of non-accidental mortality for those same areas, for 2004 and 2002. The legend under each figure lists the estimated number of cases (and 95% CI) and the estimated percent of cases (and 95% CI) when $O_3$ concentrations just meet the current standard next to the name of each location.

Figures 6-1 through 6-4 show the percent change from the current standard in risk estimates for the incidence of moderate or greater decrements in lung function (≥ 15% reduction in $FEV_1$) and moderate lung function decrements using the more precautionary definition of moderate (≥ 10% reduction in $FEV_1$) in active school age children associated with meeting alternative standards. Tables 3-11 through 3-18 in the draft risk assessment TSD show similar patterns in relative reductions estimated to occur for all school age children. Estimated risks for moderate lung function decrements (≥ 15% reduction in $FEV_1$) are reduced to a greater extent by the alternative standards than risks of moderate lung function decrements using the more precautionary definition of moderate (i.e., ≥ 10% reduction in $FEV_1$). Reducing the level of the standard to 0.07 ppm, $4^{th}$ daily max (the 74/4 scenario) results in about a 45 to 60% reduction in risk estimates for moderate lung function decrements (≥ 15% reduction in $FEV_1$), depending on whether 2004 or 2002 air quality is the basis for adjustment across the 12 urban areas. Using the more precautionary definition of moderate lung function decrements (i.e., ≥ 10% reduction in $FEV_1$), when a 0.07 ppm, $4^{th}$ daily max 8-hr standard is just met risk estimates are reduced by about 30 to 40% relative to the current standard when the two recent years are adjusted across the 12 urban areas. An alternative standard set at 0.06 ppm, $4^{th}$ daily max (the 64/4 scenario) provides greater reduction relative to the current 8-hr standard (about 75 to nearly 90% depending on the year adjusted and urban area) in the risk estimates for moderate lung function decrements (≥ 15% reduction in $FEV_1$) and by about 50 to 60% in most of the areas, with 1 area having reductions near 80%, using the more precautionary definition of moderate (≥ 10% reduction in $FEV_1$). We note that simply specifying the level of the current standard as 80 ppb (see 80/4 scenario in Figures 6-1 to 6-4), rather than as 0.08 ppm, would result in about a 20 to 25% reduction in risk estimates for moderate lung function decrements (≥ 15% reduction in $FEV_1$) and over 10 to nearly 20% reduction in risk estimates using the more precautionary definition of moderate (≥ 10% reduction in $FEV_1$) relative to the current 8-hr standard.

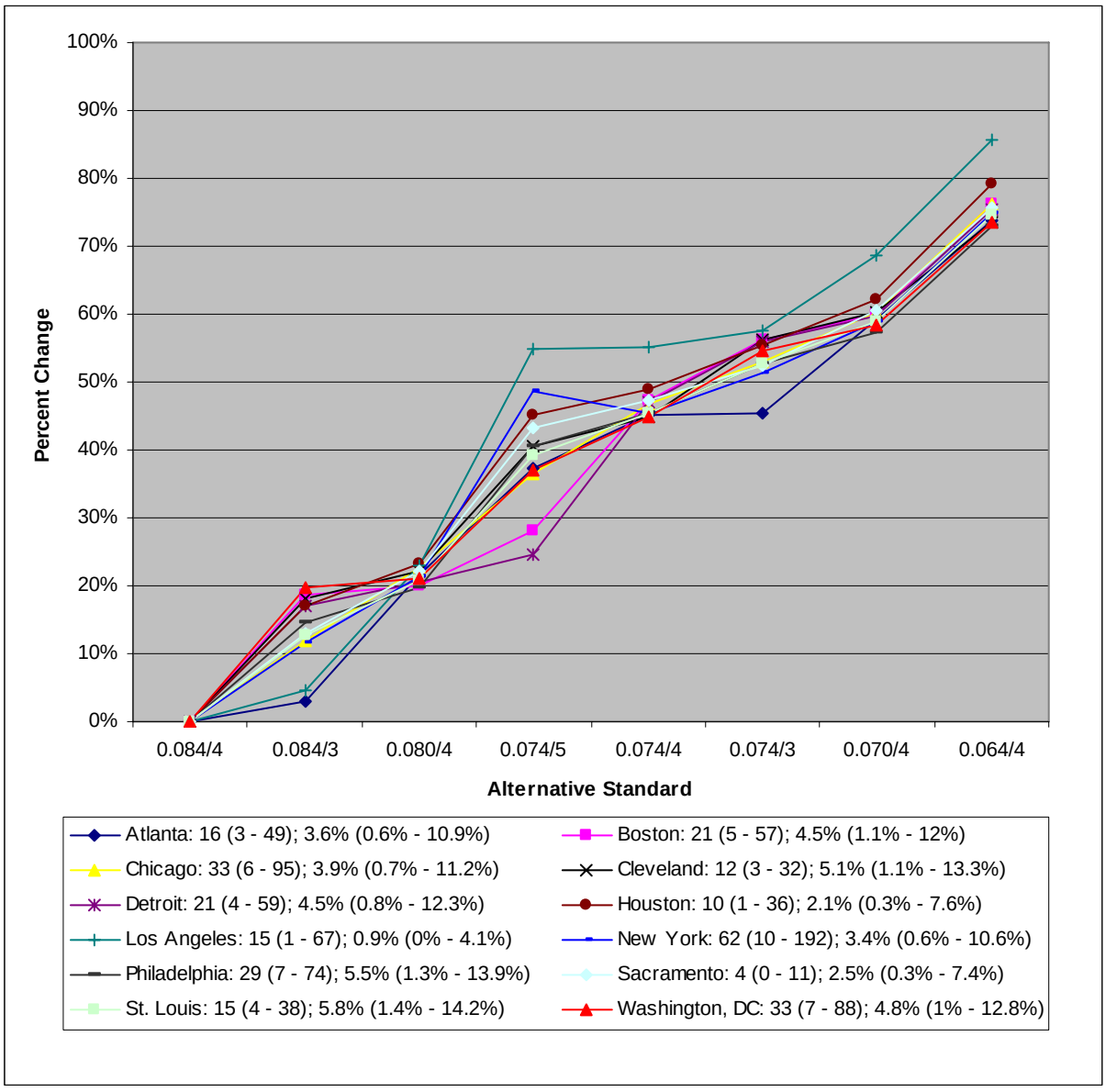
Figures 6-5 and 6-6 show the percent change from the current standard in the estimated incidence of non-accidental mortality associated with meeting alternative standards. Reducing

**Figure 6-1. Percent Changes in Numbers of Active School Age Children Experiencing at Least One Decrement in $FEV_1$ ≥15% when $O_3$ Concentrations are Reduced from Those Just Meeting the Current Standard to Those that Would Just Meet Each Alternative Standard, Based on Adjusting 2004 Data***



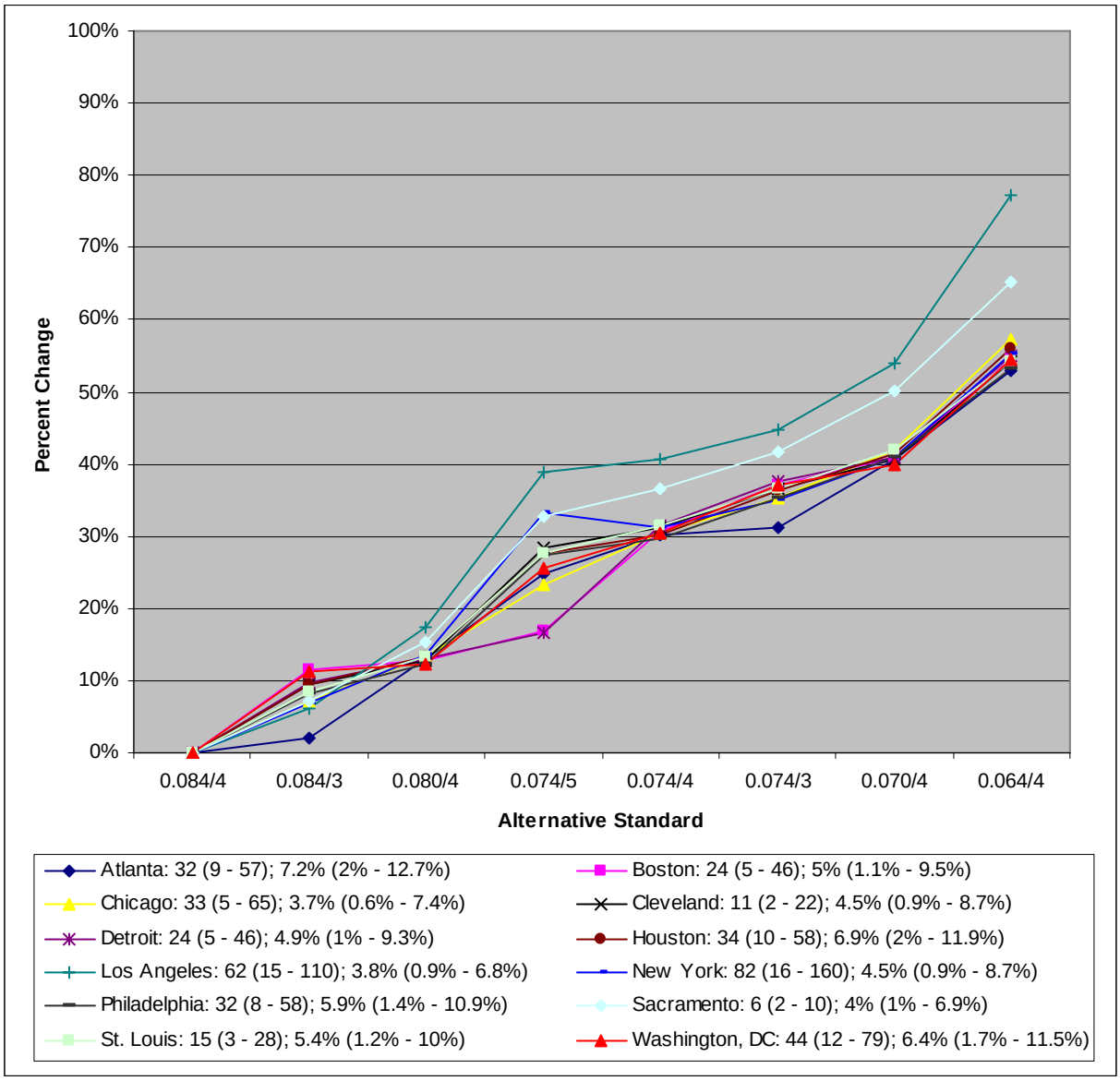

*The number of active children in thousands (and 95% CI) and the percent of active children (and 95% CI) experiencing at least one decrement in $FEV_1$ ≥15% when $O_3$ concentrations just meet the current standard (0.084/4) are shown next to the location name in the legend.

**Figure 6-2. Percent Changes in Numbers of Active School Age Children Experiencing at Least One Decrement in $FEV_1$ ≥15% when $O_3$ Concentrations are Reduced from Those Just Meeting the Current Standard to Those that Would Just Meet Each Alternative Standard, Based on Adjusting 2002 Data***



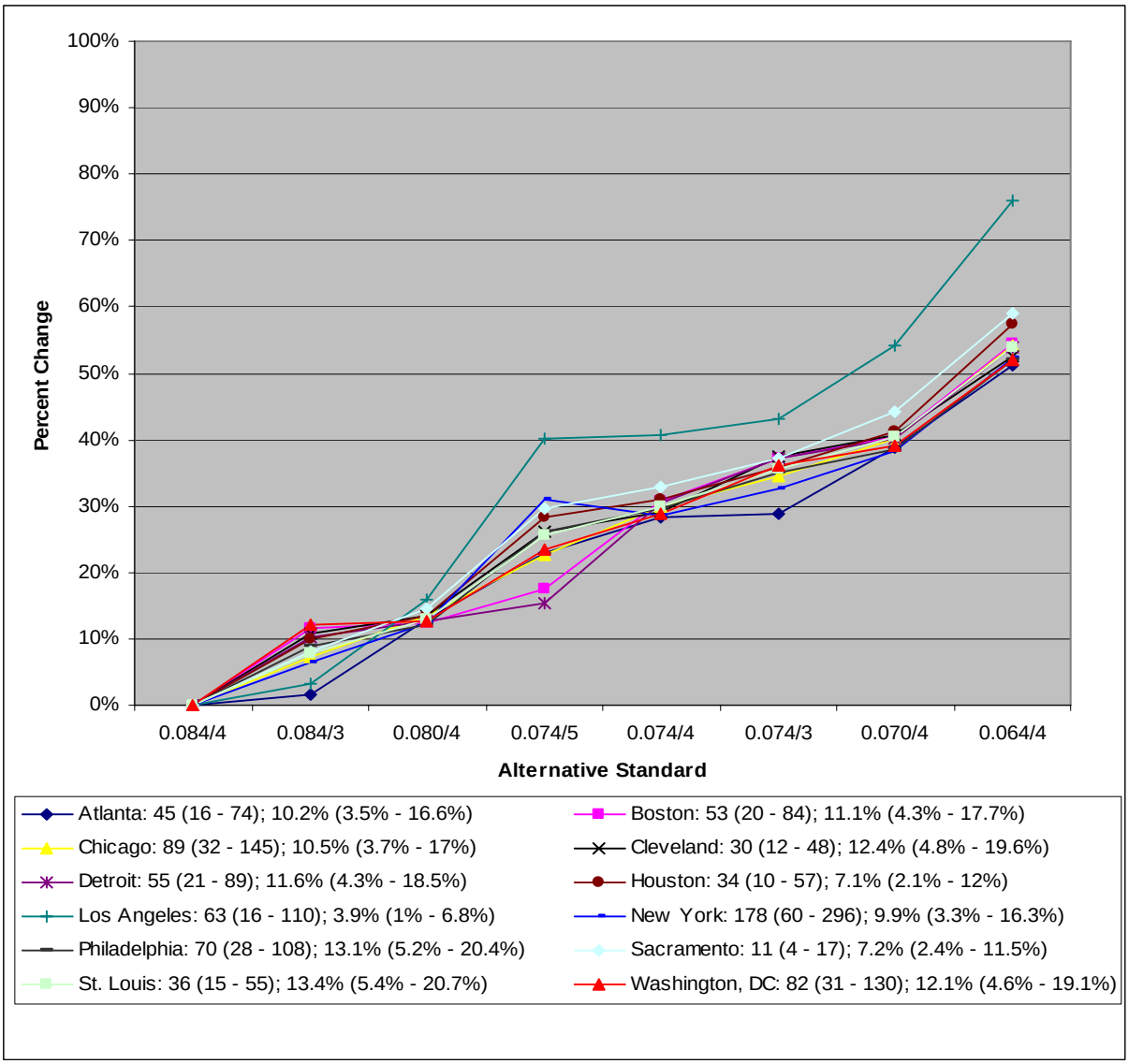

*The number of active children in thousands (and 95% CI) and the percent of active children (and 95% CI) experiencing at least one decrement in $FEV_1$ ≥15% when $O_3$ concentrations just meet the current standard (0.084/4) are shown next to the location name in the legend.

**Figure 6-3. Percent Changes in Numbers of Active School Age Children Experiencing at Least One Decrement in $FEV_1$ ≥10% when $O_3$ Concentrations are Reduced from Those Just Meeting the Current Standard to Those that Would Just Meet Each Alternative Standard, Based on Adjusting 2004 Data***



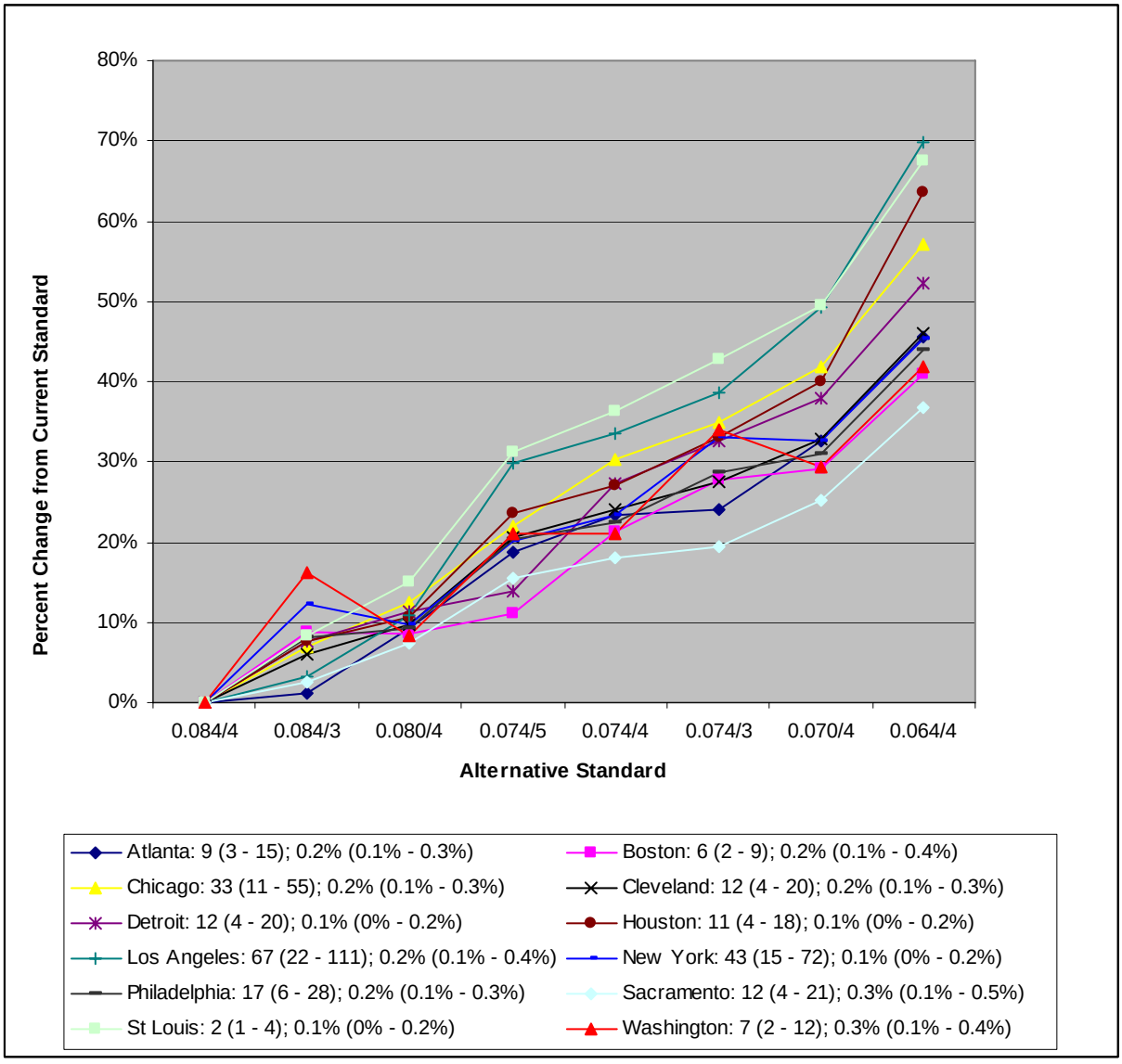

*The number of active children in thousands (and 95% CI) and the percent of active children (and 95% CI) experiencing at least one decrement in $FEV_1$ ≥10% when $O_3$ concentrations just meet the current standard (0.084/4) are shown next to the location name in the legend.

**Figure 6-4. Percent Changes in Numbers of Active School Age Children Experiencing at Least One Decrement in $FEV_1$ ≥10% when $O_3$ Concentrations are Reduced from Those Just Meeting the Current Standard to Those that Would Just Meet Each Alternative Standard, Based on Adjusting 2002 Data***



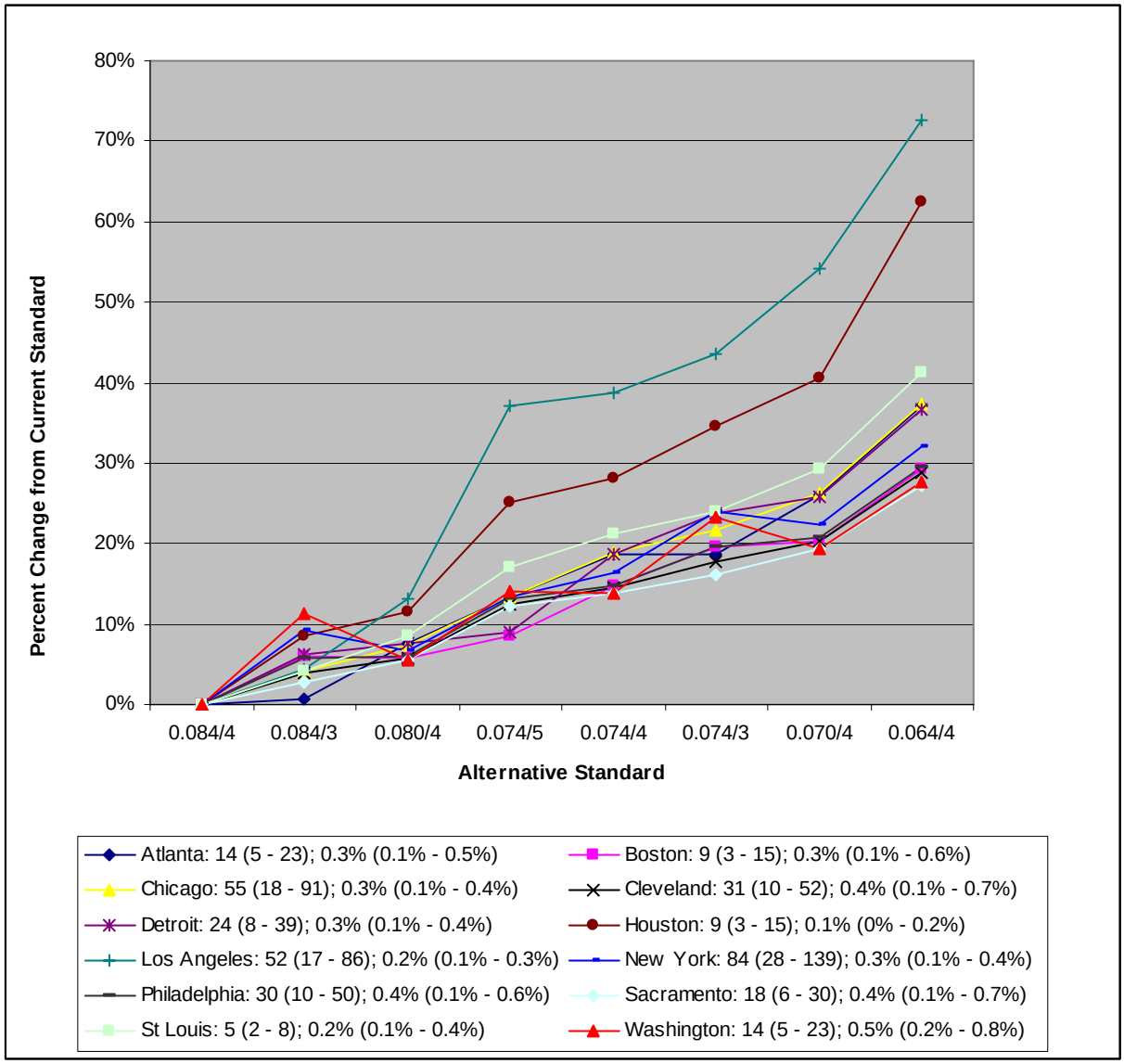

*The number of active children in thousands (and 95% CI) and the percent of active children (and 95% CI) experiencing at least one decrement in $FEV_1$ ≥10% when $O_3$ concentrations just meet the current standard (0.084/4) are shown next to the location name in the legend.

**Figure 6-5. Percent Changes in $O_3$-Related Non-Accidental Mortality Incidence when $O_3$ Concentrations are Reduced from Those Just Meeting the Current Standard to Those that Would Just Meet Each Alternative Standard, Based on Adjusting 2004 Data* (Using Bell et al., 2004 – 95 U.S. Cities)**




*The number of cases (and 95% CI) and the percent of cases (and 95% CI) of non-accidental mortality when O3 concentrations just meet the current standard (0.084/4) are shown next to the location name in the legend.

**Figure 6-6. Percent Changes in $O_3$-Related Non-Accidental Mortality Incidence When $O_3$ Concentrations are Reduced from Those Just Meeting the Current Standard to Those that Would Just Meet Each Alternative Standard, Based on Adjusting 2002 Data* (Using Bell et al., 2004 – 95 U.S. Cities)**




*The number of cases (and 95% CI) and the percent of cases (and 95% CI) of non-accidental mortality when $O_3$ concentrations just meet the current standard (0.084/4) are shown next to the location name in the legend.

the level of the standard to 0.07 ppm, 4th daily max (the 74/4 scenario) results in the risk estimates of non-accidental mortality being reduced by about 15 to over 35% (depending on the year adjusted and urban area) relative to the current standard. An alternative standard set at 0.06 ppm, 4th daily max (the 64/4 scenario) provides greater reduction relative to the current 8-hr standard (about 35 to 70% depending on the year adjusted and urban area) in the risk estimates of $O_3$-related non-accidental mortality. Simply specifying the level of the current standard as 80 ppb (see 80/4 scenario in Figures 6-5 and 6-6), rather than as 0.08 ppm, would result in about a 5 to 15% reduction in risks for non-accidental mortality relative to the current standard using the current rounding convention.

In conclusion, as discussed in the previous section addressing the adequacy of the current standard, just meeting the current 0.08 ppm, 4th daily max standard substantially reduces estimates of exposures of concern and risks of various health effects (e.g., moderate or greater lung function decrements in school age children, respiratory symptom days in moderate to severe asthmatic children, respiratory- and asthma-related hospital admissions, and non-accidental and cardiorespiratory mortality) relative to recent $O_3$ levels. Alternative standards analyzed in this draft Staff Paper and discussed in this section would provide additional protection in terms of reductions in estimated exposures of concern and health risks beyond the protection afforded by the current 8-hr standard. A standard set at 0.07 ppm, 4th daily max would provide substantial reductions in estimates of exposures of concern (i.e., 90 to 100%) and would reduce estimated health risks by15 to 60% relative to the current standard depending on health outcome, urban area, and air quality year adjusted. The most stringent standard analyzed, 0.06 ppm, 4th daily max, is estimated to essentially eliminate exposures of concern and would further reduce estimated health risks; however, there is increasing uncertainty associated with these estimated reductions as they are more heavily dependent on the assumption that the exposure-response (for lung function) and concentration-response (for non-accidental mortality) relationships go down to background levels. There also is increased uncertainty about the simulation of $O_3$ air quality that would occur upon just meeting a 0.06 ppm, 8-hr standard, since the level of air quality required to meet this scenario is well below the levels observed in some of the locations analyzed (e.g., Houston and Los Angeles). Taking the evidence, exposure- and risk-based information, and important uncertainties into consideration, staff concludes that it is appropriate for the Administrator to give primary consideration to alternative standards with a level ranging from 0.07 ppm to the current level of 0.08 ppm.

### 6.3.5 Form

In 1997 the primary $O_3$ NAAQS was changed from a "1-expected-exceedance" form[6] to a concentration-based statistic, specifically the 3-year average of the annual fourth-highest daily maximum 8-hr concentrations. The principal advantage of the concentration-based form is that it is more directly related to the ambient $O_3$ concentrations that are associated with the health effects. With a concentration-based form, days on which higher $O_3$ concentrations occur would weigh proportionally more than days with lower concentrations, since the actual concentrations are used in determining whether the standard is attained. That is, given that there is a continuum of effects associated with exposures to varying levels of $O_3$, the extent to which public health is affected by exposure to ambient $O_3$ is related to the actual magnitude of the $O_3$ concentration, not just whether the concentration is above a specified level.

In evaluating alternative forms for the primary standard, the adequacy of the public health protection provided is the foremost consideration. In addition, we recognize that it is important to have a form of the standard that is stable and insulated from the impacts of extreme meteorological events that are conducive to $O_3$ formation. Such instability can have the effect of reducing public health protection, because frequent shifting in and out of attainment due of meteorological conditions can disrupt an area's ongoing implementation plans and associated control programs. Providing more stability is one of the reasons that EPA moved to a concentration-based form in 1997.

During the 1997 review, consideration was given to a range of alternative forms, including the second-, third-, fourth- and fifth-highest daily maximum 8-hr concentrations in an $O_3$ season, recognizing that the public health risks associated with exposure to a pollutant without a clear, discernable threshold can be appropriately addressed through a standard that allows for multiple exceedances to provide increased stability, but that also significantly limits the number of days on which the level may be exceeded and the magnitude of such exceedances. Consideration was given to setting a standard with a form that would provide a margin of safety against possible, but uncertain chronic effects, and would also provide greater stability to ongoing control programs. The fourth-highest daily maximum was selected because it was decided that the difference between the protection against potential chronic effects afforded by the alternatives within the range was not well enough understood to use as a basis for choosing the most restrictive forms. On the other hand, the relatively large percentage of sites that would experience $O_3$ peaks well above 0.08 ppm and the number of days on which the level of the

[6]The 1-expected-exceedance form essentially requires that the fourth-highest air quality value in 3 years, based on adjustments for missing data, be less than or equal to the level of the standard for the standard to be met at an air quality monitoring site.

standard may be exceeded even when attaining a fifth-highest 0.08 ppm concentration-based standard, argued against choosing that form.

In selecting alternative standards to include in our exposure and risk analyses, we considered two concentration-based forms, the nth-highest maximum concentration and a percentile-based form. A percentile-based statistic is useful for comparing datasets of varying length because it samples approximately the same place in the distribution of air quality values, whether the dataset is several months or several years long. However, a percentile-based form would allow more days with higher air quality values in locations with longer $O_3$ seasons relative to places with shorter $O_3$ seasons. An nth-highest maximum concentration form would more effectively ensure that people who live in areas with different length $O_3$ seasons receive the same degree of public health protection. For this reason, our exposure and risk analyses were based on a form specified in terms of an nth-highest concentration, with n ranging from 3 to 5.

The results of some of these analyses are shown in Figures 6-1a and b and 6-2a and b, discussed above in section 6.3.4. These figures illustrate the estimated percent change in risk estimates for the incidence of moderate or greater decrements in lung function (≥ 15% reduction in $FEV_1$) and moderate lung function decrements using the more precautionary definition of moderate (≥ 10% reduction in $FEV_1$) in active school age children, associated with going from meeting the current standard to meeting alternative standards with alternative forms. Figures 6-3a and b illustrate the estimated percent change in the estimated incidence of non-accidental mortality, associated with going from meeting the current standard to meeting alternative standards. These results are generally representative of the patterns found in all of the analyses. The estimated reductions in risk associated with different forms of the standard, ranging from third- to fourth-highest daily maximum concentrations at 0.08 ppm, and from third- to fifth-highest daily maximum concentrations at 0.07 ppm, are generally less than the estimated reductions associated with the different levels that were analyzed. As seen in these figures, there is much city-to-city variability, particularly in the percent changes associated with going from a fourth-highest to third-highest form at the current level of 0.08 ppm, and with estimated reductions associated with the fifth-highest form at a 0.07 ppm level. In most cities, there are generally only small differences in the estimated reductions in risks associated with the third- to fifth-highest forms at a level of 0.07 ppm.

Because there is not a clear health-based threshold for selecting a particular nth-highest daily maximum form of the standard from among the ones analyzed, staff concludes that it is appropriate to consider retaining the current form, the fourth-highest daily maximum concentration. Alternatively, we believe that consideration could also be given to alternative forms within the range analyzed, taking into account the extent to which the alternative form

limits the number and concentration of high $O_3$ days and also allows for some yearly variability to ensure a stable target for control programs to maintain appropriate public health protection.

### 6.3.6 Summary of Staff Conclusions on Primary $O_3$ NAAQS

Staff's conclusions about options for the Administrator's consideration in making decisions on the primary $O_3$ standard, together with supporting conclusions from sections 6.3.2 to 6.3.5, are briefly summarized below. We recognize that selecting from among alternative standards will necessarily reflect consideration of qualitative and quantitative uncertainties inherent in the relevant evidence and in the assumptions of the quantitative exposure and risk assessments. Any such standard should protect public health against health effects associated with exposure to $O_3$, alone or in combination with related photochemical oxidants, taking into account both evidence-based and exposure- and risk-based considerations, and the nature and degree of uncertainties in such information. In identifying these options for consideration, we are mindful that the Act requires standards that, in the judgment of the Administrator, are requisite to protect public health with an adequate margin of safety. The standards are to be neither more nor less stringent than necessary. Thus, the Act does not require that NAAQS be set at zero-risk levels, but rather at levels that reduce risk sufficiently to protect public health with an adequate margin of safety.

(1) It is appropriate to continue to use $O_3$ as the indicator for a standard that is intended to address effects associated with exposure to $O_3$, alone or in combination with related photochemical oxidants. Based on the available information, we conclude that there is no basis for considering any alternative indicator at this time. While the new body of time-series epidemiological evidence cannot resolve questions about the relative contribution of other photochemical oxidant species to the range of morbidity and mortality effects associated with $O_3$ in these types of studies, control of ambient $O_3$ levels is generally understood to provide the best means of controlling photochemical oxidants in general, and thus of protecting against effects that may be associated with individual species and/or the broader mix of photochemical oxidants, independent of effects specifically related to $O_3$.

(2) It is appropriate to continue to use an 8-hr averaging time for the primary $O_3$ standard because it provides protection against both short-term and prolonged exposures and it continues to be more directly associated with health effects of concern from controlled human exposure studies at lower concentrations than do shorter averaging periods. We conclude that there is currently not sufficient evidence to consider a longer averaging

time, as there is not sufficient evidence upon which to draw conclusions about the need for a separate standard with a longer averaging time that might more directly protect against potential effects that may be associated with long-term exposure to $O_3$.

(3) It is appropriate both to consider retaining the current standard and to consider various options with regard to revising the level and form of the primary $O_3$ standard that would afford greater public health protection than that afforded by the current standard.

(a) Consideration could be given to retaining the current 8-hr $O_3$ standard. Consideration of this option might generally reflect a view that places more weight on the lack of clear evidence that statistically significant respiratory effects occur in controlled human exposure studies below the level of the current standard and on the observation that quantitative risk estimates based on results of controlled human exposure studies (e.g., demonstrating $O_3$-induced decreases in lung function, especially for $\geq$15 percent decrements in $FEV_1$) are now in general appreciably lower than estimated in the last review. Such a view might place more limited weight on evidence of more serious morbidity (e.g., associations with hospital admissions) and mortality effects derived from time-series epidemiological studies, which might be characterized as being a more uncertain basis for reaching decisions on the level and form of a standard that would protect public health with an adequate margin of safety.

(b) Consideration could be given to revising the current $O_3$ standard by setting a more protective standard within the range of alternative 8-hr standards that were included in staff's exposure and risk assessments. Within that range, staff concludes that consideration might primarily focus on an $O_3$ level of 0.07 ppm, with a range of forms from the third- through fifth-highest daily maximum 8-hr average concentration. Consideration of a standard set at this level might generally reflect a view that places particular importance on the evidence of greater respiratory effects in people with asthma in conjunction with consideration of risk estimates associated with a more precautionary definition of moderate decreases in lung function (i.e., >10 percent decrements in $FEV_1$). Such a view might also place more weight on epidemiological evidence, including evidence of more serious effects such as hospitalization and mortality, taking into consideration the extent to which statistically significant effects may be associated with $O_3$ exposure in areas that likely would have met the current standard. This view might also place weight on consideration of a broader pyramid of effects

that are likely associated with exposure to $O_3$, alone and in combination with other photochemical oxidants, but for which the evidence is not sufficient to include in a quantitative risk assessment (e.g., a range of effects in susceptible populations, such as increased medication use, missed school and work days, and increased visits to EDs or physician offices).

## 6.4 SUMMARY OF KEY UNCERTAINTIES AND RESEARCH RECOMMENDATIONS RELATED TO SETTING A PRIMARY $O_3$ STANDARD

We believe it is important to continue to highlight the uncertainties associated with establishing standards for $O_3$ during and after completion of the NAAQS review process. Research needs go beyond what is necessary to understand health and welfare effects, population exposures, and the risks of exposure for purposes of setting standards. Research can also support the development of more efficient and effective control strategies. It should be noted, however, that a thorough discussion of research needs related to control strategy development is beyond the scope of this document.

Following completion of the 1996 Ozone Staff Paper (EPA, 1996), the EPA held a research needs workshop and produced a draft document[7] for review by the CASAC at a public meeting held November 16, 1998. Based on our review of scientific information contained in the 2006 CD, we have concluded that $O_3$ health research needs and priorities have not changed substantially since the above document was written. Key uncertainties and research needs that continue to be high priority for future reviews of the health-based primary standards are identified below:

(1) An important aspect of risk characterization and decision making for air quality standard levels for the $O_3$ NAAQS is the characterization of the shape of exposure-response functions for $O_3$, including the identification of potential population threshold levels. Recent controlled human exposure studies conducted at levels below 0.08 ppm $O_3$ provide evidence that measurable lung function effects occur in some individuals for 6-8 hr exposures in the range of 0.08 to as low as 0.04 ppm. A major limitation of these data is that they were collected in one laboratory located in an area of the U.S. that typically experiences higher ambient air levels of $O_3$; therefore, prior attenuation of subject response may have been a factor in the responses observed. Considering the importance of estimating health risks in the range of 0.04 to 0.08 ppm $O_3$, additional research is needed to evaluate responses in healthy and asthmatic individuals in the range of 0.04 to 0.08 ppm for 6-8 hr exposures while engaged in moderate exertion.

[7] "Ozone Research Needs to Improve Health and Ecological Risk Assessment" (EPA, 1998)

(2) Similarly, for health endpoints reported in epidemiological studies such as hospital admissions, ED visits, and premature mortality, an important aspect of characterizing risk is the shape of concentration-response functions for $O_3$, including identification of potential population threshold levels. Most of the recent studies and analyses continue to show no evidence for a clear threshold in the relationships between $O_3$ levels and these health endpoints or have suggested that any such thresholds must be at very low levels approaching policy relevant background levels. Whether or not exposure errors, misclassification of exposure, or potential impacts of other copollutants may be obscuring potential population thresholds is still unknown.

(3) The extent to which the broad mix of photochemical oxidants and more generally other copollutants in the ambient air (e.g., PM, $NO_2$, $SO_2$, etc.) may play a role in modifying or contributing to the observed associations between ambient $O_3$ and various morbidity effects and mortality continues to be an important research question. Ozone has long been known as an indicator of health effects of the entire photochemical oxidant mix in the ambient air and has served as a surrogate for control purposes. A better understanding of sources of the broader pollutant mix, of human exposures, and of how other pollutants may modify or contribute to the health effects of $O_3$ in the ambient air, and vice versa, is needed to better inform future NAAQS reviews.

(4) As epidemiological research has become a more important factor in assessing the public health impacts of $O_3$, methodological issues in epidemiological studies have received greater visibility and scrutiny. Investigations of questions on the use of generalized additive models in time-series epidemiologic studies have raised model specification issues. There remains a need for further study on the selection of appropriate modeling strategies and appropriate methods to control for time-varying factors, such as temperature, and to better understand the role of copollutants in the ambient air.

(5) Limited controlled human exposure and epidemiology research has provided suggestive evidence of both direct and indirect effects of $O_3$ on the cardiovascular system, cardiovascular hospital admissions, and cardiovascular mortality. However, additional work will be needed to examine biologically plausible mechanisms of cardiovascular effects and to determine the extent to which $O_3$ is directly implicated or works together with other pollutants in causing adverse cardiovascular effects in sensitive individuals and in the general population.

(6) Most epidemiologic studies of short-term exposure effects have been time-series studies in large populations. Time-series studies remain subject to uncertainty due to use of ambient fixed-site data serving as a surrogate for ambient exposures, to the difficulty of determining the impact of any single pollutant among the mix of pollutants in the ambient air, to limitations in existing statistical models, or to a combination of all of these factors. Independent variables for air pollution have generally been measurements made at stationary outdoor monitors, but the accuracy with which these measurements actually reflect subjects' exposure is not yet fully understood. Also, additional research is needed to improve the characterization of the degree to which discrepancy between stationary monitor measurements and actual pollutant exposures introduces error into statistical estimates of pollutant effects in time-series studies.

(7) Improved understanding of human exposures to ambient $O_3$ and to related copollutants is an important research need. Population-based information on human exposure for healthy adults and children and susceptible or at-risk populations including asthmatics to ambient $O_3$ concentrations, including exposure information in various icroenvironments, is needed to better evaluate current and future $O_3$ exposure models. Such information is needed for sufficient periods to facilitate evaluation of exposure models throughout the $O_3$ season.

(8) Information is needed to improve inputs to current and future population-based $O_3$ exposure and health risk assessment models. Collection of time-activity data over longer time periods is needed to reduce uncertainty in the modeled exposure distributions that form an important part of the basis for decisions regarding air quality standard for $O_3$ and other air pollutants. Research addressing energy expenditure and associated breathing rates in various population groups, particularly health and asthmatic children, in various locations, across the spectrum of physical activity, including sleep to vigorous physical exertion is needed.

(9) An important consideration in the $O_3$ NAAQS review is the characterization of policy relevant background levels. There still remain significant uncertainties in the characterization of 8-hr daily maximum O3 background concentrations. Further research to improve the evaluation of the GEOS-CHEM model which has been used to characterize estimates of policy relevant background levels would help reduce uncertainties in estimating health risks relevant for standard setting (i.e., those risks

associated with exposure to O3 in excess of policy relevant background levels) and would aid in the development of associated control programs.

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# 7. POLICY-RELEVANT ASSESSMENT OF WELFARE EFFECTS EVIDENCE

## 7.1 INTRODUCTION

This chapter presents information critical to the review of the secondary NAAQS for $O_3$. Welfare effects addressed by a secondary NAAQS include, but are not limited to, effects on soils, water, crops, vegetation, man-made materials, animals, wildlife, weather, visibility and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and on personal comfort and well-being. Of these welfare effects categories, the effects of $O_3$ on vegetation, including agricultural crops, trees in managed and unmanaged forests, and herbaceous and woody species growing in natural settings are of most concern at concentrations typically occurring in the U.S. As stated in earlier reviews, "of the phytotoxic compounds commonly found in the ambient air, $O_3$ is the most prevalent, impairing crop production and injuring native vegetation and ecosystems more than any other air pollutant" (U.S. EPA, 1989, 1996b).

Ozone can also affect other ecosystem components such as soils, water, wildlife, and habitat, either directly, or indirectly, through its effects on vegetation. These individual ecosystem components are associated with one or more of six essential ecological attributes (EEAs) recently described in *A Framework for Assessing and Reporting on Ecological Condition: an SAB report* (Young and Sanzone, 2002) as part of a conceptual framework useful for assessing and reporting on ecological condition (see Figure 7-19 and discussion in section 7.7). This framework can be used to link $O_3$ effects at the species level to potential impacts at higher levels in the hierarchy (e.g., EEAs). Some of these species level impacts have direct, quantifiable economic value, while others are currently not quantifiable, but still have societal value. In the absence of sufficient research to allow quantification of $O_3$ impacts at the ecosystem level, including impacts on ecosystem goods and services, only a qualitative discussion is included. However, the staff infers, based on the linkages described in the SAB framework, that increasing protection for vegetation from $O_3$ related effects would also improve the protection afforded to ecosystems and their related public welfare categories.

Other $O_3$ related welfare effects categories include damage to certain manmade materials (e.g., elastomers, textile fibers, dyes, paints, and pigments) and climate interactions. The amount of damage to actual in-use materials and the economic consequences of that damage are poorly characterized, however, and the scientific literature contains very little new information to adequately quantify estimates of materials damage from photochemical oxidants (EPA, 1996a, b,

2006). Therefore, staff judges that there is insufficient information in the materials damage literature to inform secondary standard setting and so it will not be discussed further. Interested readers are referred to Chapter 11 in the CD (EPA, 2006). In contrast, the welfare impact of $O_3$ on local, regional and global climates has received more attention in recent years. Ozone enhances the heat capacity of the atmosphere. The overall body of scientific evidence suggests that high concentrations of $O_3$ on a regional scale could have a discernable influence on climate, leading to surface temperature and hydrological cycle changes. However, the CD states that confirming this effect will require further advances in monitoring and improvement in chemical transport and regional-scale modeling. Thus, staff concludes that insufficient information is available at this time to quantitatively inform the secondary NAAQS process with regard to this aspect of the $O_3$-climate interaction and will not address it further. Another aspect, e.g., potential modification of plant response to $O_3$ under conditions of changing climate, will be included in the discussion of factors that can modify the predicted vegetation responses (See Section 7.4.2).

To summarize, this chapter includes an integrated discussion of the key policy relevant science regarding $O_3$-related effects on vegetation (sections 7.2 through 7.4) and ecosystems (section 7.7), as described in the previous CD (EPA, 1996a ) and reiterated in the current CD (EPA, 2006). The remaining sections (7.5 and 7.6) of this chapter are focused on a discussion of the analyses that have been conducted in support of this current NAAQS review that update and expand upon the exposure, risk and benefits assessments conducted in the last review (EPA, 1996b). These updated assessments incorporate newer data, models, and approaches, and take into account alternative $O_3$ air quality scenarios under consideration. The environmental assessment technical support document, *Technical Report on Ozone Exposure, Risk, and Impacts Assessments for Vegetation* (Abt, 2006) (hereafter cited as "draft Environmental Assessment TSD") presents a detailed description of the exposure, risk and impacts analysis methodology. Results from these assessments, along with key uncertainties and limitations, are also described in sections 7.5 and 7.6. This information forms the basis for a discussion in Chapter 8 of preliminary conclusions and a range of options identified for the Administrator to consider with respect to the secondary $O_3$ NAAQS.

## 7.2 MECHANISMS GOVERNING PLANT RESPONSE TO OZONE

The interpretation of predictions of risk associated with vegetation response at ambient $O_3$ exposure levels can be informed by scientific understanding regarding $O_3$ impacts at the genetic, physiological, and mechanistic levels. In most cases, the mechanisms of response are similar regardless of the degree of sensitivity of the species. The information assessed in the 1996 CD (EPA 1996a) regarding the fundamental hypotheses concerning $O_3$-induced changes in

physiology continues to be valid. However, during the last decade, our understanding of the cellular processes within plants has been further clarified and enhanced. Therefore, this section reviews the key scientific conclusions identified in 1996 $O_3$ CD (EPA, 1996a), and incorporates new information from the current CD (EPA, 2006). This section describes: (1) $O_3$ uptake, (2) cellular to systemic $O_3$ response, (3) plant compensation and defense mechanisms, (4) $O_3$– induced changes to plant metabolism, and (5) plant response to chronic exposures.

### 7.2.1 Ozone Uptake: Canopy, Plant and Leaf

To cause injury, $O_3$ must first enter the plant through the stomata of the leaves. Leaves exist in a three dimensional environment called the plant canopy, where each leaf has a unique orientation and receives a different exposure to ambient air, microclimatological conditions, and sunlight. In addition, a plant may be located within a stand of other plants which further modifies ambient air exchange with individual leaves. Not all $O_3$ entering a plant canopy is absorbed into the leaves, but may be adsorbed to other surfaces e.g., leaf cuticles, stems, and soil (termed non-stomatal deposition) or scavenged by reactions with intra-canopy biogenic VOCs and naturally occurring NOx emissions from soils. Because $O_3$ does not penetrate the leaf's cuticle, it must reach the stomatal openings in the leaf for absorption to occur. The movement of $O_3$ and other gases such as $CO_2$ into and out of leaves is controlled primarily through the stomata. The aperture of the stomata are controlled by guard cells, which respond to a variety of internal species-specific factors as well as external site specific environmental factors such as light, humidity, $CO_2$ concentration, soil fertility and water status, and in some cases the presence of other air pollutants, including $O_3$ (See Section 7.4.2). These modifying factors produce stomatal conductance that vary across the diurnal cycle, days and seasons. Once $O_3$ is inside the leaf, a phytotoxic effect will only occur if sufficient amounts of $O_3$ reach sensitive cellular sites that are subject to the various physiological and biochemical controls within the leaf cells (see the discussion in section 7.2.3 below – Compensation and Detoxification).

A measure of $O_3$ flux is attractive because it incorporates both relevant environmental factors and physiological processes, and is considered the measure that most closely links exposure to plant response. Unfortunately, measurement of flux is very complex, making it difficult to extrapolate uptake from an individual leaf to that of a whole plant or canopy. Since the last review, interest has been increasing, particularly in Europe, in using mathematically tractable flux models for $O_3$ assessments at the regional and national scale (Emberson et al., 2000a, b). Though significant new research has been done with respect to flux model development, it has still not advanced to a point of being generally applicable across a range of

species and environments at a national scale. These topics are discussed in more detail in Appendix A of this document and in the 2006 CD (EPA, 2006).

### 7.2.2 Cellular to Systemic Response

Once $O_3$ diffuses into the leaf air spaces it can react with varied biochemical compounds that are exposed to the air (path 1) or is solubilized into the water lining the cell wall of the air spaces (path 2). Having entered the aqueous phase, it can be rapidly altered to form oxidative products that can diffuse more readily into and through the cell and react with many biochemicals. The initial sites of membrane reactions seem to involve transport properties and, possibly, the external signal transducer molecules (EPA, 2006). The alteration in plasma membrane function is clearly an early step in a series of $O_3$ -induced events that lead to leaf injury.

Under certain circumstances, $O_3$ reacts with organic molecules to generate peroxides, including hydrogen peroxide ($H_2O_2$). The role of hydrogen peroxide as a signaling molecule in plants is now better understood. The primary set of metabolic reactions that $O_3$ triggers clearly includes those typical of "wounding" responses generated by cutting of the leaf or by pathogen/insect attack. One aspect of this total response is the production of $O_2$ and $H_2O_2$ by the cell (Lamb and Dixon, 1997). The presence of higher-than-normal levels of $H_2O_2$ within the apoplastic space is a potential trigger for the normal, well-studied pathogen defense pathway.

Ethylene is another compound produced when plants are subjected to biotic or abiotic stressors. Increased ethylene production by plants exposed to $O_3$ stress was identified as a consistent marker for $O_3$ exposure decades ago (Tingey et al., 1976). These studies suggested that increased production of stress- ethylene correlated well with the degree of foliar injury that developed within hours or days after $O_3$ exposure. Thus, one could postulate that $O_3$ generates a wounding response with a production of ethylene, which would, in turn, generate a change in stomatal conductance and photosynthesis.

### 7.2.3 Compensation and Detoxification

Ozone injury will not occur if (1) the rate and amount of $O_3$ uptake is small enough for the plant to detoxify or metabolize $O_3$ or its metabolites or (2) the plant is able to repair or compensate for the $O_3$ impacts (Tingey and Taylor, 1982; EPA, 1996a). Leaves may physically exclude $O_3$ from sensitive tissues. A few studies have documented a direct stomatal closure or restriction in response to the presence of $O_3$ ranging from within minutes to hours or days of exposure (Moldau et al., 1990; Dann and Pell, 1989; Weber et al., 1993). However, exclusion of $O_3$ also restricts the uptake of $CO_2$, thus limiting photosynthesis and growth.

Additionally, plants can also effectively protect tissue against damage by dissipating excess oxidizing power using antioxidants. Since 1996, the role of detoxification in providing a level of resistance to $O_3$ has been further investigated. A number of antioxidants, including ascorbate, glutathione peroxidase, and sulfuroxide dimutase which are highly reactive, can detoxify the chemicals generated by $O_3$. The pattern of changes in these antioxidant proteins varies greatly among different species and conditions. Most recent reports indicate that ascorbate within the cell wall provides the first significant opportunity for detoxification to occur. The balance between the total $O_3$ flux and the detoxification process has been defined as the "effective flux" (Dämmgen et al., 1993; Grünhage and Haenel, 1997; Musselman and Massman, 1999).

In spite of the new research, however, it is still not clear as to what extent detoxification protects against $O_3$ injury. Specifically, data are needed especially on the potential rates of antioxidant production and on the subcellular location of the antioxidants. Potential rates of antioxidant production are needed to assess whether they are sufficient to detoxify the $O_3$ as it enters the cell. The subcellular location(s) is needed to assess whether the antioxidants are in cell wall or plasmalemma locations that permit contact with the $O_3$ before it has a chance to damage subcellular systems. In addition, generation of these antioxidants in response to $O_3$-induced stress potentially diverts resources away from other sinks and expends energy. Thus, scientific understanding of the detoxification mechanisms is not yet complete and requires further investigation (EPA, 2006).

Once $O_3$ injury has occurred in leaf tissue, some plants are able to repair or compensate for the impacts (Tingey and Taylor, 1982). In general, plants have a variety of compensatory mechanisms for low levels of stress including reallocation of resources, changes in root/shoot ratio, production of new tissue, and/or biochemical shifts, such as increased photosynthetic capacity in new foliage and changes in respiration rates, indicating possible repair or replacement of damaged membranes or enzymes. Since these mechanisms are genetically determined, not all plants have the same complement or degree of tolerance, nor are all stages of a plant's development equally sensitive to $O_3$. It is not yet known to what degree or how the use of plant resources for repair processes affects the overall carbohydrate budget or subsequent plant response to $O_3$ or other stresses (EPA, 1996a, EPA, 2006).

### 7.2.4 Changes to Plant Metabolism

Ozone inhibits photosynthesis, the process by which plants produce energy rich compounds (e.g., carbohydrates) in the leaves. This impairment can result from direct impact to chloroplast function and/or $O_3$-induced stomatal closure resulting in reduced uptake of $CO_2$. A large body of literature published since 1996 has further elucidated the mechanism of effect of

$O_3$ within the chloroplast. Pell et al. (1997) showed that $O_3$ exposure results in a loss of Rubisco, the central carboxylating enzyme that plays an important role in the production of carbohydrates. Due to its central importance, any decrease in Rubisco may have severe consequences for the plant's productivity. Several studies have found that $O_3$ had a greater effect as leaves aged, with greatest impact of $O_3$ on the oldest leaves (Fiscus et al., 1997; Reid and Fiscus, 1998; Noormets et al., 2001; Morgan et al., 2004). The loss of Rubisco and its messenger RNA as a function of increasing $O_3$ exposure is also linked to an early senescence or a speeding up of normal development leading to senescence. If total plant photosynthesis is sufficiently reduced, the plant will respond by reallocating the remaining carbohydrate at the level of the whole organism (see section 7.3 below) (EPA, 1996a, 2006).

### 7.2.5 Plant Response to Chronic/Long-term Exposures

Many changes that occur with $O_3$ exposure can be observed within hours, or perhaps days, of the exposure, including those connected with wounding and elicitor-induced changes in gene expression. Other effects due to $O_3$, however, take longer to occur and tend to become most obvious under long periods of low-$O_3$ concentrations. These have been linked to senescence or some other physiological response very closely linked to senescence. The understanding of how $O_3$ affects long-term growth and resistance to other biotic and abiotic insults in long-lived trees is unclear. Often, the conditions to which a tree is subjected to in one year will affect or "carry over" the response of that tree into the next year (EPA, 2006). In other words, a condition in an earlier year sets the stage for a reaction in the next year; thereby giving a "cause-effect" scenario (EPA 2006). In perennial plant species, growth affected by a reduction in carbohydrate storage may result in the limitation of growth the following year (Andersen et al., 1997). Carry-over effects have been documented in the growth of tree seedlings (Hogsett et al., 1989; Sasek et al., 1991; Temple et al., 1993; EPA, 1996a) and in roots (Andersen et al., 1991; EPA, 1996a). Accumulation of carry-over effects over time will affect survival and reproduction. Understanding of how $O_3$ interacts with the plant at a cellular level has dramatically improved in recent years. However, additional work remains to more fully elucidate the translation of those cellular mechanisms into altered cell metabolism, whole plant productivity, and other physiological effects.

## 7.3 NATURE OF EFFECTS ON VEGETATION

Science published since the conclusion of the 1996 review continues to support and strengthen key conclusions regarding $O_3$ effects on vegetation and ecosystems found in the previous CD (EPA 1996a) and reiterated in the current CD (EPA, 2006). For additional detail the reader is referred to Chapter 9 and AX9 in the current CD (EPA, 2006)

### 7.3.1 Vegetation Effects Endpoints

Ozone injury at the cellular level, when it has accumulated sufficiently, will be propagated to the level of the whole leaf or plant. These larger scale effects can include: visible foliar injury and premature senescence; reduced carbohydrate production and reallocation; reduced growth or reproduction; and reduced plant vigor. Much of what is now known about $O_3$ exposure-plant response relationships, as summarized below, is based on research that was available in the last review. Thus, the present discussion is largely based on the conclusions of the 1978, 1986, and 1996 CDs (EPA, 1978; 1986; 1996a). Further, research results published since 1996 have not invalidated the earlier EPA conclusions (EPA, 1978, 1986, 1996a) and in some cases have expanded and strengthened those conclusions. The paragraphs below describe our current understanding of the physiological effects of $O_3$ on vegetation

**Visible Foliar Injury and Premature Senescence.** Cellular injury can and often does become visible. Acute injury usually appears within 24 hours after exposure to $O_3$ and, depending on species, can occur under a range of exposures and durations from 0.04 ppm for a period of 4 hours to 0.41 ppm for 0.5 hours for crops, and 0.06 ppm for 4 hours to 0.51 ppm for 1 hour for trees and shrubs (Jacobson, 1977). Chronic injury may be mild to severe. In some cases, cell death or premature leaf senescence may occur. The significance of $O_3$ injury at the leaf level depends on how much of the total leaf area of the plant has been affected, as well as the plant's age, size, developmental stage, and degree of functional redundancy among the existing leaf area. As a result, it is not presently possible to determine with consistency across species and environments what degree of injury at the leaf level has significance to the vigor of the whole plant. However, even the presence of visible symptoms due to $O_3$ exposures can reduce the market value of certain crops and ornamentals where leaves are the product (such as spinach, lettuce, petunia, geranium, and poinsettia) and affect the aesthetics of scenic vistas in protected natural areas such as national parks and wilderness areas.

Foliar injury symptoms on mature trees have also been documented and studied. In recent years, field surveys have become more common, with greater attention to the standardization of methods and the use of reliable indicator species (Campbell et al., 2000; Smith et al., 2003). Specifically, the Unites States Forest Service (USFS) through the Forest Health Monitoring Program (FHM) (1990 - 2001) and currently the Forest Inventory and Analysis (FIA) Program collects data regarding the incidence and severity of visible foliar injury on a variety of $O_3$ sensitive plant species throughout the U.S. (Coulston et al. 2003, 2004; Smith et al. 2003). Section 7.6.3.2 contains additional information on the use of foliar injury incidence on bioindicator species as a measure of the occurrence of phytotoxic levels of $O_3$ in the ambient air. Previous CDs have noted the difficulty in relating foliar injury symptoms to other vegetation

effects such as individual tree growth, stand growth, or ecosystem characteristics (EPA, 1996a). This difficulty remains to the present day**.**

**Carbohydrate Production and Allocation** When total plant photosynthesis is sufficiently reduced, the plant will respond by reallocating the remaining carbohydrate at the level of the whole organism. Many studies have demonstrated that root growth is more sensitive to $O_3$ exposure than is stem or leaf growth (EPA, 2006). When less carbohydrate is present in the roots, less energy will be available for root-related functions such as acquisition of water and nutrients. Mycorrhizal fungi in the soil form a symbiotic relationship with many terrestrial plants. For host plants, these fungi improve the uptake of nutrients, protect the roots against pathogens, produce plant growth hormones, and may transport carbohydrates from one plant to another (CD, 1996a). Ozone can disrupt the association between mycorrhizal fungi and host plants by inhibiting photosynthesis and the amount of carbohydrates available for transfer to the roots. This effect has recently been documented in the field. Data from a long-studied pollution gradient in the San Bernardino Mountains of southern California suggest that $O_3$ substantially reduces root growth in natural stands of ponderosa pine. Root growth in mature trees was decreased at least 87% in a high-pollution site as compared to a low-pollution site (Grulke et al., 1998), and a similar pattern was found in a separate study with whole-tree harvest along this gradient (Grulke and Balduman, 1999). Though effects on other ecosystem components were not examined, a reduction of root growth of this magnitude could have significant implications for the below ground communities at those sites. In contrast, a study in Great Smoky Mountains National Park in Tennessee (Neufeld et al., 2000) found no statistically significant effects of $O_3$ exposure on stem or root biomass for several tree species. The difference in the results from these two studies may reflect the species specific nature of the symbiont-host relationship.

Unlike root systems, effects on leaf and needle carbohydrate content under $O_3$ stress range from a reduction (Barnes et al., 1990; Miller et al., 1989), to no effect (Alscher et al., 1989), to an increase (Luethy-Krause and Landolt, 1990). Therefore, studies that only examine above-ground vegetative components may miss important $O_3$-induced changes below ground. These below-ground changes could signal a shift in nutrient cycling with significance at the ecosystem level (Young and Sanzone, 2002).

**Growth and Reproduction.**

Studies of the growth response of trees to $O_3$ have established that, individual deciduous trees are generally less sensitive to $O_3$ than are most annual plants, with the exception of a few genera such as *Populus*, which are highly sensitive and in some cases (for instance, poplars and black cherry), are as sensitive to $O_3$ as annual plants. The $O_3$ sensitivity of seedlings and mature

trees within species and between species varies widely. In general, mature deciduous trees are likely to be more sensitive to $O_3$ compared to seedlings, while mature evergreen trees are likely to be less sensitive than seedlings. Based on these results, stomatal conductance, $O_3$ uptake, and $O_3$ effects cannot be assumed to be equivalent in seedlings and mature trees.

Depending on exposure duration, concentrations of $O_3$ currently in the United States are sufficient to affect the growth of a number of tree species during the annual growing season. However, these conclusions do not take into account the possibility of "carry over" effects on growth in subsequent years, an important consideration in the case of long-lived species. Given that multiple-year exposures may cause a cumulative effect on the growth of some trees (Hogsett et al. 1989; Simini et al., 1992; Temple et al., 1993), it is likely that a number of species currently are being impacted.

Other research in the U.S. in the last 10 years has focused on perennial forage crops (EPA, 2006). Recent results confirm that yields and quality of multiple-year forage crops are reduced at sufficient magnitude to have nutritional and possibly economic implications to their use as ruminant animal feed at $O_3$ exposures that occur in some years over large areas of the U.S... Ozone may also reduce the quality or nutritive value of annual species.

Recent studies have also further demonstrated $O_3$ effects on different stages of reproduction. Effects of $O_3$ have been observed on pollen germination, pollen tube growth, fertilization, and abortion of reproductive structures, as reviewed by Black et al. (2000). For seed-bearing plants, reproductive effects will culminate in seed production. The recent scientific literature supports the conclusions of the 1996 CD that ambient $O_3$ concentrations are reducing the yield of major crops in the U.S. For example, the yield reductions for soybean are generally similar to those reported previously (EPA, 2006).

**Reduced Plant Vigor**. Though $O_3$ levels over most of the U.S. are not high enough to kill vegetation directly, current levels have been shown to reduce the ability of many sensitive species and genotypes within species to adapt to or withstand other environmental stresses. These may include increased susceptibility to freezing temperatures, pest infestations and/or root disease, compromised ability to compete for available resources. For example, when species are grown in mixtures, $O_3$ exposure can increase the growth of $O_3$ -tolerant species while exacerbating the growth decrease of $O_3$ -sensitive species. In the long run, the result of this loss in vigor may be plant death.

## 7.4 IMPACTS ON PUBLIC WELFARE

### 7.4.1 What Constitutes an Adverse Vegetation Impact from Ozone Exposure?

Ozone can cause a variety of effects, beginning at the level of the individual cell and accumulating up to the level of whole leaves, plants, plant populations, communities and whole ecosystems. Not all $O_3$-related effects, however, have been classified as "adverse" to public welfare. Previous reviews have classified $O_3$ vegetation effects as either "injury" or "damage" to help in determining adversity. Specifically, injury is defined as encompassing all plant reactions, such as reversible changes in plant metabolism (e.g., altered photosynthetic rate), altered plant quality, or reduced growth, that does not impair the intended use or value of the plant (Guderian, 1977). In contrast, damage includes those injury effects that also reduce or impair the intended use or value of the plant. Damage includes reductions in aesthetic values (e.g., foliar injury in ornamental species) as well as losses in terms of weight, number, or size of the plant part that is harvested (yield loss). Yield loss also may include changes in crop quality, i.e., physical appearance, chemical composition, or the ability to withstand storage. While this construct has proved useful in the past, it appears most useful in the context of evaluating effects on single plants or species grown in monocultures such as agricultural crops or managed forests. It is less clear how it might apply to potential effects on natural forests or entire ecosystems such as shifts in species composition or nutrient cycling where the intended use or value of the system is not specifically quantified.

A more recent construct for assessing risks to forests described in Hogsett et al. (1997) suggests that "adverse effects could be classified into one or more of the following categories: (1) economic production, (2) ecological structure, (3) genetic resources, and (4) cultural values." This expands the context for evaluating the adversity of $O_3$ related effects beyond the species level. In another recent publication, *A Framework for Assessing and Reporting on Ecological Condition: an SAB report* (Young and Sanzone, 2002), additional support is provided for expanding the consideration of adversity by making explicit the linkages between stress (e.g. $O_3$) related effects at the species level and higher levels within an ecosystem hierarchy. Staff suggests that consideration of adverse effects undertaken within the context of such a broader paradigm would be appropriate in the context of this secondary NAAQS review.

### 7.4.2 Factors That Modify Functional and Growth Response

The caveat that must be placed on results from any experimental study on the response of living organisms to a stressor in a specific setting is that uncertainty is introduced when attempting to extrapolate or apply those results outside that specific setting (e.g., to a different set of organisms, scales, or exposure/growing conditions). The description of plant response to $O_3$ is no different. Because staff must necessarily rely on experimental data produced under very

specific sets of conditions in conducting this assessment, it is important to understand the range of factors that can influence plant response to $O_3$ and the magnitude and direction of that response, in order to better assess the likelihood of observing the experimentally predicted response in the ambient environment.

Plant response to $O_3$ exposure is a function of the plant's ongoing integration of genetic, biological, physical and chemical factors both within and external to the plant. The corollary is also true that $O_3$ exposure can modify the plant's subsequent integrated response to other environmental factors, both by influencing the plant response directly, and by contributing to altered climatic factors that influence plant response through its greenhouse gas forcing properties.

The 1996 $O_3$ CD (EPA, 1996a) concluded with a statement that our understanding regarding modifying factors was too fragmented to permit drawing many general conclusions. Unfortunately, in the interval since the 1996 criteria document little additional information has become available and this earlier conclusion remains unchanged. Therefore, only a brief overview of the current understanding from this research is provided. The reader is referred to the 1996 CD (EPA 1996a) and the current 2006 CD (EPA 2006) for further information.

#### 7.4.2.1 Genetics

Plant response to $O_3$ is determined by genes that are directly related to oxidant stress and to an unknown number of genes that are not specifically related to oxidants but instead that control leaf and cell wall thickness, stomatal conductance, and the internal architecture of the air spaces. It is unlikely that single genes are responsible for $O_3$ tolerance, except in rare cases (Engle and Gabelman, 1966). Recent studies using molecular biological tools and with transgenic plants have begun to positively verify the role of various genes and gene products in $O_3$ tolerance and are beginning to increase the understanding of $O_3$ toxicity and differences in $O_3$ sensitivity. Specifically, $O_3$ has been shown to trigger the production of a number of compounds (e.g. ethylene) and the signaling of these molecules determines in some cases the $O_3$ susceptibility of plants (EPA, 2006). Because the genetic code is species specific, species vary greatly in their responsiveness to $O_3$. Even within a given species, individual genotypes or populations can also vary significantly with respect to $O_3$ sensitivity. Thus, caution should be taken when ranking species categorically as having an absolute degree of sensitivity to $O_3$.

#### 7.4.2.2 Biological Factors

The biological factors within the plant's environment that may directly or indirectly influence its response to $O_3$ in a positive or negative manner encompass insects, other animal

pests, diseases, weeds, and other competing plant species. Ozone and other photochemical oxidants may influence the severity of a disease or infestation by either direct effects on the causal species, or indirectly by affecting the host, or both. Likewise, mutually beneficial relationships or symbioses involving higher plants and bacteria or fungi may also be affected by $O_3$. Ozone can also have indirect effects on herbivorous animals due to $O_3$-induced changes in feed quality.

New evidence with regard to insect pests and diseases has done little to remove the uncertainties noted in the 1996 CD (EPA 1996a). Most of the large numbers of such interactions that may affect crops, forest trees, and other natural vegetation have yet to be studied. With respect to any particular $O_3$-plant-insect interaction, we are still far from being able to predict its likelihood, or its severity. The situation is only a little clearer with respect to interactions involving facultative necrotrophic plant pathogens, with $O_3$ generally leading to increased disease. In contrast, with obligate biotrophic fungal, bacterial, and nematode diseases there are twice as many reports indicating $O_3$-induced inhibitions than enhancements. At this time, therefore, although some diseases may become more widespread or severe as a result of exposure to $O_3$, it is still not possible to predict which diseases are likely to present the greatest risks to crops and forests.

The latest studies on $O_3$ interactions with root symbionts present a more complex picture than was described in the last review. In addition to adverse effects of $O_3$ on the functioning of tree root symbioses with mycorrhizae (discussed in section 7.3.1), there is also evidence that the presence of mycorrhizae may help plants overcome root diseases stimulated by $O_3$ and/or encourage the spread of mycorrhizae to the roots of uninfected trees.

The few recent studies of the impact of $O_3$ on intraspecific plant competition have again confirmed that grasses frequently show greater resilience than other types of plants. In grass-legume pastures, the leguminous species suffer greater growth inhibition. Separately, the suppression of ponderosa pine (*Pinus ponderosa*) seedling growth by blue wild-rye grass was markedly increased by $O_3$ (Andersen et al. 2001). Due to the limited number of species studied under competitive situations to date, however, we are far from being able to predict the outcome of $O_3$ exposure on other specific competitive situations, such as successional plant communities or crop-weed interactions. Clearly, however, $O_3$ stress creates a selective pressure in some vegetative communities that can lead to a shift in community composition. This community change may be undesirable in some settings.

#### 7.4.2.3 Physical Factors

A plant's interaction with its physical environment (e.g., light, temperature, relative humidity, soil moisture and wind speed/turbulence) influences the degree and or nature of the plant response to $O_3$ exposure. Light is an essential "resource" whose energy content drives photosynthesis and $CO_2$ assimilation. It has been suggested that increased light intensity may increase the sensitivity of light-tolerant species to $O_3$ while decreasing the $O_3$ sensitivity of shade-tolerant species, but this appears to be an oversimplification with many exceptions.

Temperature affects the rates of all physiological processes based on enzyme-catalysis and diffusion, and each process and overall growth (the integral of all processes) has a distinct optimal temperature range. Although some recent field studies have indicated that $O_3$ impact significantly increases with increased ambient temperature, other studies have revealed little effect of temperature. But temperature is unquestionably an important variable affecting plant response to $O_3$ in the presence of the elevated $CO_2$ levels contributing to global climate change (see below). In contrast, evidence continues to accumulate to indicate that exposure to $O_3$ sensitizes plants to low temperature stress by reducing below-ground carbohydrate reserves, possibly leading to responses in perennial species ranging from rapid demise to impaired growth in subsequent seasons.

High relative humidity of the ambient air has generally been found to increase the adverse effects of $O_3$ by increasing stomatal conductance and thereby increasing $O_3$ flux. Similarly, abundant evidence indicates that the ready availability of soil moisture results in greater sensitivity to $O_3$. The opposite condition, drought, has been observed in field experiments and modeled in computer simulations to provide partial "protection" against the adverse effects of $O_3$ as would be expected. However, there is also compelling evidence that $O_3$ can predispose plants to drought stress. Hence, the response will depend to some extent upon the sequence in which the stresses occur, and the species-specific nature of the response. Regardless of the interaction, however, the net result of drought on growth in the short-term is negative, although in the case of tree species, other responses such as increased water use efficiency could be a benefit to long-term survival.

Wind speed and air turbulence affect the thickness of the boundary layers over leaves and canopies and, hence, affects gas exchange rates. These factors can have a significant impact on the relationship between ambient air exposures and actual exposure concentrations at the leaf or canopy surface.

#### 7.4.2.4 Chemical Factors

Mineral nutrients in the soil, other gaseous air pollutants, and agricultural chemicals constitute chemical factors in the environment. The evidence regarding interactions with

specific nutrients is still too contradictory to permit any sweeping conclusions. Somewhat analogously with temperature, it appears that any shift away from the nutritional optimum may lead to greater sensitivity, but the shift would have to be substantial before a significant effect on response to $O_3$ was observed.

Interactions of $O_3$ with other air pollutants have received relatively little recent attention. The situation with $SO_2$ remains inconsistent, but seems unlikely to pose any additional risk to those related to the individual pollutants. With NO and $NO_2$, the situation is complicated by their nutritional value as N sources. In leguminous species, it appears that $NO_2$ may reduce the impact of $O_3$ on growth, with the reverse in other species, but the nature of the exposure pattern, i.e., sequential or concurrent, also determines the outcome. Much more investigation is needed before we will be able to predict the outcomes of different $O_3$-NO-$NO_2$ scenarios. The latest research into $O_3$ × acid rain interactions has confirmed that, at realistic acidities, significant interactions are unlikely. A continuing lack of information precludes offering any generalizations about interactive effects of $O_3$ with $NH_3$, HF, or heavy metals. More evidence has been reported that the application of fungicides affords some protective effects against $O_3$.

Over the last decade, considerable emphasis has been placed on research into $O_3$ interactions with two components of global climate change: increased atmospheric $CO_2$ and increased mean global temperature. Most of these studies, however, have tended to regard increased $CO_2$ levels and increased mean temperatures as unrelated phenomena, in spite of the crucial role of temperature as a climatic determinant (Monteith and Elston, 1993). Thus, experiments that examine the effects of doubled $CO_2$ levels at today's mean ambient temperatures are not particularly helpful in trying to assess the impact of climate change on responses to $O_3$, since most of the biotic and chemical interactions with oxidants may be modified by these climatic changes. Though it is now known from limited experimental evidence and evidence obtained by computer simulation that an atmosphere sufficiently enriched with $CO_2$ (e.g., 600 + ppm) would more than offset the impact of $O_3$ on responses as varied as wheat yield or the growth of young Ponderosa pine trees, the concurrent increase in temperature would reduce, but probably not eliminate, the net gain.

Little if any experimental evidence exists related to three-way interactions, such as $O_3$ × $CO_2$ × disease or $O_3$ × $CO_2$ × nutrient availability. Increased use of computer simulations may be important in suggesting outcomes of the many complex interactions of $O_3$ and various combinations of environmental factors. However, the results obtained will only be as reliable as the input data used for their parameterization. Thus, additional data from organized, systematic study is needed.

It is important to recognize that wide variations in net impacts of climate change in different geographic areas are expected. Many regions are predicted to experience severe,

possibly irreversible, adverse effects due to climate change. The EPA is currently leading a research effort that uses regional-scale climate models with the goal of identifying changes to $O_3$ and PM concentrations that may occur in a warming climate. An assessment of the results of this effort is expected to be available for consideration in the next review of the $O_3$ NAAQS.

## 7.5 CHARACTERIZATION OF VEGETATION EXPOSURES TO OZONE

### 7.5.1 Key Considerations in Vegetation Exposure Characterization

In the last review, the Administrator chose to make the secondary NAAQS equal to the primary standard set as the 4$^{th}$ highest daily maximum 8-hr average at the level of 0.08 ppm. While recognizing this as a reasonable policy choice, she also recognized that "a SUM06 seasonal standard is more biologically relevant and, therefore, … also appropriate to consider." (62 FR 38877). This conclusion by the Administrator in 1997 is again supported by the recent body of science reviewed in the 2006 $O_3$ CD (EPA, 2006). Staff, therefore, continue to express hourly $O_3$ monitoring data in terms of both average and seasonal cumulative index forms for comparison. Staff considers the cumulative, concentration weighted SUM06 and W126 index forms discussed in the 1996 Staff Paper (EPA, 1996b). The rationale for including the W126 will emerge from the discussions of current patterns of air quality and of policy-relevant background (PRB) in the remainder of this section. Below are the definitions of the three index forms considered in this review and how they will be referred to in the rest of this document:

Current 8-hr form: 4$^{th}$ highest daily maximum 8-hr average over the $O_3$ season.

12-hr SUM06: 3-month sum of all 1-hr average $O_3$ concentrations greater than or equal to 0.06 ppm observed during the daily 12-hr period between 8 am and 8 pm.

12-hr W126: Sigmoidally weighted 3-month sum of all 1-hr average $O_3$ concentrations observed from 8 am to 8 pm.

More specifically, W126 is defined in Lefohn et al., 1988 as:

$$W126 = \sum_{i=8AM}^{i<8PM} w_{C_i} C_i, where\ C_i = hourly\ O3\ at\ hour\ i, and\ w_{C_i} = \frac{1}{1 + 4403e^{-0.126C_t}}$$

Staff selected two levels of air quality to evaluate for each of these alternative standard forms. Specifically, we looked at the 0.084 and 0.070 ppm, the 25 and 15 ppm-hr, and the 21 and 13 ppm-hr levels for the 8-hr average, the SUM06 and the W126 forms, respectively.

Since the conclusion of the last review, significant improvements in monitored $O_3$ air quality have occurred in some areas of the U.S.. In the eastern U.S., these improvements may be attributable in part to the reductions in NOx emissions resulting from the initiation of Phase II of Title IV in 1997 (The Ozone Report: Measuring Progress through 2003, EPA, 2004) and the NOx SIP call in 2002 (Chapter 2 of this SP). In addition, efforts to attain the current NAAQS have no doubt contributed to some air quality improvements, including lower hourly maximum values and fewer occurrences of those maximum values at some sites. One example of this is at the Crestline site in California, where the number of days with concentrations $\geq$ 95 ppb have been declining steadily over the last decade, matched by a decline in peak 1-hr concentrations and 12-hr SUM06 values. These declines match a similar trend in NOx and reactive organic gases (2006 CD section AX9-207, Figure AX9-17) (EPA 2006; Lee et al 2003). However, not all areas in the U.S. show this trend. Staff urge that caution be used, however, in making assumptions about trends in future years (see discussion of national parks below), as 2005 air quality does not always appear to follow this trend.

The 1997 final rule recognized that "it remained uncertain as to the extent to which air quality improvements designed to reduce 8-hr $O_3$ concentrations would reduce $O_3$ exposures measured by a seasonal SUM06 index" (62 FR 38876). At that time, staff undertook an analysis to explore that question. Results of that analysis suggested that improvements in national air quality from attaining an 8-hr average standard within the recommended range of levels would also reduce levels below those of concern for vegetation in those same areas. However, considerable uncertainty remained as to the exact strength of the relationship, especially between urban $O_3$ air quality and distributions that occur in non-monitored rural or remote areas. Using recent (2001-2004) county-level air quality data, staff has performed a similar analysis to compare the degree to which the 8-hr form appears to control air quality of concern for vegetation expressed in terms of the SUM06. Figures 7-1 and 7-2 depict plots county air quality in terms of both the current secondary standard 8-hr average form (Y axis) and the 1996 proposed SUM06 form (X axis) for the years 2002 (a relatively high $O_3$ year) and 2004 (a relatively low $O_3$ year). Both the 25 and 15 ppm-hr cutpoints for SUM06 were considered. For 2002, only a few (5) counties would have both a SUM06 higher than the 1996 proposed standard level of 25 ppm-hrs while meeting the 0.08 level of the current 8-hr form. When a lower SUM06 cutpoint of 15 ppm-hr is used, an additional 35 counties would fit that category. By contrast, the relatively low year (2004) shows that 16 counties were above the SUM06 of 25 ppm-hr while meeting the 8-hr standard level. When the lower SUM06 level of 15 ppm-hr is compared, a much larger number of counties (128) fall in that category. Based on this comparison, air quality levels associated with adverse vegetation response can be occurring in many areas that meet the current 8-hr secondary NAAQS.

Thus, staff suggests caution should be used in evaluating the likely vegetation impacts associated with a given level of air quality expressed in terms of the 8-hr form in the absence of parallel SUM06 or W126 information. Unfortunately, much of the data published both in this review and in other Agency reports only depicts trend information in terms of the 8 hr average index Additionally, staff plans to further assess the strength of the relationship between the 8-hr average and cumulative forms at a subset of more rural and remote sites, including high elevation national parks, prior to finalizing this draft Staff Paper.

National Parks represent nationally recognized areas of ecological significance afforded a higher level of protection. Therefore, staff has also focused on air quality in the subset of National Park sites and important natural areas. Two recent reports present some discussion of $O_3$ trends in a subset of National Parks (See discussion in The Ozone Report: Measuring Progress through 2003 (EPA, 2004) and 2005 Annual Performance and Progress Report: Air Quality in National Parks (NPS, 2005). Unfortunately, much of this information is presented only in terms of the current 8 hr average standard form. Therefore, staff has selected a subset of National Parks and other significant natural areas representing 4 general regions of the U.S to analyze air quality changes in terms of the 12-hr W126 levels over the 4 year period (2001 – 2004, Figures 7-3 and 7-4). A subset of parks had air quality data available for 2005 and it is also included on the Figures. From these graphs it can be seen that many national parks and natural areas have $O_3$ levels above those being considered in this review and which have been shown to decrease plant growth. For example, a 12-hr W126 of 24 ppm-hr has been estimated to cause a 10% biomass loss in 50% of 51 tree seedling cases studies (Lee and Hogsett, 1996) and sensitive tree species such as black cherry and aspen have been reported to have 10% yield losses at levels as low as 4 and 11 ppm-hr (Lee and Hogsett, 1996).

Another key aspect to be considered when evaluating exposure levels of concern to vegetation is distinguishing between pollution levels that can be controlled by U.S. regulations (or through international agreements with neighboring countries) from levels that are generally considered uncontrollable by the U.S., e.g., policy-relevant-background (PRB). As described in Chapter 2 of this SP, the global photochemical transport model GEOS-CHEM (Fiore et al., 2003) was used to estimate PRB levels. This model shows that PRB $O_3$ concentrations, which vary as a function of season, altitude and total surface $O_3$ concentration, are generally predicted to be in the range of 0.015 to 0.035 ppm at the surface in the afternoon, and they decline under conditions conducive to $O_3$ episodes. They are highest during spring and decline into summer. Higher values tend to occur at higher elevations during spring due to contributions from hemispheric pollution and stratospheric intrusions. The stratospheric contribution to surface $O_3$

is typically well below 0.020 ppm and only rarely elevates $O_3$ concentrations at low-altitude sites and only slightly more often elevate them at high-altitude sites (EPA, 2006, AX3-148).

The modeled range of 0.015 to 0.035 ppm in the 2006 CD is lower than the 0.03 to 0.05 ppm range used as background $O_3$ in the 1996 $O_3$ NAAQS Review (EPA, 2006). This is significant for the secondary standard review because the higher end of the range (0.05 ppm) provided an important policy consideration for staff in 1996 for selecting the cumulative SUM06 exposure index that did not weight concentrations below 0.06 ppm. Thus, SUM06 was not influenced by concentrations thought to be at background levels in the 1996 $O_3$ NAAQS review.

Partially on the basis of these lower estimates of PRB, as well as declining peak $O_3$ levels at some sites, staff has re-evaluated the usefulness of using the sigmoidally weighted W126 index to capture more of the vegetation relevant exposures below 0.06 ppm. Though the W126 index weights all concentrations, the concentrations below 0.04 ppm receive substantially smaller weights (3 percent or less) so as not to contribute significantly to the value of the index (Lefohn et al. 1988). In addition, because the W126 form does not contain an absolute threshold like the SUM06 form, it is more in keeping with scientific consensus that there is no threshold for exposures that cause effects on vegetation (Heck and Cowling 1997, EPA 2006). Therefore, staff have incorporated 12-hr W126 in the vegetation risk analyses where feasible to do so. Figure 7-5 shows the relationship between W126 and SUM06 as measured at $O_3$ monitors in 2001. The metrics are highly correlated, though it appears that in some cases SUM06 underestimates exposures compared to W126. This difference between the metrics is most likely because of the inclusion of weighting hourly concentrations between 0.04 and 0.06ppm in W126. Because the inflection point of W126 is approximately 0.06ppm, SUM06 metric is essentially a simple approximation of the sigmoidally weighted W126 form and it is not surprising that the two metrics measure $O_3$ exposures in a very similar way at most monitoring stations (Lee et al. 1988).

**Figure 7-1.** 2002 Air Quality Relationships

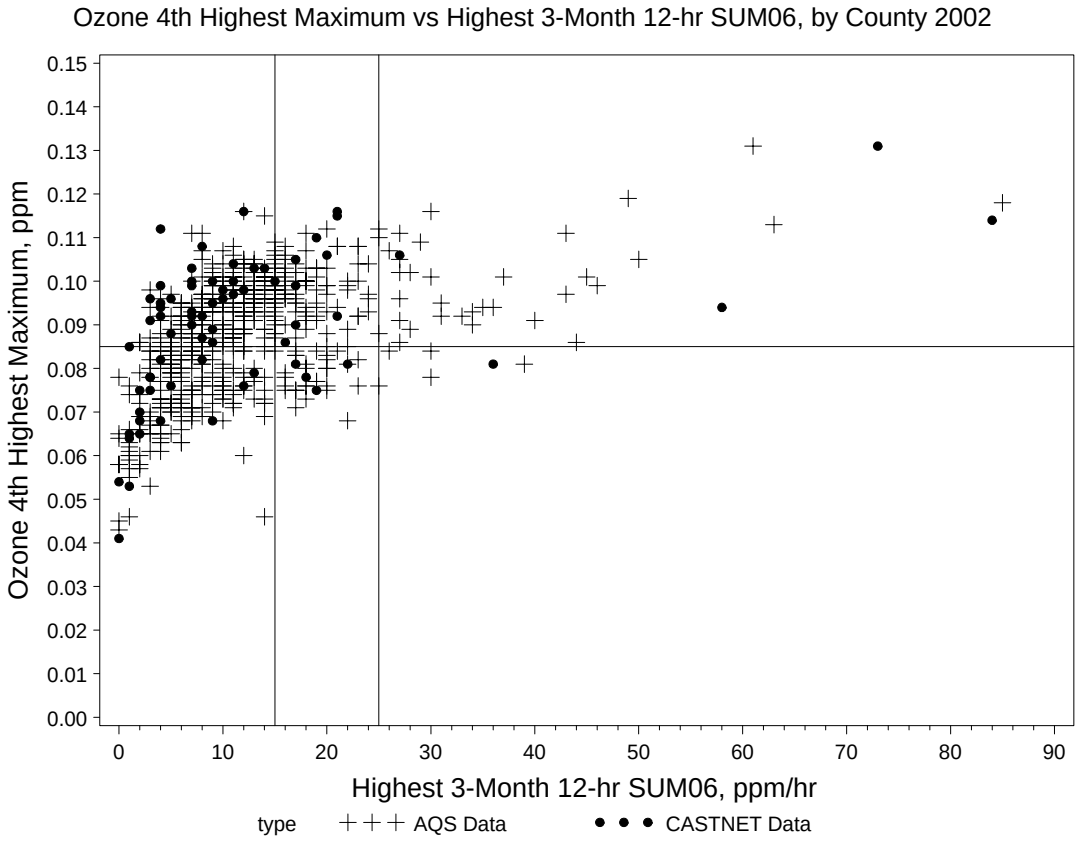


**Figure 7-2. 2004 Air Quality Relationships**

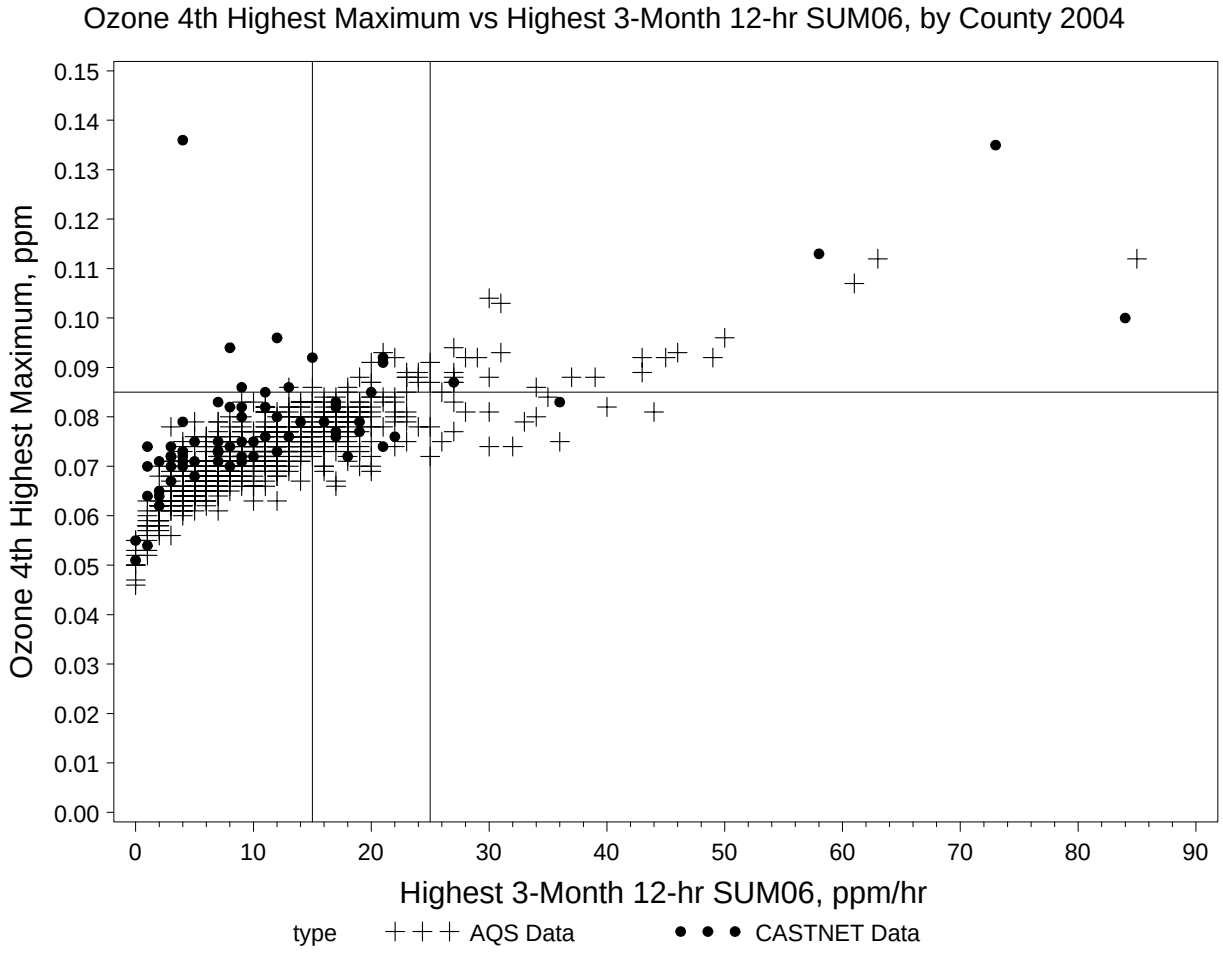
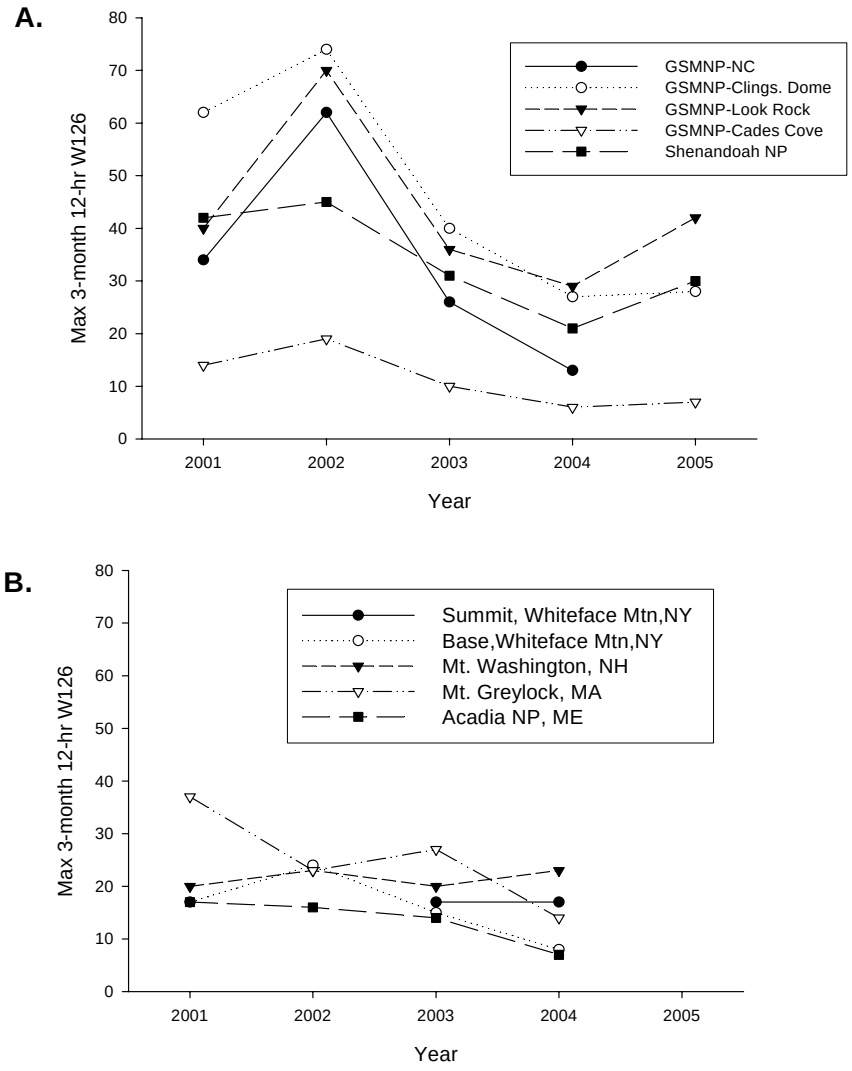


**Figure 7-3. 3 month maximum 12-hr W126 values from monitors in National Parks and other natural areas in the Southeast (A) and Northeast (B). Monitors designated as GSMNP are found in different areas of the Great Smoke Mountain National Park.**



### 7.5.2 Monitor Networks: National Coverage

Hourly $O_3$ monitor data is available from two national networks: (1) Air Quality System (AQS; http://www.epa.gov/ttn/airs/airsaqs) and (2) Clean Air Status and Trends Network (CASTNET; http://www.epa.gov/castnet/). The locations of these monitors are presented in Figure 7-6 and are described in section 2.3.1 and 2.3.2 of Chapter 2. The AQS monitoring network currently has over 1100 active $O_3$ monitors which are generally sited near population centers. However, this network also includes approximately 36 monitors located in National Parks. CASTNET is the nation's primary source for data on dry acidic deposition and rural, ground-level ozone. It consists of over 80 sites across the eastern and western U.S. and is cooperatively operated and funded with the National Park Service. Due to the overall stability in these monitoring networks and standardized, rigorous QA/QC and data handling protocols, they provide useful information regarding long term trends in air quality across regions and at specific sites. For more on the AQS protocols, see section 2.3.1 of this Staff Paper or Code of Federal Regulations, Title 40, Part 58 (40 CFR Part 58). CASTNET, in terms of data quality, achieved 98% to 99% of all precision and accuracy audits being within the ±10% criteria for both precision and accuracy. Overall, CASTNET $O_3$ monitors are stable and show only very small variation (U.S. EPA 2003, p.22). Both networks take $O_3$ measurements on an hourly time step which allows for quick comparisons between different air quality index forms and different averaging times.

In spite of the size and quality of these monitoring networks, however, vast rural areas of the U.S., where important crops and natural vegetation occur, still do not have $O_3$ monitor coverage (Figure 7-6). As was the case in the 1996 review, staff found it necessary to select a method that could be used to characterize $O_3$ air quality over broad geographical areas of concern (see sections 7.5.3 and 7.5.4 below) to support a national scale risk assessment of the effects of ambient $O_3$ exposures on vegetation and ecosystems. Staff's review of the monitor data showed that within the five most recent years available (2000 to 2004), 2001 was a fairly moderate $O_3$ year. Based on this information, and because it coincided with the most recently available air quality model data (see section 7.5.3. below), 2001 was selected as the initial (base) air quality year for most of the quantitative vegetation risk analyses conducted in this review. In a few cases (e.g. foliar injury and tree growth modeling), monitor data from other air quality years were used.

**Figure 7-4. 3 month maximum 12-hr W126 values from monitors in National Parks in the Mountain West (A) and California (B).**

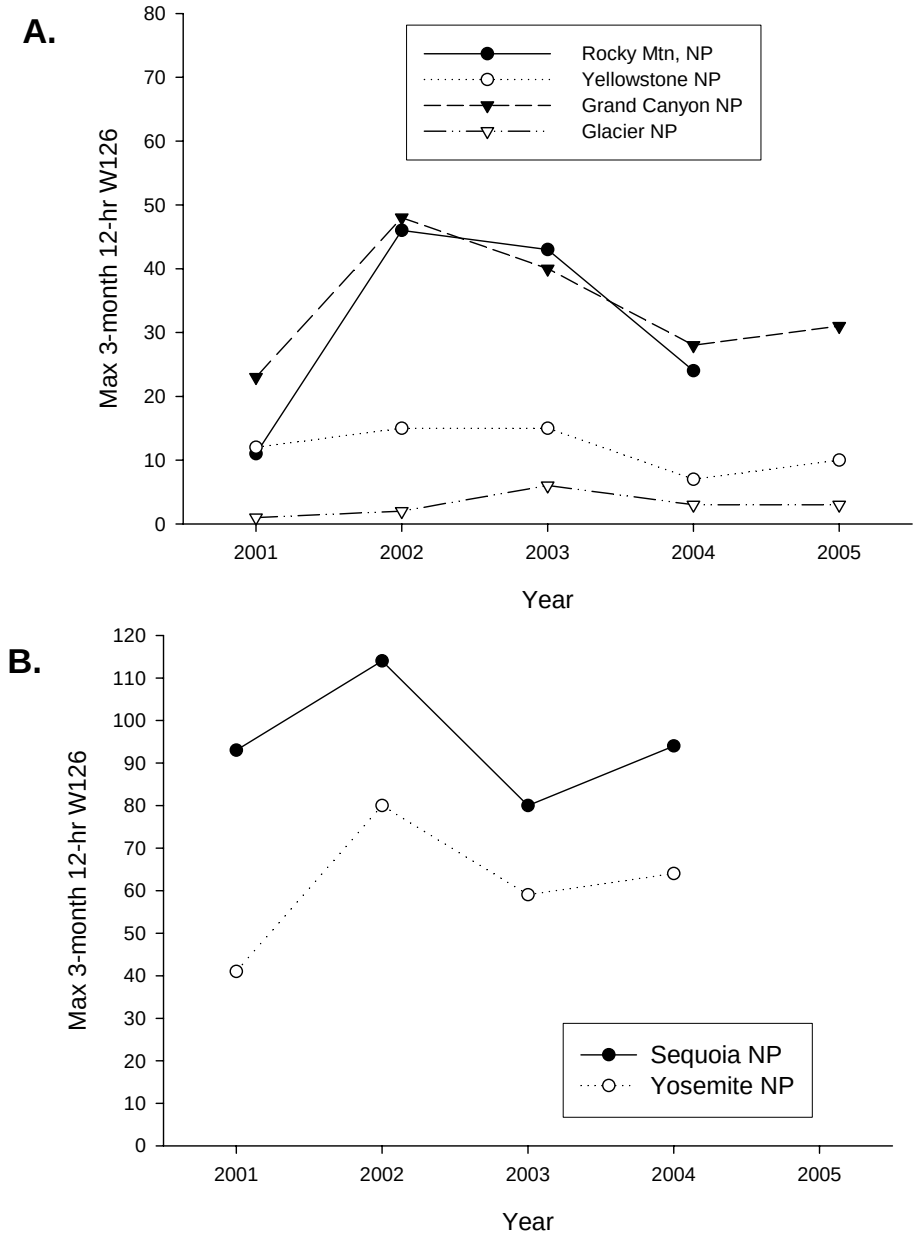


**Figure 7-5. Maximum 3-month 12-hr SUM06 plotted against maximum 3-month 12-hr W126. Data points are from the AQS and CASTNET $O_3$ monitors for the year 2001.**

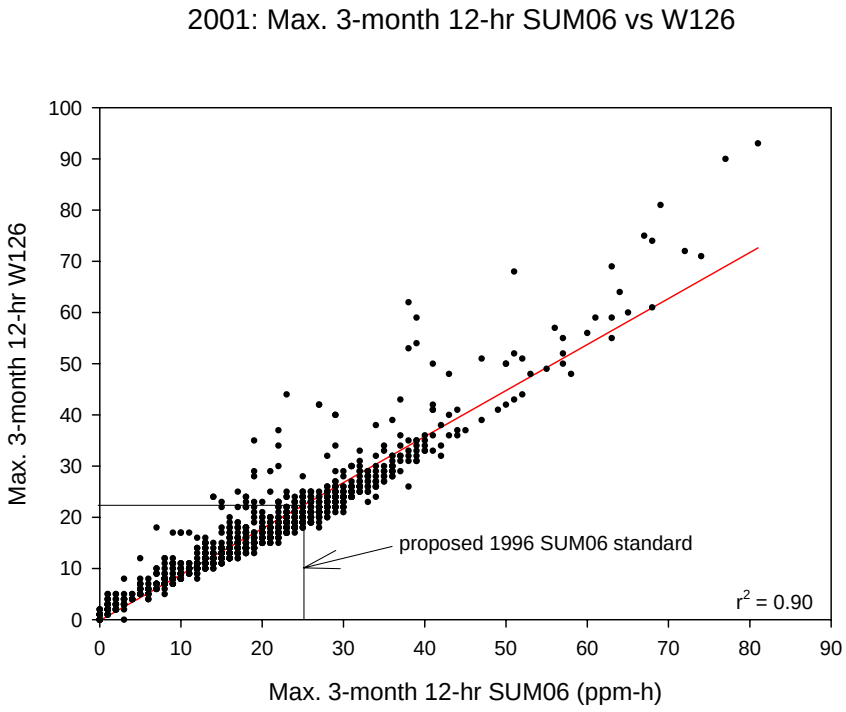
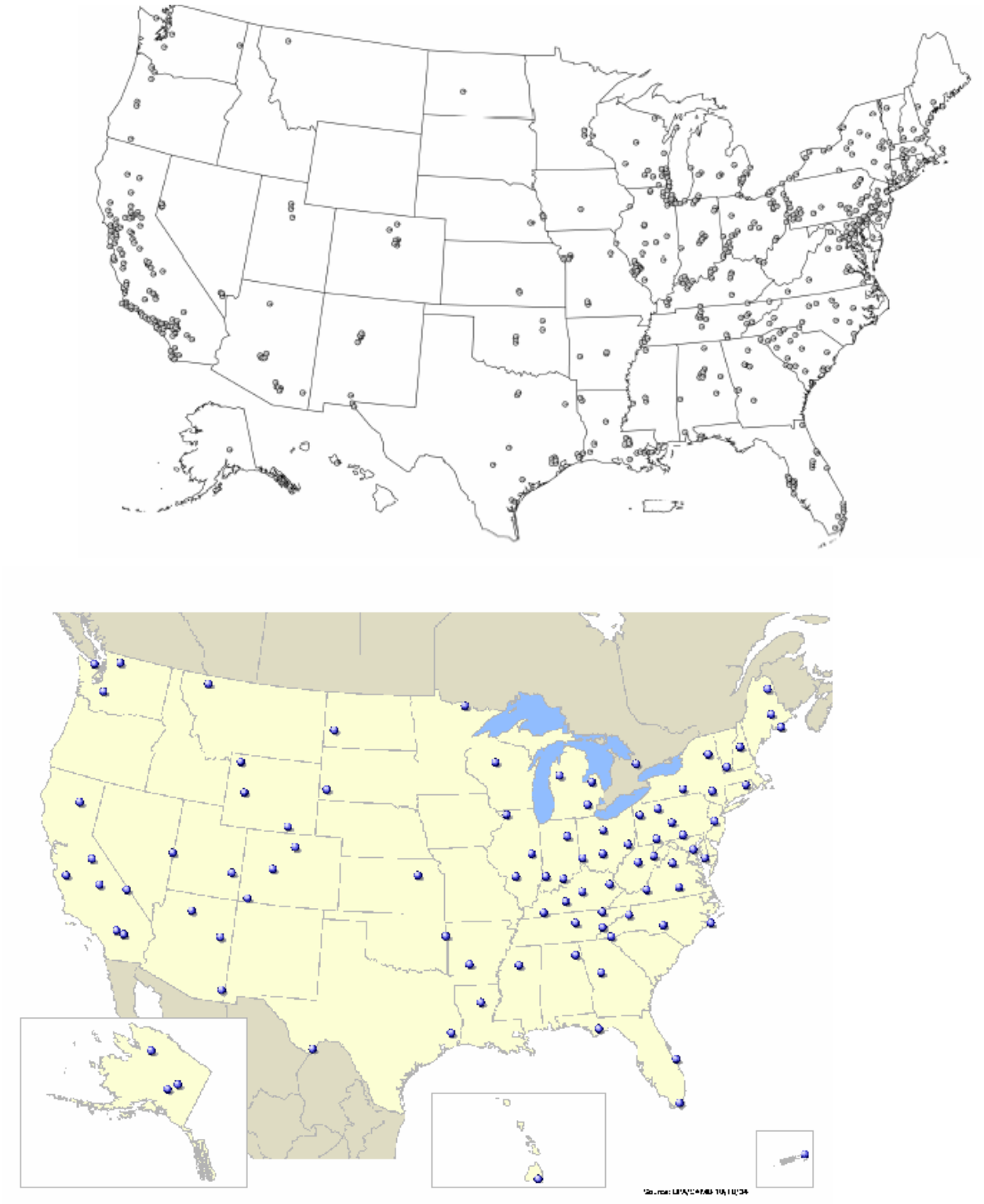


**Figure 7-6.** Locations of AQS monitors (top) and CASTNET monitoring stations (bottom)



### 7.5.3 Community Multi-scale Air Quality Model (CMAQ)

Staff investigated the appropriateness of using the $O_3$ outputs from the EPA/NOAA Community Multi-scale Air Quality model system (http://www.epa.gov/asmdnerl/CMAQ, Byun and Ching, 1999; Arnold et al. 2003, Eder and Yu, 2005) to improve spatial interpolations based on the regionally limited and unevenly distributed $O_3$ monitoring network in the western U.S. (see section 7.5.2). The CMAQ model is a multi-pollutant, multiscale air quality model that contains state-of-science techniques for simulating all atmospheric and land processes that affect the transport, transformation, and deposition of atmospheric pollutants and/or their precursors on both regional and urban scales. It is designed as a science-based modeling tool for handling many major pollutants (including photochemical oxidants/$O_3$, particulate matter, and nutrient deposition) holistically. The CMAQ model can generate estimates of hourly $O_3$ concentrations for the contiguous U.S., making it possible to express model outputs in terms of a variety of exposure indices (e.g., SUM06, 8-hr average). Due to the significant resources required to run CMAQ, however, model outputs are only available for a limited number of years. For this review, 2001 outputs from CMAQ version 4.5 were the most recent data available. This version of CMAQ utilizes the more refined 12 km x 12 km grid for the eastern U.S., while using the 36 km x 36 km grid for the western U.S. The 12 km x 12 km domain covers an area from roughly central Texas, north to North Dakota, east to Maine, and south to central Florida. More detailed information on CMAQ can be found in Appendix 7B. Section 7.5.4 below describes the very limited capacity in which staff used the CMAQ results. As explained below, in the final analysis, staff opted not to use $O_3$ values calculated from the CMAQ model, but instead only used model results to scale interpolations in the western U.S.

### 7.5.4 Generation of Potential Ozone Exposure Surfaces (POES)

Staff evaluated ten approaches for interpolating $O_3$ air quality across the U.S. which included (1) use of the CMAQ model alone; (2) use of the monitor data only Voronoi Neighbor Averaging (VNA) technique; and (3) use of a combination of monitor and CMAQ information called enhanced Voronoi Neighbor Averaging (eVNA). The evaluations were based on how well the CMAQ model or interpolation techniques were able to predict the 12-h SUM06, 12-h W126 and the 4$^{th}$ highest 8hr max average at each monitor. For VNA and eVNA evaluations each monitor was dropped out sequentially and a value for the monitor was interpolated with the remaining monitors. At each monitor site Normalized Mean Bias (NMB), Normalized Mean Error (NME), Absolute Mean Bias (AMB) and Absolute Mean Error (NME) were calculated

(Table 7-1, for more details see discussion under Uncertainties below and in the draft Environmental Assessment TSD). From the results of these evaluations, the eVNA and VNA performed equally in many cases and CMAQ model alone performed the poorest. The staff chose to use separate interpolation techniques in the east and the west. The simpler VNA approach was chosen for the eastern U.S. since it was determined that enhancing the interpolation with CMAQ did not add much information to the eastern U.S. interpolation where the monitoring network has greater coverage than in the west (Figure 7-4). Using the simpler VNA approach in the east also allowed staff to maintain the option of producing eastern U.S. interpolations for other years without the need for CMAQ results. In the west, eVNA was chosen because of the sparse monitoring network in those states. Although the VNA and eVNA interpolation approaches are not as complex or sophisticated as some techniques (e.g. Bayesian methods), they have the advantages of relying on readily available data, being relatively inexpensive to run, and being able to quickly produce estimates of any exposure index, for multiple months or years, and for different air quality scenarios.

To generate the POES, a set of geographical locations for which $O_3$ data would be interpolated was needed. Ideally these locations would be regularly spaced, cover the continental US, and be close enough to each other to provide a good spatial resolution. Staff chose to use the regularly spaced grid structure of the CMAQ model as a basis for these locations. Specifically, the center of each grid cell was identified both for cells in the 12km x 12km grid (which covers only the Eastern U.S.), and the 36km x 36km grid (the Western US). This approach produced the densest possible non-redundant "composite" grid of 44432 regularly spaced grid cell center locations throughout the U.S. Using VNA in the eastern U.S. and eVNA in the West, $O_3$ values were interpolated for each grid cell center in the composite grid (see draft Environmental Assessment TSD for more details).

To support the vegetation exposure and risk assessments, ambient $O_3$ exposures were projected using seasonal $O_3$ air quality for the 2001 base year in terms of the 3-month 12-hr SUM06 (Figure 7-7) and W126 exposure indices (Figure 7C-1 in appendix 7C). The uncertainties of this interpolation are discussed below. Taking the uncertainties into account, in the absence of more complete monitoring data, staff find the POES serves as a useful tool for identifying areas across the country where exposure levels would be expected to exceed those known to produce yield or biomass loss at given levels for crops and trees, respectively. Figure 7-7, suggests that under the base year (2001) air quality, a large portion of California has seasonal SUM06 above 38 ppm-hr, while broader multistate regions in the east and west are predicted to have SUM06 above 25 ppm-hr which is greater than the secondary standard proposed in 1996. Much of the east and Arizona and California have seasonal SUM06 values above 15 ppm-h. Thus, the staff concludes that current air quality levels could result in

significant impacts to vegetation. However, these exposures may be overestimated with respect to vegetation with canopy heights below monitor inlet heights, e.g., crops and tree seedlings. In the crop risk/benefit assessments, staff tested an adjustment of monitored $O_3$ to take into account the vertical $O_3$ gradient that exists from the height of the monitoring probe (~4 meters) to the approximate height of crops and seedlings (See Section 7.6.2.3 for details).

To evaluate changing vegetation exposures and risks under changing air quality, maps were also generated for selected "just meet" scenarios (Figures 7-8, 7-9, 7-10, 7-11) by analytically adjusting air quality distributions with the quadratic method to reflect "just meeting" the level of various alternative primary and secondary standard options (see Horst and Duff, 1995; Rizzo, 2006; Lee, 2006). This technique combines both linear and quadratic elements to reduce larger $O_3$ concentrations more than smaller ones. In this regard, the quadratic method attempts to account for reductions in emissions without greatly affecting lower concentrations near ambient background levels. The following "just meet" air quality scenarios were generated:

- 4th highest daily maximum 8-hr average of 0.084 ppm (current EPA standard)
- $4^{th}$ highest daily maximum 8-hr average of 0.070 ppm (alternate standard)
- 3-month, 12-hr. SUM06 of 25 ppm-hr (alternate standard proposed in the 1996 review)
- 3-month, 12-hr. SUM06 of 15 ppm-hr (alternate standard)

These maps of "just meet" scenarios, used in estimating benefits of improved air quality, can also depict areas which might experience residual risk after attainment of the standard. When 2001 air quality is rolled back to attaining the current 0.08 ppm, 8-hour $4^{th}$ highest max average primary and secondary NAAQS, the overall seasonal 12-hr SUM06 exposures do not improve very much (Figure 7-8). Under this attainment scenario, there are still many areas of the country that have seasonal $O_3$ levels above the level of the secondary standard proposed in 1996 (12-hr SUM06 of 25 ppm-hr). Thus, staff concludes that attaining the current (primary and secondary) NAAQS may not provide adequate protection of vegetation.

In contrast, the exposure maps generated for the 0.07 ppm, 8-hour $4^{th}$ highest max. average and SUM06 of 25 and 15 ppm-hr alternatives (Figures 7-9, 7-10, 7-11) show a markedly improved picture of $O_3$ air quality compared to Figures 7-8. In the 0.07 ppm, 8-hour $4^{th}$ highest max average scenario (Figure 7-9) only California, Nevada, and Arizona have areas predicted to exceed the 1996 proposed secondary standard (SUM06 of 25 ppm-hr). Obviously, rollback scenarios to SUM06 of 25 and 15 ppm-hr improve the air quality the most for vegetation. Thus, the staff concludes that the 0.07 ppm, 8-hour $4^{th}$ highest max average and SUM06 of 25 and 15

ppm-hr alternative standards, when attained at all locations, would be expected to provide significantly improved protection of vegetation from seasonal $O_3$ exposures of concern.

***Uncertainties***

Staff recognizes there are inherent uncertainties in the interpolation that must rely on sparse data representative of urban and near-urban areas with little representation of rural areas. This network could bias the picture of the $O_3$ exposure estimate especially in the western U.S. where monitoring sites can be very far apart. Intuitively, it is expected that the eVNA approach with spatial scaling from CMAQ approach would be an improvement over a simple interpolation in the West. However, it is difficult to test for this because the lack of monitoring in the western U.S. To quantify the uncertainty of the exposure surface, each monitor was sequentially dropped out of the interpolation and recalculated with the remaining monitors. At each monitor site Normalized Mean Bias (NMB), Normalized Mean Error (NME), Absolute Mean Bias (AMB) and Absolute Mean Error (NME) was calculated. These statistics are defined below:

$$NMB = average_{i \in dropouts}\left(100 * \frac{predictedMETRIC_i - actualMETRIC_i}{actualMETRIC_i}\right)$$

$$NME = average_{i \in dropouts}\left(100 * \frac{\left|predictedMETRIC_i - actualMETRIC_i\right|}{actualMETRIC_i}\right)$$

$$AMB = average_{i \in dropouts}(predictedMETRIC_i - actualMETRIC_i)$$

$$AME = average_{i \in dropouts}(|predictedMETRIC_i - actualMETRIC_i|)$$

This method of evaluation will be a slight overestimation of error for the exposure surface since dropping out monitors loses information that interpolation uses in that local area. Summary error and bias metrics are presented in Table 7-1a and b. More detailed information from this analysis is presented in the draft Environmental Assessment TSD. As expected the interpolation performed better in the East than in the West. Using all the monitors, the Eastern U.S. interpolation had an NME of about 26% for the 12-h SUM06 metric. Western interpolation had a much higher NME of approximately 57%. However, since SUM06 and W126 values are often low numbers, NME can be calculated to be large while the absolute difference is small. For example, if a monitor with a SUM06 of 4 ppm-hr is measured and the interpolation predicts a SUM06 of 6 ppm-hr then the NME would be 50%. Therefore, staff thought it was useful to also

report the absolute mean bias and error. In absolute terms the average bias for SUM06 was slightly low (-1.83 ppm-h in the East and -2.41 ppm-h in the West). CASTNET monitors are also presented to illustrate how well the interpolation techniques predicted air quality in that rural monitoring network. In general, the interpolations in the East and West under-predicted the 12-hr SUM06 values. This under-prediction is likely a result of the averaging inherent in the interpolation. Similar results are seen for the 12-h W126 and SUM06 (Table 7-1b). However in almost all cases the interpolation was able to predict monitored W126 slightly better than SUM06. The calculation of error and bias metrics for the interpolation represents a notable improvement over the 1996 assessment which did not have an evaluation of the exposure surface.

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**Figure 7-7. Estimated 12-Hour SUM06 Ozone Exposure – Max 3-months for 2001**

"As Is" scenario

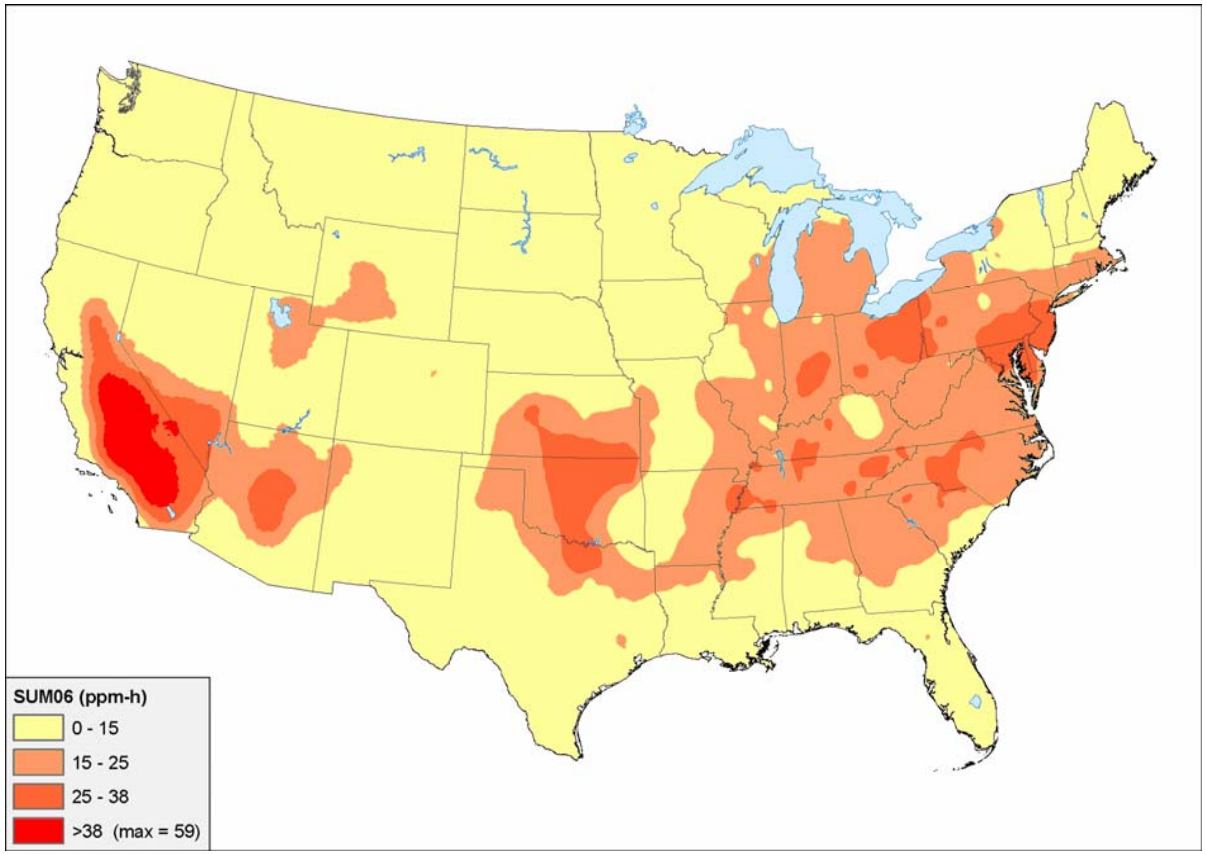


**Table 7-1a. Evaluation statistics for the 3 month 12-hr SUM06 interpolations of the Eastern and Western US domains. NMB is Normalized Mean Bias, NME is Normalized Mean Error, AMB is Absolute Mean Bias and AME is Absolute Mean Error. Explanation of these metrics are given in the text.**

| Region | Monitors | NMB (%) | NME (%) | AMB (ppm-h) | AME (ppm-h) |
|---|---|---|---|---|---|
| Eastern US | All monitors | -0.06 | 25.54 | -1.83 | 4.07 |
| Eastern US | CASTNET only | -7.87 | 19.90 | -2.66 | 4.45 |
| Western US | All monitors | 16.56 | 57.39 | -2.41 | 6.05 |
| Western US | CASTNET only | -18.19 | 19.81 | -3.21 | 3.35 |

**Table 7-1b: Evaluation statistics for the 3 month 12-hr W126 interpolations of the Eastern and Western US domains**

| Region | Monitors | NMB (%) | NME (%) | AMB (ppm-h) | AME (ppm-h) |
|---|---|---|---|---|---|
| Eastern US | All monitors | -1.08 | 21.76 | -1.21 | 2.97 |
| Eastern US | CASTNET only | -6.61 | 17.62 | -1.73 | 2.95 |
| Western US | All monitors | 14.37 | 43.38 | -1.37 | 4.27 |
| Western US | CASTNET only | -7.58 | 9.48 | -1.23 | 1.43 |

**Figure 7-8. Estimated 12-Hour SUM06 Ozone Exposure – Max 3-months for 2001**

Quadratic Rollback to just meet 4th Highest 8-hour Maximum of >0.084

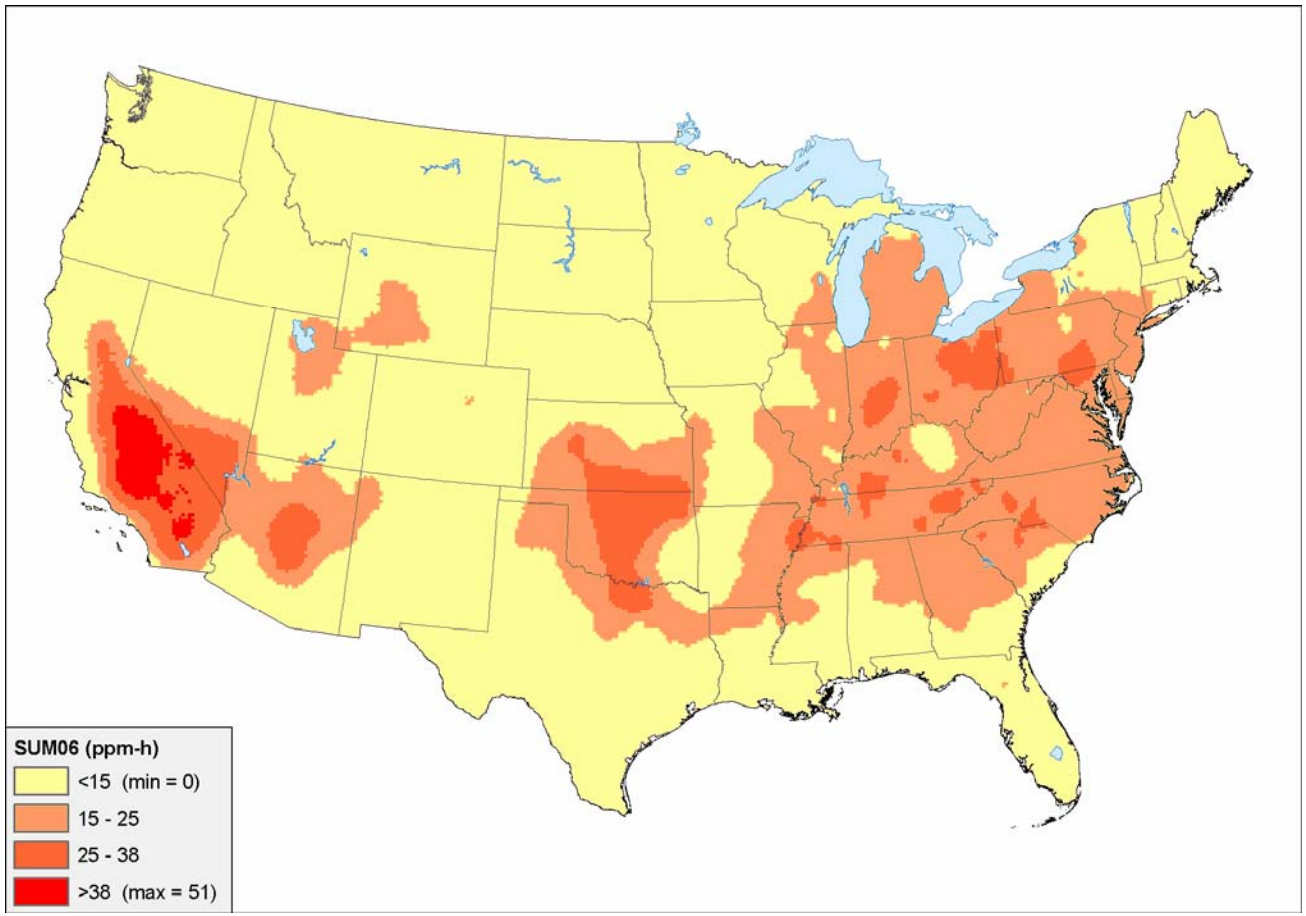


**Figure 7-9. Estimated 12-Hour SUM06 Ozone Exposure – Max 3-months for 2001**

Quadratic Rollback to just meet 4th Highest 8-hour Maximum of >0.070

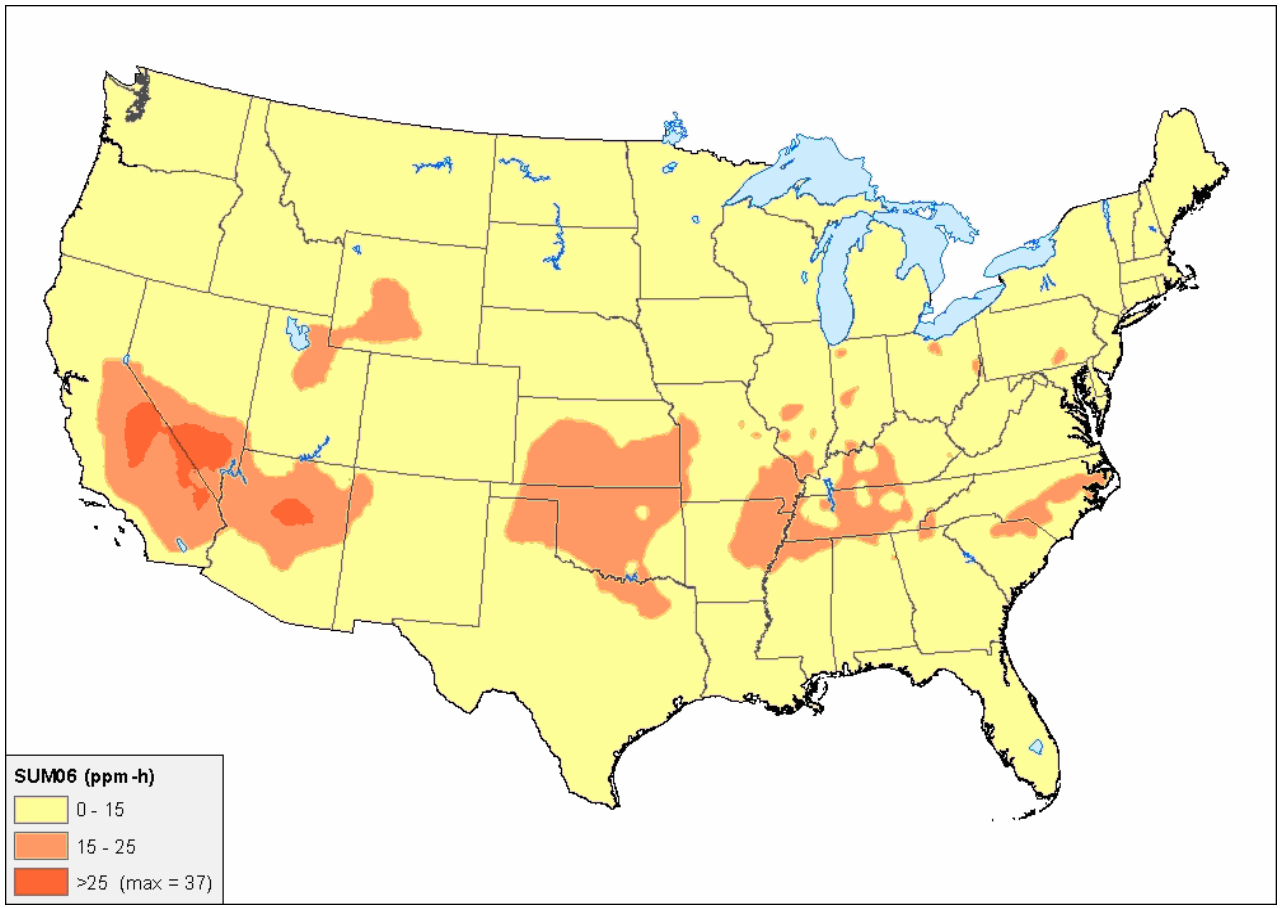


**Figure 7-10. Estimated 12-Hour SUM06 Ozone Exposure – Max 3-months for 2001**

Quadratic Rollback to just meet 12-hr SUM06 of 25 ppm-hr, secondary standard proposed in 1996

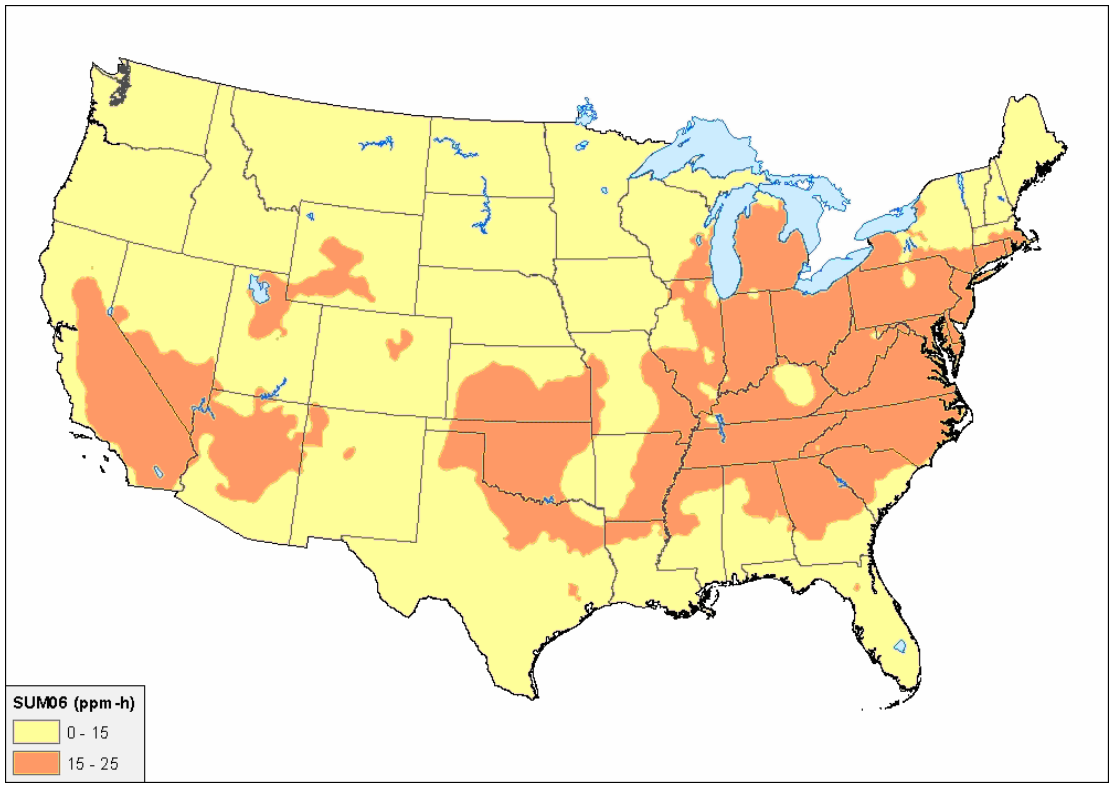
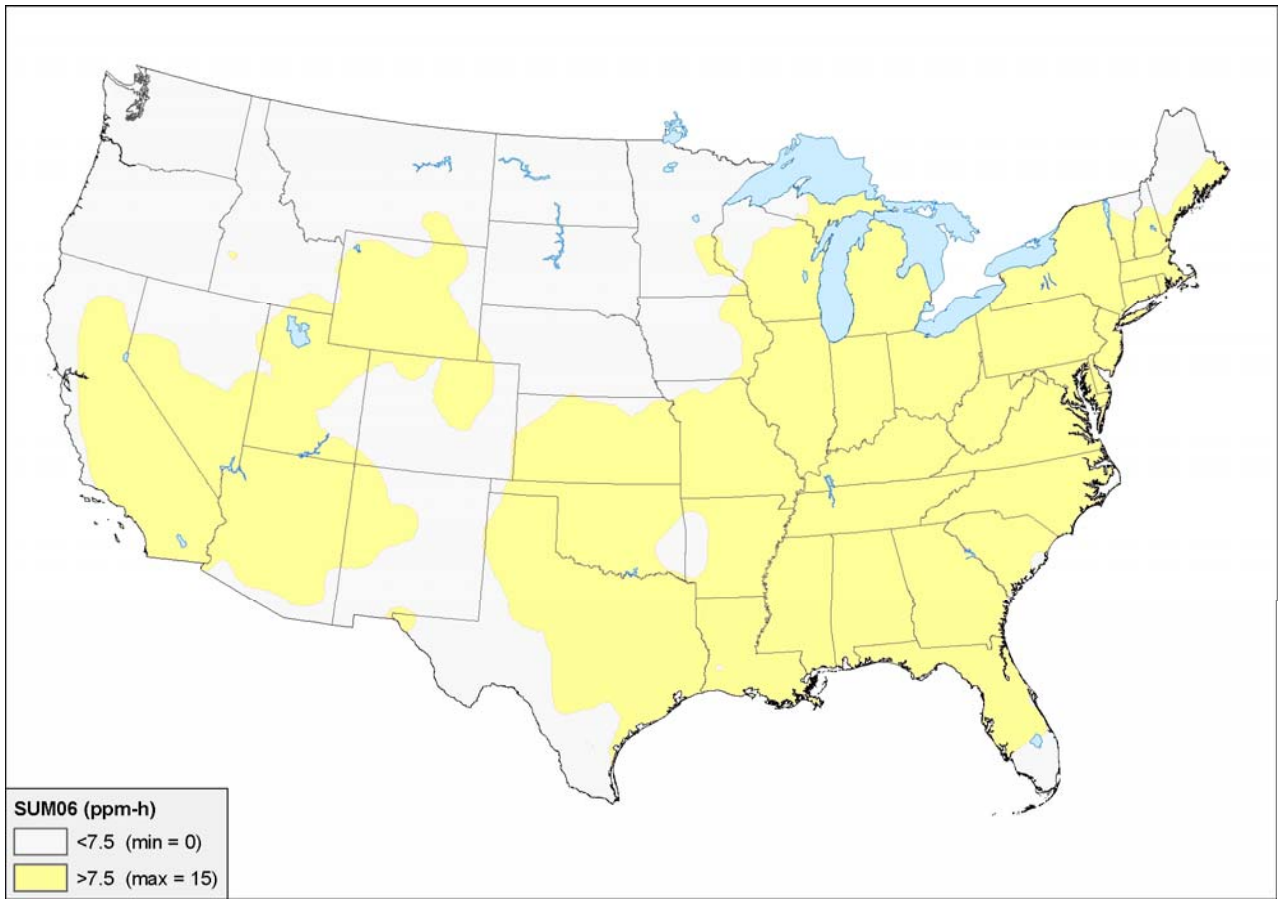


**Figure 7-11. Estimated 12-Hour SUM06 Ozone Exposure – Max 3-months for 2001**

Quadratic Rollback to just meet 12-hr SUM06 of 15 ppm-hr

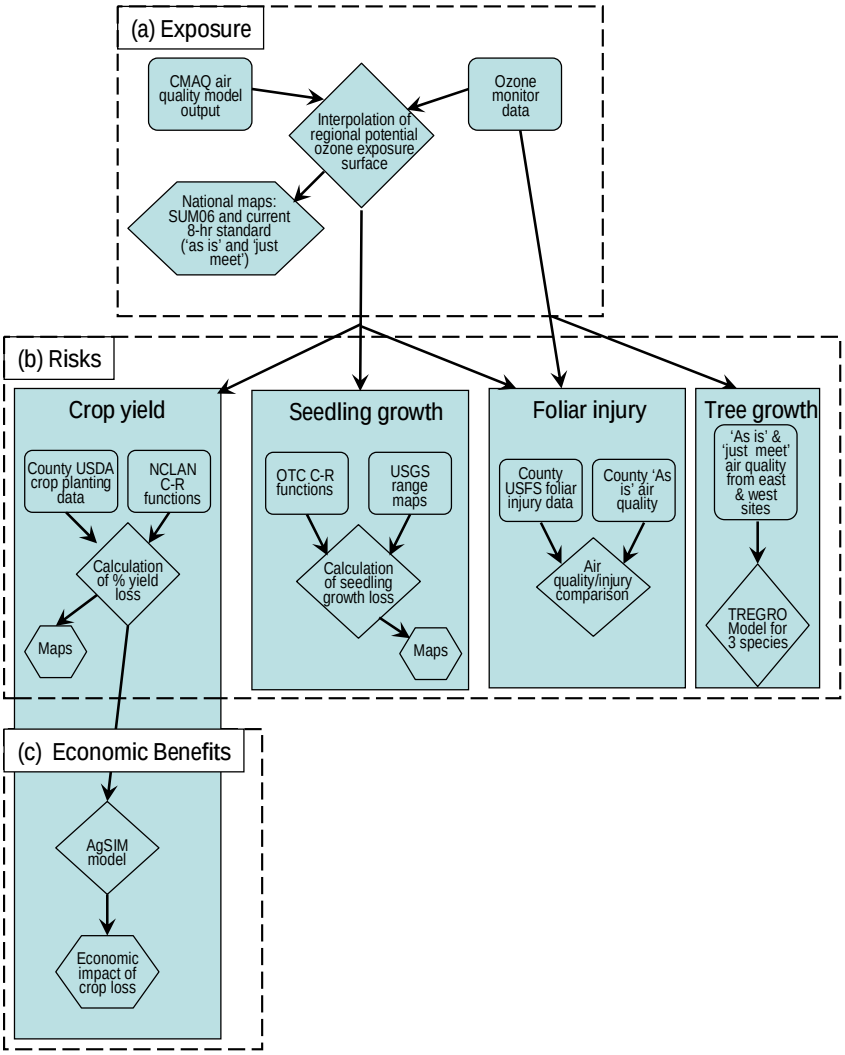


## 7.6 CHARACTERIZATION OF VEGETATION RISKS

### 7.6.1 Scope of Vegetation Risk Assessment

The vegetation impact assessment conducted for the current review (see Figure 7-12a-c), consists of exposure, risk and benefits analyses and is meant to improve and build upon the similar analyses performed in support of the 1996 secondary NAAQS review. The vegetation exposure assessment was discussed above in section 7.5. The organization of this section reflects the remaining risk and benefit components of the assessment. The vegetation risk discussion which follows is divided between the crop and tree analyses. The crop analysis discussed in section 7.6.2 includes estimates of the risks to crop yields from current and alternative $O_3$ exposure conditions and the associated change in economic benefits expected to accrue in the agriculture sector upon meeting the levels of various standards. The tree risk analysis described in section 7.6.3 includes three distinct lines of evidence: (1) estimates of seedling growth loss under current and alternative $O_3$ exposure conditions; (2) observations of foliar injury in the field linked to monitored $O_3$ air quality for the years 2001 - 2004; and (3) simulated mature tree growth reduction using the TREGRO model to simulate the effect of meeting alternative air quality standards on a single western species (ponderosa pine) and two eastern species (red maple and tulip poplar). These analyses reflect earlier input received during a consultation with the CASAC $O_3$ Panel in October 2005. This second draft Staff Paper also includes both quantitative and qualitative discussions of known sources and ranges of uncertainties associated with the components of this assessment.

**Figure 7-12 (a-c). Major Components of Vegetation Risk Assessment**



### 7.6.2 Characterization of Crop Risks and Associated Economic Benefits

#### 7.6.2.1 Exposure Methodologies Used in Vegetation Research

In the 1996 review, $O_3$ exposure studies were dominated by the use of various versions of the open-top chamber (OTC), first described by Heagle et al. (1973) and Mandl et al. (1973). Hogsett et al. (1985, 1987) described in detail many of the various modifications to the original OTC designs that appeared subsequently. The OTC method continues as a widely used technique in the U.S. and Europe for exposing plants to varying levels of $O_3$ (EPA, 2005b).

Chambered systems, including open-top chambers, have several advantages. For instance, they can provide a range of treatment levels including charcoal-filtered (CF), clean-air control, and above ambient for $O_3$ experiments. Depending on experimental intent, a replicated, clean-air control treatment is an essential component in many experimental designs. The OTC can provide a consistent, definable exposure because of the constant wind speed and delivery systems. From a policy prospective, the statistically robust concentration-response (C-R) functions developed using such systems are necessary for evaluating the implications of various alternative air quality scenarios on crop response.

Nonetheless, there are several characteristics of the OTC design and operation that can lead to exposures that might differ from those experienced by plants in the field. First, the OTC plants are subjected to constant turbulence, which, by lowering the boundary layer resistance to diffusion, results in increased uptake. This may lead to an overestimation of effects in areas with less turbulence (Krupa et al., 1995; Legge et al., 1995). As with all methods that expose vegetation to modified $O_3$ concentrations in the field, OTCs create internal environments that differ from ambient air. This so-called "chamber effect" refers to the modification of microclimatic variables, including reduced and uneven light intensity, uneven rainfall, constant wind speed, reduced dew formation, and increased air temperatures (Fuhrer, 1994; Manning and Krupa, 1992). However, staff notes that the uncertainties associated with the influence of other modifying factors occurring in the field such as water and nutrient availability (see discussion above in section 7.4.2) are likely to be greater than the uncertainties in the data due to the influence of OTCs. Because of the standardized methodology and protocols used in NCLAN, the database can be assumed to be internally consistent.

While it is clear that OTCs can alter some aspects of the microenvironment and plant growth, the question to be answered is whether or not these differences affect the plant's response to $O_3$. As noted in the 1996 $O_3$ CD (EPA, 1996a), evidence from a number of comparative studies of OTCs and other exposure systems suggested that responses were

essentially the same regardless of exposure system used and chamber effects did not significantly affect response. For example, a study of chamber effects examined the responses of tolerant and sensitive white clover clones (*Trifolium repens*) to ambient $O_3$ in greenhouse, open-top, and ambient plots (Heagle et al., 1996). The response found in OTCs was the same as in ambient plots. The California Air Resources Board (CARB), during its recent $O_3$ standard review, came to a similar conclusion about the usefulness of OTC data. Its review states "there is little scientific justification for the categorical discounting of ozone yield-response relationships obtained using the OTC technology" (CEPA, 2005).

In recent years, a few studies have employed a modified Free Air $CO_2$ Enrichment (FACE) method to expose vegetation to elevated $O_3$ without using chambers. This exposure methodology was originally developed to expose vegetation to elevated levels of $CO_2$, but has been modified to include $O_3$ exposure in Illinois and Wisconsin for soybean and deciduous trees, respectively (Dickson et al., 2000; Morgan et al., 2004). The FACE method releases gas (e.g., $CO_2$, $O_3$) from a series of orifices placed along the length of the vertical pipes surrounding a circular field plot and uses the prevailing wind to distribute it. This exposure method may more closely replicate conditions in the field and, more importantly for forest research, has the benefit of being able to expand vertically with the growth of the trees, allowing for exposure experiments to span numerous years.

The FACE methodology has a different set of limitations than those of the OTC. Most importantly, it is not possible with FACE to produce a number of replicated treatment levels, including $O_3$ concentrations below ambient that are needed to build the statistically robust C-R functions possible with OTCs. Despite the differences in these two exposure methods, recent evidence obtained using FACE and OTC systems appear to support the results observed in OTC studies used in the 1996 review. For example, a series of studies undertaken using free-air $O_3$ enrichment in Rhinelander, WI (Isebrands et al., 2000, 2001) showed that $O_3$-symptom expression was generally similar in OTCs, FACE, and ambient-$O_3$ gradient sites, and supported the previously observed variation among trembling aspen clones (*Populus tremuloides* L.) using OTCs (Karnosky et al., 1999). As more FACE data become available, a more quantitative comparison of findings from these two systems would be useful. An example of this type of comparison is presented in section 7.6.2.2 below.

Other exposure methods described both in the 1996 and 2006 $O_3$ CDs (EPA, 1996a; EPA 2006) also provide useful information on plant responses to $O_3$ exposure. For example, Gregg et al. 2002, found significant effects of $O_3$ on the growth of poplars along an ambient $O_3$ gradient in the New York City area, similar to those reported in OTCs. Other exposure methods include but are not limited to chemical protectants (e.g. EDU), exclusion, and passive monitors. Nonetheless, given a continued policy need for robust C-R functions, provided by OTC studies,

to evaluate vegetation response under alternative air quality scenarios and that other approaches confirm OTC results, staff conclude that the robust C-R functions derived using the OTC methodology are currently the most useful in a policy context and we continue to rely on them in the following analyses.

#### 7.6.2.2 Basis for C-R Functions

The 1996 crop assessment was built upon the NCLAN (National Crop Loss Assessment Network) $O_3$ C-R functions. Since very few new studies have published C-R functions that would be useful in an updated assessment, C-R functions from NCLAN remain the best data available for a national assessment of crop loss under various $O_3$ air quality scenarios. The NCLAN protocol was designed to produce crop C-R data representative of the areas in which the crops were typically grown. The U.S. was divided into 5 regions over which a network of field sites was established. In total, 15 crop species (corn, soybean, winter wheat, tobacco, sorghum, cotton, barley, peanuts, dry beans, potato, lettuce, turnip, and hay [alfalfa, clover, and fescue]), were studied. The first 12 of these 15 listed species were analyzed for the 1996 review and included 38 different cultivars studied under a variety of unique combinations of sites, water regimes, and exposure conditions, producing a total of 54 separate cases. Figure 7-13 uses the regression equations for each of the 54 cases to graph predicted relative yield loss at various exposure levels in terms of a 12-hr SUM06 (Figure 7D-1 presents a similar figure with the 4$^{th}$ highest 8-hr max. average). Figure 7-14a-c shows composite graphs for some individual crops from NCLAN and the variations in sensitivity between important crops. According to the most recent USDA National Agricultural Statistical Survey (NASS) data, the 12 species analyzed in the the last review account for greater than 70% of principal crops acreage planted in the U.S. in 2004.[1] Corn, soybean, and winter wheat alone accounted for 62% of principal crop acreage planted. For the economic analysis described in section 7.6.2.4, a reduced list of 9 species (69% of principal crop) were included (e.g., cotton, field corn, grain sorghum, peanut, soybean, winter wheat, lettuce, kidney bean, potato), with tobacco, turnip and barley not evaluated.

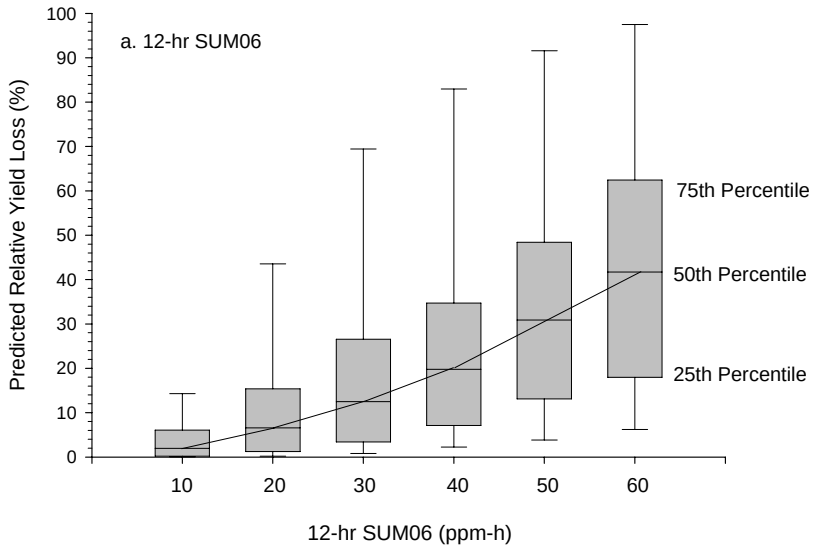
Since the NCLAN studies were performed during the years 1980 to1988, there is some uncertainty whether the crop cultivars tested in NCLAN are representative of crops grown today. In general, new crop varieties are not specifically bred for $O_3$ tolerance. The fact that $O_3$ levels are not consistent from year to year does not allow crop breeders to select for $O_3$ tolerance under natural conditions. Additionally, the cultivars used today were bred from the same very narrow

[1] Principal crops as defined by the USDA include corn, sorghum, oats, barley, winter wheat, rye, Durum wheat, other spring wheat, rice, soybeans, peanuts, sunflower, cotton, dry edible beans, potatoes, sugar beets, canola, proso millet, hay, tobacco, and sugarcane. Acreage data for the principal crops was taken form the USDA NASS 2005 Acreage Report (http://usda.mannlib.cornell.edu/reports/nassr/field/pcp-bba/acrg0605.pdf )

genetic stock available in the 1980's and it is not expected that there would be much difference in $O_3$ tolerance between cultivars used today and when the NCLAN studies were done. Since the last review there has been little evidence that crops are becoming more tolerant of $O_3$ (EPA, 2006). For cotton, some newer varieties have been found to have higher yield loss due to $O_3$ compared to older varieties (Olszyk et al. 1993, Grantz and McCool 1992). In a meta-analysis of 53 studies, Morgan et al. (2003) found consistent deleterious effects of $O_3$ exposures on soybean from studies published between 1973 and 2001. Further, early results from the SoyFACE experiment in Illinois indicate a lack of any apparent difference in the $O_3$ tolerance of old and recent cultivars of soybean in a study of 22 soybean varieties (Long et al. 2003).

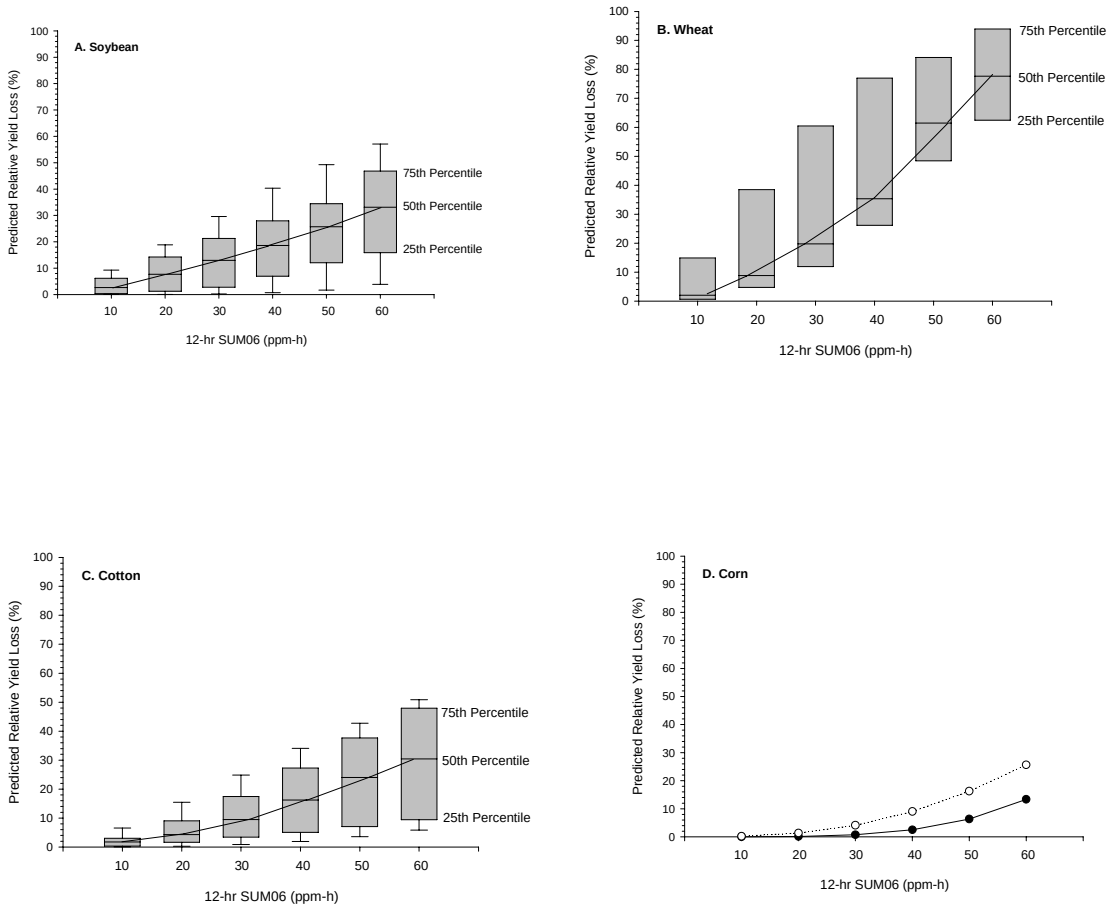
Soybean (Pioneer cultivar) yield loss data from a two year study at the SoyFACE (free air exposure) experimental site in Illinois was recently published (Morgan et al. 2006). This provided staff with an opportunity to test how well the soybean C-R function derived from NCLAN studies predicted observed yield losses at a field FACE site. This type of analysis is useful, given staff's necessary reliance on these functions for the foreseeable future to conduct national exposure assessments. Using the NCLAN median soybean C-R function, staff predicted soybean yield losses that would be expected to occur at the same exposure levels used in the Illinois SoyFACE experiment and compared them to the yield losses actually observed in the study. The 3-month, 12hr SUM06 and W126 values measured at the SoyFACE site before harvest in the ambient and elevated treatments are given in Table 7-2. When ambient hourly $O_3$ concentrations were increased by approximately 20%, measured yields decreased by 15% and 25% in 2002 and 2003, respectively (Morgan et al. 2006). The median NCLAN C-R function for soybean in SUM06 and W126 slightly over-predicted (2-5%) the yield loss of soybean in 2002 (Table 7-2), while it under-predicted (9-13%) the yield losses in 2003. However, researchers reported that in 2003 a spring hail storm significantly damaged the soybean crop and may have contributed to exacerbating the $O_3$ effect on soybean yield. Thus, it might be expected that NCLAN derived C-R functions would underestimate losses with the additional hail storm stress in 2003. Staff believes this limited analysis gives further evidence that the NCLAN C-R functions are able to estimate the relative magnitude of yield loss due to $O_3$ in sensitive crops in the field.

**Figure 7-13. Median crop yield loss from NCLAN crops characterized with the 12-hr SUM06**




Distribution of yield loss predictions from Weibull exposure-response models that relate yield to $O_3$ exposure characterized with the 12-hr SUM06 statistic using data from 31 crop studies from National Crop Loss Assessment Network (NCLAN). Separate regressions were calculated for studies with multiple harvests or cultivars, resulting in a total of 54 individual equations from the 31 NCLAN studies. Each equation was used to calculate the predicted relative yield or biomass loss at 10, 20, 30, 40, 50, and 60 ppm-h, and the distributions of the resulting loss were plotted. The solid line represents the Weibull fit at the 50th percentile. Source: EPA, 1996a; Lee and Hogsett 1995.

**Figure 7-14 (A-D). Median soybean (A), wheat (B), cotton (C) and corn (D) yield loss from NCLAN crops characterized with the 12hr SUM06**




Distribution of yield loss predictions from Weibull exposure-response models that relate yield to $O_3$ exposure characterized with the 12-hr SUM06 statistic using data from 22 soybean, 7 wheat, 9 cotton and 2 corn studies from National Crop Loss Assessment Network (NCLAN). Separate regressions were calculated for studies with multiple harvests or cultivars. Each equation was used to calculate the predicted relative yield loss at a 12-h SUM06 of 10, 20, 30, 40, 50, and 60 ppm-h, and the distributions of the resulting loss were plotted. Source: EPA, 1996a; Lee and Hogsett 1995.

**Table 7-2. Air quality and soybean yield loss data from the SOYFACE experiment in Illinois.**

| Year | Metric | Ambient $O_3$ | Elevated $O_3$ | Pred. PRYL (%) | Meas. PRYL (%) |
|---|---|---|---|---|---|
| 2002 | 12-h SUM06 | 26.37 | 56.87 | 20 | 15 |
| 2003* | 12-h SUM06 | 14.04 | 41.37 | 16 | 25 |
| | | | | | |
| 2002 | 12-h W126 | 25.07 | 51.52 | 17 | 15 |
| 2003* | 12-h W126 | 10.59 | 34.32 | 12 | 25 |

NOTE: Reported are the ambient and elevated 3-month 12-hr SUM06 and W126 exposures measured in the ambient and elevated ozone treatment plots. Predicted Percent Relative Yield Loss (PRYL) was calculated from the median soybean C-R function NCLAN and measured PRYL was the measured yield loss reported by Morgan et al. (2006).

*In 2003 there was hail-storm that severely damaged the soybean plants.

### 7.6.2.3 Considerations for Exposures at Crop Canopy Height

An additional consideration when predicting crop yield and/or tree seedling biomass loss using monitored $O_3$ exposure levels is the potential positive exposure bias associated with the height at which the measurement is taken. Inlets to ambient monitors are typically at heights of 3 to 5 meters, and thus are located in the inner part of the planetary boundary layer (EPA, 2005b). It is well known that within this layer $O_3$ reacts with vegetation and volatile compounds and can create a vertical gradient of decreasing $O_3$ concentration from the inlet height of the monitors to the surface of vegetation. The magnitude of the gradient is determined in large part by the intensity of turbulent mixing in the surface layer. During daytime hours, the vertical $O_3$ gradient is relatively small because turbulent mixing maintains the downward flux of $O_3$. For example, Horvath et al. (1995) calculated a 7% decrease in $O_3$ going from a height of 4 meters down to 0.5 meters above the surface during unstable (or turbulent) conditions in a study over low vegetation in Hungary [See Section AX3.3.2. of the 2006 CD (EPA, 2006)]. This is compared to a 20% decrease during stable conditions which usually occur during the night. The average decrease for all times measured was 10%. The daytime versus nighttime bias is an important distinction considering the assessments outlined below rely heavily on daytime metrics such as the12-hr SUM06 and W126. Thus, staff selected 10% as a daytime downward adjustment factor to apply to hourly monitor-derived exposures (including interpolated values) prior to estimating crop yield and tree seedling biomass loss values. We consider this 10% adjustment at the upper-end of the differences between the monitor height and top of the canopy of low vegetation in the daytime.

Staff recognizes that a 10% adjustment to hourly monitor data across the country is a very simple method to deal with a complicated issue. The exchange of $O_3$ between the atmosphere and vegetation is controlled by complex interactions of meteorological and biological processes. Ideally one should account for the exact height of each monitor, canopy roughness for each crop and the seasonal and diurnal nature of turbulence. This was not possible in our analyses and therefore, there is uncertainty with applying a 10% adjustment is to all monitors and crop canopies. To quantify the effect of the 10% adjustment, staff plans to perform a sensitivity analysis by also calculating crop benefits without an adjustment and/or alternative adjustment levels taking into account future CASAC advice. However, at this time only results with the 10% are available.

The 10% hourly adjustment had a dramatic effect on the predicted 12hr SUM06 and W126 exposures. Reducing each hourly value by 10% over the entire interpolated surface resulted in an average reduction of the 3 month 12-hr SUM06 by 53% and an average reduction

of 42% in the 3month 12hr W126. These dramatic reductions in the SUM06 and W126 exposures are most likely a result of many hourly concentrations measured at the monitor inlets near the cut-off point for SUM06 and the inflection point for W126 (approximately 0.06 ppm). When these "mid-level" hourly $O_3$ values are reduced by 10%, many fall below 0.06 ppm, dramatically decreasing the amount of hourly values counted (SUM06) or contributing to (W126) these metrics.

Given the somewhat lesser impact of the 10% adjustment on exposures using the W126 and the lack of evidence for a biological threshold for effects at 0.06 ppm, staff concluded that the W126 index form would be the more appropriate for conducting the crop yield and tree seedling biomass loss risk assessment. Other information that supports this decision includes: 1) studies that document effects on crops and other sensitive vegetation at concentrations below 0.06 ppm [e.g., exposures as low as a 0.04 ppm 7-hr seasonal average (EPA 2006)]; 2) the high degree of correlation between both forms when describing ambient exposures (see Figure 7-5) and their similar predictive power of NCLAN crop data results in retrospective analyses (Lee et al., 1988; EPA, 1996, 2006); and 3) the use of the 12-hr W126 metric in the crop assessment performed for the 1996 Staff Paper. It should be noted that in some cases, W126 is calculated to be higher than SUM06. Though this is due to the inclusion of concentrations below 0.06 ppm, exposures below 0.04 ppm are not significantly weighted (Lefohn et al. 1988) and so is not significantly influenced by policy relevant background levels (0.02 to 0.035 ppm).

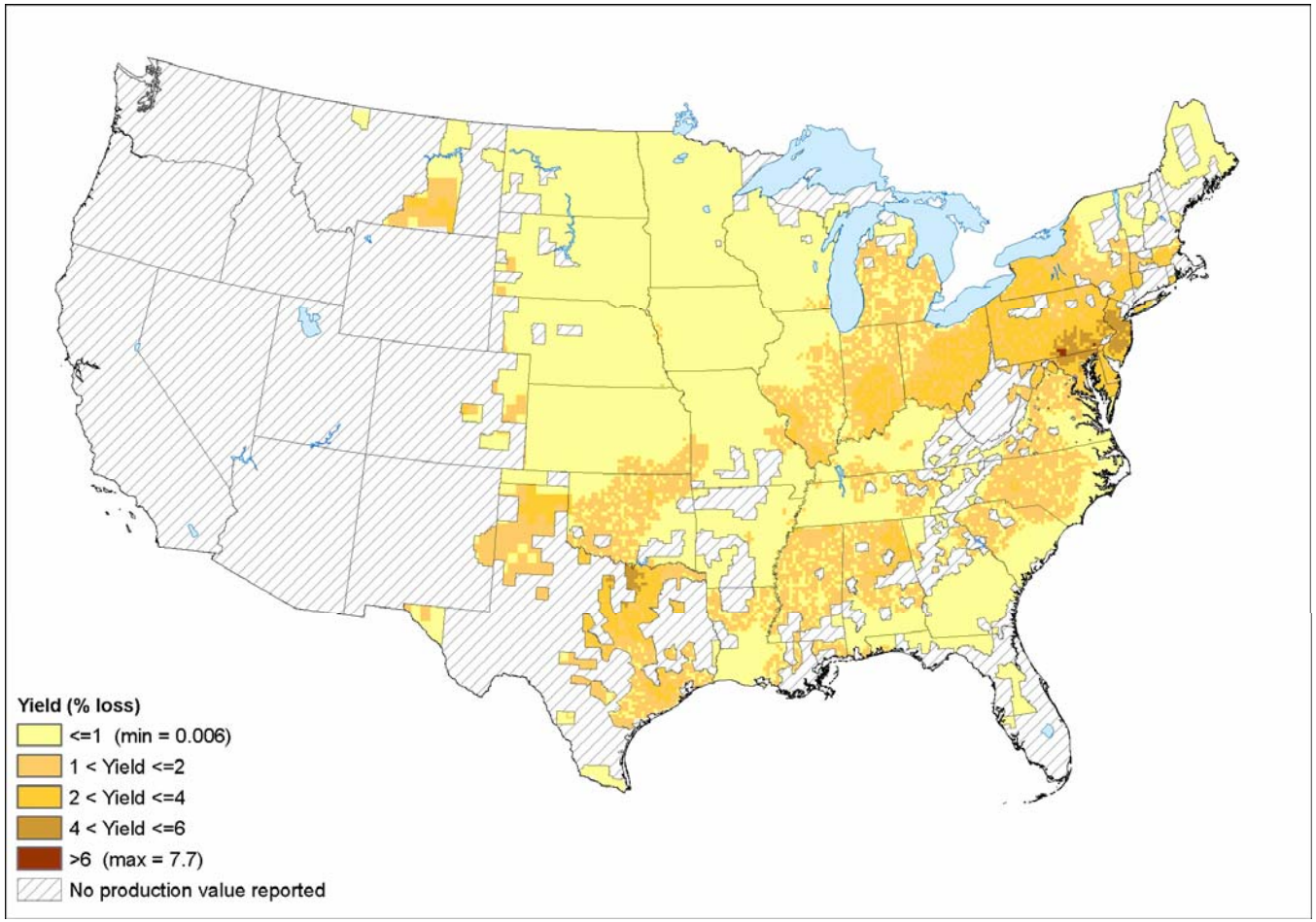
#### 7.6.2.4 Quantifiable Risk of Yield Loss In Select Commodity, Fruit and Vegetable Crops

The 2001 county-level crop planting data were obtained for the 9 commodity crops (corn, soybean, winter wheat, sorghum, cotton, peanuts, kidney bean, potato & lettuce) from USDA-NASS (National Agricultural Statistics Service; http://www.usda.gov/nass). The appropriate NCLAN C-R functions (available in the 12-hr W126 format) were identified for each of the nine commodity crops from the analysis done for the 1996 staff paper (Table 7E-1). The appropriate C-R functions (available in the 7-hr or 12-hr average format) for six fruit and vegetable species (Tomatoes-processing, grapes, onions, rice, cantaloupes, Valencia oranges) were identified from the 1996 California fruit and vegetable analysis (Table 7E-2). Staff combined these C-R functions with the crop planting information and with projections of 2001 $O_3$ exposure based on a 12-hr W126 calculated for the 3 months prior to the harvest date for each commodity crop and the appropriate 7-hr or 12-hr average used for the fruits and vegetables. Calendar periods used for computing W126, 7-hr and 12-hr exposure statistics are based on the harvest date and are done on a state-specific basis. This allows for geographic variation and better reflects actual $O_3$

exposure during the true growing period of the crop so that calculated expected yield change for each crop, fruit and vegetable is specific to where they were planted.

The results of this risk assessment are presented in Appendix 7E in Table 7E-4. This table depicts the relative change in crop yield loss under air quality scenarios of just meeting various alternative standard options under consideration. Maps of predicted yield loss for selected major rops are presented in Appendix 7F. Figure 7-15 shows a map of predicted yield loss for soybean from 2001 using the 10% adjusted "as is" estimated $O_3$ exposure scenario. Soybean is predicted to have the largest yield loss in southwestern Pennsylvania, southern New Jersey and east Texas. However, these areas are not places of high soybean production. In a high soybean producing state, such as Illinois, yield loss was predicted to reach a maximum range of 2-4%. Corn, another major commodity crop, was not predicted to have any loss in 2001. This is because the two corn cultivars studied in NCLAN were not sensitive to $O_3$. In contrast, cotton, a more sensitive crop, had predicted yield loss above 10% in southern California (see Appendix 7F).

**Figure 7-15.** Estimated soybean yield loss based on interpolated 2001 3-month 12-hr W126.



### 7.6.2.5 Economic Benefits Assessment – AGSIM

This section presents results of the quantitative economic benefits analysis associated with attaining alternate standards. Adequate data are currently available to assess economic benefits for 9 of the commodity crops studied in the NCLAN project and 6 fruit and vegetable species. Fruits and vegetables were evaluated in the 1996 review using a separate regional benefits model due to the fact that only regional data was available at the time for those fruits and vegetables. In the current benefits assessment, both commodity crops and fruits and vegetables are evaluated together in the same national scale model. However, because fruit and vegetables are a large part of the U.S. agricultural sector and are especially susceptible to $O_3$ pollution because much of the production is located in the San Joaquin Valley region of California, which has very high levels of $O_3$ exposure (CEPA, 2005), information on fruits and vegetables is also sometimes presented separately. For example, in 2004, cash income from California fruit and nut production was worth more than 9.6 billion dollars and over 7.2 billion dollars for vegetable crops (California Agricultural Resource Directory, 2005, http://www.cdfa.ca.gov/).

The Agriculture Simulation Model (AGSIM) (Taylor, 1994; Taylor et al., 1993) has been utilized recently in many major policy evaluations.[2] AGSIM is an econometric-simulation model used to calculate agricultural benefits of changes in $O_3$ exposure and is based on a large set of statistically estimated demand and supply equations for agricultural commodities produced in the U.S. A number of updates to AGSIM were performed before running this analysis: (1) an update of the commodity data for 2001, (2) incorporation of the most recent version of the official USDA baseline model, (3) an econometric component added to AGSIM to compute total farm program payments for different levels of farm program parameters, and (4) farm payment program component added to the economic surplus module. The AGSIM model was run to provide benefit estimates for nine major commodity crops (soybeans, corn, winter wheat, cotton, peanuts, sorghum, potato, lettuce, kidney bean) and six fruits and vegetables mainly grown in California (tomatoes-processing, grapes, onions, rice, cantaloupes, Valencia oranges). As described earlier, hourly $O_3$ exposures were adjusted downward by 10% before calculating the W126, 7-h or 12-h exposure metrics.

Percent relative yield losses (PYRL) calculated as the change in yield occurring between just meeting 'as is' air quality and various alternative standard scenarios were the relevant input

[2] For example, AGSIM© has been used in EPA's prospective study of the benefits derived from the Clean Air Act Amendments of 1990 required by section 812-B of the Clean Air Act, non-road land-based diesel engine rule, and proposed Clear Skies legislation.

parameters to the AGSIM model. The AGSIM model predicted acreage, production, supply and price parameters for each crop for each year, as well as yield per harvested acre, based on calculated new yield-per-planted acre values, as well as on lagged price data, ending stocks from the previous year and other variables. From these results and demand relationships embedded in the model, AGSIM calculated the utilization of each crop (i.e., exports, feed use, other domestic use, etc), as well as change in consumer surplus, net crop income, deficiency payments and other government support payments. Total undiscounted economic surplus was calculated as the crop income plus consumer surplus. The AGSIM model was run for 14 years for each scenario in order for the model parameters to adjust to the initial change in yield. Annual changes in total undiscounted economic surplus were calculated for each of the 14 years. The annual averages for the 14 years are reported in Table 7-3.

Table 7-3 presents the results from applying the AGSIM model to determine commodity crop benefits based on meeting the level of the current 8-h standard and three alternative standards. The 0.070 4$^{th}$ highest maximum average $O_3$ scenario was chosen as a possible alternative primary standard level. Alternative secondary standards are expressed in maximum 3 month 12-h SUM06. For the SUM06 index, the level 25 ppm-hr is the level proposed in the 1996 review and is associated with a yield loss prevention of about 10% in 50% of crops studied in the NCLAN experiments. The other 12-h SUM06 of 15 ppm-hr is associated with a yield loss prevention of about 10% in 75% of crops studied in the NCLAN experiments. Staff plans to also add two equivalent levels of a 12-h W126 (21 and 13 ppm-hrs) for the final $O_3$ Staff Paper.

In summary, this analysis estimates a range of benefits using both the available minimum and maximum yield loss equations for each crop. Results are presented in annual 2001 dollars for the commodity crops, fruits and vegetables and total agricultural sector. Overall, benefits from the fruit and vegetable species in this analysis accounted for a relatively large portion of the total agricultural benefits compared with the commodity crops. This is likely because many of the fruits and vegetables are grown in parts of California with high $O_3$ exposures and any rolling back of air quality produced greater changes in $O_3$ levels, resulting in higher changes in yield. All of the alternative standards analyzed showed positive incremental benefits greater than those associated with just meeting the level of the current 8-hr standard. Meeting the SUM06 of 25 proposed in the last review produced an additional incremental benefit of $102-$134 million for the total agricultural sector. Of all the scenarios, SUM06 of 15 ppm-hrs and 0.07 4$^{th}$ highest maximum 8 hour average had the largest economic benefit. Meeting the alternative SUM06 of 15 produced incremental benefits of $275-$436 million for the total agricultural sector. It is important to note that these results represent a macro-analysis of the U.S. agricultural economy. Farmers in areas that have higher $O_3$ levels are more adversely affected than farmers that are in areas with low $O_3$ levels. These important effects are difficult to quantify in a macro-analysis.

The current CD reports very few studies have been conducted on the economic effect of $O_3$ on U.S. agriculture. A study by Murphy et al. (1999) confirmed the general magnitude of economic effects reported by the two key studies performed a decade earlier (Adams, 1986; Adams et al., 1985). Specifically, Murphy et al. (1999) evaluated benefits to eight major crops associated with several scenarios concerning the reduction or elimination of $O_3$ precursor emissions from motor vehicles in the United States. Their analysis reported a $2.8 to 5.8 billion (1990 dollars) benefit from complete elimination of $O_3$ exposures from all sources, i.e., ambient $O_3$ reduced to a background level assumed to be 0.025 to 0.027 ppm. In comparison, AGSIM calculates up to $800 million (2001 dollars) in economic benefit when $O_3$ levels are reduced to near background. These analyses are quite difficult to compare for many reasons: different economic models, different air quality years, how farm payment programs are counted, dollar value unadjusted for inflation, etc. However, it is apparent that the benefits for this assessment are substantially lower than in past analyses. Staff suspects a major factor is the 10% adjustment of the hourly $O_3$ data measured at monitoring height and the use of different economic models. For the final draft staff paper, we will present economic benefits without the 10% adjustment factor. Also, 2001 was a moderate $O_3$ year and it would be expected that benefits would be notably greater if this analysis was run for a higher $O_3$ year like 2002. Staff are considering expanding the analysis to include another year if air-quality for comparison.

It is important to restate and summarize the uncertainties associated with the results of the AGSIM analysis presented above. Uncertainties are introduced by: (1) the extrapolation of limited air quality monitoring data to national air quality distributions; (2) the application of exposure-response functions from open-top chamber studies extrapolated to 2001 ambient air exposure patterns and crop production; (3) the use of a quadratic rollback methodology to project the "just attain" air quality distributions without a direct link to an emissions control strategy; and (4) the inherent uncertainties associated with use of an economic model such as AGSIM. It is also important to note that the range of results from this analysis represents impacts associated only with available NCLAN experimental data and a limited number of fruits and vegetable studies. Not all crops have been subjected to exposure-response experiments and effects on those crops would be missed. Despite the amount of uncertainty, this analysis provides useful insights for comparing the relative benefits obtained as a result of attaining alternative regulatory scenarios.

**Table 7-3. Agricultural model results**

| Average Annual Changes in Total Undiscounted Economic Surplus for the Current 8hr Standard and Alternative Standards (millions $ 2001) | | | | | | |
|---|---|---|---|---|---|---|
| **Standard** | **Commodity Crops** | | **Fruits & Vegetables** | | **Total Ag.** | |
| | Minimum | Maximum | Minimum | Maximum | Minimum | Maximum |
| 0.08 4th highest | $7 | $22 | $63 | $74 | $70 | $96 |
| 0.07 4th highest | $46 | $199 | $310 | $365 | $356 | $564 |
| SUM06 = 25 | $14 | $50 | $158 | $180 | $172 | $230 |
| SUM06 = 15 | $56 | $195 | $289 | $337 | $345 | $532 |

### 7.6.3 Tree Risk Assessments

In the last review (EPA 1996b), analyses of the effects of $O_3$ on trees were limited to 11 tree species for which C-R functions for the seedling growth stage had been developed from OTC studies conducted by NHEERL-WED. Since the last review, only a few studies have developed C-R functions for additional tree seedling species (EPA, 2006). Section 7.6.3.1 describes how staff updated the tree seedling risk analysis performed in the last review. Section 7.6.3.2. discusses the approach for assessing $O_3$ effects on vegetation in natural settings using visible foliar injury data. Section 7.6.3.3 discusses the analysis and results for modeling $O_3$ impacts on mature trees in the Eastern and Western U.S. The tree and/or forest analyses outlined below will enable staff to begin to assess important long-term effects of various secondary standard levels on forest ecosystem health and services.

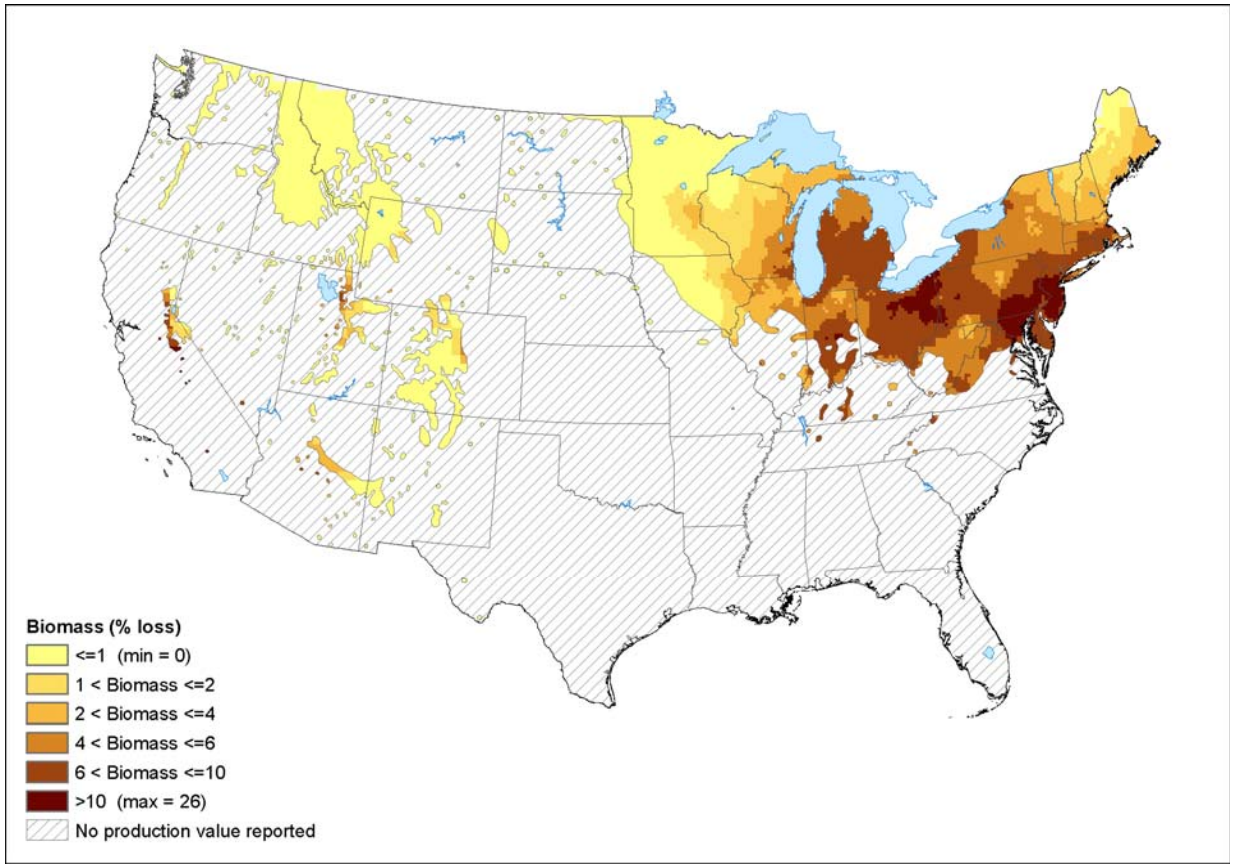
#### 7.6.3.1 Quantifiable Risk of Biomass Loss In Select Tree Seedling Species

In a process similar to that used for crops above (7.6.2.4), C-R functions for biomass loss for a subset of seedling tree species taken from the CD (Table 7E-3) and information on tree growing regions derived from the U.S. Department of Agriculture's Atlas of United States Trees (Little, 1971) were combined with projections of air quality based on 2001 POES, to produce estimated biomass loss for each of the seedling tree species individually. The results of this risk assessment are presented in Table 7E-5 in Appendix 7E. In addition, maps depicting these results for selected tree seedling species are found in Appendix 7G

Figure 7-16 shows an example of the aspen tree species. The aspen map shows significant variability in projected seedling biomass loss across its range for 2001. Aspen seedling biomass loss is projected to be greater than 6% over much of its geographic range, though it can reach as high as 26% in some areas. In Appendix 7G there are additional maps of Ponderosa pine and black cherry along with maps of seedling biomass gain when various standards levels are met. These biomass gain maps indicate that substantial improvements in seedling biomass growth may be achieved when the alternative standards are met, especially the 0.07ppm 4$^{th}$ highest max. and SUM06 of 15ppm-hr. It should be noted that the species mapped are generally sensitive and they are also important tree species in ecosystems across vast areas of the U.S. Though each map shows the geographical range for a species, it does not indicate that an individual of that species will be found at every point within its range. It should also be recognized that the production of these maps incorporates several separate sources of uncertainty, beginning with the C-R functions produced for seedlings in OTCs to the uncertainties associated with the inputs used to generate the POES. Furthermore, percent

biomass loss in tree seedlings is not intended to provide any information on expected biomass loss in mature trees of the same species (see section 7.6.3.3 for modeling of mature tree growth). Studies indicate that mature trees can be more or less sensitive than seedlings depending on the species. Further, seedling biomass loss cannot be considered comparable to percent yield loss in agricultural crops. This is because a small biomass loss per year in a perennial tree species, if compounded over multiple years of exposure could have a large effect on the growth of that tree, while yield loss in annual crops is only affected by the $O_3$ exposure for that year. In summary, this analysis indicates that current air quality can produce significant seedling biomass loss in the areas which those trees grow. Meeting the level of alternative standards is expected to improve biomass growth in the seedlings analyzed.

**Figure 7-16.** Estimated aspen seedling annual biomass loss based on interpolated 2001 maximum 3-month 12-hr W126. This map indicates the geographic range for aspen, but it does not necessarily indicate that aspen will be found at every point within its range.



### 7.6.3.2 Foliar Injury Incidence

The use of sensitive plants as biological indicators to detect phytotoxic levels of $O_3$ is a longstanding and effective methodology (Chappelka and Samuelson, 1998; Manning and Krupa, 1992). Some well defined bioindicators for ambient $O_3$ include blackberry, black cherry, green ash, milkweed, quaking aspen, sassafras, yellow poplar, and white ash. Each of these bioindicators exhibits typical $O_3$ injury symptoms when exposed under appropriate conditions. These symptoms are considered diagnostic as they have been verified in exposure-response studies under experimental conditions. Typical visible injury symptoms on broad leaved plants include: 1) acute exposure (pigmented lesions (stippling), flecking, surface bleaching, and/or bifacial necrosis); 2) chronic exposure (pigmentation (bronzing), chlorosis or premature senescence). Typical visible injury symptoms for conifers include: 1) chlorotic banding or tipburn (acute exposure); 2) flecking or chlorotic mottling, premature senescence of needles (chronic exposure). Though common patterns of injury develop within a species, these foliar lesions can vary considerably between and within taxonomic groups. Furthermore, the degree and extent of visible foliar injury development varies from year to year and site to site, even among co-members of a population exposed to similar $O_3$ levels, due to the influence of co-occurring environmental and genetic factors. It is important to note that the foliar injury occurs only when sensitive plants are exposed to elevated $O_3$ concentrations in a predisposing environment. Thus great care must be taken when assessing the response of bioindicators to ambient $O_3$ (Flagler, 1998).

The Unites States Forest Service (USFS) through the Forest Health Monitoring Program (FHM) (1990 - 2001) and currently the Forest Inventory and Analysis (FIA) Program has been collecting data regarding the incidence and severity of visible foliar injury on a variety of $O_3$ sensitive plant species throughout the U.S. (Coulston et al. 2003, 2004; Smith et al. 2003). FIA biomonitoring sites are located throughout the country and analysis of foliar injury within these sites follows a set of established protocols (for more details see http://fiaozone.net/). Since the conclusion of the 1996 NAAQS review, the FIA monitoring program network and database has continued to expand. The visible foliar injury indicator has been identified as a means to track stress trends in the nation's natural plant communities as a result of changes in $O_3$ air quality in EPA's most recent Report on the Environment (EPA, 2003; http://www.epa.gov/indicators/roe). EPA staff also considers it important to assess the degree to which $O_3$-induced visible foliar injury observed *in situ*, corresponds with monitored $O_3$ air quality in recent years. In a collaborative effort with FIA staff, EPA staff conducted an analysis to compare the incidence of foliar injury at different levels of air quality (e.g., the current

standard and alternative levels under consideration) by county throughout the US. This analysis potentially provides a measure of the effectiveness and degree of protection provided by the current form/level of the secondary standard for this welfare effect.

The major confounding effect for $O_3$ induced foliar injury is the amount of soil moisture (local rainfall) available to a plant during the year that the foliar injury is being assessed. This is because lack of soil moisture decreases stomatal conductance of plants and therefore, limits the amount of $O_3$ entering the leaf that can cause injury. Many researchers have shown that dry periods in local areas tend to decrease the incidence and severity of foliar injury caused by $O_3$ in plants measured by the USFS (Smith et al. 2002). Therefore, the incidence of foliar injury is not always higher in years with higher $O_3$, especially when there is drought in areas where foliar injury is assessed.

Due to a congressional requirement that the US Forest Service protect landowner privacy, FIA cannot publicize the exact locations of their biosites. As a result, all data in our analysis are reported on a county-level. County-level foliar injury data were available for the years 2001 to 2004 for all areas of the U.S. except the Mountain West region. However, according to the FIA staff, no $O_3$ injury was reported at any site in that region. Figure 7-17, shows that the incidence of foliar injury in 2001 was widespread across the eastern and western U.S. The 2001 data are indicative of the incidence of foliar injury in the years 2001 to 2004. (see appendix 7H for 2002). This indicates that $O_3$ levels are above phytotoxic levels sufficient to cause adverse effects in natural plant populations in many areas. It is important to note that direct links between $O_3$ induced visible foliar injury symptoms and other adverse effects (e.g., biomass loss), are not always found. However, in a few cases, visible foliar symptoms have been correlated with decreased vegetative growth (Karnosky et al., 1996; Peterson et al., 1987; Somers et al., 1998) and with impaired reproductive function (Black et al., 2000; Chappelka, 2002). Though visible injury is a valuable indicator of the presence of phytotoxic concentrations of $O_3$ in ambient air it is not always reliable indicator of damage or other injury endpoints. The lack of visible injury does not indicate a lack of phytotoxic concentrations of $O_3$ nor a lack of non-visible $O_3$ effects.

In an attempt to assess how meeting various $O_3$ standard levels affected the incidence of foliar injury, staff matched up county-level $O_3$ monitoring data with counties that had US Forest Service biosites. In counties containing multiple $O_3$ monitors, staff used the monitor measuring the highest $O_3$ to characterize county air quality. Because visible foliar injury symptoms reflect the $O_3$ stress of the year in which they are observed, staff looked at yearly snapshots of county-level air quality data. Between 235 and 286 FIA biomonitoring sites have been surveyed in counties containing an $O_3$ monitor for the years 2001 – 2004, respectively (see Table 7-4). However, because the specific locations of the USFS biosite are not publicly available, staff was

unable to determine how close the biosites within each county are to the $O_3$ monitor selected to represent that county. Air quality was evaluated in terms of both the current 8 hr. average and 12-h SUM06 forms, using a number of different cutpoints. Table 7-4 shows the percentage and number of counties with and without visible foliar injury at or below various standard levels for the 2001-2004 period. Because the FIA program reorganized the locations of biosites in 2002 and expanded the number of biosites in 2003 and 2004, the total number of counties containing both an $O_3$ monitor and an FIA biosite changed each year and it is difficult to interpret changes in the number of counties in different categories between years. Therefore, staff found it more informative to present results in terms of percent of total counties with or without injury under different levels of air quality. Firstly, this table illustrates that foliar injury is occurring in areas that are attaining the current 8-h standard. The table also illustrates that the secondary standard option of a SUM06 of 25 ppm-hrs proposed in 1996 did not appear to offer more protection from foliar injury than the current 8 hr. standard form. By comparison, the SUM06 of 15 ppm-hrs and the 8 hour average of 0.074 provided more protection across all years than either the 0.084 8-h or SUM06 of 25 standards. At the 0.084, 8 hr. average, the percent of counties showing injury ranged from 21% to 39%. Under a SUM06 of 25 ppm-hrs., percent of counties with injury increased slightly, ranging from 26% to 49%. For the two lower air quality alternatives (0.074 ppm 8 hr avg. and SUM06 of 15 ppm-hrs), values ranged from 12% injured to 30% and 35%, respectively.

In summary, this analysis indicates that incidence of $O_3$ induced foliar injury is widespread across the eastern and western U.S. Foliar injury was observed in counties that are attaining the current level of the 8-h standard and secondary standard option of a SUM06 of 25 ppm-hrs proposed in 1996. Lower standards in the 8-hr and SUM06 forms would be expected to have lower incidences of foliar injury. However, the level of protection would depend heavily on local environmental variable such as soil moisture. Finally, in the consensus workshop on held on the secondary $O_3$ standard, researchers were in agreement that a 3 month 12-h SUM06 value of 8 to 12 ppm-h should be considered for protection from foliar injury to natural ecosystems (Heck and Cowling, 1997). The analysis above supports this recommendation that these levels would reduce the incidence of foliar injury to natural ecosystems.

**Figure 7-17. 2001 County-level incidence of visible foliar injury in the eastern and western U.S. as measured by the US Forest Service FIA program.**

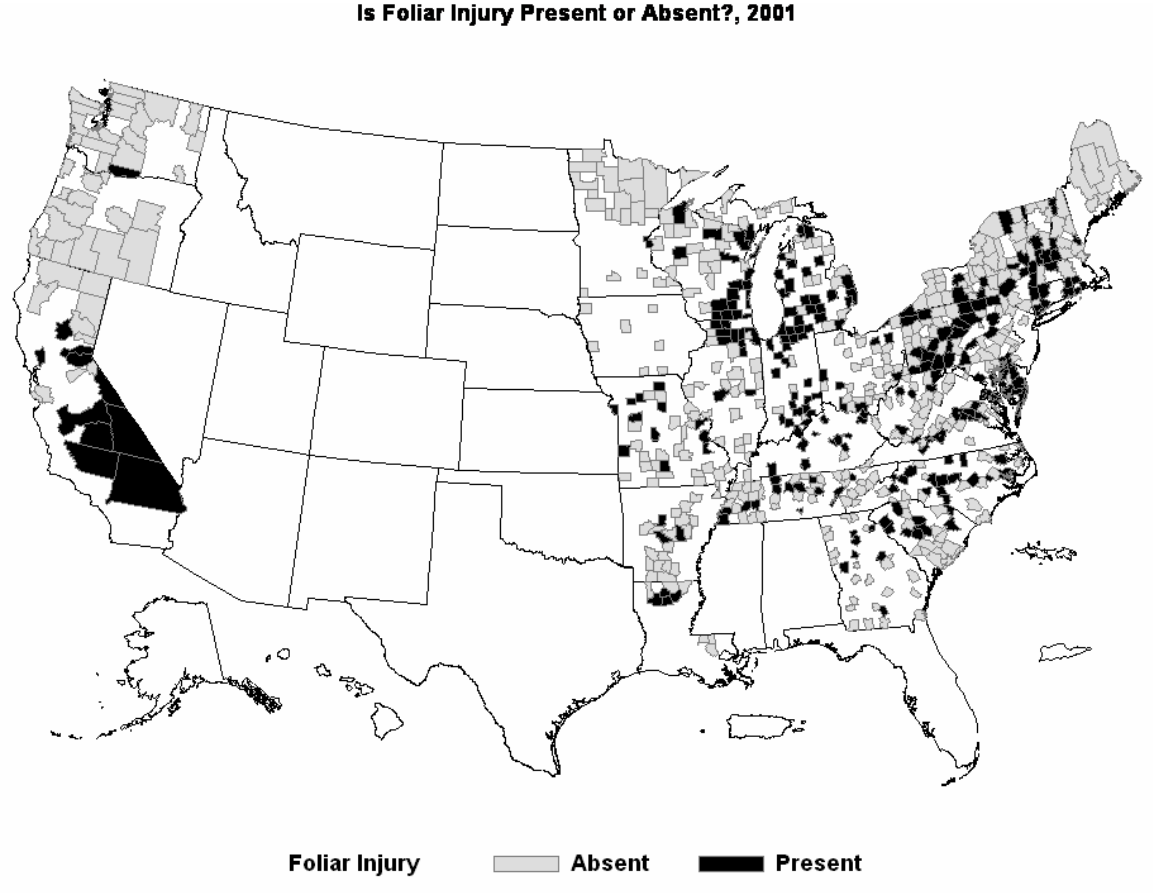


**Table 7-4. Percentage and number of counties with visible foliar injury and without injury (none) below various standard levels for the years 2001-2004. Each county had an $O_3$ monitor and a USDA forest service FIA plot tracking visible foliar injury due to $O_3$ exposure.**

| Year | | ≤0.084* | ≤0.074* | ≤SUM06 25 | ≤SUM06 15 | Total Counties with $O_3$ monitoring & FIA site |
|---|---|---|---|---|---|---|
| **2001** | Tot. counties | 99 | 36 | 134 | 48 | 235 |
| | % injured | 39% (39) | 25% (9) | 49% (65) | 23% (11) | |
| | % not injured | 61% (60) | 75% (27) | 51% (69) | 77% (37) | |
| **2002** | Tot. counties | 89 | 43 | 129 | 59 | 270 |
| | % injured | 21% (19) | 12% (5) | 26% (33) | 12% (7) | |
| | % not injured | 79% (70) | 88% (38) | 74% (96) | 88% (52) | |
| **2003** | Tot. counties | 185 | 61 | 236 | 135 | 285 |
| | % injured | 28% (52) | 11% (7) | 34% (81) | 25% (34) | |
| | % not injured | 72% (133) | 89% (54) | 66% (155) | 75% (101) | |
| **2004** | Tot. counties | 260 | 159 | 249 | 220 | 286 |
| | % injured | 35% (91) | 30% (47) | 37% (91) | 35% (76) | |
| | % not injured | 65% (169) | 70% (112) | 63% (158) | 65% (144) | |

*These standard levels represent the annual 4$^{th}$ highest 8hr max average

#### 7.6.3.3 Modeled Mature Tree Growth Response: Eastern and Western Species Case Studies

In the 1996 $O_3$ Staff Paper, evaluations of $O_3$ impacts on tree growth were limited to the seedling growth stage. At that time, robust C-R functions were available only for 11 tree seedlings developed from OTC data. Few studies had been done comparing seedling sensitivity to that of a mature tree of the same species. Recent experiments using the FACE methodology have been able to expose 3 tree species to $O_3$ beyond the seedling growth stage. However, this methodology has not yielded C-R functions at this time, due to the limited number of exposure regimes used. Findings from FACE publications, however, do show decreased biomass growth under elevated $O_3$ in trees beyond the seedling stage (King et al., 2005). In order to better characterize the potential $O_3$ effects on mature tree growth, staff used a tree growth model (TREGRO) as a tool to evaluate the effect of changing $O_3$ air quality scenarios from just meeting alternative $O_3$ standards on the growth of mature trees.

TREGRO is a process-based, individual tree growth simulation model (Weinstein et al, 1990) and has been used to evaluate the effects of a variety of $O_3$ scenarios and linked with concurrent climate data to account for ozone and climate/meteorology interactions on several species of trees in different regions of the U.S. (Tingey et al., 2001; Weinstein et al., 1991; Retzlaff et al., 2000; Laurence et al., 1993; Laurence et al., 2001; Weinstein et al., 2005). The model provides an analytical framework that accounts for the nonlinear relationship between $O_3$ exposure and response. The interactions between ozone exposure, precipitation and temperature are integrated as they affect vegetation thus providing an internal consistency for comparing effects in trees under different exposure scenarios and climatic conditions (see the draft Environmental Assessment TSD for more details on TREGRO). An earlier assessment of the effectiveness of national air quality standards, in place since the early 1970s, took advantage of 40 years of air quality and climate data for the Crestline site in the San Bernardino Mountains of California to simulate Ponderosa pine growth over time with the improving air quality using TREGRO (Tingey et al., 2004).

Staff collaborated with the EPA NHEERL-WED lab to use the TREGRO model to assess growth of ponderosa pine (*Pinus ponderosa*) in the San Bernardino Mountains of California (Crestline) and the growth of yellow poplar (*Liriodendron tulipifera*) and red maple (*Acer rubrum*) in the Appalachian mountains of Virginia and North Carolina, Shenandoah National Park (Big Meadows) and Linville Gorge Wilderness Area (Cranberry), respectively. Total tree growth associated with 'as is' air quality, and air quality adjusted to just meet alternative $O_3$ standards was assessed (Table 7-5).

Ponderosa pine is one of the most widely distributed pines in western North America, a major source of timber, important as wildlife habitat, and valued for aesthetics (Burns and Honkala, 1990). Red maple is one of the most abundant species in the eastern U.S. and is important for its brilliant fall foliage and highly desirable wildlife browse food (Burns and Honkala, 1990). Yellow poplar is an abundant species in the southern Appalachian forest. It is 10% of the cove hardwood stands in southern Appalachians which are widely viewed as some of the country's most treasured forests because the protected, rich, moist set of conditions permit trees to grow the largest in the eastern U.S. The wood has high commercial value because of its versatility and as a substitute for increasingly scarce softwoods in furniture and framing construction. Yellow poplar is also valued as a honey tree, a source of wildlife food, and a shade tree for large areas (Burns and Honkala, 1990).

At the western site, staff and NHEERL-WED scientists used Crestline, CA air quality and climate data from the years 1995 to 2000 to run TREGRO, while at the eastern sites, staff used Big Meadows, VA and Cranberry, NC air quality and climate data from the years 1993 to 1995. These three years were the only years in the east with readily available $O_3$ and climate data that could be used in TREGRO. The years chosen to run the TREGRO at each site appear to have annual $O_3$ exposures typical of the last 15 years (Figure 7-18). Air quality from each site and year was adjusted using the quadratic roll-back method to 'just meet' the current 8-hr secondary standard ($4^{th}$ highest maximum average = 0.08 ppm), a 12hr SUM06 of 25 ppm-hr, and $1^{st}$ highest max average of 0.07 ppm. Staff also tested the $4^{th}$ highest 0.07 ppm level on the Cranberry and Big Meadows sites. For the ponderosa pine at Crestline, TREGRO was run for "as is" and "just meet" in four 3 year increments to increase the accountability of climate variability and the annual average biomass determined from these 4 simulations to yield an annual average biomass change over the 6 years of ozone exposure. For the yellow poplar and red maple, two sites (Big Meadows, VA and Cranberry, NC) were chosen to run TREGRO to increase the variability in climate since there were only 3 years of data available at each site. The differences between growth under "just meet" air quality and "as is" air quality were compared to evaluate the effectiveness of the current secondary standard and alternative standards in protecting these three tree species.

Results of the TREGRO simulations are presented in Table 7-5. Clearly, the greatest simulated growth benefits in the scenarios are seen in ponderosa pine at the Crestline site in California. As shown in Figure 7-18, $O_3$ levels are much higher at Crestline than the sites in the eastern US. Meeting the level of the current standard was simulated to result in an 8.63% increase annual growth and a SUM06 of 25 is expected

increase growth 10.33% in ponderosa pine. In the eastern sites (Cranberry and Big Meadows) $O_3$ levels are much lower (Figure 7-18) and had less of an affect on the simulated growth of red maple and yellow poplar. In fact, the Cranberry, NC site was below level of the current 8 hr standard and the SUM06 of 25 scenarios and therefore, no benefits were calculated for those levels. At Big Meadows, VA, the current 8hr standard and SUM06 scenarios resulted in relatively small growth increases for yellow poplar (0.03-0.07%) and red maple (0.34-0.41%). This was mostly because the Big Meadows site was close to meeting those levels in 1993-1995 (Figure 7-18). Red maple was simulated to have a similar response (~2%) to the 0.07 ppm 1$^{st}$ and 4$^{th}$ highest 8hr max. in Big Meadows and Cranberry. For the same scenarios, yellow poplar had a very different response to $O_3$ reduction at Big Meadows (0.34-0.38%) compared to Cranberry (3.91-6.54%). The climate at Cranberry is much more ideal for yellow poplar than under the cool temperatures of Big Meadows, making it much more likely that its growth would be suppressed by ozone and that, conversely, it would respond much more to ozone reductions at Cranberry. Red maple has a much larger geographical distribution, so that the temperature differences between Big Meadows and Cranberry are less likely to affect the growth response. This phenomenon was reflected in the simulations.

The effect of $O_3$ on an individual tree may be quite different than the predicted effect on a forest stand after many years. Some researchers have used the ZELIG model, a forest stand simulator, to predict stand growth using growth rates of individual species from TREGRO scenarios (Laurence et al., 2001; Weinstein et al., 2005). Small changes in growth of an individual over a short period of time have sometimes been simulated to have large changes in basal area as it develops over a long time period. For example, Weinstein et al. (2005) found a simulated $O_3$ effect on an individual ponderosa pine at Crestline to reduce growth by 6.7% in three years under normal precipitation, yet stand basal area was calculated to be reduced by 29% after 100 years. Similarly, Laurence et al. (2001) found individual yellow poplar in NC with an $O_3$ induced growth loss of 1.7% which was then calculated to reduce basal area by 14% after 100 years. This suggests that small effects on individual tree growth may result in substantial effects on forest stand growth after many years.

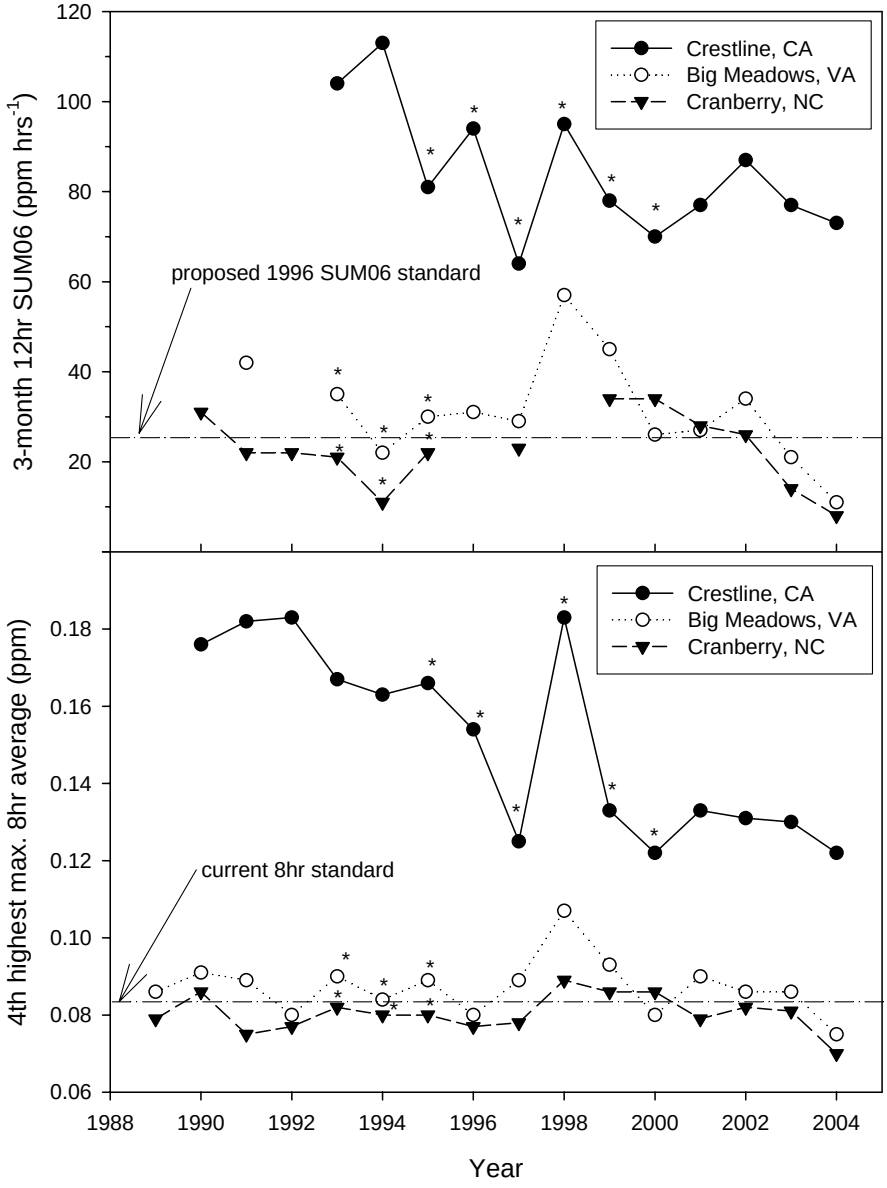
**Table 7-5. Relative increase in total annual tree biomass growth, simulated with the TREGRO model, if the level current and alternative standards are met.**

| Species | red maple | red maple | yellow poplar | yellow poplar | ponderosa pine |
|---|---|---|---|---|---|
| Site | Big Meadows, VA (1993-1995) | Cranberry, NC (1993-1995) | Big Meadows, VA (1993-1995) | Cranberry, NC (1993-1995) | Crestline, CA (1995-2000) |
| 0.08 4th highest | 0.41% | *no rollback*[1] | 0.03% | *no rollback*[1] | 8.63% |
| 0.07 1st highest | 2.71% | 2.31% | 0.38% | 6.54% | 10.81% |
| 0.07 4th highest | 2.24% | 1.38% | 0.34% | 3.91% | *n.a.*[2] |
| SUM06 = 25 | 0.34% | *no rollback*[1] | 0.07% | *no rollback*[1] | 10.33% |
| SUM06 = 15 | 4.49% | 2.99% | 0.60% | 8.26% | *n.a.*[2] |

[1]A rollback was not necessary for the Cranberry site for the 0.08 4th highest and SUM06 = 25 scenarios since air quality was at or below the levels of those scenarios.

[2] TREGRO was not run for ponderosa pine for the 0.07 4th highest scenario.

**Figure 7-18. Historical $O_3$ data as measured in the 3-month 12-hr SUM06 and 4th highest 8hr metrics for the 3 sites used to run the TREGRO model. For Big Meadows, VA and Cranberry, NC, climate and $O_3$ data from 1993 to 1995 was used to run TREGRO and for Crestline, CA, 1995 to 2000 was used. Missing data points in the top panel indicate incomplete data to calculate a SUM06. * indicates which years of data were used in the TREGRO model at each site.**



## 7.7 QUALITATIVE RISK: ECOSYSTEM CONDITION, FUNCTION AND SERVICES

Ecosystems are comprised of complex assemblages of organisms that provide distinct ecological attributes, many of which may be adversely affected by ozone (EPA, 2006). A new effort has been initiated within the Agency to identify indicators of ecological condition whose responses can be clearly linked to changes in air quality and be used to track improvements in environmental protection attributable to environmental program actions/implementation. Moreover, a recent critique of the secondary NAAQS review process published in the report by the National Academy of Sciences on Air Quality Management in the United States (NRC, 2004) stated that "EPA's current practice for setting secondary standards for most criteria pollutants does not appear to be sufficiently protective of sensitive crops and ecosystems . . .." This report made several specific recommendations for improving the secondary NAAQS process and concluded that "There is growing evidence that tighter standards to protect sensitive ecosystems in the United States are needed . . ..." However, the vast majority of information regarding the effects of ozone involves the sensitivity of individual species. Therefore, this section lays out some examples of our current understanding of how $O_3$ may be affecting ecosystems and identifies areas of research needed to address this issue.

An ecosystem is defined as comprising all of the organisms in a given area interacting with the physical environment, so that a flow of energy leads to a clearly defined trophic structure, biotic diversity, and cycling of materials between living and nonliving parts (Odum, 1963). Individuals within a species and populations of species are the building blocks from which communities and ecosystems are constructed. Classes of natural ecosystems, e.g., tundra, wetland, deciduous forest, and conifer forest, are distinguished by their dominant vegetation forms. Ecosystem boundaries are delineated when an integral unit is formed by their physical and biological parts. Defined pathways for material transport and cycling and for the flow of energy are contained within a given integrated unit.

Each level of organization within an ecosystem has functional and structural characteristics. At the ecosystem level, functional characteristics include, but are not limited to, energy flow; nutrient, hydrologic, and biogeochemical cycling; and maintenance of food chains. The sum of the functions carried out by ecosystem components provides many benefits to humankind, as in the case of forest ecosystems (Smith, 1992). Some of these benefits include food, fiber production, aesthetics, genetic diversity, and energy exchange.

A conceptual framework for discussing the effects of $O_3$ on ecosystems was developed by the EPA Science Advisory Board (Young and Sanzone, 2002). Their six essential ecological

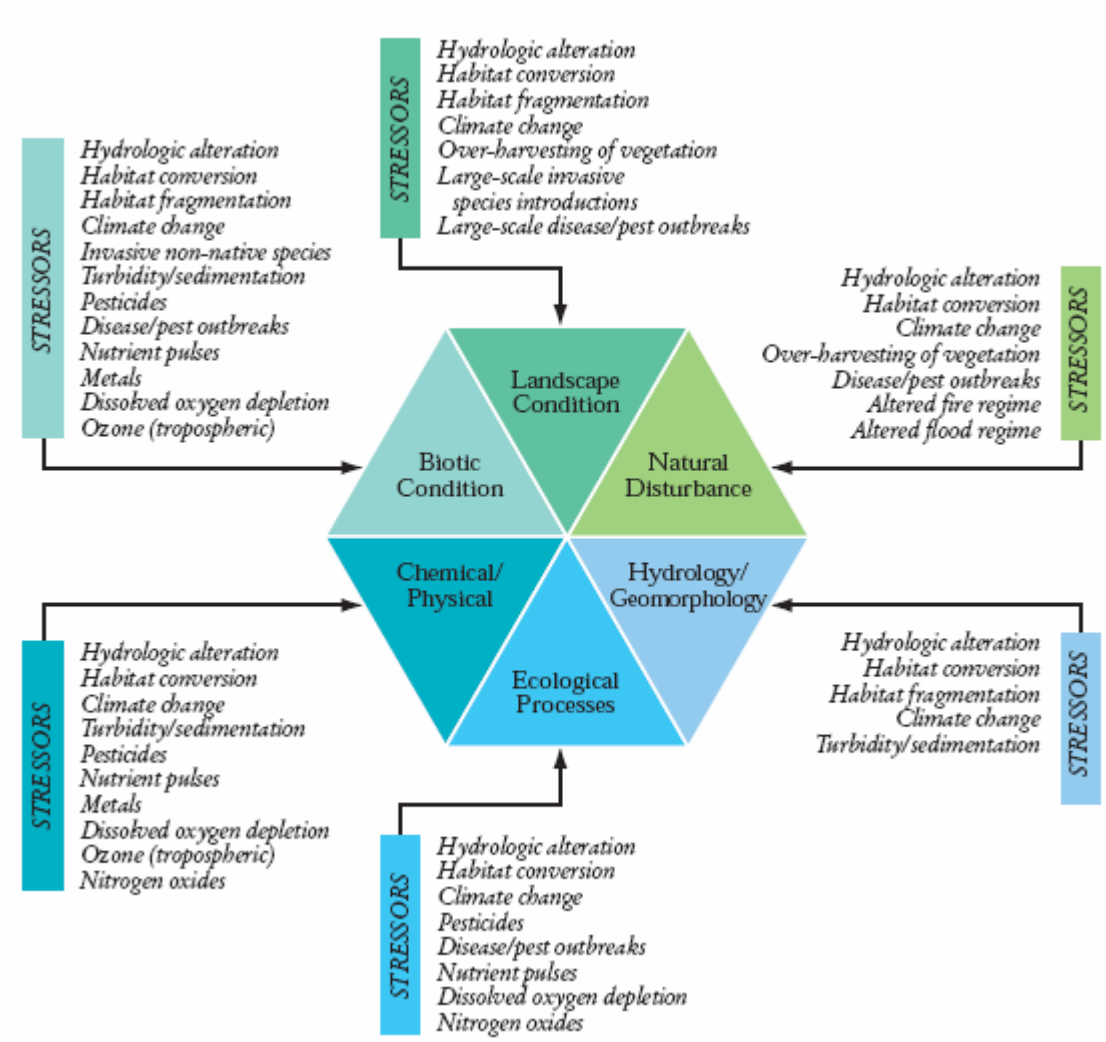
attributes (EEAs) include landscape condition, biotic condition, organism condition, ecological processes, hydrological and geomorphological processes, and natural disturbance regimes. Figure 7-19 outlines the how common anthropogenic stressors, including tropospheric $O_3$, might affect the essential ecological attributes outlined by the SAB.

There is evidence that tropospheric $O_3$ is an important stressor of ecosystems, with documented impacts on the biotic condition, ecological processes, and chemical/physical nature of natural ecosystems (EPA, 2006). Most of the effects on ecosystems must be inferred from $O_3$ exposure to individual plants and processes that are scaled up through the ecosystem affecting processes such as energy and material flow, inter- and intraspecies competition, and net primary productivity (NPP). Thus, effects on individual keystone species and their associated microflora and fauna, which have been shown experimentally, may cascade through the ecosystem to the landscape level. By affecting water balance, cold hardiness, tolerance to wind and by predisposing plants to insect and disease pests, $O_3$ may even impact the occurrence and impact of natural disturbance (e.g., fire, erosion).

Another approach to assessing $O_3$ effects on ecosystems is the identification and use of indicators. For example, the main indicators of phytotoxic $O_3$ exposures used for forest ecosystems are visible foliar injury (as described in section 7.6.3.2 above) and radial growth of trees. Systematic injury surveys demonstrate that foliar injury occurs on $O_3$-sensitive species in many regions of the United States. However, there is not always a direct relationship between the severity of the visible foliar symptoms and growth. This essentially means it is difficult to quantify or characterize the degree which EEAs may be impacted when foliar injury is found in the field. Investigations of the relationship between changes in radial growth of mature trees and ambient $O_3$, in combination with data from many controlled studies with seedlings, suggest that ambient $O_3$ is reducing the growth of mature trees in some locations. However, definitively attributing growth losses in the field to $O_3$ in a wide array of ecosystems is often difficult because of confounding factors with other pollutants, climate, insect damage and disease.

The draft CD (EPA, 2006) outlines seven case studies where $O_3$ effects on ecosystems have either been documented or are suspected. However, in most cases, only a few components in each of these ecosystems have been examined and characterized for ozone effects, and therefore the full extent of ecosystem changes in these example ecosystems is not fully understood. Clearly, there is a need for highly integrated ecosystem studies that specifically investigate the effect of $O_3$ on ecosystem structure and function in order to fully determine the extent to which ozone is altering ecosystem services.

**Figure 7-19. Common anthropogenic stressors and the essential ecological attributes they affect. Modified from Young and Sanzone (2002)**




1

### 7.7.1 Evidence of Potential Ozone Alteration of Ecosystem Structure and Function

The seven case studies listed in the 2006 CD demonstrate the potential for $O_3$ to alter ecosystem structure and function. The oldest and clearest example involves the San Bernardino Mountain forest ecosystem. In this example, $O_3$ appeared to be a predisposing factor leading to increased drought stress, windthrow, root diseases, and insect infestation (Takemoto et al., 2001). Increased mortality of susceptible tree species including ponderosa and Jeffrey pine resulting from these combined stresses has shifted community composition towards white fir and incense cedar and has altered forest stand structure (Miller et al., 1989). A shift of community composition towards white fir may make this ecosystem more susceptible to fire. Although the role of $O_3$ was extremely difficult to separate from other confounding factors, such as high N deposition, there is evidence that this shift in species composition has altered trophic structure and food web dynamics (Pronos et al., 1999) and C and N cycling (Arbaugh et al., 2003). Ongoing research in this important ecosystem will reveal the extent to which ecosystem services have been affected.

One of the best-documented studies of population and community response to $O_3$ effects are the long-term studies of common plantain (*Plantago major*) in native plant communities in the United Kingdom (Davison and Reiling, 1995; Lyons et al., 1997; Reiling and Davison, 1992c). Elevated $O_3$ significantly decreased the growth of sensitive populations of common plantain (Pearson et al., 1996; Reiling and Davison, 1992a, b; Whitfield et al., 1997) and reduced fitness as determined by decreased reproductive success (Pearson et al., 1996; Reiling and Davison, 1992a). While spatial comparisons of population responses to $O_3$ are complicated by other environmental factors, rapid changes in $O_3$ resistance were imposed by ambient levels and variations in $O_3$ exposure (Davison and Reiling, 1995). At the site of plantain seed collection the highest correlations occurred between $O_3$ resistance and ambient $O_3$ concentrations (Lyons et al., 1997). In this case study, it appears that $O_3$- sensitive individuals are being removed by $O_3$ stress and the genetic variation represented in the population could be declining. If genetic diversity and variation is lost in ecosystems, there may be increased vulnerability of the system to other biotic and abiotic stressors, and ultimately a change in the services provided by those ecosystems.

Reconstructed ecosystems in artificial exposure experiments have also provided new insight into how ozone may be altering ecosystem structure and function (Karnosky et al., 2005). For example, the Aspen Free-Air $CO_2$ Enrichment facility was designed to examine the effects of both elevated $CO_2$ and $O_3$ on aspen (*Populus tremuloides*), birch (*Betula papyrifera*), and sugar

maple (*Acer saccharum*) in a simple reconstructed plantation characteristic of Great Lakes aspen-dominated forests (Karnosky et al., 2003b; Karnosky et al., 1999). They found evidence that the effects on above- and below-ground growth and physiological processes have cascaded through the ecosystem, even affecting microbial communities (Larson et al., 2002; Phillips et al., 2002). This study also confirmed earlier observations of $O_3$-induced changes in trophic interactions involving keystone tree species, as well as important insect pests and their natural enemies (Awmack et al., 2003; Holton et al., 2003; Percy et al., 2002).

Collectively these examples suggest that $O_3$ is an important stressor in natural ecosystems, but it is difficult to quantify the contribution of $O_3$ due to the combination of stresses present in ecosystems. Continued research, employing new approaches, will be necessary to fully understand the extent to which $O_3$ is affecting ecosystem services.

### 7.7.2 Effects on Ecosystem Products and Services

Since it has been established that $O_3$ affects photosynthesis and growth of plants, $O_3$ is most likely affecting the productivity of crop and forest ecosystems. Therefore, it is desirable to link effects on growth and productivity to essential ecosystem services. However, it is very difficult to quantify ecosystem-level productivity losses because of the amount of complexity in scaling from the leaf-level or individual plant to the ecosystem level, and because not all organisms in an ecosystem are equally affected by ozone. Below is a discussion of potential effects of $O_3$ on an important ecological service.

#### 7.7.2.1 Carbon Sequestration

Terrestrial ecosystems are important in the Earth's carbon (C) balance and could help offsett emissions of $CO_2$ by humans if anthropogenic C is sequestered in vegetation and soils. The annual increase in atmospheric $CO_2$ is less than the total inputs from fossil fuel burning and land use changes (Prentice et al., 2001) and much of this discrepancy is thought to be attributable to $CO_2$ uptake by plant photosynthesis (Tans & White, 1998). Temperate forests of the northern hemisphere have been estimated to be a net sink of 0.6 to 0.7 Pg of C per year (Goodale et al. 2002). Ozone interferes with photosynthesis, causes some plants to senesce leaves prematurely and in some cases, reduces allocation to stem and root tissue. Thus, $O_3$ decreases the potential for C sequestration. For the purposes of this discussion, we define C sequestration as the net exchange of carbon by terrestrial the biosphere. However, long-term storage in the soil organic matter is considered to be the most stable form of C storage in ecosystems.

In a study including all ecosystem types, Felzer et al. (2004), estimated that US Net Primary Production (net flux of C into an ecosystem) was decreased by 2.6-6.8% due to $O_3$ pollution in the late 1980's to early 1990's. Ozone not only reduces C sequestration in existing forests, it can also affect reforestation projects (Beedlow et al. 2005). This effect, in turn, has been found to ultimately inhibit C sequestration in forest soils which act as long-term C storage (Loya et al., 2003; Beedlow et al. 2005). The interaction of rising $O_3$ pollution and rising $CO_2$ concentrations in the coming decades complicates predictions of future sequestration potential. Models generally predict that in the future C sequestration will increase with increasing $CO_2$, but often do not account for the decrease in productivity due to the local effects of tropospheric $O_3$. In the presence of high $O_3$ levels, the stimulatory effect of rising $CO_2$ concentrations on forest productivity has been estimated to be reduced by more that 20% (Tingey et al 2001; Ollinger et al. 2002; Karnosky et al. 2003).

In summary, it would be anticipated that attaining lower $O_3$ standards would increase the amount of $CO_2$ uptake many ecosystems in the US. However, the amount of this improvement would be heavily dependent on the species composition of those ecosystems. Many ecosystems in the U.S. do have $O_3$ sensitive plants. For, example forests ecosystems with dominant species such as aspen or ponderosa pine would be expected to increase $CO_2$ uptake more with lower $O_3$ than forests with more $O_3$ tolerant species.

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# 8. STAFF CONCLUSIONS ON SECONDARY OZONE NAAQS

## 8.1 INTRODUCTION

This chapter provides staff conclusions for consideration by the Administrator about whether the existing secondary $O_3$ standard should be revised and, if so, what options should be considered. Our conclusions on this standard and on options for consideration are based on the scientific and technical information contained in the CD and on staff analyses and evaluations presented in Chapters 2 and 7 of this Staff Paper.

The provisions of the Clean Air Act require the Administrator to establish secondary standards that, in the Administrator's judgment, are requisite to protect the public welfare from any known or anticipated adverse effects. In so doing, the Administrator seeks to establish standards that are neither more nor less stringent than necessary for this purpose. As noted in Chapter 7, welfare effects, as defined in section 302(h) (42 U.S.C. 7602(h)) include, but are not limited to, ''effects on soils, water, crops, vegetation, manmade materials, animals, wildlife, weather, visibility, and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and on personal comfort and well-being"(62 FR 38857). As in the last review, this review has focused on crops and other vegetation since these public welfare effects are of most concern at $O_3$ concentrations typically occurring in the U.S. In addition, by affecting commercial crops and natural vegetation, $O_3$ may also indirectly affect natural ecosystem components such as soils, water, animals, and wildlife. As discussed above in Chapter 7, insufficient new information is available on other welfare effects categories to provide a basis for selecting an averaging time and level for a distinct secondary standard to address such effects and therefore they are not discussed further.

In identifying a range of secondary standard options for the Administrator to consider, staff notes that the final decision is largely a public policy decision. A final decision regarding the adequacy of the current standard and the range of options presented will draw upon**:** (1) the most policy-relevant scientific information on vegetation effects associated with exposure to ambient levels of $O_3$; (2) staff analyses of air quality, vegetation exposure, risk, and associated economic values; and (3) judgments about how to deal with the range of uncertainties that are inherent in the relevant scientific evidence and analyses. The range of options identified by the staff for the Administrator to consider, include options regarding an appropriate pollutant indicator, averaging time, form, and level of the secondary $O_3$ NAAQS.

## 8.2 APPROACH

In evaluating whether the current secondary standard is adequate or whether consideration of revisions is appropriate, our approach in this review builds upon the general approach used in the last review by expanding and modifying the exposure, risk, and benefits assessments to reflect the availability of new tools, assessment methods, and a larger and more diverse body of evidence. In developing conclusions on the $O_3$ standard, we have taken a weight of evidence approach that evaluates information across a variety of vegetation-related research areas described in the CD, combined with assessments of air quality, exposures, risks, and both quantitative and qualitative assessments of the benefits associated with protection of commercial crops, forest tree species and ecosystems.

With respect to vegetation effects information, we have taken into account past as well as more recent evidence from chamber, free air, gradient, and field observation studies for a variety of vegetation effects endpoints. We place greater weight on U.S. studies due to the often species-, site-, and climate-specific nature of $O_3$-related vegetation response. With respect to quantitative exposure-, risk, and benefits-based considerations, we have relied on interpolated $O_3$ exposures as described in section 7.5.4 of Chapter 7. A range of alternative air quality scenarios were generated to reflect the alternative standard options under consideration. These scenarios include current "as is" air quality (2001), as well as four "just meet" scenarios for which air quality is adjusted using the rollback method to just meet the level of the alternative standard options. We have quantified the uncertainties associated with the interpolated $O_3$ exposure surface by comparing actual monitor data to the interpolated surface value at each monitor site. In the benefits assessment, staff acknowledges the presence of unknown and unquantifiable sources of uncertainty associated with use of the agronomic benefits model, AGSIM, as is typical with all such models.

Our review of the adequacy of the current secondary standard begins by considering whether the currently available body of evidence assessed in the 2006 CD suggests that revision of any of the basic elements of the standards would be appropriate. More specifically, this evaluation of the adequacy of the current standard involves addressing questions such as the following:

- To what extent does newly available information reinforce or call into question evidence of associations with effects identified in the last review?
- To what extent does newly available information reinforce or call into question any of the basic elements of the current standards?
- To what extent have important uncertainties identified in the last review been reduced and have new uncertainties emerged?

To the extent that the evidence suggests that revision of the current standards would be appropriate, we then consider whether the currently available body of evidence supports consideration of standards that are either more or less protective by addressing the following questions:

- Is there evidence that vegetation effects occur at air quality levels that are as low as or lower than had previously been observed, and what are the important uncertainties associated with that evidence?
- Are exposures of concern and vegetation risks estimated to occur in areas that meet the current standard; are they important from a public welfare perspective; and what are the important uncertainties associated with the estimated risks?

To the extent that there is support for consideration of revised standards, we then identify ranges of standards (in terms of indicators, averaging times, levels, and forms) that would reflect a range of alternative public welfare policy judgments, based on the currently available evidence, as to the degree of protection that is requisite to protect public welfare from any known or anticipated adverse effects. In so doing, staff addresses the following questions:

- Does the evidence provide support for considering a different $O_3$ indicator?
- Does the evidence provide support for considering different averaging times?
- What ranges of levels and forms of alternative standards are supported by the evidence, and what are the uncertainties and limitations in that evidence?
- To what extent do specific levels and forms of alternative standards reduce the estimated exposures of concern and risks attributable to $O_3$, and what are the uncertainties in the estimated exposure and risk reductions?

Staff's review of the secondary standard for $O_3$ is addressed in section 8.3 below, including our consideration of the adequacy of the current secondary $O_3$ standard based on key policy-relevant information on vegetation and ecosystem effects, exposures, risks, and benefits, and considerations of each of the major elements that define the $O_3$ standard: pollutant indicator, averaging time, form, and level. Section 8.4 summarizes the range of alternative secondary standard options identified by staff for the Administrator's consideration. This chapter concludes with a summary of key uncertainties and research needs related to setting a secondary $O_3$ NAAQS in section 8.5.

## 8.3 SECONDARY $O_3$ STANDARD

### 8.3.1 Background

In the final rule for the $O_3$ NAAQS published in July 1997 (62 FR 38877), the Administrator decided to replace the then existing 1-hr, 0.12-ppm secondary NAAQS with a standard that was identical in every way to the new revised primary standard of an 8-hr, 0.08 ppm annual fourth highest maximum 8-hr average standard averaged over 3 years. Her decision was based on her judgment that: (1) the then existing secondary standard did not provide adequate protection for vegetation against the adverse welfare effects of $O_3$; (2) CASAC advice ''that a secondary NAAQS, more stringent than the present primary standard, was necessary to protect vegetation from $O_3$'' (Wolff, 1996); (3) the new 8-hr average standard would provide substantially improved protection for vegetation from $O_3$-related adverse effects as compared to the level of protection provided by the then current 1-hr, 0.12-ppm secondary standard; 4) significant uncertainties remained with respect to exposure dynamics, air quality relationships, and the exposure, risk, and monetized valuation analyses presented in the proposal, resulting in only rough estimates of the increased public welfare likely to be afforded by each of the proposed alternative standards, which are important factors in selecting an appropriate secondary standard; 5) there was value in allowing more time to obtain additional information to better characterize $O_3$-related effects on vegetation under field conditions from additional research and to develop a more complete rural monitoring network and air quality database from which to evaluate the elements of an appropriate seasonal secondary standard; and 6) there was value in allowing more time to evaluate more specifically the improvement in rural air quality and in $O_3$-related vegetation effects resulting from measures designed to attain the new primary standard (62 FR 38877-78).

As discussed in Chapter 7, additional information has become available since the last review. On the basis of staff assessments that incorporate the most policy-relevant aspects of this new information, we have evaluated the adequacy of the current secondary standard in protecting public welfare.

### 8.3.2 Adequacy of Current $O_3$ Standard

More recent research has further confirmed and strengthened our earlier understanding and conclusions regarding the effects of $O_3$ on vegetation at current ambient exposures. Results from the exposure, risk and benefits assessments conducted by staff and described in Chapter 7 characterize to what degree impacts would be expected to occur upon meeting the current 8-hr secondary standard. As documented below, we have evaluated the adequacy of the current

standard both on the evidence and significance of vegetation effects at or below the level of the standard in conjunction with the additional considerations presented in discussions on indicator, averaging time, form, and level.

#### 8.3.2.1 Considerations Based on Vegetation Effects Evidence

Based on a weight of evidence approach that integrates information from across the various vegetation-related research areas described in the $O_3$ CD, including chamber and free air exposure crop yield and tree seedling biomass experimental studies, visible foliar injury data from biomonitoring plots, and modeled mature tree growth, we conclude that vegetation effects continue to occur at levels that impact public welfare at air quality levels that just meet or are below the current standard.

Staff exposure and risk assessments estimate that just meeting the current 8-hr standard would still allow significant levels of yield loss to occur in several fruit and vegetable species and major commodity crop species currently grown in the U.S. (see Table 7.3 in section 7.6.2.4 of Chapter 7). For example, grapes, cantaloupes and Valencia oranges had estimated median yield losses of 20.5, 19, and 15%, respectively, when air quality just met the level of the current standard. Fruits and vegetables are a large part of the U.S. agricultural sector and are especially susceptible to $O_3$ pollution because much of the production occurs in the San Joaquin Valley region of California. Median yield losses for the commodity crops were not as large. Cotton, for example, had estimated median yield losses of 4.8% at air quality levels that just meet the current standard. Soybean had an even smaller estimated median yield loss of 1.7% under just meet air quality for the current standard. However, soybean is grown in 40 of the lower 48 states, suggesting that even small changes in individual plant yield, when applied across large acreages, can be significant.

Another group of crops, multiple year forage crops, have also received additional study since the last review. Based on these new studies, the yields and quality of multiple-year forage crops have also been shown to be sufficiently reduced as to have nutritional and possibly economic implications for their use as ruminant animal feed at $O_3$ exposures that occur in some years over large areas of the U.S. However, it is not clear at this time to what degree they are impacted at lower levels of air quality.

Biomass loss in sensitive tree seedlings is still predicted to occur under $O_3$ exposures that just meet the level of the current secondary standard (see Table 7.5 in section 7.6.3.1 of Chapter 7). For instance, black cherry, ponderosa pine, eastern white pine and aspen had estimated median seedling biomass losses of 24, 10, 5.8, and 5.6%, respectively. Percent biomass loss in tree seedlings is not intended to provide any information on expected biomass loss in mature trees of the same species, and cannot be considered comparable to percent yield in annual crops.

However, due to the potential for compounding effects over multiple years, there is scientific consensus that biomass loss greater than 1-2% annually can be significant. Decreased seedling root growth and survivability could affect overall stand health and composition in the long term.

Visible foliar injury, not quantitatively explored in the last review, has been more fully assessed in Chapter 7 (see Table 7.6 in section 7.6.3.2). Visible injury symptoms diagnostic of phytotoxic $O_3$ exposures continue to be documented on sensitive bioindicator plants at many U.S. Forest Service Forest Inventory and Analysis biomonitoring sites throughout the U.S. at current levels of $O_3$ air quality. Staff assessments of recent data show that of the counties with air quality levels at or below that of the current 8-hr standard, 0.084 ppm that also contained FIA biomonitoring sites, incidence of foliar injury ranged from 21 to 39% during the four year period (2001-2004). These percentages suggest that phytotoxic exposures would still occur after full attainment of the current secondary standard. Additionally, the data show that foliar injury occurrence is geographically widespread and is occurring on a variety of plant species in forested systems. Though linking foliar injury to other plant effects is still problematic, its presence indicates that other $O_3$–related vegetation effects could also be present.

Our analysis using modeled mature tree growth response under different air quality scenarios for the western species (ponderosa pine) and two eastern species (red maple and tulip poplar) projected that just meeting the current standard could be reducing annual net biomass gain in simulated species (see Table 7.7 in section 7.6.3.3 in Chapter 7). This judgment is based in part on model outputs that estimate that as $O_3$ levels are reduced below those of the current standard, significant improvements in growth would occur. For instance, estimated growth in red maple increased by 4.08% and 2.99% at Big Meadows and Cranberry sites, respectively, when air quality was rolled back to just met a SUM06 of 15 ppm-hr. Yellow poplar was projected to have a growth increase between 0.6 and 8.26% under the same scenario at the two sites.

Though there is significant uncertainty associated with this analysis, we judge that this information should be given careful consideration in light of several other pieces of evidence. Specifically, limited evidence from experimental studies that go beyond the seedling stage show continued decreased growth under elevated $O_3$ in trees. Some mature trees such as red oak, have shown greater sensitivity to $O_3$ than seedlings of the same species. As indicated above, smaller growth loss increments may be significant for perennial species. The potential for cumulative "carry over" effects as well as compounding must be considered. The accumulation of such "carry-over" effects over time may affect long term survival and reproduction of individuals and ultimately the abundance of sensitive tree species in forest stands.

In summary, $O_3$ levels that would be expected to remain after meeting the level of the current secondary standard, are sufficient to cause reduced crop yields, reduced above and below

ground seedling and mature tree growth, and visible foliar injury. Other $O_3$ induced effects described in the literature include an impaired ability of many sensitive species and genotypes within species to adapt to or withstand other environmental stresses such as freezing temperatures, pest infestations and/or root disease, and reduced ability to compete for available resources. In the long run, the result of these impairments (e.g., loss in vigor) may be plant death. Though effects on other ecosystem components have not been examined, except in isolated cases, effects such as those described above, could have significant implications for plant community and associated species biodiversity and the structure and function of whole ecosystems (Young and Sanzone, 2002).

#### 8.3.2.2 Pollutant Indicator

The staff concludes that $O_3$ remains the appropriate pollutant indicator for use in a secondary NAAQS that provides protection for public welfare from exposure to all photochemical oxidants. This conclusion is based on the same rationale presented in the previous Staff Paper (U.S. EPA, 1996), which recognizes that among the other photochemical oxidants, the database for vegetation effects only raises concern at levels found in the ambient air for $O_3$ and, therefore, control of ambient $O_3$ levels provides the best means of controlling other photochemical oxidants of potential welfare concern. There is nothing in the recent literature to warrant reconsideration of this conclusion.

#### 8.3.2.3 Averaging Times

Plants, unlike people, are exposed to ambient air 24 hr a day, every day for their entire life. For annual species, this is for only a period within one year, for perennials, for multiple years, decades or centuries. Regardless of plant type, it has been well established in the literature that $O_3$ effects are cumulative, and that longer exposure durations have a greater impact than shorter durations, all else being equal. Air quality indices that account for the exposure duration overall do a better job predicting plant response than long term averages. However, $O_3$ levels are not continuously elevated and plants are not equally sensitive to $O_3$ over the course of a day, season or lifetime. Thus, it becomes necessary to identify periods of exposure that have the most relevance for plant response.

*Seasonal Window.* Many recent studies described in the 2006 CD have specifically selected exposure indices that take into account the cumulative, concentration-weighted impact of $O_3$-induced effects throughout the growing season when measuring growth and yield impacts and have substantiated the 1996 CD and 1996 Staff Paper conclusions on the importance of cumulative, seasonal exposures. In general, the period of maximum potential growth for annual crops, herbaceous species and deciduous trees and shrubs occurs within the annual period defined as the $O_3$ season, which varies on a state-by-state basis. Annual crops are typically

grown for periods of two to three months before being harvested. In contrast, perennial species may be photosynthetically active up to 12 months each year, depending on the species and where it is grown. In the 1996 Staff Paper and proposal notice, we noted that the selection of any single averaging time for a national standard would represent a compromise, given the significant variability in growth patterns and lengths of growing seasons among the wide range of vegetation species that may experience adverse effects associated with $O_3$ exposure, but concluded, based on the information available at that time, that selection of the maximum consecutive 3-month period within the $O_3$ season was reasonable, and in most cases, would most likely coincide with the periods of greatest plant sensitivity on an annual basis. Based on the information assessed in the current CD (EPA, 2006) and Chapter 7 of this document, we again conclude the maximum consecutive 3-month period within the $O_3$ season is a reasonable averaging time for vegetation.

*Diurnal Window*. Stomata are the entry points for $O_3$ into plant leaves. Over the course of a day, plant stomatal conductance varies along with light level, soil moisture and other factors. In general, stomata are most open during daylight hours in order to allow sufficient $CO_2$ uptake for use in carbohydrate production through photosynthesis. At most locations, $O_3$ concentrations are also highest during the daytime, potentially coinciding with maximum stomatal uptake. Ozone uptake impairs photosynthesis, which can then lead to impacts on plant growth, reproduction (yield) and root function. In the last review, studies had shown that by increasing the diurnal window from 7 to 12 or 24 hrs**,** the index captured more of the peak $O_3$ concentrations that occur in some environments. However, the associated reductions in growth or yield (which are a result of impaired photosynthesis) and increases in foliar injury had not been seen to increase proportionally with increasing diurnal period. Though limited work has been done recently to more fully characterize $O_3$ uptake at night and its potential contribution to total plant uptake and response, we conclude that such information remains preliminary and not generalizable at this time (see also Appendix A of Chapter 7).

Based on these considerations, as well as information assessed in the current CD (EPA, 2006) and Chapter 7 of this document, we again conclude that a 12-hr (8:00 am to 8:00 pm) diurnal window remains appropriate for a secondary NAAQS designed to protect a wide range of vegetation growing in environmental conditions found across the U.S**.**

#### 8.3.2.4 Form of the Standard

In the last review, based on a substantial body of vegetation effects literature that demonstrated the importance of taking into account exposure duration and the differential impact of higher concentrations when predicting vegetation response, the Administrator judged that a 3-month, 12-hr SUM06 seasonal secondary standard (set at a level of 25 ppm-hr) would also be

appropriate to protect public welfare from known or anticipated adverse effects given the available scientific knowledge and that such a seasonal standard "…is more biologically relevant…" (62 FR 38876 -77). On the basis of that history, Chapters 2 and 7 of this Staff Paper characterize information in terms of both the current 8-hr, 0.08 ppm secondary standard form and the alternative 3-month, 12-hr SUM06 form proposed in the last review. Due to a number of additional technical and policy-relevant considerations discussed in secion 7.5.1 of Chapter 7, we also included the W126 as an alternative cumulative, concentration weighted form.

*Comparison of 8-Hour Average and Cumulative Seasonal Forms*. The 1997 final rule recognized that "it remained uncertain as to the extent to which air quality improvements designed to reduce 8-hr $O_3$ concentrations would reduce $O_3$ exposures measured by a seasonal SUM06 index." (62 FR 38876)

An analysis undertaken by EPA at the time to explore that question showed that there was considerable overlap between areas that would be expected not to meet the range of alternative 8-hr standards being considered for the primary NAAQS and those expected not to meet the range of values (expressed in terms of the SUM06 index) of concern for vegetation. Though this result suggested that improvements in national air quality from attaining an 8-hr primary standard within the recommended range of levels would also reduce levels below those of concern for vegetation in those same areas, there was considerable uncertainty as to the exact strength of the relationship between urban $O_3$ air quality and distributions that occur in non-monitored rural or remote areas.

Using recent county-level air quality data (2001 – 2004), we again performed an analysis to compare the degree to which the 8-hr form controlled air quality of concern for vegetation expressed in terms of the SUM06. Based on data from AQS sites and the subset of CASTNET sites that had the highest $O_3$ levels for the county in which they are located, this analysis again shows that only a few counties have SUM06 values above 25 ppm-hr after attaining the current 0.08-ppm, 8-hr average standard (see Figures 7-1 and 7-2 in Chapter 7). However, these patterns varied considerably between years with differing levels of $O_3$, with the higher $O_3$ year (2002) showing a stronger association between SUM06 and the 8-hr standard, and the lower $O_3$ year (2004) showing less of one. Further, at SUM06 levels at or below 25 ppm-hr (see discussion on Level below), the relationship between the 8-hr standard and SUM06 levels potentially of concern to vegetation did not hold. Prior to finalizing this draft Staff Paper, we plan to further assess the strength of the relationship between the 8-hr and SUM06 standard forms at a subset of more rural and remote sites, including high elevation national parks.

In conclusion, meeting the current 8-hr 4$^{th}$ highest maximum average standard would result in air quality improvements that could potentially benefit vegetation in some areas. However, based on the above analysis, as well as scientific consensus supporting the use of a

cumulative concentration-weighted form to describe exposures of concern for vegetation as described in Chapter 7, we conclude that the use of the 8-hr index as a tool to track and predict vegetation risk remains problematic.

*Comparison of SUM06 and W126 Cumulative, Concentration-Weighted Forms.* In addition to evaluating the 8-hr average form, we evaluated the appropriateness of the SUM06 alternative proposed in the last review by comparing it to another cumulative, concentration-weighted form discussed in the 1996 Staff Paper, the W126. In the 1996 Staff Paper, our preference for the SUM06 over other cumulative forms was based on the following science and policy considerations:

1) All cumulative, peak-weighted exposure indices considered, including W126 and SUM06, were about equally good as exposure measures to predict exposure-response relationships reported in the NCLAN crop studies.

2) the SUM06 form would not be influenced by background $O_3$ concentrations (defined at the time as 0.03 to 0.05 ppm) under many typical air quality distributions.

In the current review, we have reconsidered whether the SUM06 form is the most appropriate cumulative form based on the following:

- Model predictions of policy-relevant background (PRB) in the range of 0.02 to 0.035 ppm for the current review are below the range of 0.03 to 0.05 ppm described as background in the previous review. Thus, background concentrations become much less of a factor influencing the choice of an appropriate cumulative index.
- There is no evidence of a biological exposure threshold for eliciting plant response in the extensive vegetation effects literature. An index with a threshold set at 0.06 ppm artificially truncates exposures that have been shown to produce vegetation effects of concern given sufficient duration. Without the policy consideration of not including PRB $O_3$ concentrations up to a level of 0.05 ppm, it may be appropriate to consider a more biologically-based form that includes concentrations below 0.06 ppm, such as the W126.

While recognizing that no one concentration-weighted exposure index can fully account for the complex relationships between $O_3$ concentrations and plant responses across a wide range of species and environments, we conclude, on the basis of the information highlighted above, that the W126 form is a more appropriate biologically-based and policy- relevant cumulative, concentration-weighted form.

#### 8.3.2.5 Level of the Standard

The level at which a secondary standard should be set depends on a blending of science and policy judgments by the Administrator as to the level of air quality which is requisite to protect the public welfare from any known or anticipated adverse effects associated with the pollutant in the ambient air. The exposure, risk and benefits assessments conducted in Chapter 7 and summarized briefly above, provide information regarding the effects associated with a number of different welfare endpoints at different levels of air quality, often expressed in terms of both the current 8-hr average form and the SUM06 (or W126) seasonal form(s).

At the end of the last review, we identified a range for a 3-month, 12-hr SUM06 standard form of 25 to 38 ppm-hr, for the Administrator's consideration. These levels were estimated to allow 10% to 20% yield loss, respectively, to occur in no more than 50% of the studied NCLAN agricultural crops. These levels were also estimated to provide an increased level of protection for other categories of vegetation such as tree seedlings and mature trees in commercial, Class I, and other forested areas in urban, rural, and remote environments. It was recognized, however, that a standard set within this range would not protect the most sensitive species or individuals within a species from all potential effects related to $O_3$ exposures. The Administrator proposed the lower end of the range (e.g., 25 ppm-hr) as necessary to provide a requisite level of protection for vegetation against the adverse effects of $O_3$.

As discussed more fully in Appendix 7A, in the interim between the 1996 proposal notice and the 1997 final rule, the results of a consensus-building workshop on the need for a long-term cumulative secondary $O_3$ standard were published. At this workshop, expert scientists expressed their judgments on what standard form(s) and level(s) would provide vegetation with adequate protection from $O_3$-related adverse effects. Consensus was reached with respect to selecting appropriate ranges of levels in terms of a 3-month, 12-hr SUM06 standard for a number of vegetation effects endpoints. We have included estimated equivalent levels in terms of the 3-month, 12-hr W126, shown in parentheses, for reference. For yield reductions in agricultural crops – a range of 15 to 20 (13 to 18) ppm-hr; for growth effects to tree seedlings in natural forest stands – a range of 10 to 15 (9 to 13) ppm-hr; for growth effects to tree seedlings and saplings in plantations – a range of 12 to 16 (11 to 14) ppm-hr; and for foliar injury to natural ecosystems – a SUM06 range of 8 to 12 (7 to 11) ppm-hr (Heck and Cowling, 1997).

In the final rule, the Administrator pointed to the results of this workshop as providing important support to her view that the then current secondary standard was not adequately protective of vegetation, contributing to her rationale that revision of the secondary standard was needed. Additionally, she felt that this consensus report foreshadowed the direction of future scientific research in this area, the results of which could be important in future reviews of the $O_3$ secondary standard (62 FR 38877).

The expert recommendations identified above informed our assessment of a range of levels appropriate for the Administrator to consider in this review. We judge that the upper bound of this range, the SUM06 level of 25 ppm-hr, as proposed in the last review, is an appropriate upper level for consideration, and that a SUM06 level of 15 ppm-hr is an appropriate lower level. We conclude that approximately equivalent levels of a W126 (13 to 21 ppm-hr) would also be appropriate to consider. The level of protection to vegetation at the upper end of this range is expected to be roughly equivalent to that provided by the current 8-hr secondary standard in most areas. Levels below the upper end but within this range would provide increased protection for vegetation over the current level of the 8-hr standard. Further, the degree of protection varies depending on the vegetation effects endpoint(s) considered. The lower end of this range, 15 ppm-hr, was selected for the following reasons: 1) it represents an increase in protection for agricultural crops studied in NCLAN to no more than 10% yield loss in 75% of studied crop species and/or cultivars; 2) it falls at or near the upper end of the range suggested as protective of tree seedling growth in natural forest stands and plantations, respectively; 3) it would provide some additional protection for visible foliar injury in natural systems.

In arriving at this conclusion, we placed greater weight on those welfare effects endpoints that could be quantified or directly assessed. For example, the crop economic benefits analysis estimates that when the current 8-hr standard is just met across the entire U.S., an average annual benefit of $70-$96 million would be realized for the total agricultural sector. Meeting a SUM06 of 25 ppm-hr produced an estimated average annual benefit of $172-$230 million for the total agricultural sector. However, at the SUM06 of 15 ppm-hr, estimated benefits increased to approximately $345-$532 million. These numbers clearly suggest a significant annual impact from $O_3$ that could reasonably be judged to be important from a public welfare perspective. We note that that these impacts would not be distributed equally across the country, but would impact certain regions disproportionately.

In addition to crops, the lower level would improve protection against decreased growth in tree seedlings and mature trees. Tree growth is an important endpoint to consider because it can be related to other aspects of societal welfare such as sustainable production of timber and related goods, recreation, and carbon ($CO_2$) sequestration. Equally important, impacts on tree growth can also affect ecosystems through shifts in community species composition and the loss of genetic diversity due to the loss of $O_3$ sensitive individuals or species. Though it is not possible to quantify all the ecological and societal benefits associated with varying levels of alternative secondary standards, based on our analyses of seedling and mature tree growth and the scientific literature we would anticipate that the lower end of the range identified for the

Administrator's consideration would improve tree growth and decrease the adverse effects of $O_3$ on forested ecosystems.

Additionally, it is anticipated that the lower end of this range would provide increased protection from the more subtle impacts of $O_3$ acting in synergy with other natural and man-made stressors to adversely affect individual plants, populations and whole systems. By disrupting the photosynthetic process, decreasing carbon storage in the roots, increasing early senescence of leaves and affecting water use efficiency in trees, $O_3$ exposure can disrupt or change the nutrient and water flow of an entire system. Weakened trees can become more susceptible to other environmental stresses such as pest and pathogen outbreaks or harsh weather conditions. Though insufficient information exists to estimate the severity of these impacts as a function of the level of alternative secondary standards, we conclude that this information should be weighed in considering the extent to which a secondary standard should be precautionary in nature in protecting against effects that have not yet been adequately studied and evaluated.

## 8.4 ALTERNATIVE SECONDARY STANDARD OPTIONS FOR CONSIDERATION

We have identified a range of options for the Administrator to consider in determining whether revisions to the secondary standard are appropriate. These options reflect the results from the environmental assessment described in Chapter 7 above, as well as a number of policy-relevant considerations identified both in the last and current reviews.

In the last review, the Administrator took into account the following in reaching her final decision: 1) the varying degrees of protection afforded by the alternative primary standards recommended in Section VI; 2) the incremental protection associated with alternative cumulative, seasonal secondary standards under consideration; and 3) the value of establishing a seasonal form for the secondary standard that is more representative of biologically relevant exposures; and 4) the extent to which a secondary standard should be precautionary in nature given the possibility of ozone impacts acting in synergy with other natural and manmade stressors to impact climate and other environmental endpoints, particularly given the potential significance at a regional scale and in Class I areas.

In the current review, several additional policy-relevant issues may warrant consideration. First, the Agency has undertaken a number of activities geared toward improving ecosystem-related program tracking and accountability and is currently engaged in efforts to identify relevant indicators for that purpose. Having a biologically-relevant air quality index would assist with that process. Secondly, the National Research Council recently published a comprehensive report titled *Air Quality Management in the United States* (NRC, 2004). In that report, the Agency was encouraged to evaluate its historic practice of setting the secondary NAAQS equal to the primary. "Whatever the reason that led EPA to use identical primary and

secondary NAAQS in the past, it is becoming increasingly evident that a new approach will be needed in the future. There is growing evidence that the current forms of the NAAQS are not providing adequate protection to sensitive ecosystems and crops."(NRC, 2004)

Based on these new policy-relevant considerations, combined with the weight of the scientific evidence, we conclude that consideration should be given to a distinct secondary standard with a more biologically relevant form, in addition to considering retaining the current standard.

The following secondary standard options encompass the breadth of policy-relevant considerations described above:

1) ***Set a biologically relevant secondary standard.*** Selecting a cumulative, seasonal, concentration-weighted form (e.g., SUM06 or W126) has the benefit of making it easier to track the expected impact to vegetation of different levels of air quality and to better link environmental improvements with Agency programs, as well as improve protection to vegetation in some areas. In Chapter 7 of this Staff Paper, we described several policy-relevant issues, including lower estimated levels of PRB and the lack of a scientific basis for a biological threshold that led to the inclusion of a W126 form for consideration as a more appropriate alternate to the previously proposed SUM06 form. Under this option, we have identified a range of levels appropriate for the Administrator to consider based on the discussions above: for SUM06, a range of 15 to 25 ppm-hr and the comparable range of 13 to 21 ppm-hr for a W126.

2) ***Continue to set secondary standard identical to primary.*** Meeting the current 0.08-ppm secondary standard would provide additional protection to vegetation and ecosystems. However, at the 0.08-ppm level, some areas of the country will still experience exposures sufficient to produce a significant level of crop yield and tree seedling biomass loss, mature tree impacts, foliar injury, economic impacts and unquantifiable ecosystem effects, taking into account expected year-to-year variability. In addition, tracking the success of the secondary NAAQS program would be more difficult without a biologically based form.

## 8.5 SUMMARY OF KEY UNCERTAINTIES AND RESEARCH RECOMMENDATIONS RELATED TO SETTING SECONDARY $O_3$ STANDARDS

Staff has identified the following key uncertainties and research questions that have been highlighted in Chapter 9 of the CD and Chapter 7 herein, associated with this review of the welfare-based secondary standards. The first set of key uncertainties and research recommendations discussed below is that associated with the extrapolation to species or growing conditions outside of specific experimental or field study conditions The second set of key

uncertainties and research recommendations pertain to our ability to assess the impact of $O_3$ on ecosystem structure and function. Thirdly, we identify research recommendations related to the development of approaches, tools, or methodologies useful in characterizing the relationship between $O_3$ and plant response in a policy context. These three areas are described below.

(1) Species-Level Extrapolations:

- To reduce uncertainties associated with extrapolating plant response for a given level of $O_3$ using composite response functions across differing regions and climates, studies using large numbers of plant species across regions where those species are indigenous are recommended. In addition, to better understand the full range of response of plant species to $O_3$, research on more species is recommended.
- To reduce uncertainty associated with estimating the risk to vegetation of differing amounts of $O_3$-induced visible foliar injury over the plant's leaf area, research to explore the relationship between visible foliar injury and other $O_3$-related effects is recommended.
- To reduce uncertainty associated with estimated or modeled flux into plants, research is recommended to evaluate the factors that affect $O_3$ flux into plants, including the species specific roles of nocturnal flux and detoxification. Research that explores the relative importance of flux rate versus total cumulative flux or dose, and that leads to a database of $O_3$ flux-response relationships for vegetation, similar to the extensive concentration-response database that currently exists is recommended to further reduce existing uncertainties.
- To reduce uncertainties in extrapolating from $O_3$ effects on juvenile to mature trees and from trees grown in the open versus those in a closed forest canopy in a competitive environment, additional research is recommended.
- To reduce uncertainties in extrapolating individual plant response spatially or to higher levels of biological organization, including ecosystems, research that explores and better quantifies the nature of the relationship between $O_3$, plant response and multiple biotic and abiotic stressors, including those associated with climate change, is recommended.

(2) Ecosystem Level Impacts:

- To reduce uncertainties associated with projections of the effects of $O_3$ on the ecosystem processes of water, carbon, and nutrient cycling, particularly at the stand and community levels, research is needed on the effects on belowground ecosystem

processes in response to $O_3$ exposure alone and in combination with other stressors. These below ground processes include interactions of roots with the soil or microorganisms, effects of $O_3$ on structural or functional components of soil food webs and potential impacts on plant species diversity, changes in the water use of sensitive trees, and if the sensitive tree species is dominant, potential changes to the hydrologic cycle at the watershed and landscape level.

- To conclusively show whether $O_3$ affects biodiversity or genetic diversity, research on competitive interactions under elevated $O_3$ levels are recommended. This research could be strengthened by modern molecular methods to quantify impacts on diversity.

- To fill the data gaps regarding interactions and potential feedback mechanisms between $O_3$ and $O_3$ precursor (e.g., volatile organic carbons) production, atmospheric processes, and climate change variables, research is recommended to evaluate whether $O_3$ will negate the positive effects of an elevated $CO_2$ environment on plant carbon and water balance, whether the likelihood of various biotic stressors such as pest epidemics and insect outbreaks would be expected to increase in the future

- To reduce uncertainties associated with scaling $O_3$ effects up from the responses of single or a few plants to effects on communities and ecosystems, additional research is recommended. Because these uncertainties are multiple and significant due to the complex interactions involved, new research will likely require a combination of manipulative experiments with model ecosystems, community and ecosystem studies along natural $O_3$ gradients, and extensive modeling efforts to project landscape-level, regional, national and international impacts of $O_3$.

(3) Approaches, Tools, Methodologies:

- To reduce uncertainties associated with valuing improved vegetation and ecosystem function from improved $O_3$ air quality, research is needed on methodologies to determine the values associated with important services and benefits derived from natural ecosystems such that these could be used in comprehensive risk assessment for $O_3$ effects on natural ecosystems

- To reduce uncertainties associated with evaluating the performance of different exposure indices given different patterns of $O_3$ exposures, experiments would need to be designed to specifically test the performance of different indices in predicting plant response under different exposure regimes.

## 8.6 REFERENCES


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