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Review of the National Ambient Air Quality Standards for Ozone:

Policy Assessment of Scientific and Technical Information

OAQPS Staff Paper – First Draft

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U.S. Environmental Protection Agency
Office of Air Quality Planning and Standards
Research Triangle Park, North Carolina

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 first draft OAQPS Staff Paper contains the preliminary draft 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 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 draft document, *Air Quality Criteria for Ozone and Related Photochemical Oxidants: 2nd External Review Draft* (USEPA, 2005b; henceforth referred to as the draft CD), prepared by EPA's National Center for Environmental Assessment (NCEA). This draft Staff Paper also presents and interprets initial results from several staff analyses (e.g., air quality analyses, human exposure analyses, and human health risk assessments) and discusses plans for a staff environmental assessment of vegetation-related impacts. Staff believes that these analyses should be considered in EPA's current review of the national ambient air quality standards (NAAQS) for ozone (O_3). This draft Staff Paper identifies alternative standard options for purposes of conducting additional exposure and risk analyses but does not present staff conclusions and recommendations as to potential revisions of the primary (health-based) and secondary (welfare-based) O_3 NAAQS.

The policy assessment to be presented in the final version of this Staff Paper is intended to help "bridge the gap" between the scientific review contained in the draft 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 final CD (targeted for completion by February 2006), identify the critical elements that EPA staff 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 staff conclusions and recommendations of options for the Administrator to consider.

This draft Staff Paper is being provided to CASAC and the public for review at a meeting planned for December 2005. Following that meeting, staff will complete the human exposure

[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.

analyses and health risk assessment and conduct an environmental assessment of vegetation-related impacts. Taking CASAC and public comments on this first draft Staff Paper into account, staff will prepare a second draft Staff Paper, to be based on the final CD, and will make that draft document available for further review and comment by CASAC and the public.

While this document should be of use to all parties interested in the O_3 NAAQS review, it is written for those decision makers, scientists, and staff who have some familiarity with the technical discussions contained in the draft 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 "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]

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[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."

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 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 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 to EPA's 1997 decision by industry and others, 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, in responding to the remand, EPA should consider the potential beneficial health effects of O_3 pollution in shielding the public from the effects of solar ultraviolet (UV) radiation.

On January 27, 2000, EPA petitioned the U.S. Supreme Court for certiorari on the constitutional issue (and two other issues) but did not request review of the D.C. Circuit ruling regarding 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 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]

On November 14, 2001, EPA proposed to respond 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 by leaving the 1997 8-hr NAAQS unchanged (66 FR 52768). Taking into account public comment on the proposed decision, EPA published its final response to this remand on January 6, 2003, reaffirming the 8-hr O_3 NAAQS set in 1997 (68 FR 614). Finally, on April 30, 2004, EPA announced (69 FR 23966) 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. For most areas the date that the 1-hr NAAQS no longer applied was June 15, 2005. (See 40 CFR 50.9 for details.)

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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)

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 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 decisions 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 assessment to be developed in the Staff Paper. 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 staff, 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.

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. The lawsuit alleged that EPA had failed to perform its mandatory duty, under section 109(d)(1), of completing the current review within the period provided by statute. *American Lung Association v. Whitman* (No. 1:03CV00778, D.D.C. 2003). An initial consent decree, entered by the court in July 2003, after an opportunity for public comment, was subsequently modified in December 2003 and in April, July, and December 2004. 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. These dates are premised on the expectation that a series of interim milestones will be met, including the release of a final CD by February 28, 2006, and release of a second draft Staff Paper by April 2006, followed by CASAC and public review by July 2006, with completion of a final Staff Paper by September 2006.

1.3 GENERAL APPROACH AND ORGANIZATION OF THE DOCUMENT

The policy assessment in this draft Staff Paper is based on staff's evaluation of the policy implications of the scientific evidence contained in the draft CD and initial results of quantitative analyses based on that evidence. Taken together, this information informs preliminary staff conclusions and recommendations on certain elements of the O_3 standards under review. While the draft 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 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 air quality data 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 draft 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 initial results from those assessments. Chapter 6 includes a preliminary discussion of the adequacy of the current primary standard and identifies alternative primary standards that staff believes are appropriate to consider in completing the human exposure and health risk assessments.

Chapters 7 and 8 will 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 staff is planning to use in conducting vegetation-related exposure and risk assessments. Chapter 8 will be added in the second draft Staff Paper, and it will include discussions of the adequacy of the current secondary standard and staff recommendations related to the secondary O_3 standard.

Staff conclusions and recommendations, to be presented in the second draft Staff Paper, will be informed by comments received from CASAC and the public in their reviews of this draft

Staff Paper. The final Staff Paper will be informed by further comments received from CASAC and the public in their review of the 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 staff's overall evaluation of the adequacy of the current primary and secondary NAAQS; and 3) staff conclusions and recommendations as to whether any revisions are appropriate to address public health and welfare effects associated with exposure to O_3. For these purposes, the staff will assess and integrate new scientific and technical findings with information gained in previous reviews in the context of those critical elements that the staff believes should be considered.

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2. AIR QUALITY CHARACTERIZATION

2.1 INTRODUCTION

This Chapter summarizes the origin and status of ozone (O_3) concentrations in the ambient air. Section 2.2 summarizes the physical and chemical properties of O_3 including its formation, transport, and fate. The section also summarizes the differences between tropospheric and stratospheric O_3 and how O_3 and ultraviolet radiation interact. Section 2.3 describes the various sources of ground level O_3 data and the monitoring methodology that gives rise to these data and issues regarding the monitoring methodology. Section 2.4 describes O_3 monitoring methods and issues. Section 2.5 describes the spatial and temporal variation found in ground level O_3 data. Section 2.6 characterizes O_3 episodes and Section 2.7 describes background levels of ground level O_3.

2.2 CHEMICAL AND PHYSICAL PROPERTIES, FORMATION, AND TRANSPORT

2.2.1 Chemical and Physical Properties

Ozone and other oxidants form in polluted areas mainly by chemical reactions in the atmosphere involving two classes of precursor pollutants, volatile organic compounds or VOCs and nitrogen oxides (NO_x). Ozone is, therefore, a secondary pollutant. Carbon monoxide (CO) is also important for ozone 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 (draft CD, pp.2-1 – 2-27).

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 (draft CD, p.AX2-88).

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 nitric oxide (NO) and a ground-state oxygen atom, $O(^3P)$, which then reacts with molecular oxygen to form O_3 (draft CD, p.2-2).

In urban areas, compounds representing all forms of 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 (draft CD, p.2-2 and 2-3).

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. Oxidized nitrogen compounds are emitted to the atmosphere mainly as NO which rapidly interconverts with NO_2. Consequently, NO and NO_2 are often grouped together into their own family called NO_x (draft CD, p.2-3). NO_x is considered a good surrogate for NO_y and is monitored more often and its emissions are more widely reported (see Table 2-2).

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. They are observed over the mid-Atlantic region, the central U.S. and California. 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 limits mixing as in Los Angeles and Mexico City and will result in a higher frequency and duration of days with high O_3 concentrations (draft CD, p.2-9).

2.2.4 Precursors, Sources and Emissions

Although there are direct sources of ozone (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 2-1 (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 2-2 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 troposphere, in particular in the PBL (draft 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 (draft CD, p.AX2-88).

Table 2-1. 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 2-1. 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

Table 2-2. 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 2-2. 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

2.3 DATA SOURCES

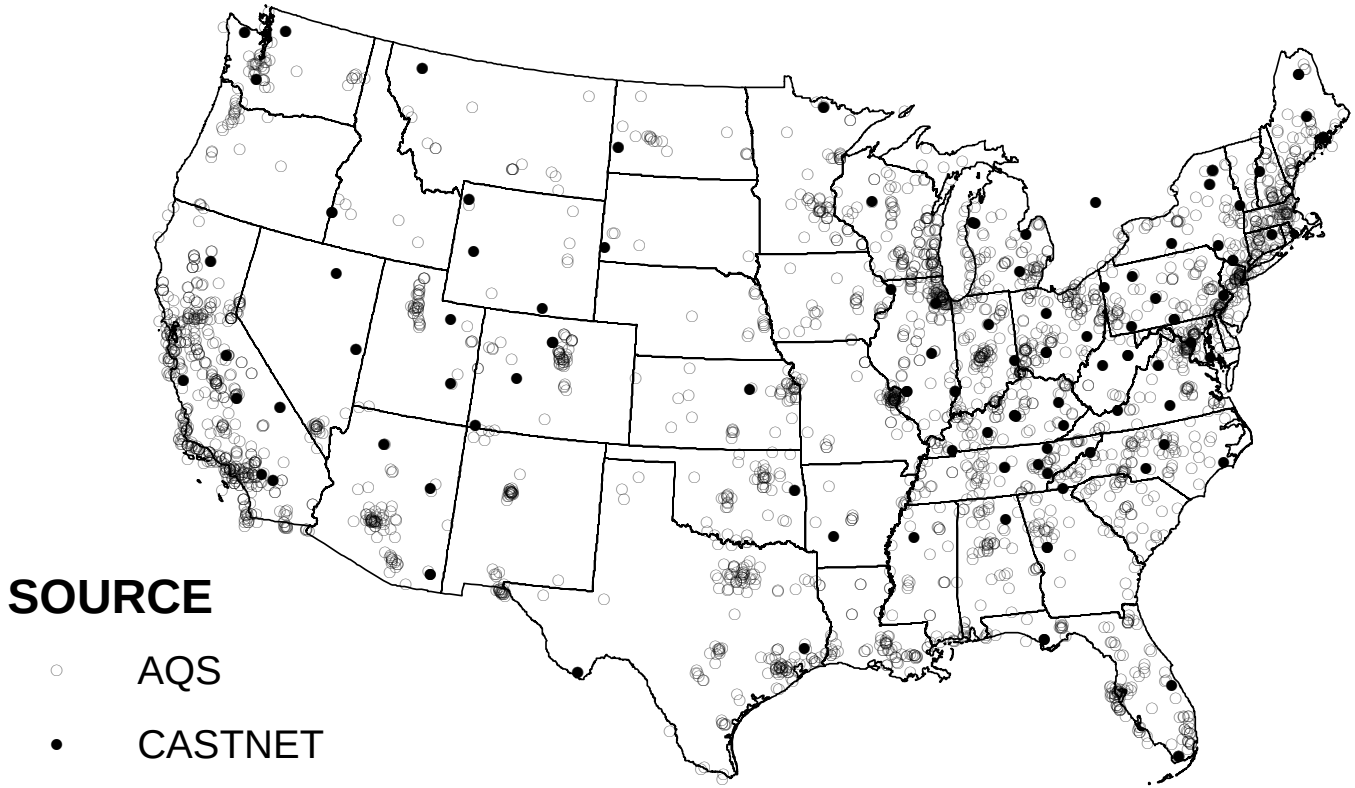
Two main sources of data were used for this assessment, the state-supplied data from various types of monitors housed in the Air Quality System (AQS) data base and the Clean Air Status and Trends Network (CASTNET). The vegetation exposure/risk analyses (see Chapter 7) will depend heavily on using the Community Multi-scale Air Quality (CMAQ) modeled data for 2001 in conjunction with 2001 monitor data. Both monitor and model values will be combined using the spatial interpolation tool in BenMAP to create an interpolated surface to fill in the gaps left by a sparse rural monitoring network. 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 ozone 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 organic and inorganic chemical relationships associated with the formation of ozone, as well as sulfate, nitrate, and organic aerosols.

2.3.1 Air Quality System (AQS)

The Code of Federal Regulations, Title 40, Part 58 (40 CFR Part 58) contains the EPA's ambient air quality surveillance regulations. 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

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



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 ozone 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 ozone 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 ozone. 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 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 ozone monitors are stable and show only very small variation (U.S. U.S. EPA 2003, p.22).

2.4 OZONE MONITORING METHODS AND ISSUES

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) (draft CD, p.2-21).

Several reports in the reviewed scientific literature have investigated interferences in O_3 detection via UV radiation absorption. These include the effects of water vapor, VOC's, aromatic compounds and their oxidation products, and other organic and inorganic compounds on instruments based on both UV absorption and chemiluminescence. 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 (draft CD, p.2-24).

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 (draft CD, p.AX2-146).

New techniques are being developed, but UV absorption remains the method of choice for ambient O_3 monitoring near the Earth's surface. These commercial UV absorption detectors are available at a moderate price. They show good absolute accuracy with only minor cross sensitivity in clean to moderately polluted environments; they are stable, reliable, and sensitive (draft CD, p.AX2-147).

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, and two seasonal cumulative statistics, SUM06 and W126 are summarized to show how O_3 varies over space and time. 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:am, then average the 1-hr values from 2:00am to 9: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. Both the SUM06 and the W126 statistics were calculated using all 1-hr values from 8:00am to 8:00pm and finding the largest 3-month sum of these values in an O_3 monitoring season according to the secondary standard proposed in 1996 (FR Dec 13, 61(241) 1996 p. 65750). The SUM06 cumulative statistic is calculated by summing all 1-hr values that are greater than or equal to 0.06ppm for every day in a month. The W126 seasonal cumulative statistic is calculated similarly to the SUM06 statistic. The only difference is the weighting function. 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. The W126 statistic is a continuous, sigmoidal weighting function with an inflection point between 0.06ppm and 0.07ppm (Lefohn and Runeckles, 1987).

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 8-Hour and 1-Hour Statistics

High 8-hr average O_3 concentrations tend to occur near larger urban areas in the same patterns as the 8-hr concentrations. Elevated levels occurring in smaller urban and non-urban areas are most likely caused by transport (see Figure 2-2). These 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 2-2) (Fitz-Simons, *et al., 2005*). High 1-hr O_3 concentrations levels occur in the same patterns as the 8-hr concentrations (see Figure 2-3). The highest levels occur in California. (Fitz-Simons, *et al., 2005*).

2.5.2.2 Cumulative Seasonal Statistics

High SUM06 and W126 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 show higher values. The spatial patterns for SUM06 and W126 are very similar (See Figure 2-4, 2-5, 2-6, 2-7). (Fitz-Simons, *et al., 2005*).

Figure 2-2. 4th Highest Daily Maximum 8-hour Values in U.S. Counties, 2002-2004.

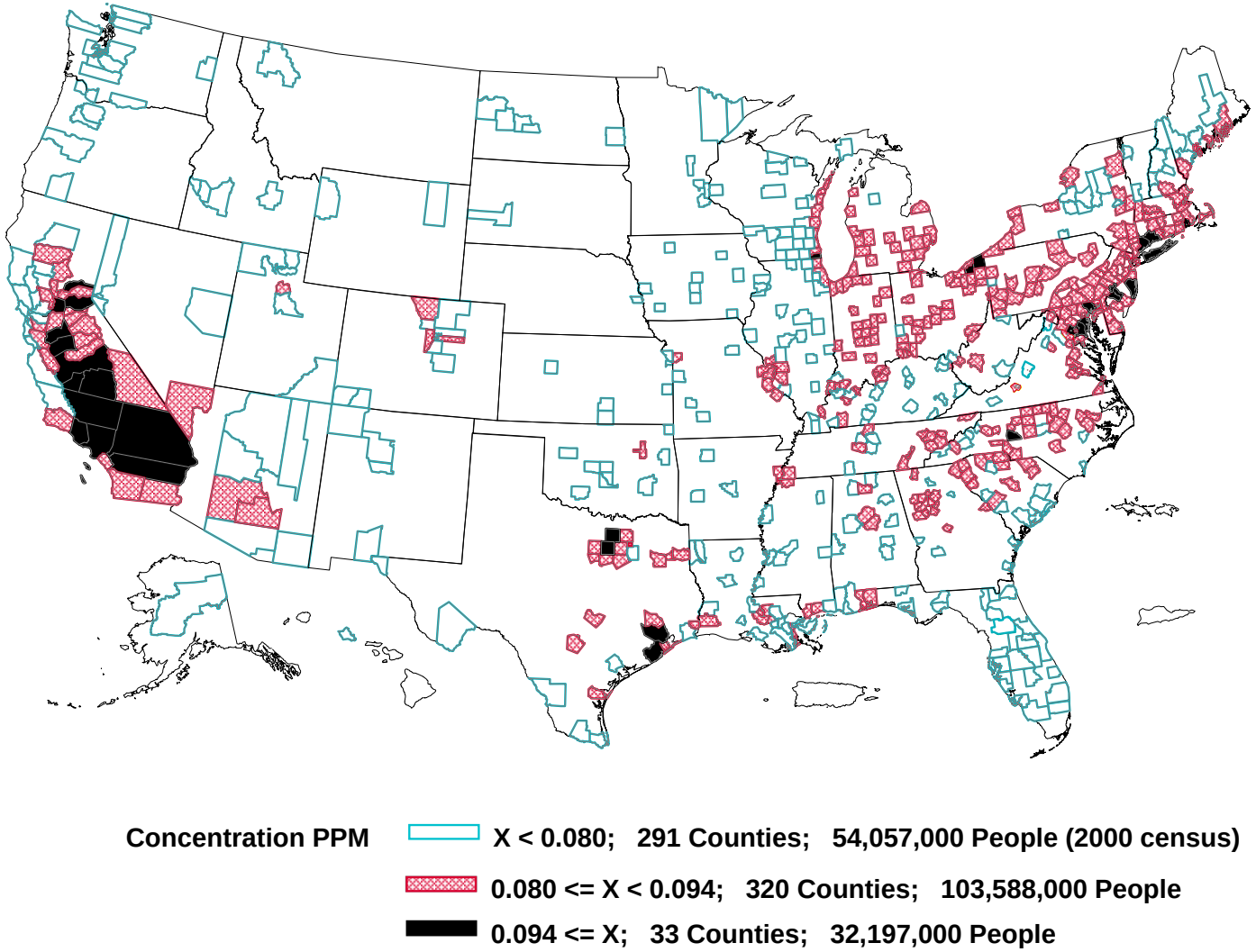
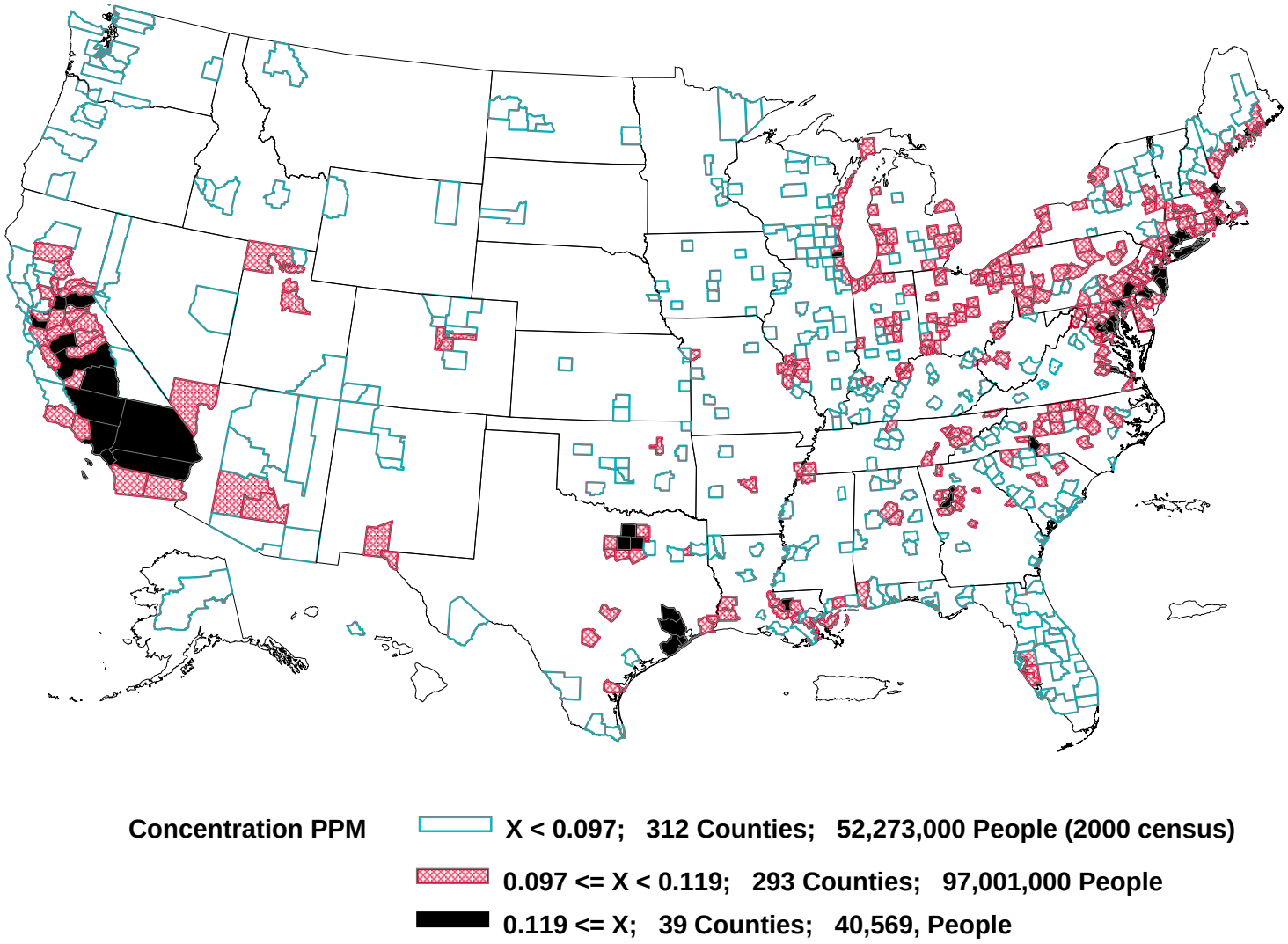


Figure 2-3. 2nd Highest Daily Maximum 1-Hour Values in U.S. Counties, 2002-2004.



2.5.3 Temporal Variability

Temporal variability consists of several time frames when considering characterization of ground level air quality data. Multi-year trends characterize long term variability or year to year variability. Trends can usually give evidence as to 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-hr 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 ozone values are presented in Figures 2-8 and 2-9. Figure 2-8 presents data from sites in the AQS that meet trends criteria and have locations described as Urban and Center City. Figure 2-9 presents data from CASTNET which are rural locations.

The trends are similar. The urban trends have more data and more variation. The rural means are slightly lower that 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 ozone values are presented in Figures 2-10 and 2-11. Figure 2-10 presents data from sites in the AQS that meet trends criteria and have locations described as Urban and Center City. Figure 2-11 presents data from CASTNET which are rural locations. The trends are similar. As in the 8-hr data, urban trends have more data and more variation with the means for the urban trends being 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 ozone 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 short term variation (see Evaluating Ozone Control Programs in the Eastern United States: NO_X p.17, U.S. EPA*, 2005b*).

Figure 2-4. Highest 3-Month SUM06 Exposure Index in U.S. Counties, 2001 AQS Data.

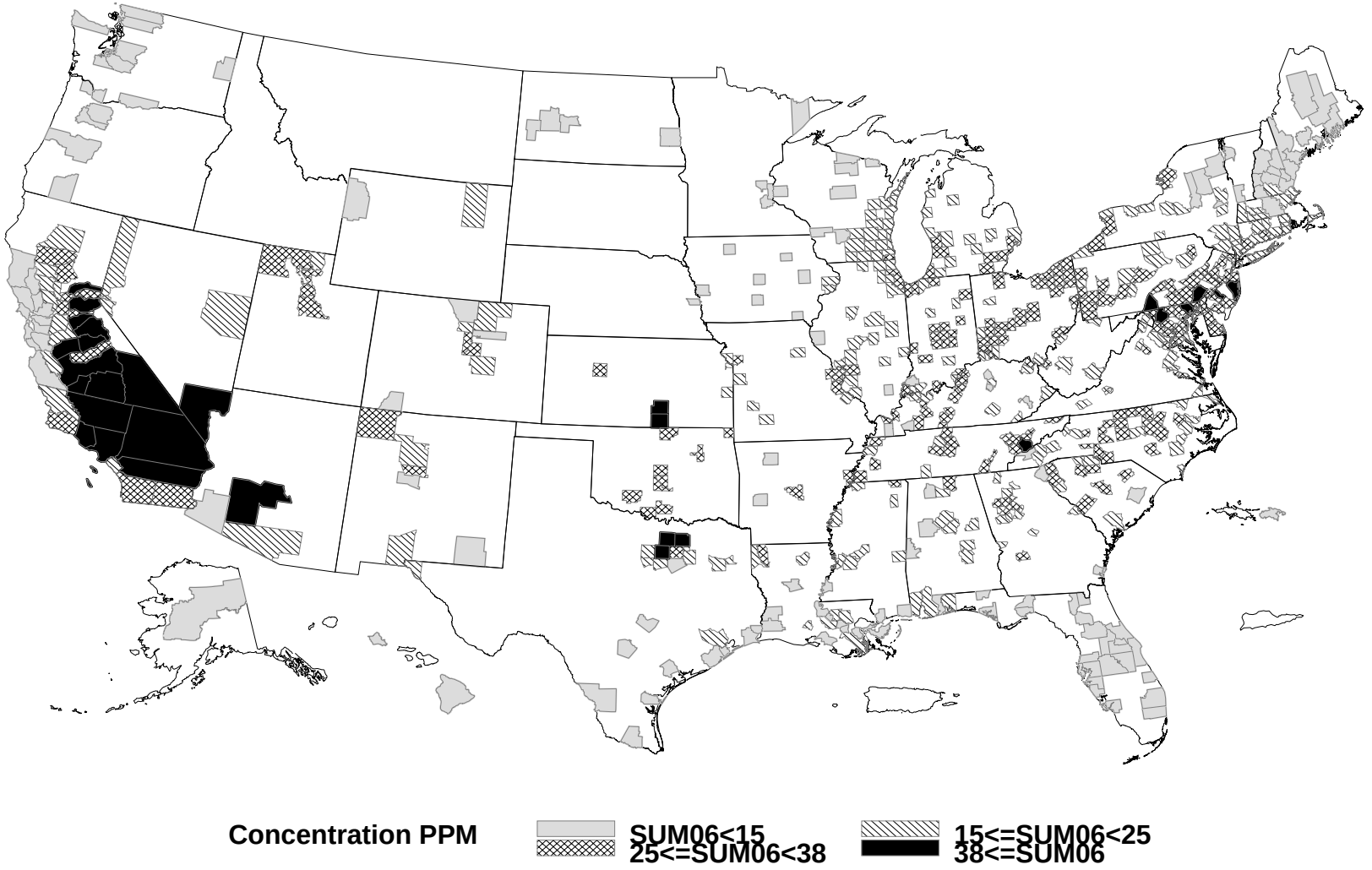


Figure 2-5. Highest 3-Month W126 Exposure Index in U.S. Counties, 2001 AQS Data.

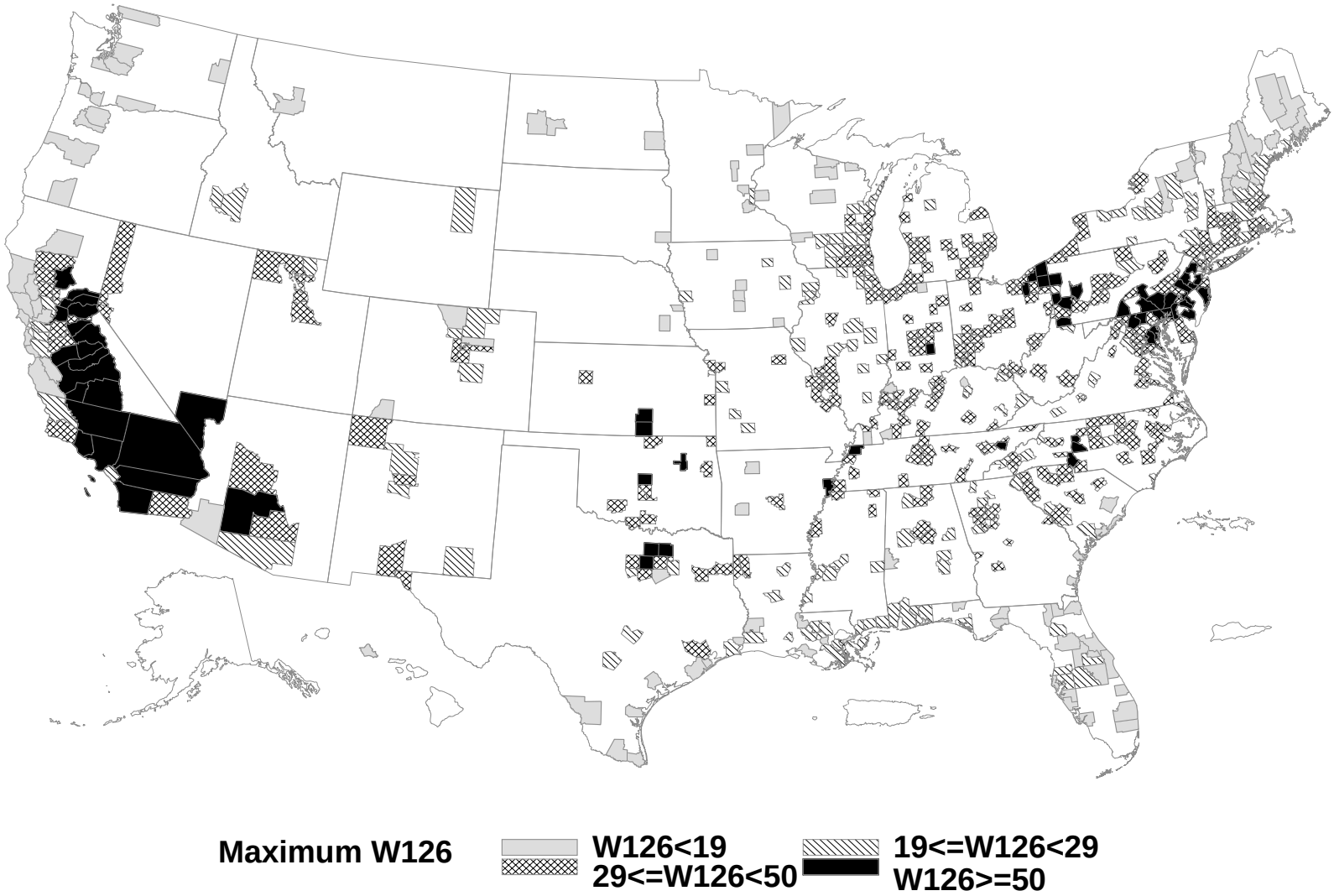


Figure 2-6. Highest 3-month SUM06 Exposure Index in U.S. Counties, 2001 CASTNET Data.

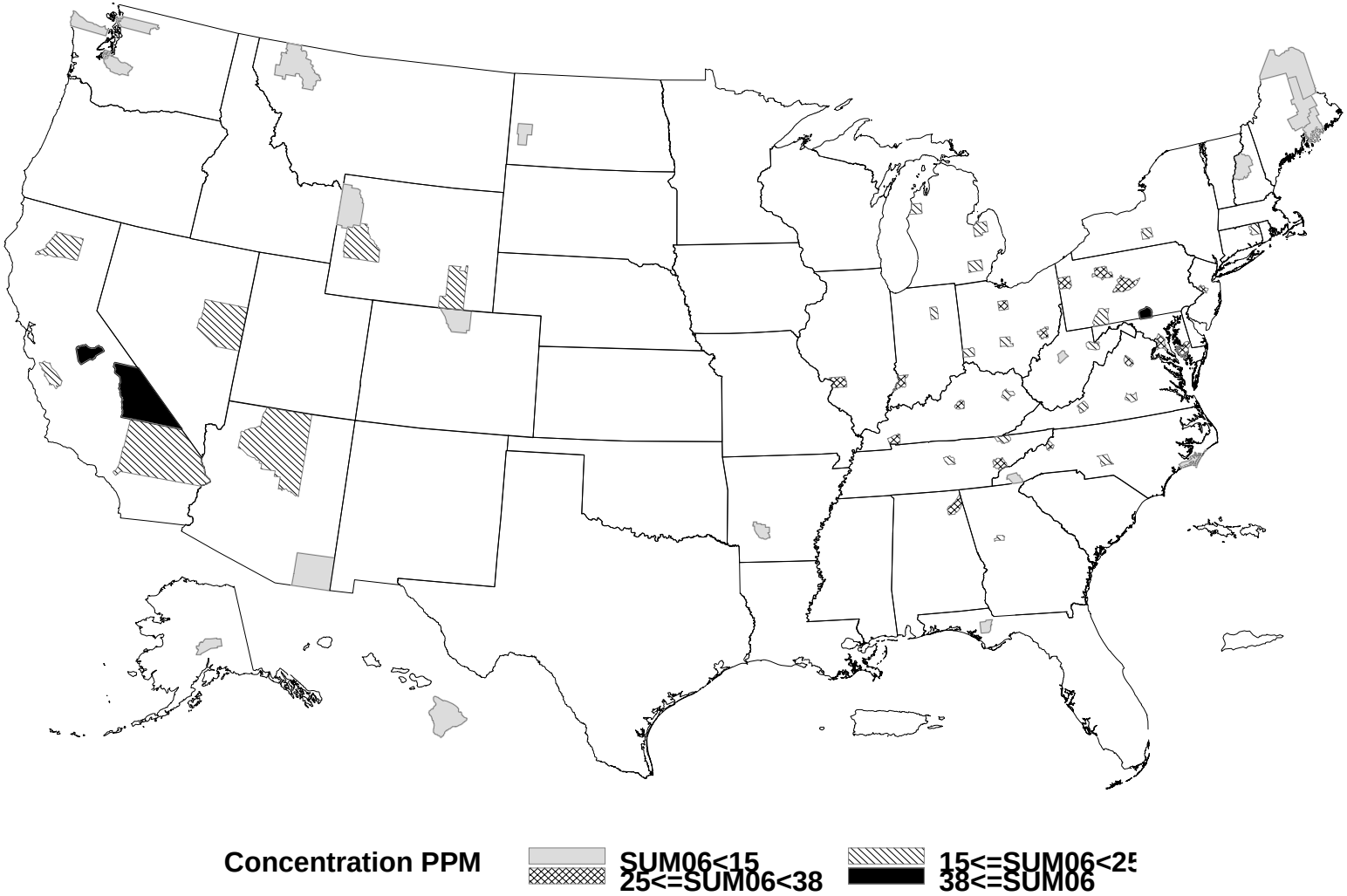


Figure 2-7. Highest 3-Month W126 Exposure Index in U.S. Counties, 2001 CASTNET Data.

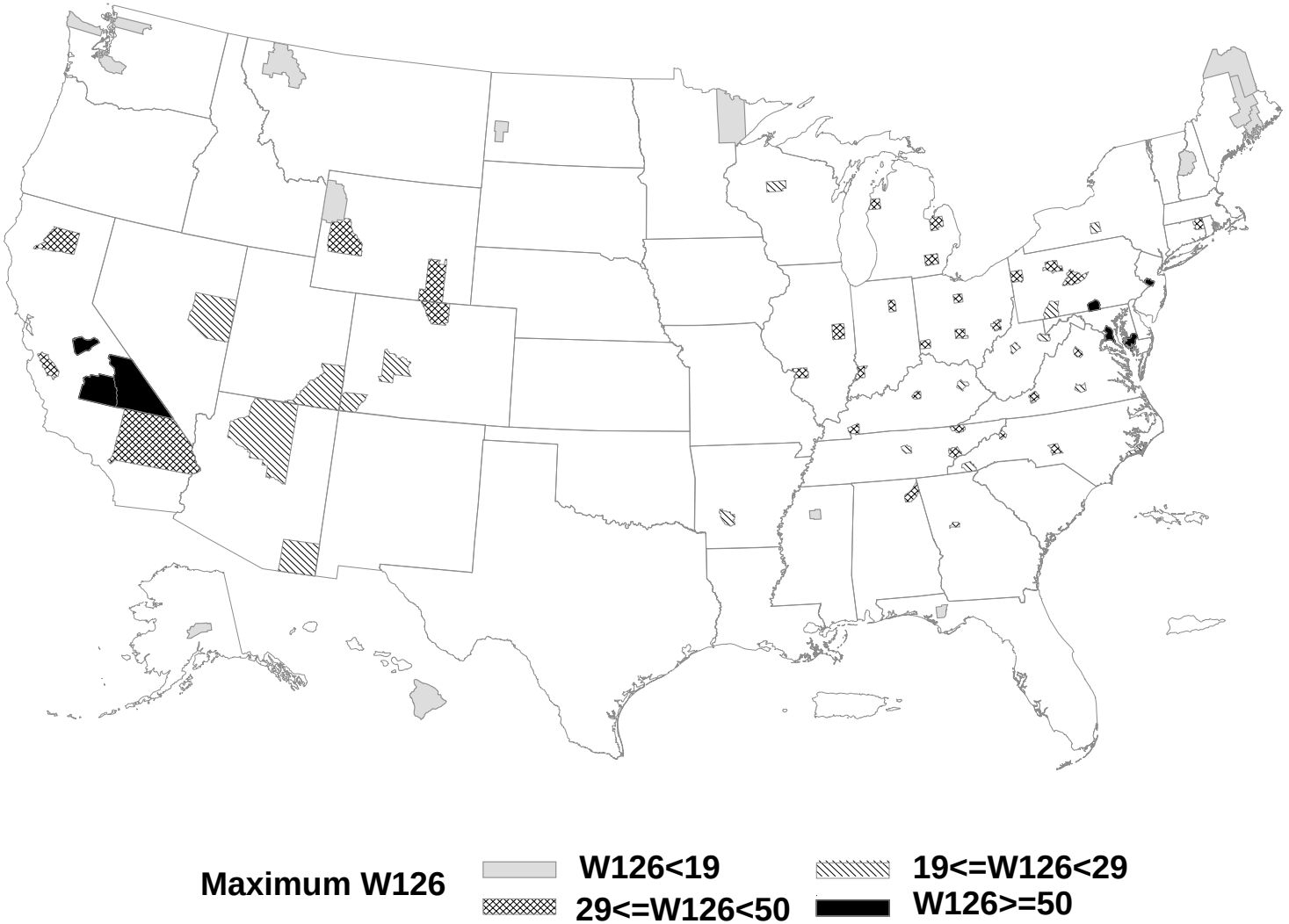


Figure 2-8. 4th Highest Daily Maximum 8-hour Ozone Values 1990-2004 (Urban).

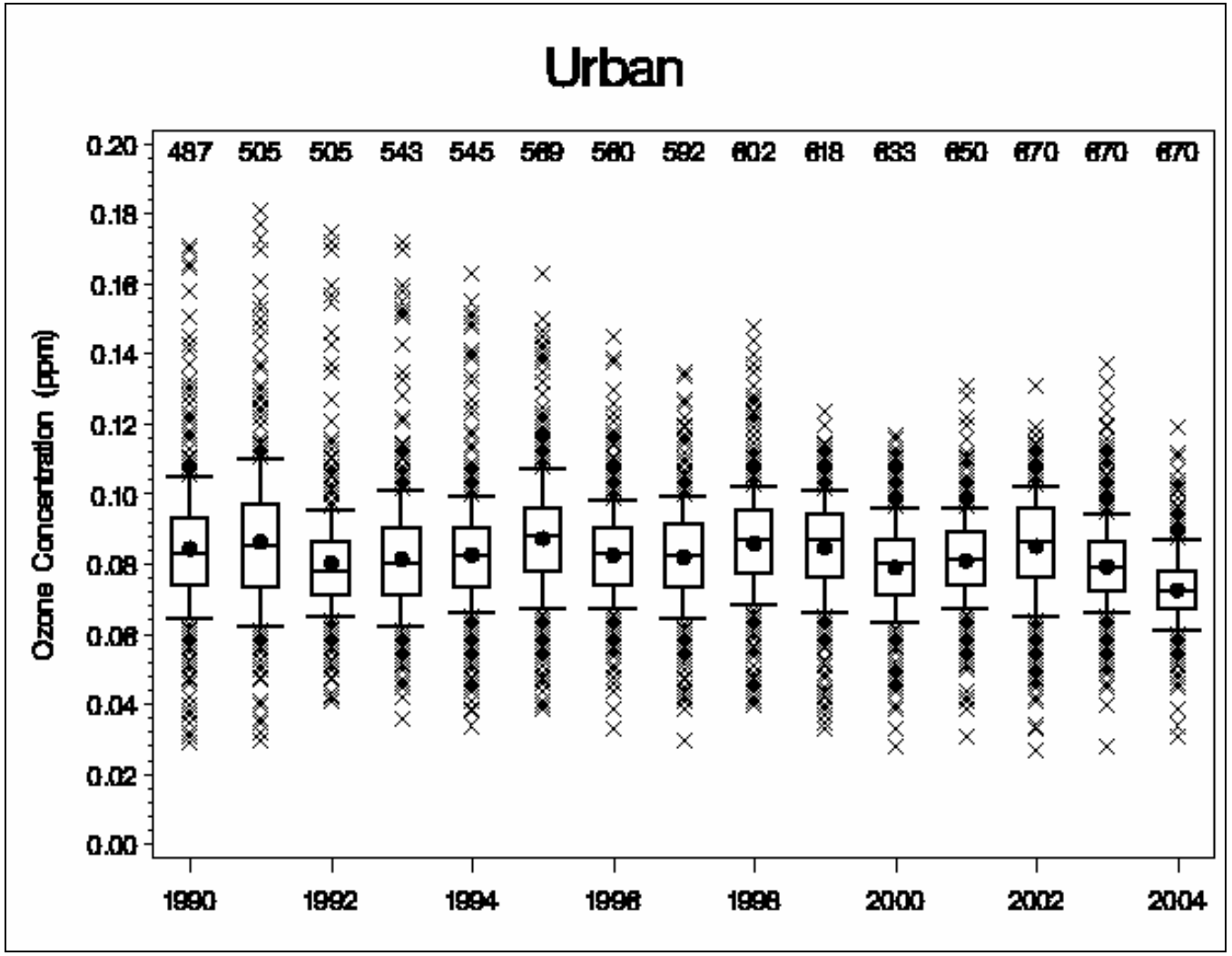


Figure 2-9. 4th Highest Daily Maximum 8-hour Ozone Values 1990-2004 (Rural).

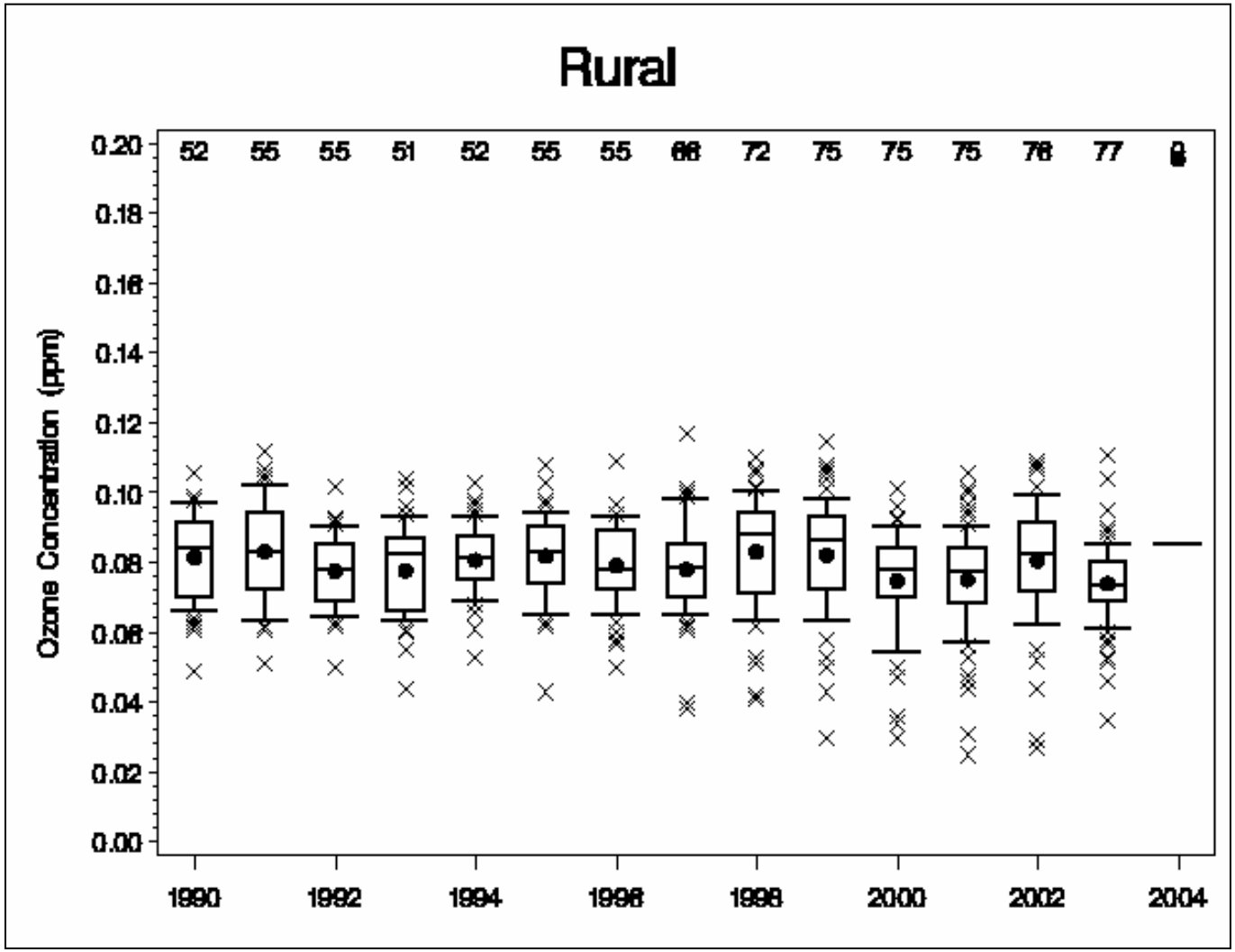


Figure 2-10. 2nd Highest Daily Maximum 1-hour values 1990-2004 (Urban).

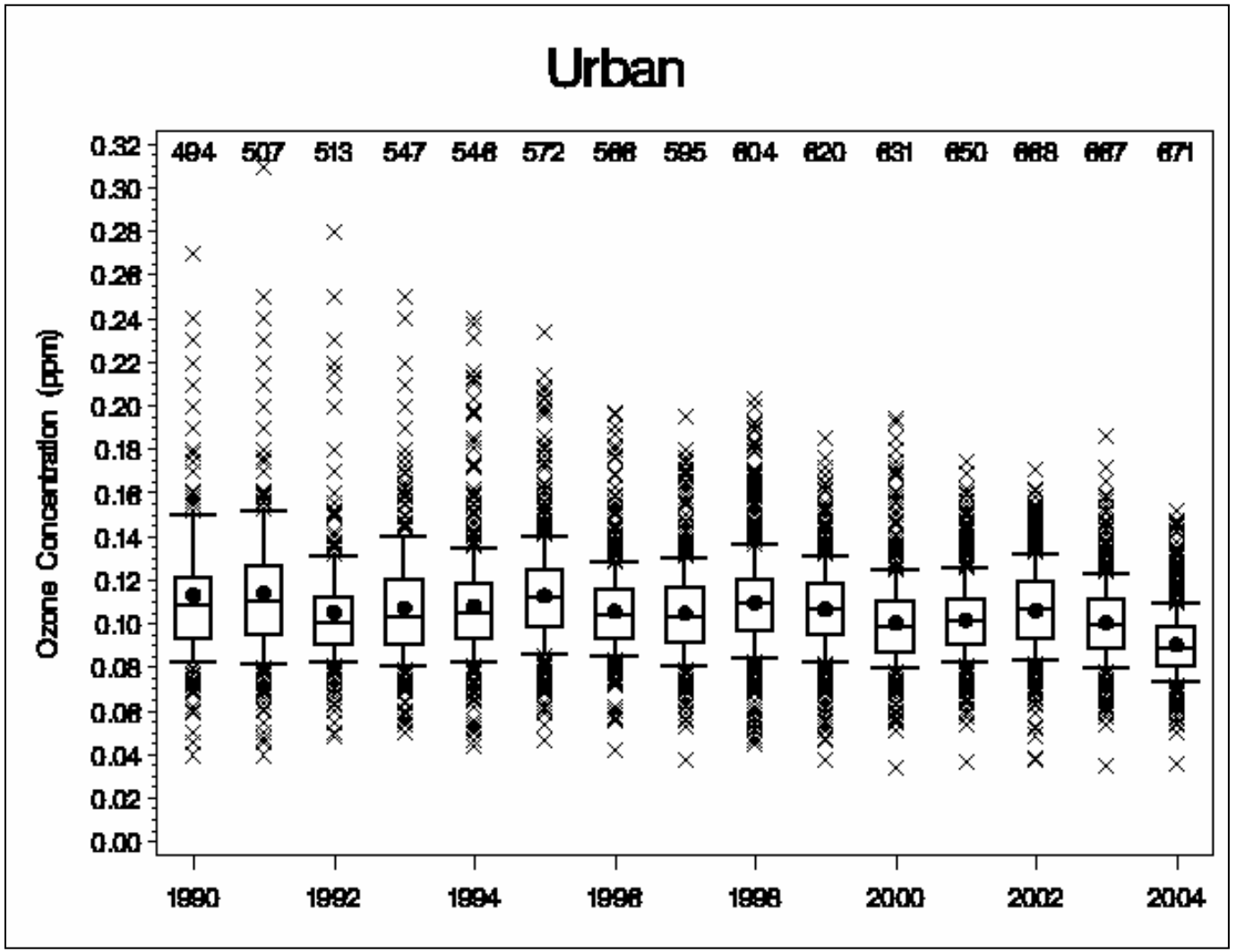
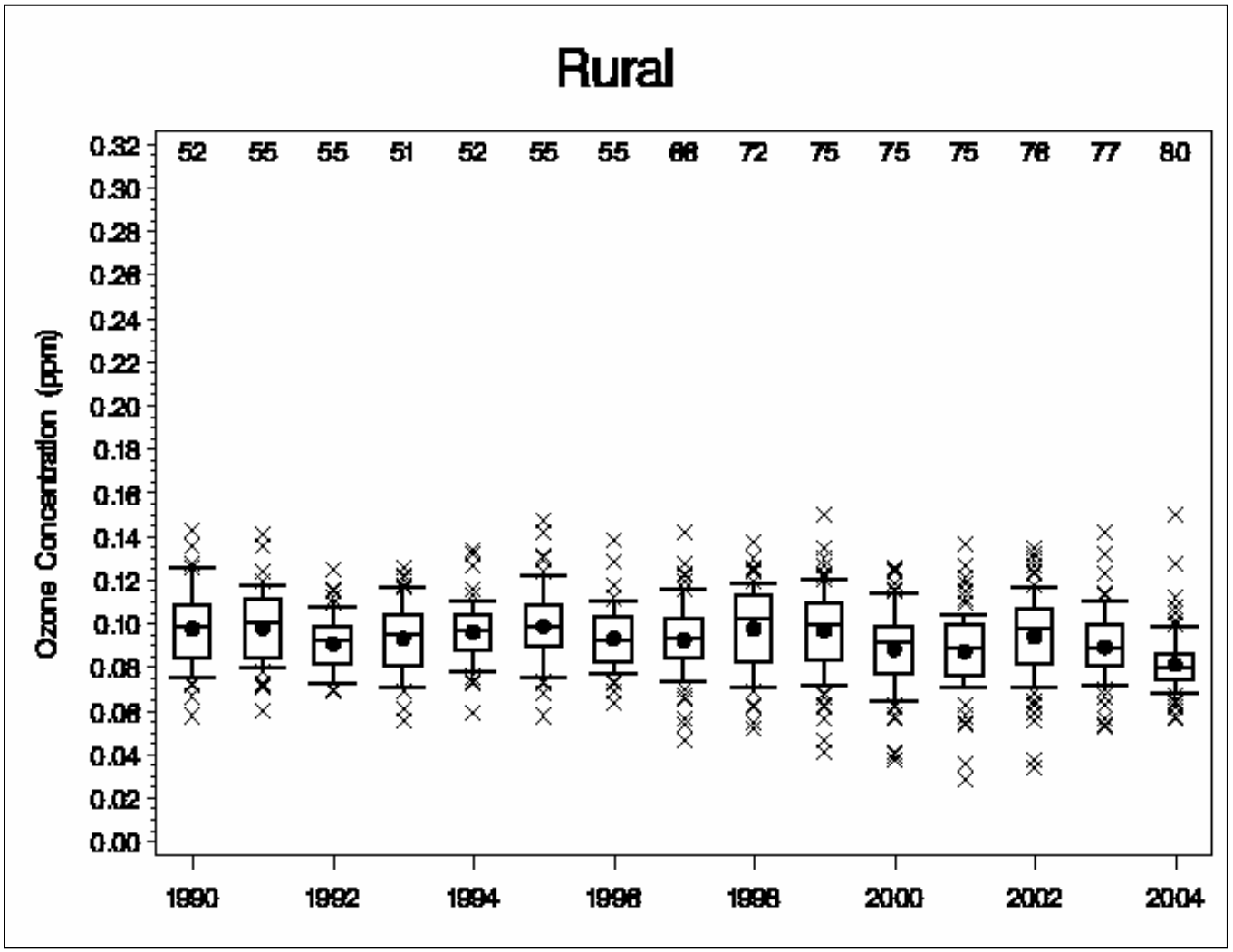


Figure 2-11. 2nd Highest Daily Maximum 1-hour Ozone Values 1990-2004 (Rural).



2.5.3.2 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 2-12 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 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 2-13 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*).

2.5.3.3 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.

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 2-14 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 2-15 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

Figure 2-12. 2nd Highest Daily Maximum 1-hour Ozone Values from 2004 by Month.

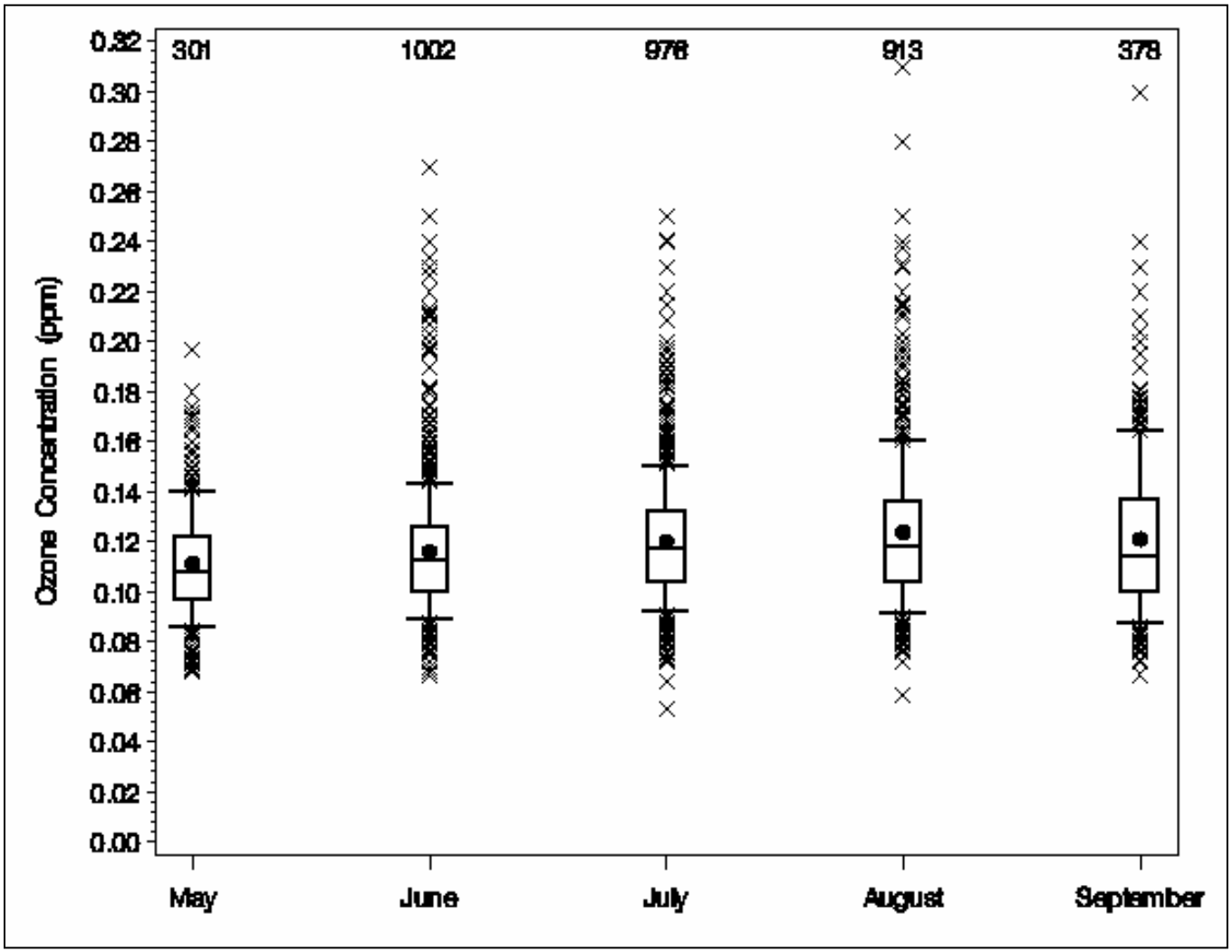


Figure 2-13. 4th Highest Daily Maximum Ozone Values from 2004 by Month.

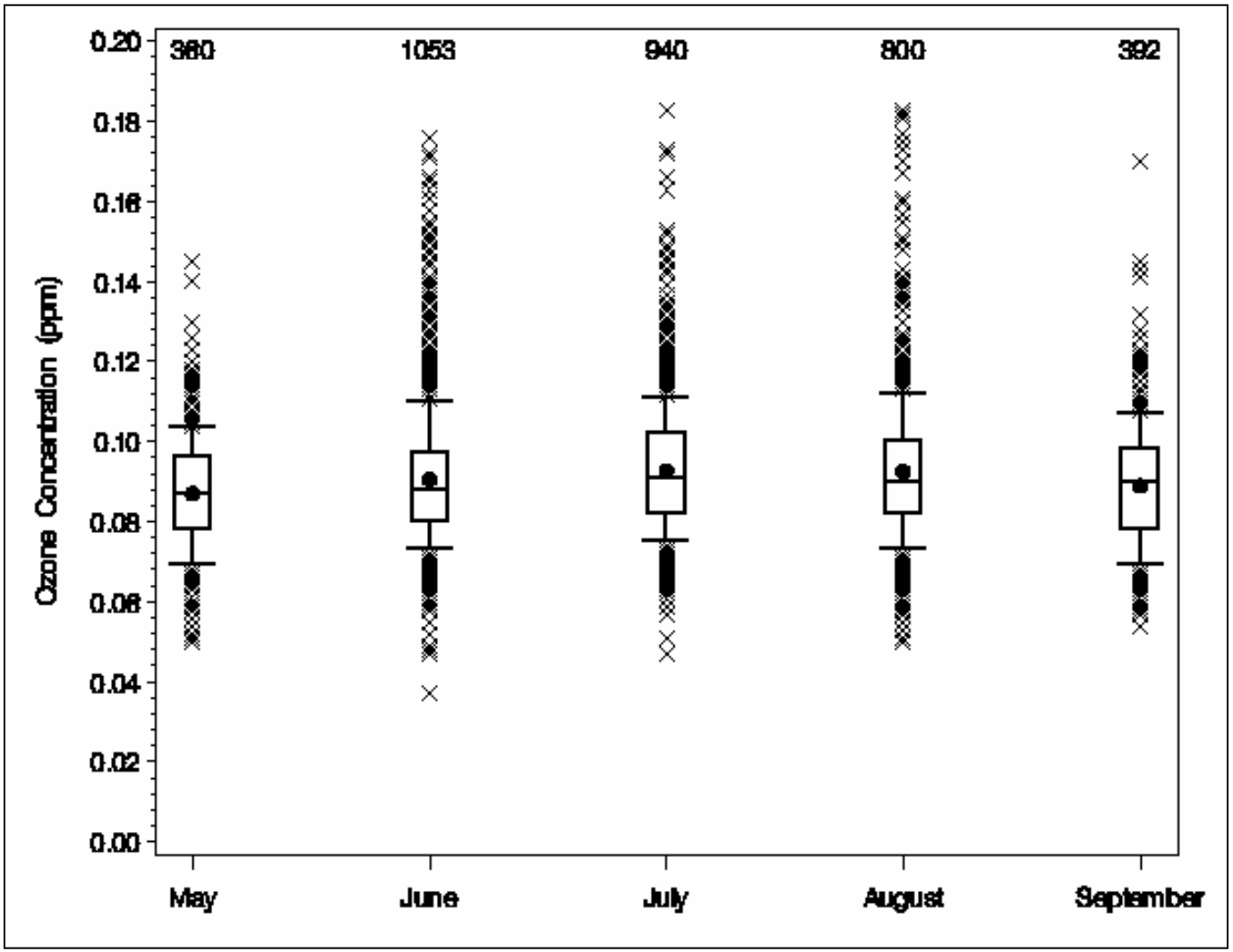


Figure 2-14. 1-Hour Diurnal Week Day Pattern for Urban Sites, May Through September 2004.

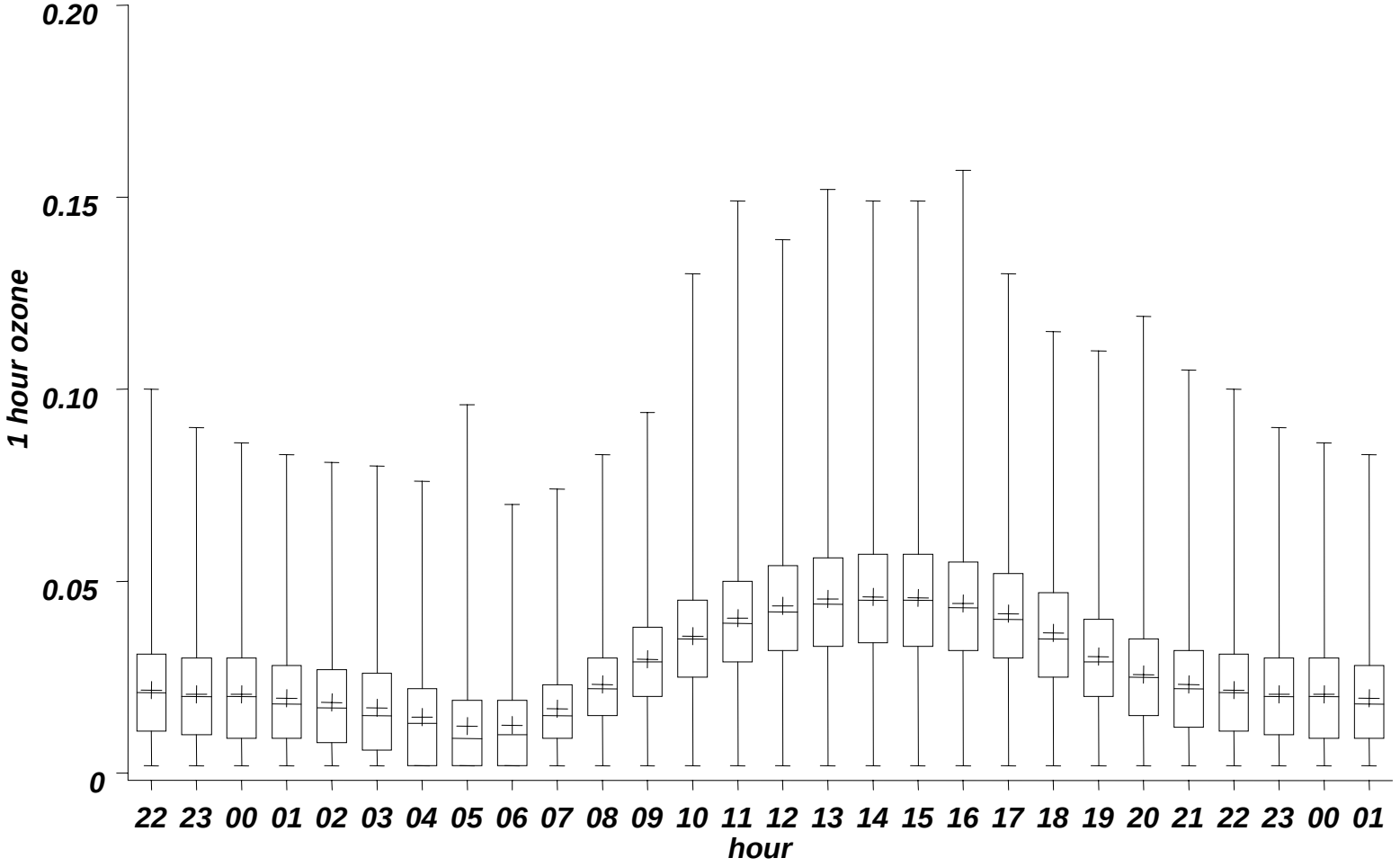
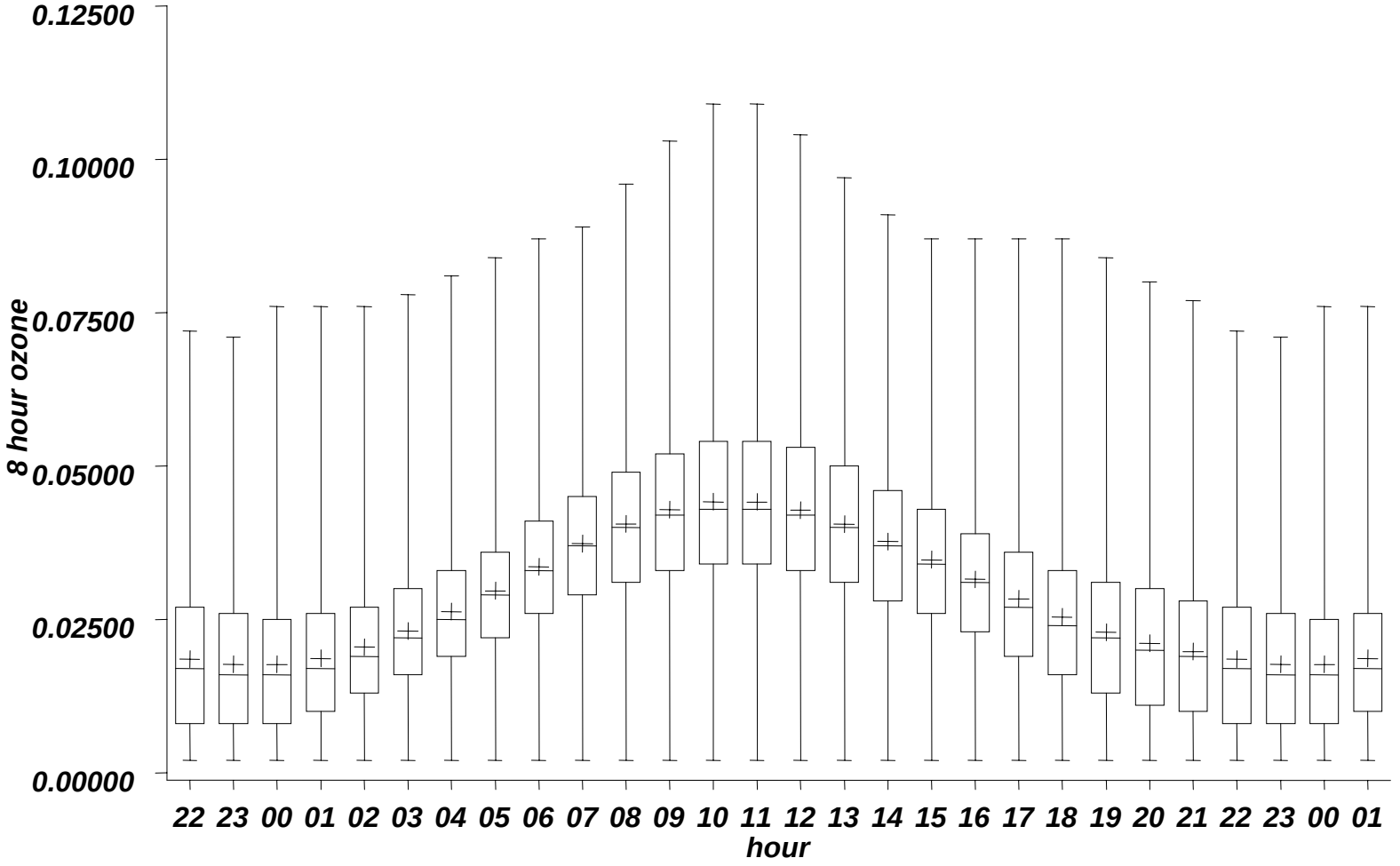


Figure 2-15. 8-Hour Diurnal Week Day Pattern for Urban Sites, May through September



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 2-16 through 2-19 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 is 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 has a smooth sinusoidal pattern but reaches 2 peaks in the day (12:00 midnight and 12:00 noon). The week end pattern 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*).

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 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. 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 2-10 and 2-20). As the length of these episodes increase, 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*).

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 2-8 and 2-21). 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*).

Figure 2-16. 1-Hour Diurnal Week Day Pattern for Rural Sites, May through September 2004.

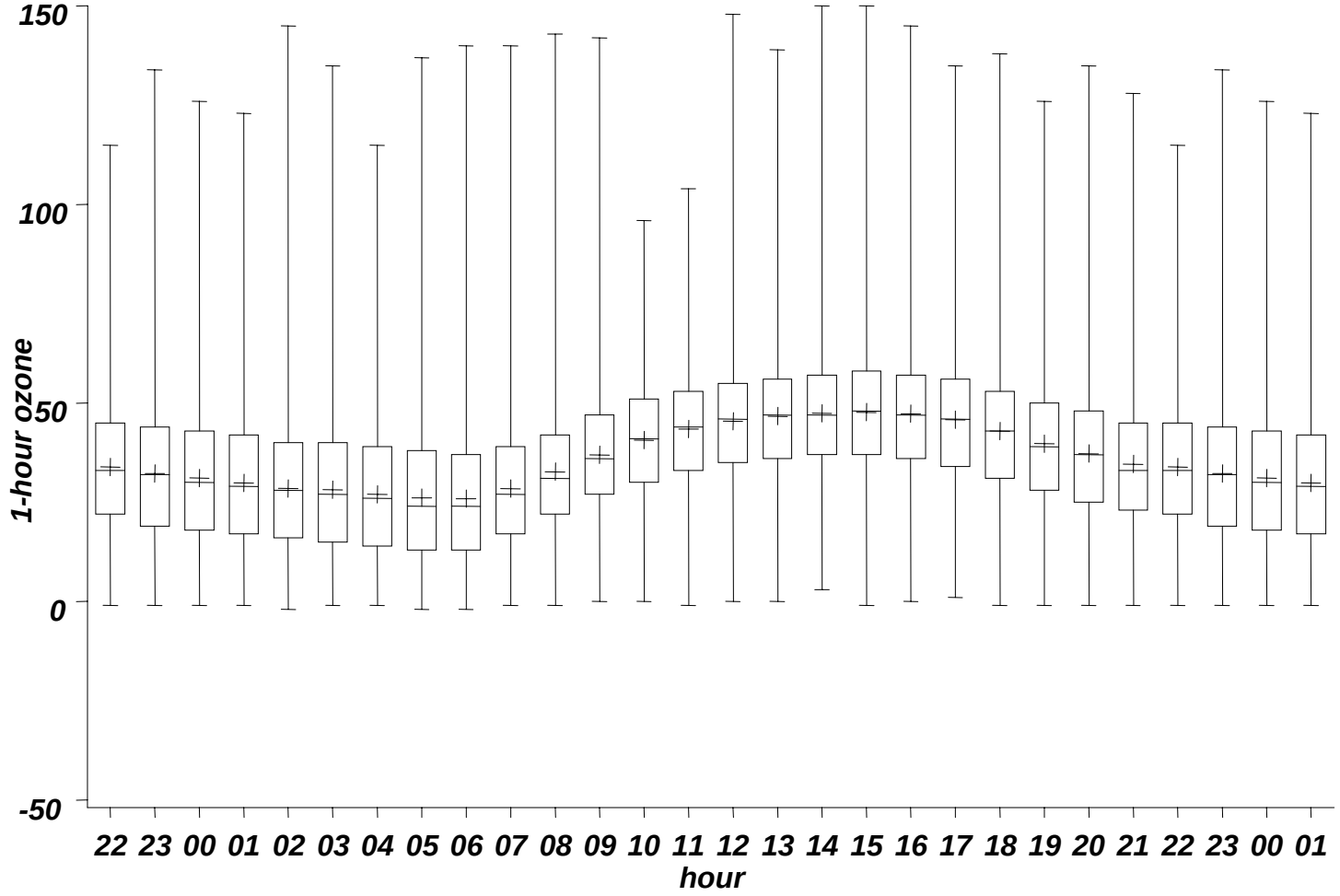


Figure 2-17. 1-Hour Week End Diurnal Pattern for Rural Sites, May through September 2004.

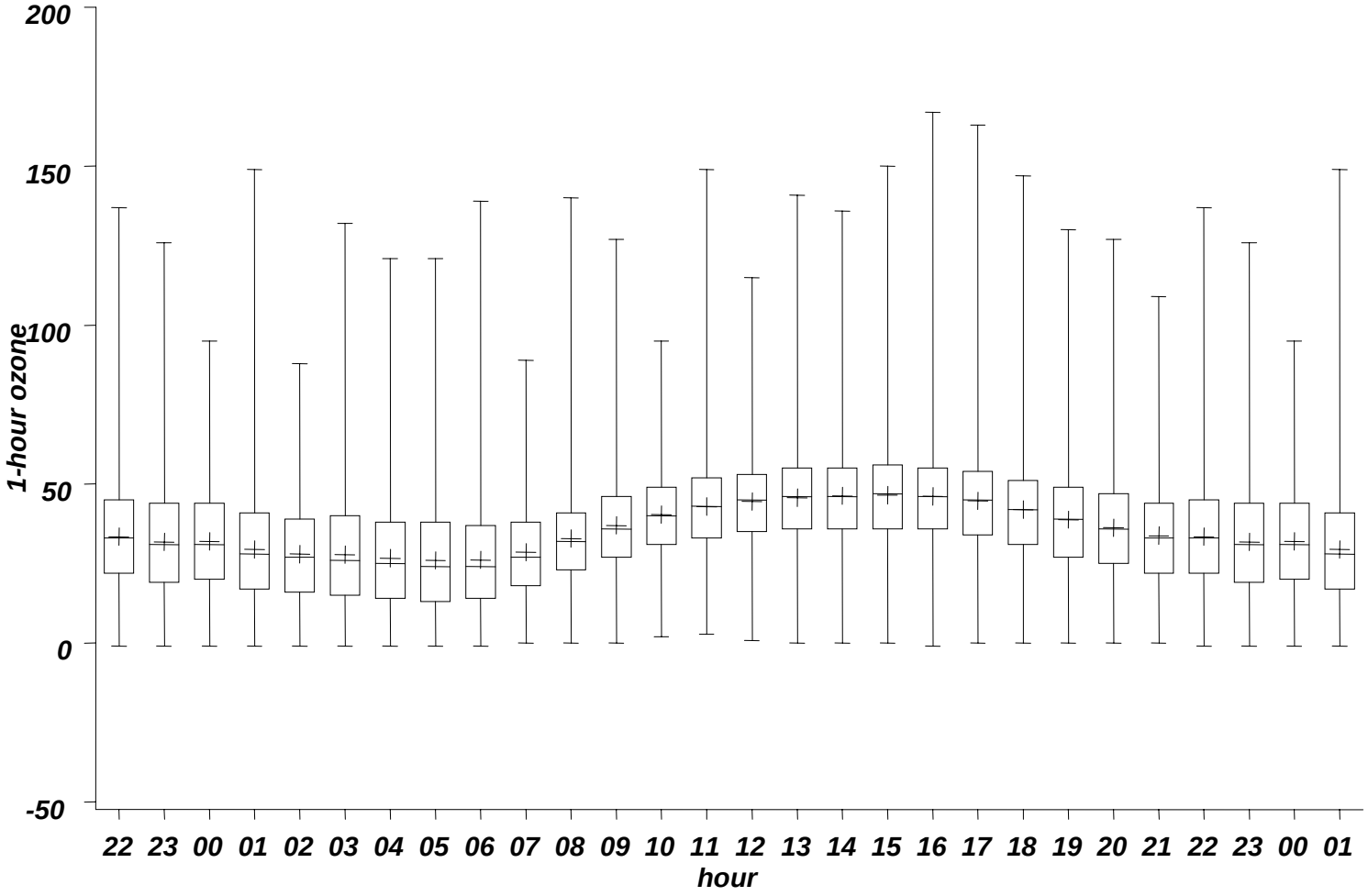


Figure 2-18. 8-Hour Week Day Diurnal Pattern for Rural Sites, May through September 2004.

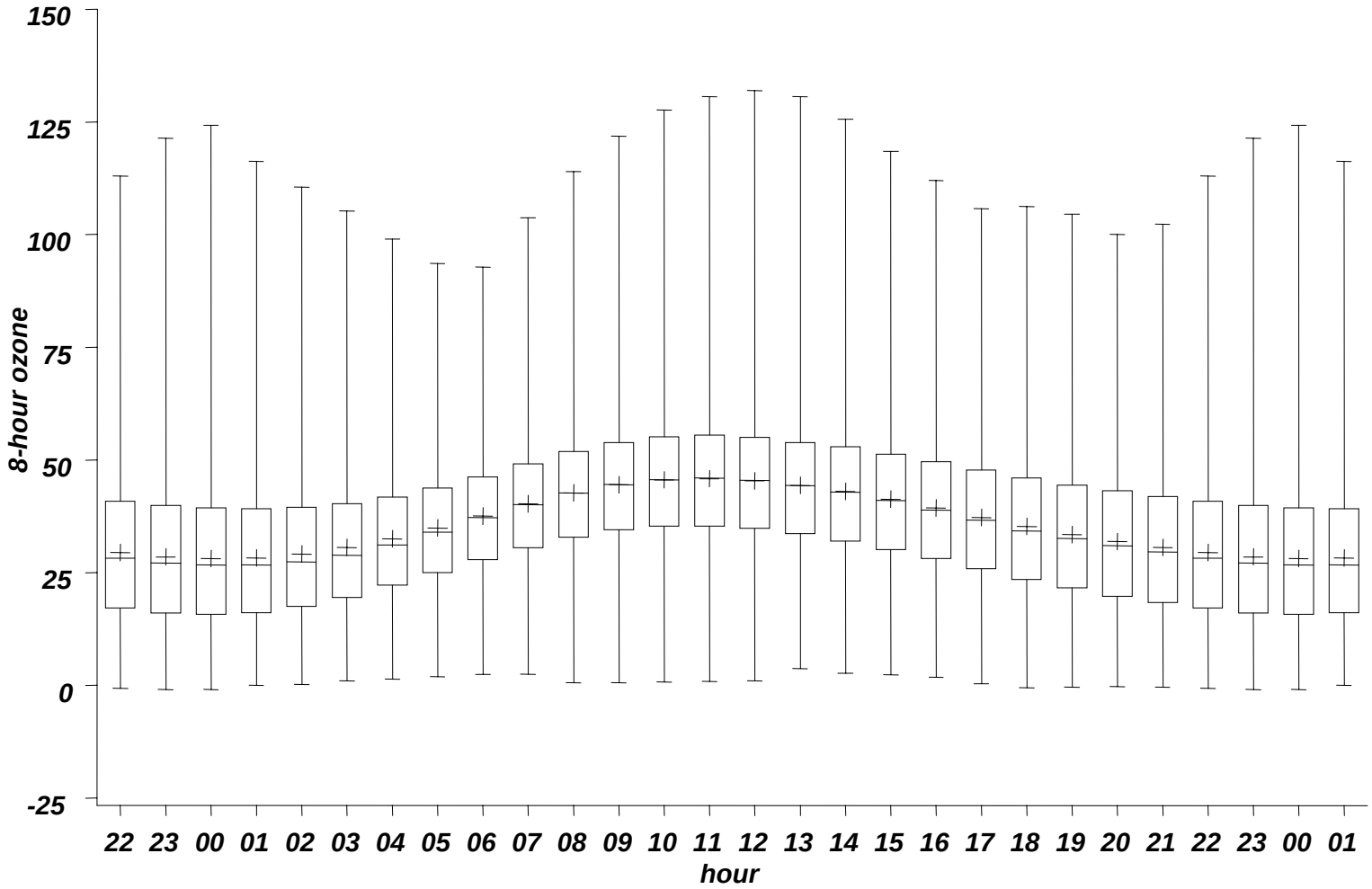


Figure 2-19. 8-Hour Week End Diurnal Pattern for Rural Sites, May through September 2004.

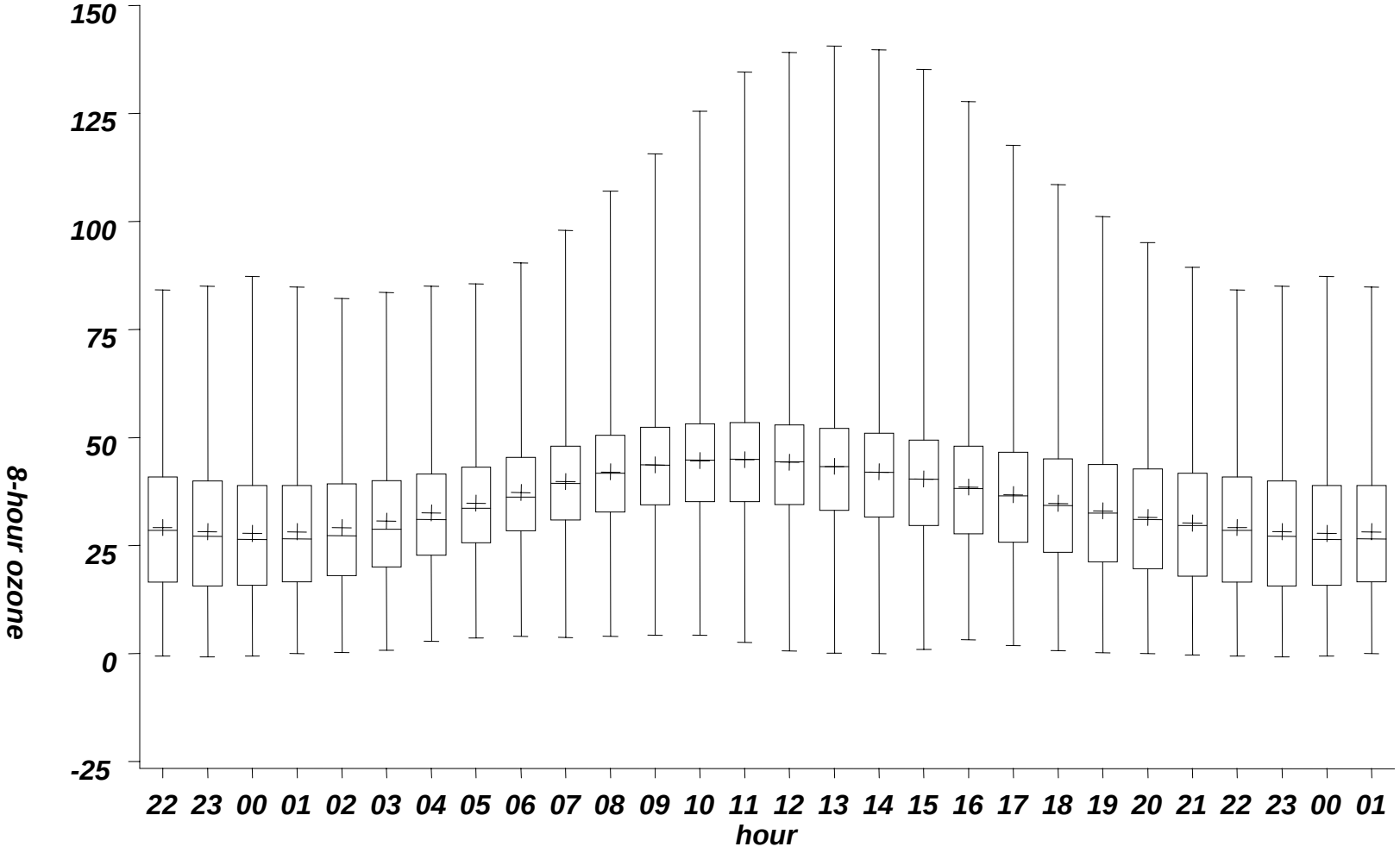


Figure 20. Length of Episodes over 0.12 ppm by Year for 1-hour O_3 Data

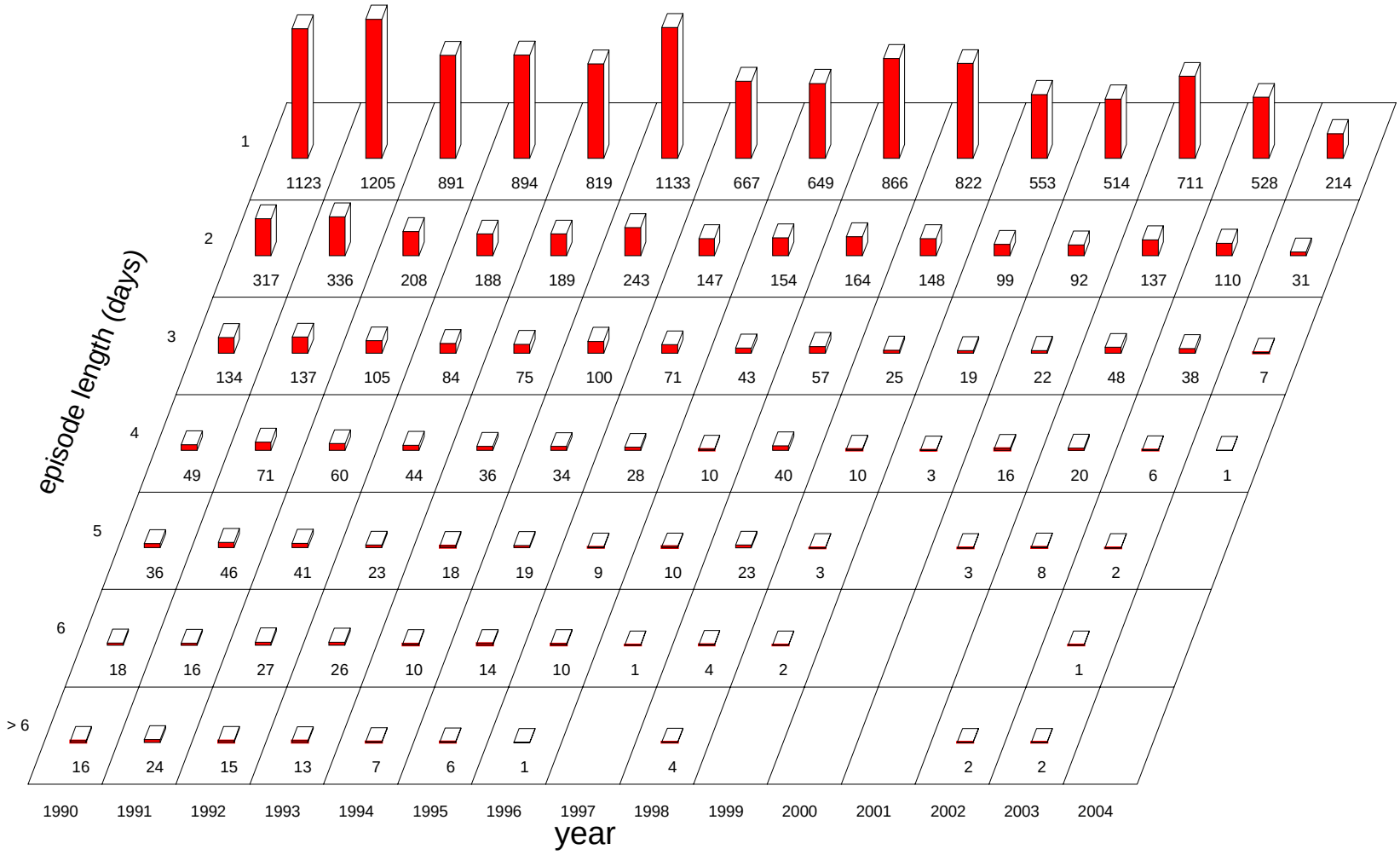
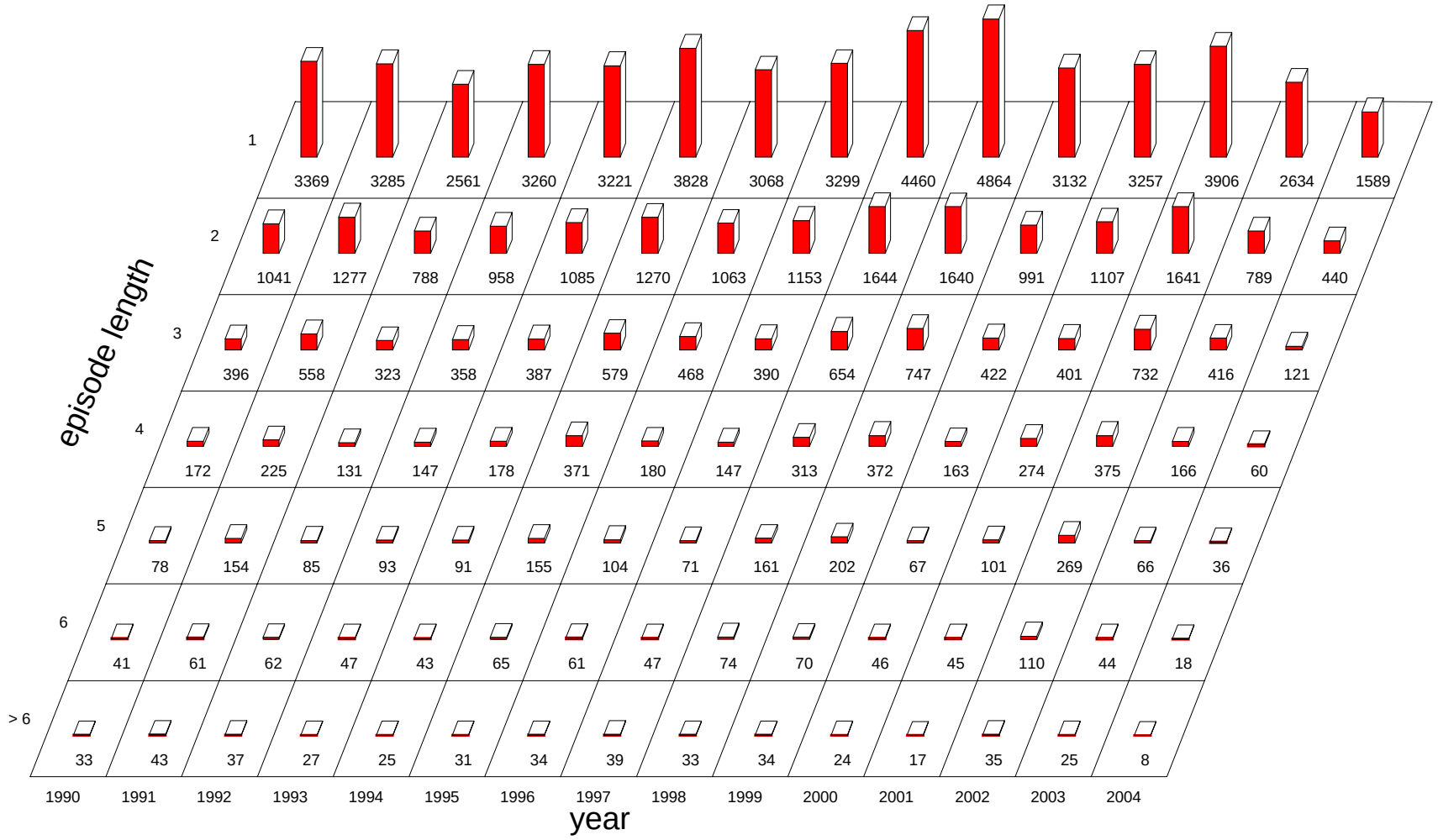


Figure 2-21. Length of Episodes over 0.08 ppm by Year for 8-hour O_3 data



As episode length and level increase for both 1-hr and 8-hr O_3 data the frequency decreases (Figure 2-22 and 2-23). 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 2-24). 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 33-34 days (see Figure 2-25). The frequencies for these episodes are so small compared to the frequencies of the 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 BACKGROUND LEVELS

Policy relevant background (PRB) concentrations are those concentrations that would result in the United States in the absence of anthropogenic emissions in North America (including Canada and Mexico) (U.S. EPA, 2005a, AX3-130). Background concentrations include contributions from global natural sources and from anthropogenic sources outside North America. As discussed in Chapter 5 of this Staff Paper, PRB concentrations enter into the assessment of risk to human health.

Contributions to background levels of O_3 include: photochemical interactions involving natural emissions of VOCs, NOX, 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 (draft 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). This 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.

Figure 2-22. Length of Episodes over Levels for 1-hour O3 Data (2002-2004).

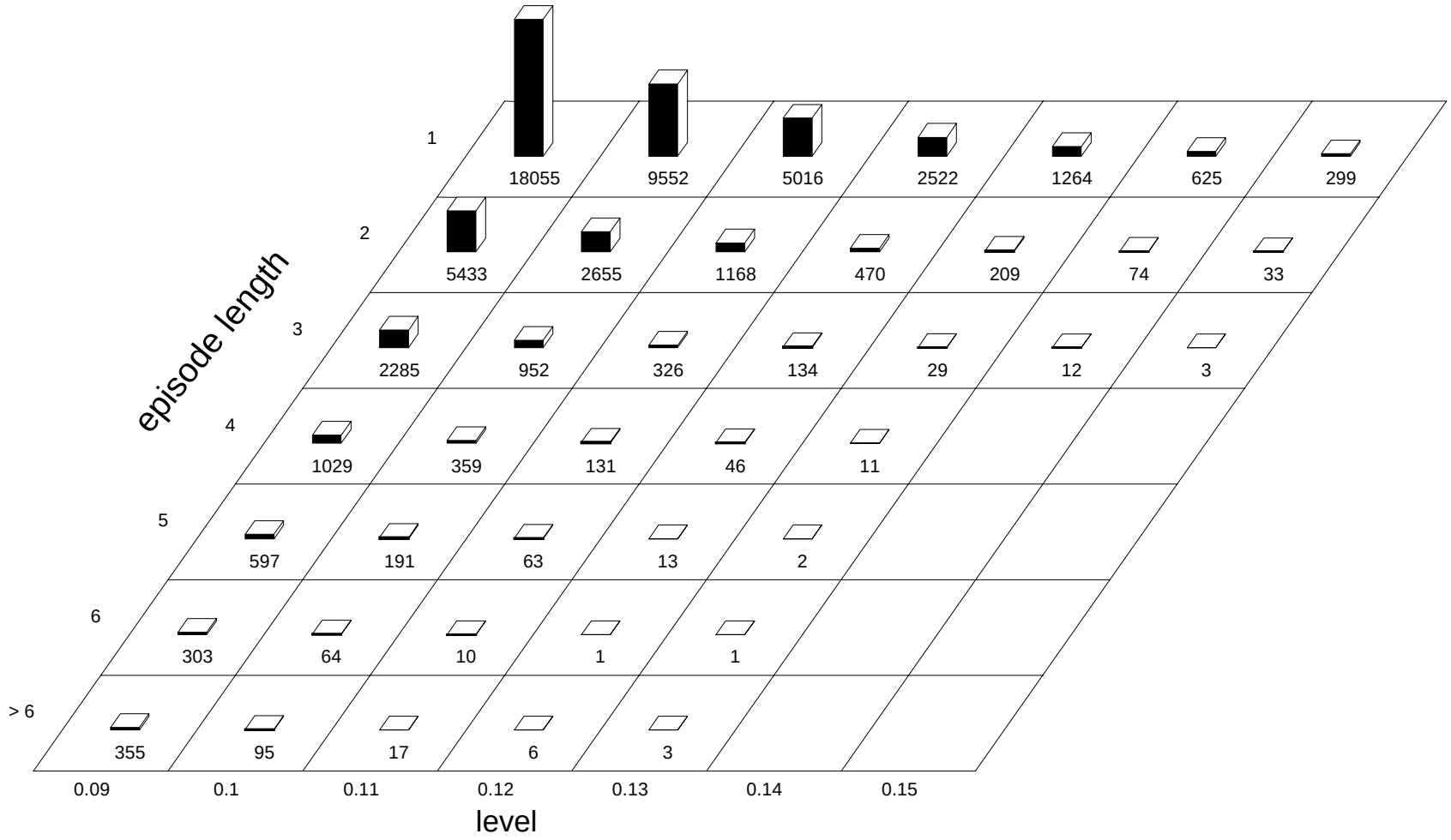


Figure 2-23. Length of Episodes over Levels for 8-hour O_3 Data (2000-2004).

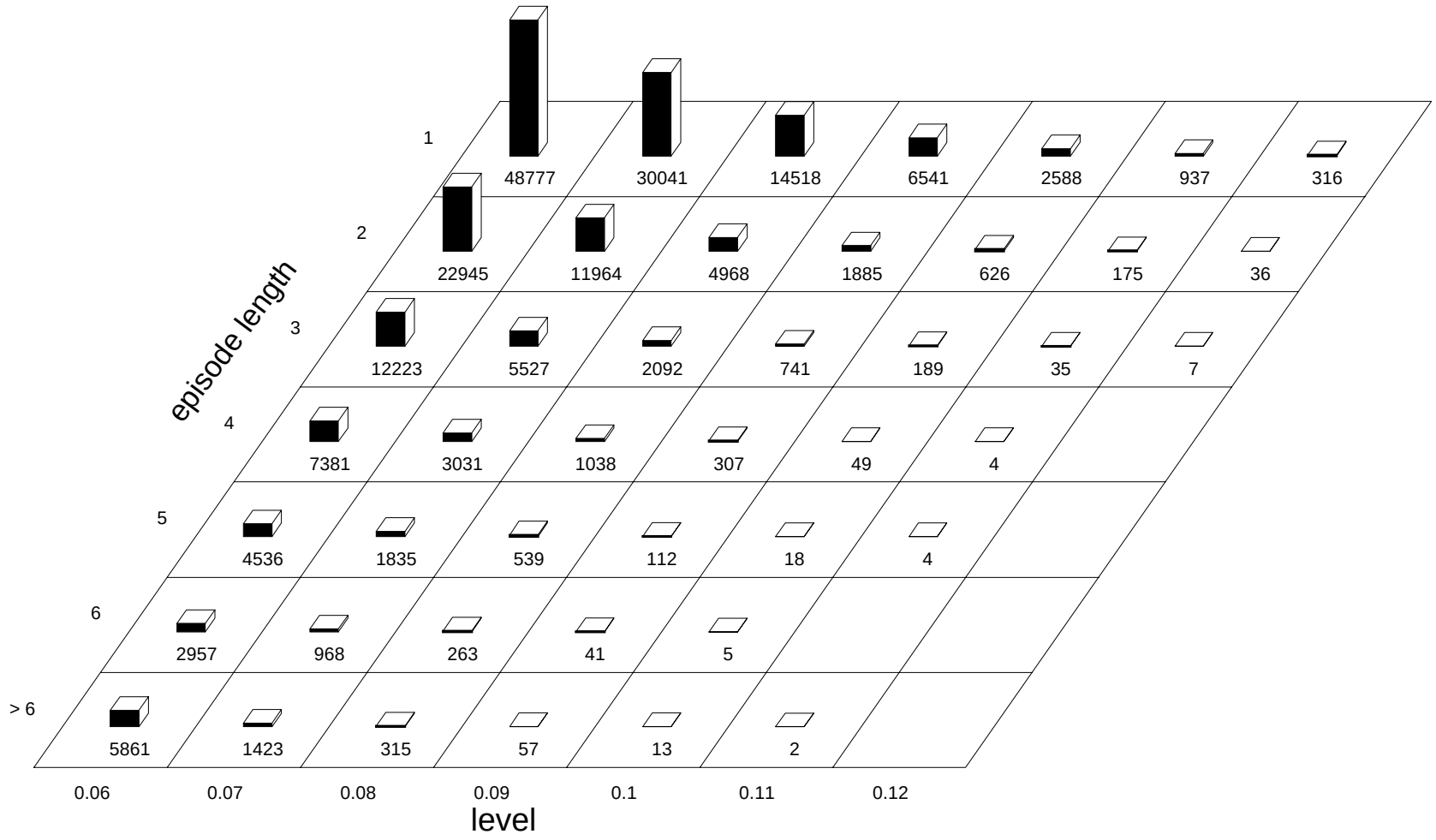


Figure 2-24. Length of Gaps in Days Between Episodes over 0.08 ppm for 8-Hour Data (2000-2004).

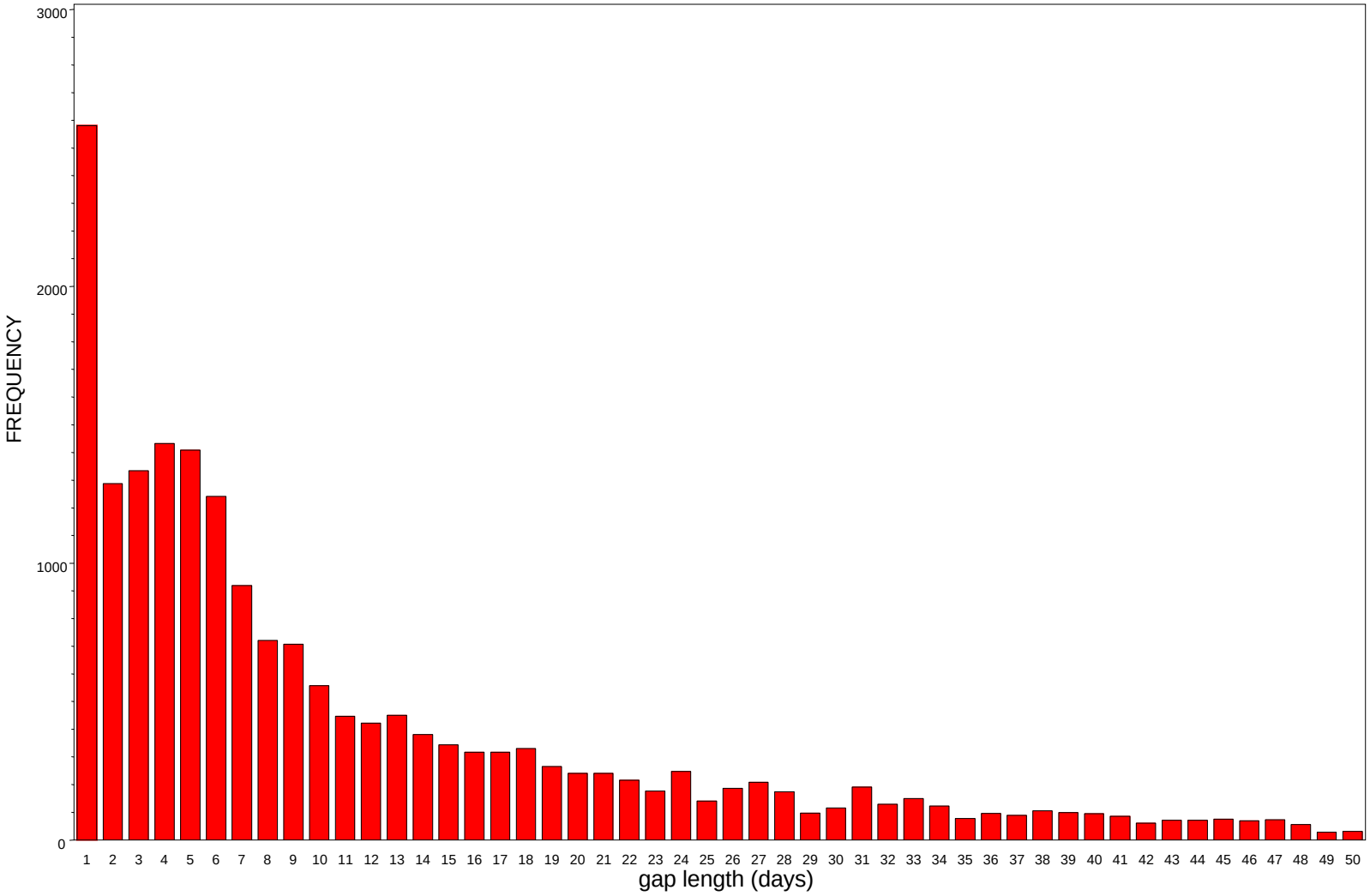
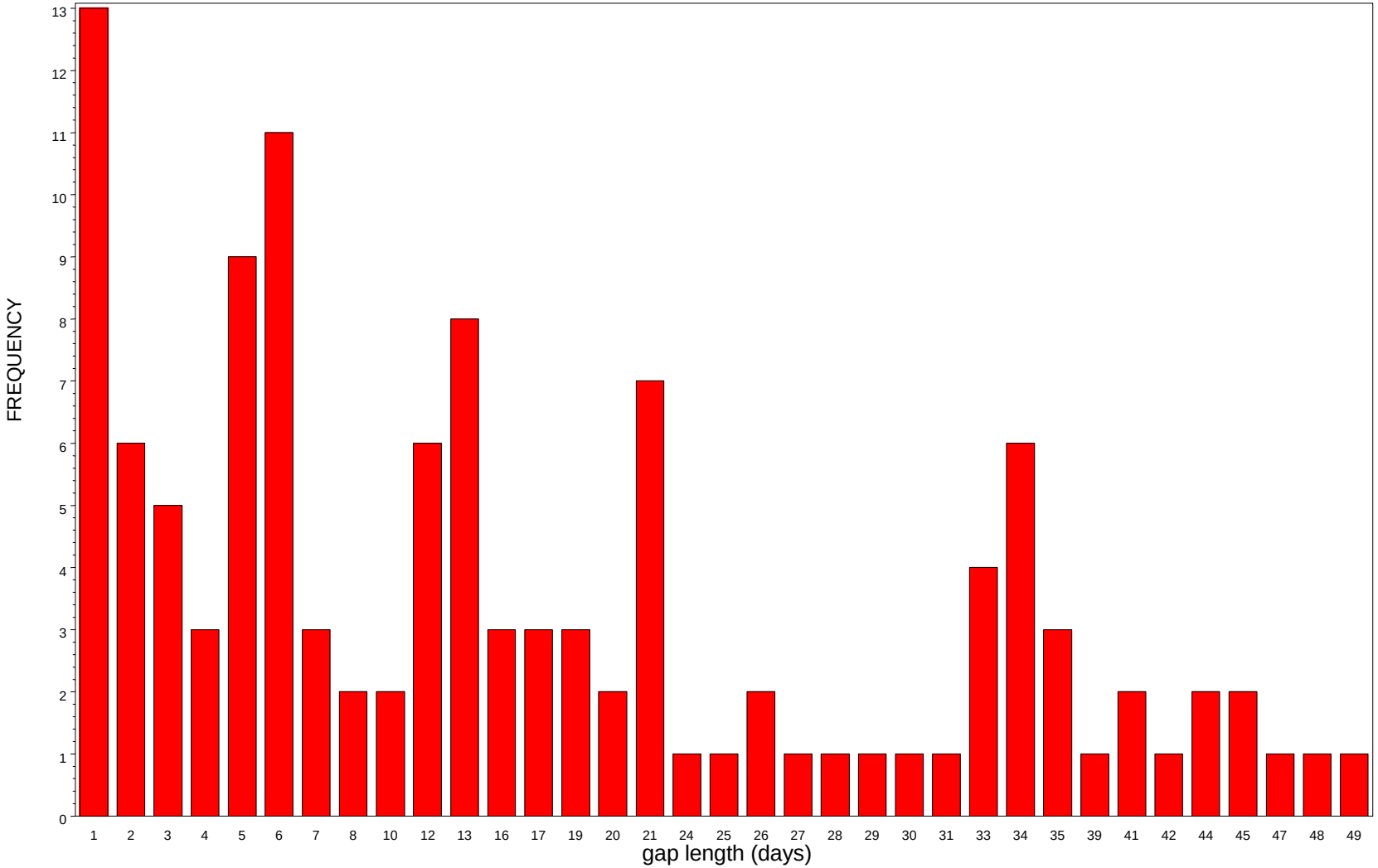


Figure 2-25. Length of Gaps in Days Between Episodes over 0.12 ppm for 8-hour O_3 Data (2000-2004).



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).

Ozone concentrations measured at remote monitoring sites in the Northern Hemisphere show a broad range in mean and median concentrations, as do annual maximum 1-hr concentrations. Generally, concentrations increase with elevation and the highest concentrations are found during spring. The overall average of the annual median O_3 concentrations at all remote sites in the continental United States is about 30 ppb and excluding higher elevation sites it is about 24 ppb. Maximum concentrations may be related to stratospheric intrusions, wildfires, and intercontinental or regional transport of pollution. However, it should be noted that all of these sites are affected by North American anthropogenic emissions to some extent making an interpretation based on these data alone problematic (draft CD, p.AX2-147).

Background estimates of hour O_3 concentrations from observations tend to be at the higher end of the range of PRB estimates (25 to 45 ppbv), while the observational results, as well as those from prior modeling studies, indicate that background O_3 concentrations in surface air are usually below 40 ppbv. The background O_3 concentrations derived from observations may be overestimated if observations at remote and rural sites contain some influence from regional pollution. Natural O_3 concentrations are generally in the 10 to 25 ppbv range and never exceed 40 ppbv. The range of the hemispheric pollution enhancement (the difference between the background and natural O_3 concentrations) is typically 4 to 12 ppbv and only rarely exceeds 20 ppbv (< 1% total incidences). The stratospheric contribution is usually below 10 ppbv (draft CD, p.AX2-149).

In addition to policy relevant background concentrations, a second component of more rare episodic high-concentration events over shorter periods of time (e.g., days or weeks) both within and outside the U.S., Canada, and Mexico (e.g., volcanic eruptions, large forest fires). Specific natural events such as stratospheric intrusions (STE), wildfires, and volcanic eruptions, both of U.S. and international origin, can lead to very high levels of O_3 comparable to, or greater than, those driven by man-made emissions in polluted urban atmospheres. Because such excursions can be essentially uncontrollable, EPA has in place policies that can remove consideration of them, where appropriate, from decisions when implementing the NAAQS (U.S. EPA, 1986).

Currently, estimates of PRB O_3 concentrations used in this document are based on predictions obtained by the global scale, three dimensional, chemical transport model GEOS-CHEM (Fiore et al., 2003). Estimates of PRB O_3 concentrations cannot be derived solely from

measurements of O_3 at relatively unpolluted sites because of long-range transport from anthropogenic source regions within North America. 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 estimated to be in the range of 0.015 to 0.035 ppm from 1300 to 1700 local time, 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. The maximum probability of stratospheric intrusions reaching about 1800 m altitude was less than 1 %. Stratospheric intrusions occur with higher probabilities of 1 to 2 % at about 4100 m, and 10 % at about 5400 m. Thus, stratospheric intrusions only rarely elevate O_3 concentrations at low-altitude sites and only slightly more often elevate them at high-altitude sites.

The analysis used in Chapter 4 and 5 uses the estimates of PRB from the GEOS-CHEM model. The 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 in hourly values for the 2001 warm season. The model estimated the PRB and total ozone concentrations at each grid point.

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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 contained in Chapters 4 through 7 of the draft 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 O_3 NAAQS is to be based. It is intended to provide a coherent framework for assessment of human health effects posed by ambient O_3 in the U.S. and to facilitate consideration of the key policy-related issues to be addressed in this draft Staff Paper.

This chapter summarizes that evidence as a basis for future development of staff conclusions and recommendations related to primary standards for O_3. These staff conclusions and recommendations will be discussed in Chapter 6 of the second draft Staff Paper. Furthermore, this assessment addresses key issues relevant to quantitative assessment of controlled human exposure and epidemiological evidence so as to provide a foundation for quantitative health risk assessment, as discussed in Chapter 5 of this draft Staff Paper.

The decision in the last O_3 primary NAAQS review was focused substantially on short-term and prolonged controlled-exposure studies reporting lung function decrements, respiratory symptoms, and respiratory inflammation in humans. The current review of the draft CD has emphasized a large number of epidemiological studies with these and additional health endpoints, including acute and long-term effects of O_3 on premature mortality, enhanced respiratory symptoms and lung function decrements in asthmatic individuals, school absences, emergency room visits and hospital admissions for respiratory causes, published since the last review, with some important new information also coming from toxicology, dosimetry, and controlled human exposure studies. As discussed in more detail in section 3.3 of this draft Staff Paper, highlights of the new evidence include:

- Newly available, large multicity studies, designed specifically to examine the acute effects of PM and O_3 on mortality, provide much more robust and credible information than was previously available in the last NAAQS 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]) showed positive and significant O_3 effect estimates for all cause (nonaccidental) mortality.

- 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 emergency department visits for respiratory diseases and a significant O_3 effect on respiratory hospital admissions.

- New controlled human-exposure studies offer evidence of increased airway responsiveness to allergens in subjects with allergic asthma exposed to O_3 and of increased airway allergen responsiveness in subjects with allergic rhinitis following exposure 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, dosimetry, increased susceptibility to respiratory infection, and the biological plausibility of acute effects and chronic, irreversible respiratory damage.

The scientific evidence and conclusions presented in this chapter are based upon information contained in the draft CD's evaluation of health evidence from various disciplines. Section 3.2 is an overview of potential mechanisms by which exposure to O_3 may result in health effects, discussed in Chapters 5, 6, and 7 of the draft CD. Section 3.3 summarizes the nature of effects induced by O_3 exposure, and draws on information contained in Chapters 5, 6 and 7 of the draft CD. Section 3.4 presents several issues important to staff's interpretation and quantitative assessment of epidemiological studies. Section 3.5 discusses biological plausibility and coherence of evidence for O_3-induced adverse health effects, including short-term respiratory effects, short-term cardiovascular effects, long-term health effects, and mortality-related health endpoints. Also drawing from the draft CD's integrative synthesis, section 3.6 discusses factors that modify responsiveness to O_3; potentially susceptible and vulnerable populations groups; public health impacts of exposure to ambient O_3; and what constitutes an adverse health impact from ambient O_3 exposure. Finally, in section 3.7, staff builds upon the draft CD's detailed

evaluation and integration of the scientific evidence available on these issues to draw conclusions regarding the use of health study results in quantitative evaluation and risk assessments that will be relied upon in developing future staff recommendations on potential revisions to the primary O_3 NAAQS to be presented in Chapter 6 of the second draft of the Staff Paper.

3.2 MECHANISMS

This section provides an overview of evidence covered in the draft CD (chapters 5 and 6) on possible mechanisms by which exposure to O_3 may result in acute and chronic health effects. Evidence from dosimetry, toxicology, and human exposure studies has contributed to an understanding of the mechanisms which 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.

Scientific evidence discussed in the draft CD indicates that reactions with lipids and antioxidants are the initial step in mediating deleterious health effects of O_3. 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 (CD, sec. 8.4.1). According to the draft 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. Most of these mechanisms of action were based on animal toxicology studies with some support from human exposure studies.

3.2.1 Direct Pulmonary Effects

Potential direct pulmonary effects of O_3 include changes in breathing pattern, symptoms of breathing discomfort, lung function changes, and airway hyperreactivity. Subjects who engage in physical activity for multiple hrs while exposed to O_3 may experience subjective respiratory tract symptoms and acute physiological changes. Airway irritation is consistently the most typical symptomatic response reported in studies and is accompanied by several physiological changes, depending on individual responsiveness to O_3. These physiological changes include bronchoconstriction, airway hyperresponsiveness, airway inflammation, immune system activation, and epithelial injury. Severity of symptoms and magnitude of response depend on dose of inhaled O_3, individual sensitivity to O_3, and extent of tolerance resulting from previous O_3 exposures. Development of effects is time-dependent with a substantial degree of overlap of increasing and receding effects. Time sequences, magnitudes, and types of responses of this series of events, in terms of development and recovery, indicate

that several mechanisms, activated at different times, contribute to the overall lung function response. (CD, pp. 6-8 to 6-9) For the full discussion of the mechanisms of pulmonary function responses, see section 6.2.5 of the draft CD.

3.2.1.1 Breathing Pattern Changes

Human controlled-exposure studies have consistently found that inhalation of O_3 alters the breathing pattern without significantly affecting minute ventilation (CD, pp. 6-10 to 6-11). A progressive decrease in tidal volume and an increase in frequency of breathing to maintain steady ventilation during exposure of human subjects suggest a direct impact on ventilation. These changes are similar to responses in many animal species exposed to O_3 and other respiratory irritants. Bronchial C-fibers and rapidly adapting receptors appear to be the primary modulators of O_3-induced changes in ventilation rate and O_3 penetration in both humans and animals (CD, section 6.2.5.1).

3.2.1.2 Symptoms and Lung Function Changes

In addition to changes in ventilatory control, O_3 inhalation by humans induces a variety of symptoms, reduces vital capacity (VC) and related functional measures, and increases airway resistance (CD, pp. 6-11 to 6-12). The reduction in VC caused by exposure to O_3 is a reflex action and not a voluntary cessation of breathing resulting from discomfort. While O_3-induced symptom responses (mediated in part by bronchial C-fibers) are substantially reduced by inhaled topical anesthetic, the anesthetic had a minor and irregular effect on pulmonary function decrements and rapid, shallow breathing. Since respiratory symptom responses were largely abolished, these findings support reflex inhibition of VC due to stimulation of both bronchial and pulmonary C-fibers. Intersubject variability in FEV_1 responses is not explained by differences in O_3 doses between similarly exposed individuals (CD, section 6.2.5.1).

3.2.1.3 Airway Hyperresponsiveness

Bronchial or airway hyperresponsiveness (AHR) refers to a condition in which the propensity for the airways to constrict due to specific (e.g., allergens and antigens) or nonspecific (e.g., histamine and cold air) stimuli becomes increased (CD, section 6.8). Despite a common mechanism (CD, p. 5-49, pp.6-12 to 6-13), post-O_3 exposure pulmonary function changes and AHR (either early or late phase) are poorly correlated. Neither does post-O_3 exposure AHR seem to be related to baseline airway reactivity. These findings imply that the mechanisms are either not related or are activated independent in time. Indeed, O_3-induced increases in AHR appear to persist longer than pulmonary function and symptom responses to O_3. Animal studies (with limited support from human studies) have suggested that that stimulation of C-fibers can lead to increased responsiveness of bronchial smooth muscle independently of systemic and

inflammatory changes which may be absent. Characteristic O_3-induced inflammatory, airway neutrophilia, which at one time was considered a leading AHR mechanism, appears to be only temporally correlated with AHR. This observation does not rule out involvement of other cells in AHR modulation. However, there is some evidence that release of inflammatory mediators might sustain AHR and bronchoconstriction. Late AHR observed in some studies is plausibly due to sustained damage of the airway epithelium and continual release of inflammatory mediators. Thus, O_3-induced AHR appears to be a product of many mechanisms acting at different time periods.

3.2.2 Extrapulmonary Effects

Ozone reacts rapidly on contact with lipids and antioxidants in the epithelial lining fluid (ELF) and is not absorbed or transported to extrapulmonary sites (CD, p. 6-40, p. AX6-126). Laboratory animal studies suggest that reaction products formed by the interaction of O_3 with respiratory system fluids or tissues may produce effects measured outside the respiratory tract—either in the blood, as changes in circulating blood or as changes in the structure or function of other organs, such as the parathyroid gland, the heart, the liver and the central nervous system. However, very little is known about the mechanisms by which O_3 could cause extrapulmonary effects (CD, sections AX6.10 and 5.4). Human exposure studies discussed in previous criteria documents (U.S. EPA, 1986, 1996) failed to demonstrate any consistent extrapulmonary effects. More recent human exposure studies have identified specific markers of exposure to O_3 in the blood, such as a reduction in the serum levels of a free radical scavenger after O_3 exposure (CD, sections 6.10 and AX6.10).

Alterations in heart rate and/or rhythm are thought to reflect pathophysiologic changes which may represent mechanisms by which pollutants like O_3 may induce acute adverse cardiovascular health effects. Decreased heart rate variability (HRV) has been suggested as a predictor of increased cardiovascular morbidity and mortality (CD, p. 7-55). Heart rate variability, resting heart rate, and blood pressure are modulated by a balance between the sympathetic and parasympathetic nervous systems, and decreased HRV predicts an increased risk of cardiovascular morbidity and mortality in the elderly and those with significant heart disease. Decreased parasympathetic input to the heart may provide an important mechanistic link between air pollution and cardiovascular mortality by promoting fatal arrhythmias (CD, section 7.2.7.1). The impact of O_3 exposure on the cardiovascular system is discussed in section 3.3.1.4 of this draft Staff Paper.

3.3 NATURE OF EFFECTS

When the primary O_3 NAAQS was last reviewed, the decision was based largely upon evidence of pulmonary function decrements, respiratory symptoms, and indicators of inflammation collected in experimental controlled exposure studies of human subjects. Less consistent, but supportive evidence was provided by epidemiological studies that reported associations between ambient O_3 levels and hospital admissions or emergency room (ER) visits for respiratory causes, as well as school absences, work loss days, and restricted activity days. In addition, toxicological studies demonstrated morphological changes and altered host defense mechanisms with O_3 exposure (U.S. EPA, 1996)

The current draft CD provides some new evidence of lung function, symptom, and inflammatory effects in controlled exposure studies that supports the findings of the previous CD. However, the most significant body of new studies in this review is the recent epidemiological evidence of associations between short-term exposure to O_3 and effects such as premature mortality, hospital admissions and ER visits for respiratory (e.g., asthma) and cardiovascular causes.

The following discussions of O_3-induced health effects are based on scientific evidence critically reviewed in chapters 5, 6, and 7 of the draft CD, as well as the draft 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 draft CD's annexes AX5, AX6, and AX7. Conclusions drawn about O_3-induced health effects depend on the full body of evidence from controlled-exposure human, epidemiological and toxicological data contained in the draft CD. Staff first focuses on the broad array of morbidity effects that have been associated with O_3 exposure, including both acute and chronic exposures, in section 3.3.1. Section 3.3.2 then discusses 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 briefly summarizes evidence from toxicological, controlled human exposure and epidemiological studies on respiratory and cardiovascular effects associated with exposure to O_3, based on the draft CD's assessment in Chapters 4, 6 and 7. Evidence of O_3-related hospital admissions and emergency room visits is discussed in section 3.3.2.1, followed by discussion of the effects of short-term and long-term exposure to O_3 on the respiratory system in sections 3.3.2.2 and 3.3.2.3, and O_3-related cardiovascular effects in section 3.3.2.4.

3.3.1.1 Emergency Department Visits/Hospital Admissions for Respiratory Causes

In the last review of the O_3 NAAQS, the 1996 CD evaluated emergency room visits and hospital admissions as possible outcomes following exposure to O_3 (CD, section 7.3.1). The evidence was limited for emergency department visits, but results of several studies generally indicated that short-term exposures to O_3 were associated with respiratory emergency department visits (Bates et al., 1990; Cody et al., 1992; Weisel et al., 1995; White et al., 1994). 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 (Bates and Sizto, 1983, 1987, 1989; Burnett et al., 1994; Lipfert and Hammerstrom, 1992; Thurston et al., 1992, 1994). 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 were associated with exacerbation of respiratory disease (CD, p. 7-57, 7-58).

In the past decade, a number of studies have examined the temporal associations between O_3 exposures and emergency department visits for respiratory causes (CD, section 7.3.2). These studies are summarized in the draft CD (Table AX7-3, Chapter 7 Annex). Respiratory causes for emergency room 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 emergency department visits for total respiratory complaints (Delfino et al., 1997b, 1998b; Hernandez-Garduno et al., 1997; Ilabaca et al., 1999; Jones et al., 1995; 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. 7-59) provides effect estimates for associations between emergency department 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. 7-60). Several of the studies reported significant associations between O_3 concentrations and emergency department 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 emergency department visits. This has led the draft CD (p. 7-62) to conclude that the body of evidence remains inconclusive regarding effects of O_3 on the risk of emergency department visits.

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 emergency department 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). In a 16-city Canadian study, Burnett et al. (1997) found the strongest association at a 1-day lag and a decline in magnitude and significance of effect estimates with longer lag periods for O_3 exposure. In five European cities, Anderson et al., (1997) investigated the association between O_3 and unscheduled daily hospital admissions for COPD and found that the largest risk estimates were for 0- and 1-day lags. Also, among all pollutants examined, the most consistent and significant findings were for O_3. According to the draft CD (p. 7-67), other studies conducted in one or two cities over a five year period or longer provided substantial additional evidence regarding O_3 effects on respiratory hospital admissions (Anderson et al., 1998; Burnett et al., 1999, 2001; Moolgavkar et al., 1997; Petroeschevsky et al., 2001; Ponce de Leon et al., 1996; Sheppard et al., 1999 [reanalysis Sheppard, 2003]; Yang et al., 2003). The draft CD observes that in some areas with low ambient O_3 concentrations, authors reported that significant associations between O_3 exposure and respiratory hospitalization were not found but did not provide quantitative results (e.g., Lin et al., 2004).

Overall, the draft CD concludes that positive and robust associations were found between ambient O_3 concentrations and hospital admissions, when focusing particularly on results of warm-season analyses. Recent studies have also reported associations with ER visits for respiratory diseases, though the draft CD finds this evidence to be less consistent (CD, p. 7-177).

3.3.1.2 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 more subtle effects such as including morphological changes in the respiratory tract, pulmonary function decrements, respiratory inflammation, increased airway responsiveness, morphological effects, changes in host defense

capability, and effects on exercise performance. Short-term O_3 exposure has also been associated with increases in respiratory symptoms, restricted activity days, and school absences.

3.3.1.2.1 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 lower O_3 concentrations, as low as 0.08 ppm, and at lower minute ventilation (i.e., moderate exercise) than the shorter duration studies (CD. p. 6-5).

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 V_E 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 develop a tolerance to successive exposures, as demonstrated by an attenuation of responses, which is lost after about a week without exposure (CD, p. 6-1).

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 hrs in duration are summarized in Table AX6-1 of the draft CD (p. AX6-5 to AX 6-7). 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 hrs to O_3 concentrations from as low as 0.08 ppm up to 0.40 ppm, at rest or with 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 CE 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 of > 15% and 7% had decrements of > 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; Adams 2003) have reported statistically significant responses and increased symptoms and spirometric responses with increasing duration of exposure, O_3 concentration, and total minute ventilation. Based on review of several prolonged exposure studies, the draft 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. Triangular exposure studies (Hazucha et al., 1992; Adams, 2003) suggest that depending upon the profile of the exposure, the triangular exposure, which is more representative of actual ambient exposures, can potentially lead to greater FEV_1 decrements than square wave exposures at overall equivalent O_3 doses (CD, p. 6-8). McDonnell (1996) 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. However, about 18% of the exposed subjects had moderate functional decrements (10 to 20%), and about 8% experienced large decrements (>20%). This demonstrates that while average responses may appear small and insignificant, some individuals can experience much more significant and severe effects.

A relatively large number of field studies investigating the effects of ambient O_3 concentrations on lung function decrements and respiratory symptoms have been published since 1996 and are reviewed and summarized in the draft CD (sections 7.2.3, 7.2.4, and 8.4.2.1.1). 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 are closely correlated to ambient O_3 concentrations. Pre-1996 field studies focused primarily on children attending summer camps (Spektor et al., 1988a, 1991; Avol et al., 1990; Raizenne et al., 1987, 1989; Higgins et al., 1990). The newer studies have expanded into looking at O_3-induced effects on outdoor workers (Brauer et al., 1996; Romieu et al., 1998), athletes (Höppe et al.,

1998, 2003), the elderly (Schindler et al, 2001; Höppe et al., 2003), hikers (Korrick et al., 1998), school children (Ulmer et al., 1997; Linn et al., 1996; Scarlett et al., 1996), and asthmatics (Höppe et al., 2003; Romieu et al, 2002). 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 Korrick et al. (1998) hiker study, 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 subgroup who reported having asthma or wheezing, and those who hiked for longer periods of time, thus increasing the exposure period (CD, p. 7-27, 7-31).

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 8.4.2.1.1). 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 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. 7-40). 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 other studies report statistically significant associations between O_3 exposure and reduced PEF in asthmatics (Gielen et al., 1997; Jalaludin et al., 2000; Just et al., 2002; Ross et al., 2002; Thurston et al., 1997), other studies did not (Hilterman et al., 1988; Delfino et al., 1997a), 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).

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. 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.7-38). In most laboratory animals studied, biochemical

markers of lung injury and associated morphological changes were not found to be attenuated. Although there are no data available on pulmonary function changes in animals chronically exposed to O_3, earlier work of repeated exposures of rats to an episodic profile of O_3 demonstrated small but significant decrements in lung function consistent with early indicators of focal fibrogenesis in the proximal alveolar region (CD, p. 8-26).

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 8.4.2.1.1). 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 CD observes that there are a number of well-conducted, albeit smaller, studies (Avol et al., 1998; Chen et al., 1998; Delfino et al., 1996, 1997a, 1998a; Gielen et al., 1997; Jalaludin et al., 2004; Ostro et al., 2001; Taggart et al., 1996) which showed only limited or a lack of evidence for symptom increases associated with O_3 exposure.

The draft CD (p. 7-48) concludes that the asthma panel studies as a group 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.

3.3.1.2.2 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. 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. 8-29). 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 individual with preexisting allergic asthma and that its influence may be both immediate and persist for long periods (CD, p. 8-29).

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 (Jörres 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).

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 O_3 concentrations. 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.

The draft CD concludes that exposure is linked with increased AHR (CD, p. 6-43, 6-44). 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, 8.4.2.4.2). Increases in AHR do not appear to be strongly associated with decrements in lung function or increases in symptoms (CD, p. 6-30). These findings suggest that different mechanisms underlie reported changes in AHR and changes in lung function or respiratory symptoms.

3.3.1.2.3 Respiratory Inflammation and Permeability

Short-term exposures to O_3 can cause acute respiratory inflammation and increased permeability in the lungs of humans and experimental animals (CD, sections 5.2.3, 6.9, 7.2.5 and 8.4.1.4.3). 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 draft 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 hrs required concentrations of 0.26 ppm to induce epithelial permeability thought there was no effect on inflammation. The lowest O_3 concentration that affected epithelial permeability of inflammation in the rat was 0.5 ppm for a 3 hr exposure (CD, p. 8-32). After acute exposures, the influence of the time of exposure increases as the concentration of O_3 increases. The exact role of inflammation in causation of lung disease is not known, nor is the relationship between inflammation and lung function (CD, section 5.2.3).

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 draft 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 (CD, p. 6-31).

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. 8-33). 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 to occur among adults exposed to 0.08 ppm O_3 for 6.6 hrs with exercise (Devlin et al., 1990). Another study (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 hrs, with light IE) that did not affect pulmonary function.

Since 1996, a substantial number of human exposure studies have been published which have provided important new information on lung inflammation and epithelial permeability. One publication (Mudway and Kelly, 2004) examined O_3-induced inflammatory responses and epithelial permeability with a meta-analysis of 21 controlled human exposure studies. Results of the analysis suggest that for a 1 hr exposure to 0.12 ppm O_3, the threshold dose for early phase

PMN response would not be exceeded unless an individual was engaged in very heavy exercise (minute ventilation of 90 L/min). For 8 hr exposures to 0.08 ppm O_3, early phase PMN dose threshold could be reached during relatively light sustained activity (minute ventilation of 17 L/min). For these 1- and 8-hr exposure scenarios, BAL fluid protein levels would be predicted to increase by about 1.1 fold. For late phase PMN responses, threshold dose was 26% greater than for early phase responses. Mudway and Kelly (2004) indicated that their threshold doses were for average PMN responses in healthy adults and that some individuals would respond at lower doses.

A number of more recent 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. Markers from BAL fluid following both 2-hr (Devlin et al., 1997) and 4-hr (Christian et al., 1998; Jörres 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.

The draft CD (p. 8-35) concludes that interaction of O_3 with constituents of ELF and induction of oxidative stress is implicated in injury and inflammation. Alterations in the expression of cytokines, chemokines, and adhesion molecules, indicative of an ongoing active 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.

3.3.1.2.4 Changes in Host Defense Capability

As discussed in section 8.4.1.4.2 of the draft CD, acute exposures to O_3 have been shown to impair host defense capabilities in both humans and experimental animals by depressing alveolar macrophage functions and by altering the mucociliary clearance of inhaled particles and microbes. Acute 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 acute exposures to O_3 levels as low as 0.08 ppm (CD, p. 8-36). 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 (CD, p. 8-36).

Ozone exposure has also been show 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. 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. Although the available information suggests that acute O_3 exposures can impair host defense capability by interfering with AM functions, there is no compelling evidence from animal or human studies that O_3 increases the incidence of respiratory viral infection in humans (CD, p, 8-36).

A single 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 induced decrements in the ability of alveolar macrophages (AMs) to phagocytose microorganisms; several other studies reported similar effects but with higher exposure concentrations (CD, p. 6-39). Few new controlled human exposure studies are available in this draft CD (section 6.9.6). Integrating the recent study results with evidence available in the 1996 CD, the draft CD concludes that evidence supports the conclusion that short-term O_3 exposures have an adverse impact on host defense capability, even for exposures as low as 0.08 ppm to 0.10 ppm (CD, p. 6-39).

3.3.1.2.5 Morphological Effects

In the 1996 CD, it was 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 this region receives the greatest dose of O_3 delivered to the lower respiratory tract (CD, p. 8-30). Ciliated cells in the nasal cavity and airways, as well as Type I cells in the gas-exchange region, are also identified as targets. Differences in distribution of antioxidants in the CAR of the lungs are responsible for differences in injury and morphological effects observed in nonhuman primates and rodents. 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 dependent on species and O_3 dose.

Recent studies continue to show that short-term 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 5.2.4.1 and 5.2.4.2). New work (Hotchkiss et al., 1998) has shown that a topical anti-inflammatory corticosteroid can prevent these effects in nasal epithelia, while exposure to bacterial endotoxin can potentiate effects (Fanucchi et al., 1998). 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 (Dormans et al., 1999).

New studies of susceptibility factors demonstrated that ferrets and monkeys have similar inflammatory and necrotic responses to 1 ppm O_3, which differs from lesser injury seen in rats (Sterner-Kock et al., 2000). Rats with induced allergic rhinitis are more susceptible to 0.5 ppm O_3 than are controls (Cho et al., 1999b). Important new work has demonstrated variability of local O_3 dose and subsequent injury in the respiratory tract due to depletion of glutathione (GSH) (Plopper et al., 1998). 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. 5-32).

Based on evidence from animal toxicological studies, the draft CD concludes that short-term exposures to O_3 can cause morphological changes in the respiratory systems of a number of laboratory animal species (CD, p. 5-38). Little evidence is available from human studies.

3.3.1.2.6 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 reported that endurance exercise performance and VO_{2max} may be limited by acute exposure to O_3 (Adams and Schelegle, 1983; Schelegle and Adams, 1986; Gong et al., 1986; Foxcroft and Adams, 1986; Folinsbee et al., 1977; Linder et al., 1988). Gong et al. (1986) and Schelegle and Adams (1986) 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 draft CD.

Thus, as in the 1996 CD, the draft 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. 6-29).

3.3.1.2.7 Increased School Absences

The association between school absenteeism and ambient O_3 concentrations was assessed in three relatively large field studies (CD, section 7.2.6). One study (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. Another study (Gilliland et al., 2001) studied O_3-related absences among 1,933 4th 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. A third study (Park et al., 2002) investigated associations between air pollution and school absences in 1,264 students (1^{st} to 6^{th} grades) in Seoul, Korea and reported that same day O_3 concentrations were positively associated with illness-related absences. Models of PM_{10} alone and of both PM_{10} and O_3 showed positive associations with illness-related absences, with a slightly greater effect seen for O_3.

The draft CD concludes that these studies of school absences suggest that ambient O_3 concentrations on the same day, as well as accumulated over two to four weeks, may be associated with school absenteeism, but further replication is needed before firm conclusions can be reached regarding this effect (CD, p. 7-52).

3.3.1.3 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. 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. 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. One important toxicological study (Tyler et al., 1988) reported that young monkeys exposed to seasonal ambient O_3 patterns, but not daily exposures, experienced increases in total lung collagen content, chest wall compliance, and inspiratory capacity, suggesting a delay in lung maturation in seasonally-exposed animals. 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 new morphological effects studies of long-term exposures are listed in Table AX5-6 (CD, Annex AX5) and of new morbidity effects epidemiological studies long-term exposure are listed in Table AX7-7 (CD, Annex AX7).

3.3.1.3.1 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 found that growth-related increases in lung function over the summer season were reduced in relation to seasonal mean O_3 levels. 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. Another 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 compared to children living in areas with lower ambient O_3 levels. Another Austrian study (Ihorst et al., 2004) 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 draft CD (p. 7-102), these studies collectively indicate that seasonal O_3 exposure is associated with smaller increases in lung function in children and that there is limited evidence that seasonal O_3 also may affect young adults.

3.3.1.3.2 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 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. In the current draft 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 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. Another analysis (Peters et al., 1999b) examined the relationship between 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. In a separate study (Gauderman et al., 2000) of 4th, 7th, and 10th grade students, a longitudinal analysis of 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 lung function in children. 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}. 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 lung function, but further study is needed to address this question (CD, p. 7-104). Three other studies (Frisher et al., 1999; Ihorst et al, 2004; Horak et al., 2002a) conducted in Austria and Germany also found no associations between increases in lung function parameters and mean summer O_3 levels over a three- to five-year period of study.

Evidence for a significant relationship between long-term O_3 exposures and decrements in maximally attained lung function was reported in a nationwide study (Galizia and Kinney, 1999; Kinney et al., 1998) of first year Yale students. 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. 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. An autopsy pathologic study (Sherwin et al., 2000) examined subjects for CAR alterations in LA and in Miami, FL. A trend toward greater extent and severity of CAR alterations in LA residents was observed, and it was suggested that this effect might be related to higher O_3 exposures in LA.

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. 7-106). Limited evidence is available from studies of adults and college studies to suggest that long-term O_3 exposure may affect lung function or respiratory symptoms (CD, p. 7-105).

Overall, the draft CD concluded that this body of evidence was generally inconclusive for effects of long-term O_3 exposure on respiratory symptoms or lung function (CD, p. 7-178).

3.3.1.3.3 Long-term O_3 Exposure and Respiratory Inflammation

As noted earlier in section 3.3.1.2 of this Staff Paper and in the draft 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 (8hr/day for 90 days) (CD, p. 8-32).

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. 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 series of studies (Calderon-Garciduenas et al., 1995, 1997, 1999) 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. Significantly higher DNA damage was reported in children living in Mexico City compared to nonurban children and in older compared to younger children. A more recent study (Calderon-Garciduenas et al., 2003) of Mexico City children reported that they exhibited nasal abnormalities (22%), hyperinflation (67%), interstitial markings (49%), and a mild restrictive pattern by spirometry (10%), while a control group of nonurban children showed no significant abnormalities. Another marker of inflammation, urinary eosinophil, was analyzed in an Austrian school children study (Frischer et al., 2001), and it was reported that O_3 exposure was significantly associated with eosinophil inflammation.

In assessing these studies, the draft CD (p. 7-110) 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.

3.3.1.3.4 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, and new cases of asthma were defined as self-reported doctor-diagnosed asthma at either the 1987 or 1992 follow-up questionnaire among those who had not reported having asthma when the enrolled in 1977. 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 per 10 ppb increase in annual mean O_3 (no exposure metric given) as observed in males, compared to a nonsignificant relative risk of 0.94 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 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 follow-up studies provides 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. 7-111).

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 (mean 1-hr max O_3 of 75.4 ppb over four years) and six low-O_3 (50.1 ppb) 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.

The draft CD (p. 7-111) suggests that playing sports may indicate outdoor activity when O_3 levels would be higher, as well as an increased ventilation rate, both of which could increase

O_3 exposure and dose. These results, however, were based on a small number (29) of new-onset asthma cases among children who played three or more sports. Future replication of these findings in other cohorts would help support a causal interpretation.

3.3.1.3.5 Morphological Effects

The progression of morphological effects 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 5.2.4.3). Epithelial hyperplasia follows a somewhat similar pattern. In contrast, fibrotic changes in the tissue increase very slowly over months of exposure, and, after exposure ceases, the changes sometimes persist or increase. 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. The long-term study of Plopper et al. (1998) 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. The only epidemiological study (Sherwin et al., 2000) that investigated severity of CAR alterations in human lungs compared autopsy results of lungs for Miami and LA residents. The results indicate a significantly greater extent and severity of CAR alterations in LA residents, suggesting that the CAR alterations may be related to higher O_3 levels in LA. These findings advance earlier information regarding possible injury-repair processes occurring with seasonal O_3 exposures (CD, p. 5-36).

3.3.1.3.6 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. In contrast to the supportive evidence from animal studies with chronic exposures, epidemiological studies of new asthma development and longer-term lung function declines remain inconclusive at present (CD, p. 7-118).

3.3.1.4 Effects on the Cardiovascular System

Epidemiological studies of cardiovascular effects have investigated associations with several air pollutants, including O_3, PM, CO, NO_2 and SO_2, most often with a focus on PM health

endpoints (CD, p. 7-54). Several studies also have examined associations of O_3 and other gaseous pollutants with heart rate variability (HRV) in the elderly and the increased risk of myocardial infarction associated with exposure to air pollution. One study (Liao et al. 2004) reported larger effect estimates for PM_{10} than those for the gaseous pollutants such as O_3; however, the findings are suggestive of short-term effects of O_3 and other pollutants on HRV. Another study (Park et al., 2005) reported that in analyses by ischemic heart disease, hypertension, and diabetes status, stronger associations of HRV and both O_3 and $PM_{2.5}$ were observed for individuals with ischemic heart disease and hypertension than those without these preexisting conditions. These results were consistent with another study (Holguin et al., 2003) conducted in Mexico City, which reported an association between decreased HRV with O_3 in subjects with hypertension. Other studies did not provide evidence for an O_3 effect on cardiac arrhythmias; however, the draft CD notes that the O_3 concentrations in these studies were low (CD, p. 7-57).

Some new epidemiological studies have reported associations with more severe effects, such as myocardial infarction. Peters et al. (2001) reported positive, but not statistically significant associations between ozone and the incidence of myocardial infarction in Boston (CD, p. 7-55). The effect estimate for the association with O_3 averaged over 2 hrs prior to the myocardial infarction was substantially larger than that reported for an association with 24-hr average O_3 (Peters et al., 2001). In France, Ruidavets et al. (2005) reported a statistically significant association between ambient O_3 concentrations and incidence of myocardial infarction (CD, p. 7-55).

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 draft CD, the results of these studies are inconsistent (CD, p. 7-72). In addition, in Denver, (Koken et al., 2003) reported associations between hospitalization for specific cardiovascular diseases and ambient O_3 concentrations; the associations were inconsistent, however, and generally not statistically significant.

There is limited controlled-exposure human experimental information available which suggests that O_3 exposure induces cardiovascular effects (CD, sections 6.10 and AX6.10). In one study, Gong et al. (1998) monitored numerous cardiac variables in both healthy and hypertensive subjects. Results suggested that by impairing the alveolar-to-arterial oxygen transfer, the O_3 exposure could potentially lead to adverse cardiac events by decreasing oxygen supply to the myocardium. The subjects in the Gong et al. (1998) study had sufficient functional reserve so as not to experience significant ECG changes or myocardial ischemia and/or injury; however, it was concluded that O_3 exposure could pose a cardiopulmonary risk to persons with preexisting cardiovascular disease, with or without concomitant respiratory disease. In other research,

Foster et al. (1993) demonstrated that even in relatively healthy young adults, O_3 exposure can cause ventilation to shift away from the well perfused basal lung, an effect on small airways which Foster et al. (1997) showed may persist for over 24 hr after exposure. Hypoxic pulmonary artery vasoconstriction acts to shift perfusion away from areas of low ventilation and moderate ventilation-perfusion mismatches (Santak et al., 1998). This arterial vasoconstriction is thought to be mediated by protein kinase C (Barman, 2001; Tsai et al., 2004). A more generalized (i.e., not localized to poor ventilated areas) increase in pulmonary vascular resistance in response to O_3 exposure would presumably act against the ability of the hypoxic vasoconstriction in mediating ventilation-perfusion mismatches (CD, sections 6-10 and AX6-10).

Based on epidemiological study results, the draft 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. 7-57). In the draft 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. 7-73, 7-74).

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 ozone, but conclusions could not be drawn regarding such associations (U.S EPA, 1996, p. 42). 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 still provided limited, if any, evidence for an association between chronic ozone exposure and mortality, as described in section 3.3.2.2.

3.3.2.1 Mortality and Short-term O_3 Exposure

In the 1996 CD, some, but not all, epidemiological studies had reported associations between short-term ozone exposure and mortality. Given the information available from the studies modeling for O_3 and weather, it was difficult to evaluate whether associations were possibly not achieving statistical significance due to overspecification of the weather model. Based on the limited evidence available from the epidemiological studies and the uncertainties regarding weather model specifications, the 1996 CD was unable to quantitatively assess the O_3-mortality relationship, or even provide qualitative assessment of the likelihood of O_3-mortality associations (CD, p. 7-74).

The draft CD includes results from numerous epidemiological analyses of the relationship between O_3 and mortality. Key findings are available from multicity 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 (Samet et al., 2000, reanalyzed in Dominici, 2003) and from 95 U.S. cities in an extension to the NMMAPS analyses (Bell et al., 2004), and further analyses using a subset of 19 U.S. cities and focusing on cause-specific mortality associations (Huang et al., 2005). An additional study used case-crossover design and data from 14 U.S. cities (Schwartz, 2005), to further investigate the influence of adjustment for weather variables in the O_3-mortality relationship. 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 (Touloumi et al., 1997).

In the original 90-city NMMAPS analysis, which 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. 7-86). The extended NMMAPS analysis included data from 95 U.S. cities and included data from 1987-2000 (Bell, et al., 2004), and significant associations were reported between ozone 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. 7-78). 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) (CD, p. 7-85). The authors also report that O_3-mortality associations were robust to adjustment for PM (CD, p. 7-87).

Using a subset of the NMMAPS data set, Huang et al. (2005) focused on associations between cardiopulmonary mortality and ozone exposure (24-hr average) 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. 7-78, 7-80).

As discussed in section 3.4, assessment of confounding by weather, especially temperature, is complicated by the fact that higher temperatures are important for O_3 formation. Using case-crossover study design, Schwartz (2005) 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 maximum, 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% Probability Interval: 0.13, 1.40), suggesting that associations between O_3 and mortality are not sensitive to these adjustment methods for temperature (CD, p. 7-80, 7-81).

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 4.5% change in mortality per 40 ppb O_3 (95% CI: 1.6, 7.7) in four cities (Touloumi 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. 7-81). Focusing on analyses using summer measurements, the authors report statistically significant associations with total mortality [1.8% increase per 30 ppb 8-hr ozone (95% CI: 0.8, 2.9)], cardiovascular mortality [2.7% increase per 30 ppb 8-hr ozone (95% CI: 1.2, 4.3)] and with respiratory mortality [6.8% increase per 30 ppb 8-hr ozone (95% CI: 4.5, 9.2)] (Gryparis et al., 2004; CD, p. 7-85).

Two of the recent multi-city mortality studies have also reported associations for multiple averaging times (Bell et al., 2004; Gryparis et al., 2004). Bell and colleagues (2004) reported associations between mortality and 1-hr daily maximum, 8-hr daily maximum and 24-hr average 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 average O_3, but the effect estimates did not differ statistically. 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 7-19 of the draft 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. 7-86). 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 7-20, p. 7-88).

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 draft 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 7-18, page 7-84). 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 draft 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. 7-84). 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 draft CD concludes that these studies "provide strong evidence that O_3 is associated with mortality." (CD, p. 7-84)

Taken together, the draft CD concludes that the epidemiological evidence shows robust associations between daily O_3 concentrations and mortality (CD, p. 7-96). For standardized ozone 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. 7-96). The results of multi-city studies, single-city studies and the recent meta-analyses all indicate that associations reported between O_3 and mortality are also robust to adjustment for PM in the models (CD, p. 7-89). 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 (CD, p. 7-94).

3.3.2.2 Mortality and Long-term O_3 Exposure

Little evidence was available in the previous O_3 NAAQS 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; the mortality and O_3 concentration data are presented in a figure but quantitative concentration-response functions are not available in this report (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 (Dockery et al., 1993, p. 1755).

As discussed in section 7.5.8 of the draft 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 previous prospective cohort study reports, 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) (Krewski et al., 2000, p. 150).

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 report (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).

A recent report from this study 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 (Pope et al., 2002). 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 7-24 of the draft CD, the effect estimates are near zero and sometimes negative (though

[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).

not statistically significant) for associations between long-term O_3 exposure and all-cause, cardiopulmonary, and lung cancer mortality (CD, p. 7-112).

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 lung cancer risk 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, however (Abbey et al., 1999). 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 draft CD raised concerns about the plausibility of the reported association with lung cancer (CD, p. 7-114.)

The U.S. Veterans Cohort study (Lipfert et al., 2000b) 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. 7-112).

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 ozone concentrations, the cohort is also a rather specific subgroup of the U.S. population. Overall, the draft 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. 7-114).

3.3.3 Summary

The draft 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 (CD, p. 7-177). Short-term O_3 exposure has also been associated with hospital admissions for respiratory causes in numerous new studies that support findings in the 1996 CD. The draft CD reports that warm-season

studies show evidence for positive and robust associations between ambient O_3 concentrations and respiratory admissions, and positive but less conclusive evidence for associations with respiratory ER visits (CD, p. 7-177).

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 draft CD concludes that the evidence for this group of associations is inconclusive (CD, p. 7-178).

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 myocardial infarction and hospitalization for cardiovascular diseases. The draft CD finds this body of evidence to be limited but supportive of potential effects of O_3 on the cardiovascular system (CD, p. 7-177).

The major new information presented in the draft CD 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. Recent meta-analyses also showed risk estimates that are consistent across studies and robust to control for potential confounders, providing strong evidence for an association between short-term O_3 exposure and mortality (CD, p. 7-78). The limited evidence from long-term O_3 exposure studies, however, does not provide conclusive evidence of an association with mortality.

3.4 INTEGRATIVE ASSESSMENT OF EVIDENCE FROM EPIDEMIOLOGICAL STUDIES

In Chapter 8, the draft 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. In evaluating the evidence from epidemiological studies in section 8.4, the draft CD focuses on well-recognized criteria, including: (1) the quality of the *exposure metrics*; (2) the *quality and size* of the study population; (3) the *robustness* of reported associations to the use of alternative model specifications and potential confounding by co-pollutants; (4) the *strength* of reported associations; (5) evidence for *temporality* between exposure and observed effects (CD, p. 8-10). Integrating more broadly across epidemiological and experimental evidence, the draft CD also focuses on the *coherence* and *plausibility* of observed O_3-related health effects to reach judgments about causality (Section 8.4.8); this will be the focus of section 3.5.

The following discussion summarizes the conclusions and judgments from the draft CD's integrative assessment, focusing in particular on discussions of strength, consistency, robustness,

temporality and in the epidemiological evidence. This section also addresses several issues relevant to the interpretation of epidemiological evidence. In particular, staff has focused on issues related to exposure error in O_3 epidemiological studies, potential confounding by co-pollutants, the affect of alternative model specifications on O_3-health associations, the lag periods between O_3 ambient exposure levels and health outcomes, and the nature of O_3-health concentration-response relationships.

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 (CD, p. 8-10; 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 various health outcomes are generally small in size. For example, the draft CD reports effect estimates in the range of 0.5 to 5% increase in mortality per 40 ppb increase in O_3 or equivalent (CD, p. 7-80). The magnitude of these associations, while small, is found to be relatively consistent between studies (CD, p. 8-12). As shown in Figure 8-5 in the draft CD, effect estimates for associations with emergency department visits and hospital admissions range up to 40% increases per incremental change in O_3 (CD, p. 8-47).

In considering both the magnitude and statistical strength of the associations, a pattern of positive and often statistically significant associations can be seen between mortality and respiratory morbidity and short-term exposures to O_3 (CD, pp. 7-45, 7-46, 7-74). Such associations are strong in terms of the precision of the studies; 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. Thus, while the associations reported in the more recent body of epidemiological studies are approximately characterized as being modest in terms of the magnitude of the relative risk estimates, such modest associations are generally coherent with outcomes that may reasonably be expected.

3.4.2 Robustness of Associations

In section 8.4.7, the draft CD evaluates the robustness of epidemiological associations, reporting that the health associations reported with short-term exposure to O_3 are generally robust (CD, p. 8-58). In this evaluation, the draft CD focuses on the impact of exposure error, statistical model specification, and potential confounding by co-pollutants on O_3-health associations; these issues are 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 draft CD, there are very few sources of O_3 exposure for most people other than ambient air; one potential source is O_3 emitted from office equipment (CD, p. 7-6). Exposure to ambient O_3 for individuals is influenced by factors related to the infiltration of O_3 into buildings, as well as the time spent out of doors by the individuals.

The draft 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, p. 7-7).

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. 7-7). Similarly, Zidek (1997) used data from a previous epidemiological study and observed that accounting for

exposure measurement error produced results that were similar to the conclusions of the original report, but the effect estimates were considerably larger in magnitude (CD, p. 7-7).

The draft CD concludes that ambient O_3 concentrations "may serve as valid surrogate measures for aggregate personal O_3 exposures in time-series studies. However, using ambient concentrations to determine exposure generally overestimates true personal O_3 exposures, resulting in biased descriptions of underlying concentration-response relationships." (CD, p. 7-8) The draft CD recommends caution in the quantitative use of these effect estimates as they may lead to underestimation of the overall health impact of air pollution. 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, where concern about use of ambient concentrations as a surrogate for exposure is not an issue.

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 draft 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 fine particles, especially during the summer months (CD, p. 7-130). 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. 7-14). Thus, the draft 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 draft 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. 7-131). This is particularly the situations 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. 7-132).

For mortality, the results from numerous multi-city and single-city studies are shown in Figure 7-20 of the draft 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 7-21 of the draft CD shows risk estimates for O_3-mortality associations that are fairly robust to adjustment for PM in multipollutant models (CD, p. 7-90).

Similarly, multipollutant models are presented for associations between short-term O_3 exposures and respiratory hospitalization in Figure 7-12 of the draft CD; the draft 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 were robust to adjustment for $PM_{2.5}$ (CD, p. 7-134). In reports from U.S. multi-city studies of respiratory symptoms, associations with O_3 were found to be remain statistically significant and little changed in magnitude in two-pollutant models including PM_{10} or $PM_{2.5}$ (Mortimer et al., 2002; Gent et al., 2003; CD pp. 7-45, 7-46).

Considering this body of studies, the draft CD concludes: "These findings indicate that the effects of O_3 on various health outcomes are robust and independent of the effects of other copollutants." (CD, p. 7-151) Staff will use the results of single-pollutant model results in presentation of results in this chapter and in quantitative assessments conducted as part of this review for purposes of comparing results from different studies. However, staff will also include the use of multi-pollutant model results in presenting risk estimates, where available to more completely assess the quantitative health risks associated with alternative O_3 standards.

3.4.2.3 Model Specification

The draft 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 distinguish effects associated with O_3 or the seasonal or weather variables in statistical analyses.

Section 7.1.3.4 of the draft 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). These studies generally report that associations reported with O_3 are not substantially changed with alternative modeling strategies (CD, p. 7-122). Overall, the draft CD concludes that O_3 effects are generally robust to various model specifications for temporal trend adjustment though additional research would help better understand the influence of different modeling approaches. (CD, p. 7-150)

A number of epidemiological studies have conducted season-specific analyses, as discussed in section 7.6.3.2 of the draft 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 draft 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 varies 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. The draft CD concludes: "Given the potentially significant effect of season, O_3 effect estimates computed for year-round data need to be interpreted with caution." (CD, p. 7-130) Staff has therefore focused on epidemiological findings from warm season analyses, where available, for quantitative and qualitative assessments.

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). The draft CD observes that the magnitude of effect estimates is relatively consistent across the results of recently published studies of associations between short-term

ozone exposure and mortality (CD, p. 8-41). Including results from studies conducted on several continents, the draft CD finds that effect estimates range from 0.5 to 5% increases in mortality per incremental change in O_3 (CD, p. 8-56). For associations with morbidity, the draft CD reports that there is greater variability in effect estimates between studies, but that fairly consistent positive associations between short-term ozone exposure and various respiratory health outcomes have been observed (CD, p. 8-57).

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, p. 7-84). The draft 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. In addition, as discussed previously, stronger and more consistent associations have been reported in analyses for the warm season. The meta-analysis results indicated that these two factors were important sources of variability in O_3-mortality relationships (Levy et al., 2005; CD, p. 8-57), but also reported that the associations were fairly consistent between studies; addressing these sources of heterogeneity resulted in stronger and more consistent findings. Overall, the epidemiological findings are fairly consistent for associations between short-term exposure to O_3 and both respiratory morbidity and mortality.

3.4.4 Temporality

Temporality refers to the occurrence of a cause before its purported effect, and is most relevant to studies of diseases that develop over time. This factor is difficult to investigate in situations where the pollutant concentrations are correlated over time as is the case to some degree in time series studies and to a greater degree in cohort studies. The short-term exposure studies evaluate associations between acute health outcomes and ozone measured on an hourly basis. In many studies, associations have been reported between health events and ozone measured contemporaneously. For example, in studies of total and cardiovascular mortality, the draft CD observes that effects have been most clearly linked with ozone measured on the same day or the preceding day (CD, p. 8-59). This would be expected for acute health outcomes; however, it is difficult to characterize these associations in terms of temporality. Issues related to the evaluation and selection of lag periods among studies are discussed in the next section.

3.4.5 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 ozone concentration (see

CD, sections 7.1.3.3 and 8.4.2.3). The draft 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 irritant action of ozone, 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. 7-9). For both mortality and respiratory hospital admissions, the draft CD reports that most significant associations between ozone and mortality were observed with ozone measured on the same day or a 1-day lag period in studies using individual lag periods (CD, p. 8-59). In U.S. multi-city studies, larger effect estimate sizes were reported for the ozone-mortality relationship with the distributed lag structure (CD, p. 7-80). Field studies of lung function or respiratory symptoms reported associations with ozone 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 ozone at shorter lag periods; cardiovascular health outcomes such as changes in cardiac autonomic control were associated with ozone 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 ozone with very short lag times of 1- to 4 hrs (CD, p. 7-55).

In focusing on an effect estimate reported for any individual lag period, the draft 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. 7-10). However, if the reported effect estimates vary substantially across lag periods, any result for a single day may well be biased (CD, p. 7-11). If the effect of ozone 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). Conversely, if the underlying ozone-health relationship is truly an acute effect, then a distributed lag model would likely result in reduced effect estimate size that may underestimate the effect (CD, p. 7-10).

On this basis, the draft 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, staff concludes that it is appropriate to use results from lag period analyses consistent with those reported in the draft 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). 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.

3.4.6 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 ozone exposure, individual thresholds would presumably vary substantially from person to person due to individual differences in genetic-level 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 time-series epidemiological studies have used statistical modeling approaches to evaluate whether thresholds exist in associations between short-term ozone exposure and mortality. As discussed in section 7.6.5 of the draft 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 ozone measurements from the study (Gryparis et al., 2004; CD p. 7-135). Several single-city studies also observed a monotonic increase in associations between ozone and morbidity that suggest that no threshold exists (CD, p. 7-137).

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) for an association between mortality and short-term ozone exposure during the summer months (Kim et al., 2004; CD, p. 7-136). The authors reported larger effect estimates for the association for data above the potential threshold level, suggesting that an ozone-mortality association might be underestimated in the non-threshold model. 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 ozone are found in the concentration range above about 30 ppb (1-hr maximum).

Other studies have tested associations between ozone and health outcomes after removal of days with higher ozone 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 ozone exposure and mortality was little changed when days exceeding 60 ppb (24-hr average) were excluded in the analysis (CD, p. 7-135). Using data from 8 U.S. cities, Mortimer and colleagues (2002) also reported that associations between ozone 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 average) were excluded (CD, p. 7-137). Several single-city studies are also summarized in section 7.6.5 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.

Finally, Vedal and colleagues (2003) reported a significant association between ozone and mortality in British Columbia where ozone 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 ozone concentrations suggests that any potential threshold level would be quite low in this data set.

In summary, some epidemiological analyses have suggested that no threshold levels can be found in associations between ozone and mortality or morbidity. In those studies that provide suggestive evidence of thresholds, the potential thresholds are at low concentrations (CD, p. 7-138). The draft CD finds that no definitive conclusion can be reached with regard to the existence of thresholds in epidemiological studies (CD, p. 8-24). Staff recognizes, 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 draft CD's conclusions, staff judges that there is insufficient evidence to support use of potential threshold levels in quantitative assessments, but that data should be used within the range of air quality concentrations down to a policy-relevant background level.

3.5 BIOLOGICAL PLAUSIBILITY AND COHERENCE OF EVIDENCE

This section summarizes material contained in section 8.5 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 draft 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. 8-59).

Table 3-1 (Table 8-1, CD, p. 8-60) summarizes physiological and biochemical observations which represent the knowledge base available from toxicological studies in humans and animals that underlie 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 health effects are transient and attenuate over time, the time-line for resolution of

many of the physiological and biological parameters presented in Figure 3-1 (Figure 8-9, CD, p. 8-61) 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 3-2 (Figure 8-10, CD, p. 8-62), 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. 8-62). 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 3-1 and 3-2. 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 of 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. Since quantitative extrapolation requires a combination of dosimetry, end point homology, and species sensitivity and because uncertainties continue to exist, extrapolation models have not been completely validated. However, 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, which supports the use of some animal data collected at higher O_3 exposures to help understand molecular changes in acutely exposed humans. Also of great importance are the chronic exposure studies (12 to 24 months) reporting lesions caused by long-term O_3 exposures, which may facilitate a more direct assessment of chronic health effects in humans (CD, p. 8-63).

3.5.1 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, bronchoconstriction, increased airway responsiveness, airway inflammation, epithelial injury, and immune system effects, emergency department 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

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 ↑ Frequency of breathing (rapid, shallow) ↓ inspiratory capacity (cough, breathing discomfort, throat irritation, wheezing) Mild bronchoconstriction	↓ FEV_1 ↑ Frequency of breathing (Rapid, shallow) ↓ inspiratory capacity
Airway Responsiveness:	↑ (neuronal involvement) change in lung resistance	↑ (vagal mediation) Change in lung resistance
Inflammation:	Yes ↑ inflammatory mediators	Yes ↑ inflammatory mediators
ROS	↑	↑
Host Defense:	↑ Particle clearance ↑ permeability ↓ AM phagocytosis	↑ Particle clearance ↑ permeability ↓ clearance of bacteria ↑ severity of infection ↑ Mortality & morbidity
Lung injury: Morphology	Yes	Yes
Susceptibility:	Age, Inter individual variability Disease status Polymorphism in certain genes being recognized	Species specific differences Genetic basis for susceptibility indicated
Cardiovascular Changes:	Impairment in arterial O_2 transfer Ventilation-perfusion mismatch (suggesting potential arterial vasoconstriction)	Heart rate variability (HRV) ↓ core body temperature ↑ ANF Role for PAF indicated increased pulmonary vascular resistance

[1] Controlled chamber exposure studies in human volunteers were carried out for a duration of 1-6.6 h with O_3 concentration in the range of 0.08-0.4 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 2-72h with O_3 concentration in the range of 0.1- 2.0 ppm.
[4] Various species (mice, rat, guinea pigs and rabbit) and strains.

(Reproduced from Table 8-1, CD, p. 8-60).

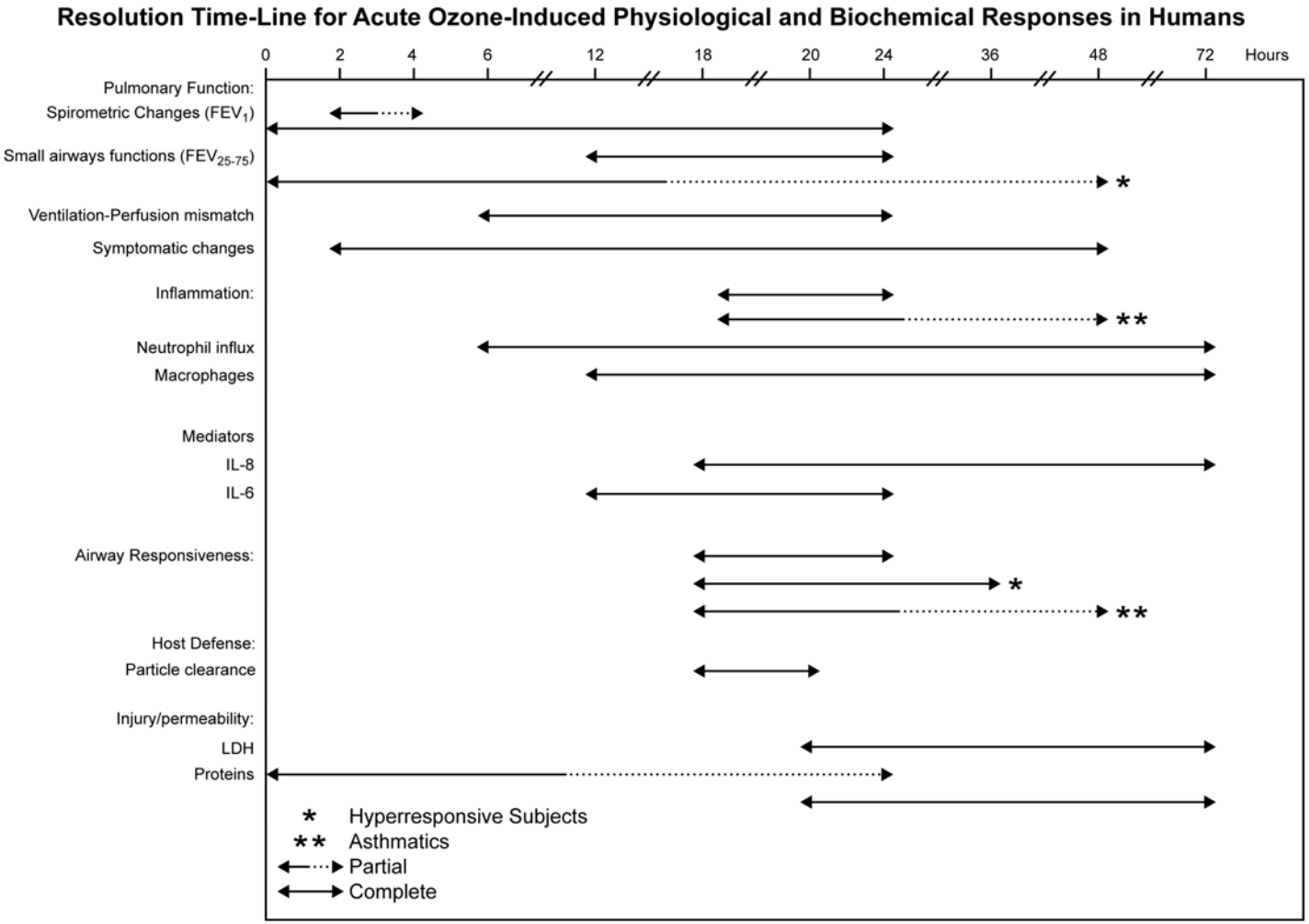


Figure 3-1. Resolution time-line for the physiological and biochemical parameters are derived from studies reported in Chapter 6 and Chapter 6 Annex. (Reproduced from Figure 8-9, CD, p. 8-61)

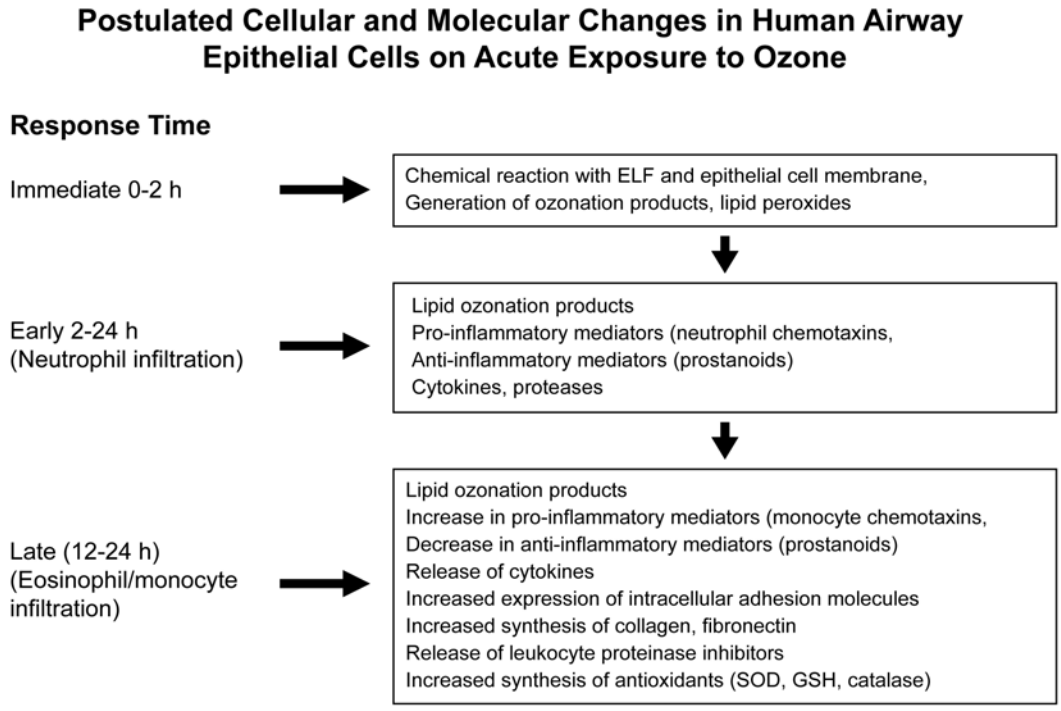


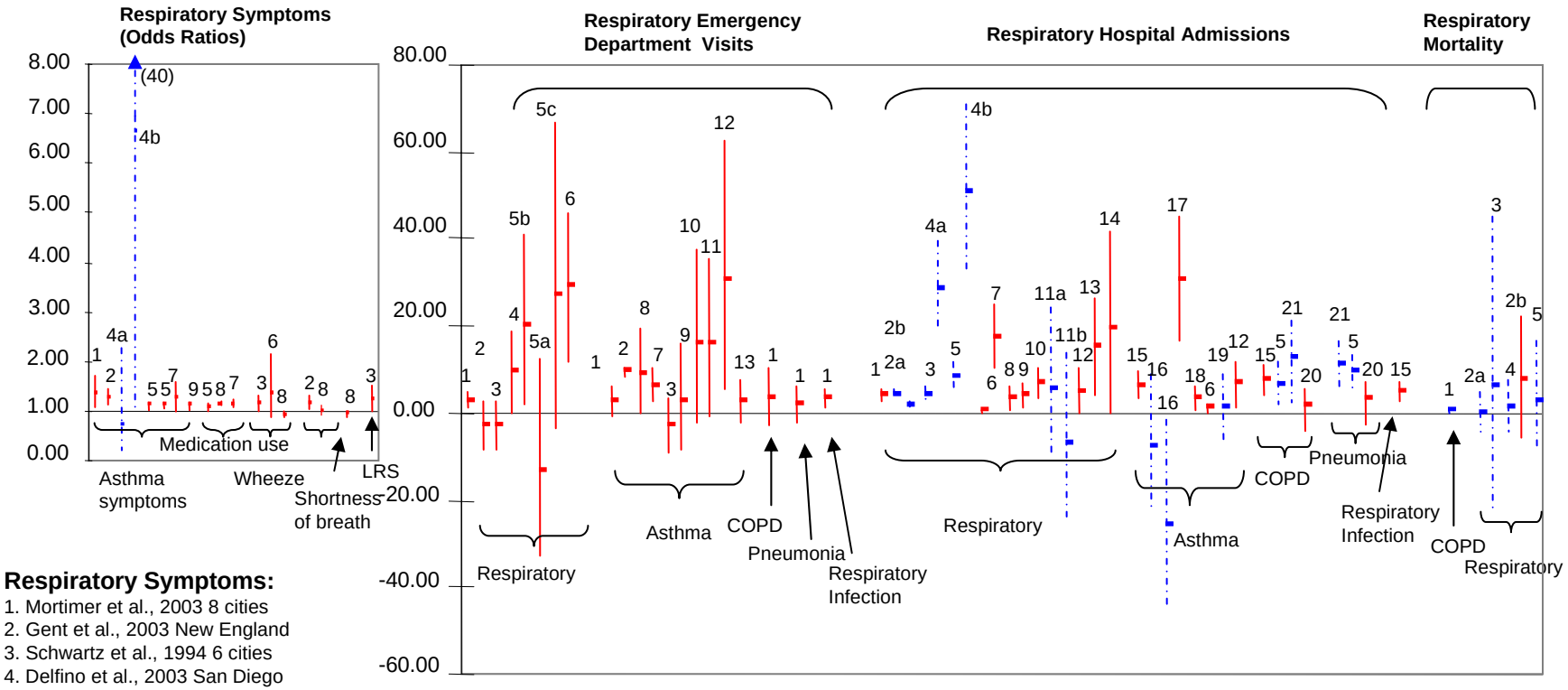
Figure 3-2. O_3-induced cellular and molecular changes and their evolution depicted here is derived from the data reported in Leikauf et al. (1995) and Mudway and Kelly (2000). (Reproduced from Figure 8-10, CD, p. 8-62)

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 and a multicity study (Mortimer et al., 2002). The draft CD 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 emergency department 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. 7-94).

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 3-3, 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 studies, the CD (section 8.5.1) discusses biological plausibility and coherence of evidence for acute O_3-induced respiratory health effects. Inhalation of O_3 for several hrs while subjects are physically active can elicit both acute pathophysiological changes and subjective respiratory tract symptoms (CD, section 8.4.2.4.1). 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 FVC and FEV_1; and increased SR_{aw}. The severity of symptoms and magnitude of response depends on inhaled dose, individual O_3 sensitivity, and the degree of attenuation resulting from previous O_3 exposures. Pulmonary 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 hrs of exposure, and attenuation in functional responses following repeated O_3 exposures is similar to those observed in humans.



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 3-3. 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

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 3-1 and 3-2), illustrate the inherent difficulty of interpreting the biological plausibility of O_3-induced cardiopulmonary health effects (CD, p. 8-64).

The interaction of O_3 with airway epithelial cell membranes and 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, p. 8-65). 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. Initial inflammatory response phase is characterized by increased PMNs in the BAL fluid and increased levels of inflammatory mediators (e.g., interleukins, prostaglandins, complement component C3a). Late inflammatory phase in the lungs is characterized by increased levels of monocytes and eosinophils and mediators, such as cytokines, leukotrienes, proteinases, and ROS. Ozone-induced lung injury and subsequent disruption of the airway epithelial barrier has been implicated in increased mucociliary clearance of particles in human subjects. Similarly, animal toxicology studies have shown that O_3 exposure increased clearance of particles and increased mortality resulting from bacterial and viral infections (CD, p. 8-65).

The draft CD concludes that the findings of O_3-induced lung function changes, respiratory symptoms, inflammation, and permeability changes in animal toxicological studies are consistent with the associations with respiratory health outcomes reported in epidemiological studies. Taken together, there appears to be substantial evidence for coherence and biological plausibility for effects of O_3 on the respiratory system.

3.5.2 Coherence and Plausibility of Effects on the Cardiovascular System

As described in sections 7.2.7 and 7.3.4, some new epidemiological studies have reported associations between short-term O_3 exposure and effects on the cardiovascular system. In the 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 draft CD concludes that the "current evidence is rather limited but supportive of a potential effect on [heart rate variability], ventricular arrhythmias, and the incidence of MI." (CD, p. 7-57)

Some studies have reported associations with hospitalization or emergency department visits for cardiovascular diseases. As shown in Figure 7-13 of the draft CD, the results are somewhat inconsistent, but a number of the associations are positive and statistically significant, especially those conducted during the warm season. The draft CD finds that the evidence from these studies is inconclusive, but the results from studies using warm season analyses suggest potential effects of O_3 on the cardiovascular system (CD, p. 7-73).

Finally, several recent studies report associations between short-term O_3 exposure and mortality from cardiovascular or cardiopulmonary causes, and numerous studies have reported statistically significant associations with total nonaccidental mortality, and cardiopulmonary causes constitute the largest category. Based on results of multi-city analyses, meta-analyses and numerous single-city analyses, the draft CD concludes that there is strong evidence for associations between short-term O_3 exposure and mortality (CD, p. 7-74). As shown in Figure 7-22 of the draft CD, all associations reported in these studies are positive, and many are statistically significant, particularly the associations reported from warm season analyses (CD, p. 7-92).

There are very few human or animal experimental studies that have investigated potential cardiovascular effects of acute O_3 exposure, in contrast to the large data base of studies indicating that O_3 exposure induces lung injury, inflammation, impaired mucociliary clearance, and increased epithelial permeability. The draft CD observes that generation of lipid ozonation products and ROS in lung tissue can influence pulmonary hemodynamics and the cardiovascular system (CD, section 5.4.2). Recent reports of interaction between O_3 and cholesterol in the lung surfactant and the generation of highly reactive products, such as oxysterols and B-epoxide, indicate a role for cardiovascular effects and atherosclerosis (CD, p. 8-66). Changes in heart rate variability, heart tissue edema, and increased tissue and serum levels of ANF have been reported in experimental animals and support the potential for cardiovascular effects induced by acute O_3 exposures. Such effects are the result of stimulation of airway irritant receptors and C-fiber activation and may result from either local or CNS involvement. Ozone-induced changes in alveolar-arterial oxygen transfer observed in controlled exposure human studies of subjects with

hypertension suggest potential complex ANF effects that require further investigation (CD, p. 8-66).

While still limited, the evidence from recent epidemiological studies suggests some coherence in effects of short-term O_3 exposure on the cardiovascular system, from subtle changes in physiological cardiac responses to hospitalization for cardiovascular disease to cardiopulmonary mortality. The draft CD also describes toxicological evidence that provides some potential plausible mechanisms or pathways for effects on the cardiovascular system.

3.5.3 Coherence and Plausibility of Effects Related to Long-Term O_3 Exposure

As discussed in section 8.5.2 of the draft CD, previous epidemiological studies have provided only inconclusive evidence for either mortality or morbidity effects of long-term O_3 exposure. The draft 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. 8-69). 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, increased incidence in asthma, mortality, and possibly lung cancer (CD, section 7.5). Considering these new findings, the draft CD concludes: "The strongest evidence is for negative seasonal effects of O_3 on lung function in adults and children. Less conclusive are longer-term studies investigating the association of chronic O_3 exposure on yearly lung function, asthma incidence, and respiratory symptoms. Chronic O_3-mortality studies observed inconsistencies across exposure periods, cause-specific mortality outcomes, and gender." (CD, p. 7-150) Thus, the epidemiological evidence suggests some potential effects on the respiratory system, but provides no evidence for associations between long-term O_3 exposure and mortality.

Human chamber studies have not evaluated effects with long-term exposures to O_3, but some evidence is 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. 8-69). Studies of monkeys that compared these two exposure scenarios found increased airway pathology only with the latter. A long-term study of 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 seasonal exposure study of monkeys exposed (0.61 ppm O_3) for a year reported increased deposition of collagen and thickening of the CAR of the deep lung. Long-term seasonal O_3 exposure studies of rats also have provided evidence of biochemical and morphological changes suggestive of

irreversible chronic damage to the lungs. One of these studies exposed rats for 20 months (0.5-1.0 ppm O_3 for 6 hr/day) and found increased deposition of collagen and thickening of the CAR of the deep lung. 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.

The draft CD concludes that the totality of evidence from animal toxicology studies strongly suggests that O_3 exposure can damage the distal airways and proximal alveoli, resulting in lung tissue remodeling thus leading to apparent irreversible damage. Such structural changes and compromised pulmonary function caused by persistent inflammation may exacerbate the progression and development of chronic lung disease (CD, p. 8-70). Together with the limited evidence available from epidemiological studies, these studies suggest coherence and plausibility for associations between long-term exposure to O_3 and adverse effects on the respiratory system; however, as noted previously, there is not clear evidence linking long-term exposure to O_3 and mortality.

3.5.4 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 draft CD (section 7-4). These mortality studies suggest a pattern of effects for causality that has a biologically plausible explanation, 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. 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 is hypothesized in the CD (p. 8-70).

The third National Health and Nutrition Examination Followup 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. 8-71). 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). Although this complex series of physiological and biochemical reactions following O_3 exposure could lead to adverse health effects in those with cardiopulmonary disease, there is no experimental data available to support such a hypothesis at this time to explain the cardiovascular mortality evaluated in the epidemiological studies. Future reevaluation may help in understanding the biological plausibility of changes in CRP in the context of O_3 and other air pollution related mortality (CD, section 8.5.3).

3.6 OZONE-RELATED IMPACTS ON PUBLIC HEALTH

The following discussion draws from section 8.6 of the draft 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 health effects that are considered adverse 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. After 18 to 20 years of age, 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 predicted for 20 year old individuals exposed to 0.12 ppm O_3, whereas similar exposure of 35 year old individuals were predicted 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 present in the ELF, are the first line of defense against oxidative stress. Ozone exposure depletes the antioxidant level in the nasal ELF by scrubbing of O_3, 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 draft 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 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, section 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. 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, as discussed below, the effect of increased exertion is consistent.

3.6.2.2 People with Lung Disease

People with preexisting pulmonary disease may be 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. Evidence contained in the 1996 CD indicated that people with asthma appear to be at least as sensitive, or more, to the acute effects of O_3 as healthy nonasthmatic individuals. The new results reviewed in Chapters 6 and 7 of the draft CD from controlled human exposure, field, and epidemiological studies continue to suggest that people with asthma are a potentially sensitive subpopulation for O_3 health effects. This information expands the understanding of the physiological basis for increased sensitivity in people with asthma. It indicates that there are slightly increased spirometric responses in mild asthmatics compared to healthy subjects. Small airways tend to be more affected in people with asthma than in healthy subjects (Alexis et al., 2000), O_3–induced FEV_1 decrements tended to be greater in people with asthma and allergic rhinitis compared to healthy controls (Jörres et al., 1996), and O_3–induced increases in sR_{aw} were reported to be greater in people with asthma compared to healthy subjects (Aris et al., 1995; Balmes et al., 1996). In a study (Horstman et al., 1995) of people with mild-to-moderate asthma exposed for longer durations (6.6 hr), FEV_1 and FEF_{25-75} decrements were

found to be significantly greater than for healthy subjects. Moreover, a significant positive correlation reported in people with asthma between O_3–induced spirometric responses and baseline lung function suggested that responses increased with severity of disease. Ozone-induced inflammatory responses also have been reported to be greater in people with asthma as compared to healthy individuals (Peden et al., 1995; Scannell et al., 1996; Holz et al. 1999). New evidence also indicates that people with asthma may have increased occurrence and duration of nonspecific airway responsiveness, and that people with pre-existing allergic asthma may have increased airway responsiveness to allergens following O_3 exposure (CD, p. 8-29).

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 (CD, p. 8-44). 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 emergency department visits, as discussed in the draft 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 (CD, p. 8-44). With regard to ambient O_3 levels and increased hospital admissions and emergency department visits for asthma and other respiratory causes, strong 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 (CD, p. 8-46). Several hospital admission and emergency department 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 emergency department visits and hospital admissions.

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 draft 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, appear to increase with age until early adulthood and then 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 draft 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 (≤65 years of age) O_3-mortality risk 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 risk 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 draft 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 age or younger populations (CD, p. 7-151).

The draft 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

New animal toxicology studies using various strains of mice and rats have identified O_3-sensitive and resistant strains and illustrated the importance of genetic background in determining O_3 susceptibility. Using subacute low exposure regimen (0.3 ppm O_3, 48h) studies on inbred strains that have been designated as inflammation prone or resistant, Kleeberger et al., (1997) identified the pro-inflammatory cytokine gene, *Tnf*-∝, as a susceptibility gene. Further characterization of this model indicated a role for TNF receptors (TNFR1, TNFR2) in O_3-induced pulmonary epithelial injury and inflammation (Cho et al., 2001). Studies on five inbred strains of mouse with differing response to O_3 exposure (acute high dose or low dose continuous exposure for 3 days), reported a protective role for clara cell secretory protein (CCSP) against O_3-induced oxidative damage (Broeckaert et al., 2003; Wattiez et al., 2003). The role for these genes and/or their orthologs in human susceptibility to O_3 exposure is yet to be examined.

Apart from age at the time of exposure, controlled human exposure studies have also indicated a high degree of interindividual variability in some of the pulmonary physiological parameters. Recent studies by David et al. (2003) and Romieu et al. (2004) reported a role for genetic polymorphism in antioxidant enzymes and genes involved in inflammation to modulate pulmonary function and inflammatory responses to O_3 exposure. Similar to mouse studies referred above, polymorphism in *Tnf*-∝ has been implicated in O_3-induced lung function changes in healthy, mild asthmatics and individuals with rhinitis. These observations suggest a potential role for these markers in the innate susceptibility to O_3, however, the validity of these markers and their relevance in the context of prediction to population studies needs additional experimentation.

Biochemical and molecular parameters extensively evaluated in these 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. No doubt, 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 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 emergency department 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 draft 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. 7-57). In the draft 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. 7-73, 7-74). 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 in section 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 significant enough that they should be 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 "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 category, 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 is much stronger across 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 fall 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, emergency room 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, but the evidence is much stronger in this review than in the 1997 review. 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 draft 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 draft CD concludes that the findings from multi-city times series, single city, and meta-analyses epidemiology studies support a 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, staff defined gradations of individual functional responses (e.g., decrements 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 below in Tables 3-2 and 3-3 below.

For active healthy people, it has been judged that 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 > 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 emergency room 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 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 the guidance for defining adverse respiratory health effects (ATS, 1985) that was published fifteen years earlier and has been used in past NAAQS reviews. 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

1

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

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 responsiveness3	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

[2] This table is reproduced from the 1996 O_3 AQCD (Table 9-1, page 9-24) (U.S. Environmental Protection Agency, 1996).
[3] 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 [4]	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

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

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 3-2 above.

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, and is reproduced in the draft CD (section 8.4.1). Similarly, section 8.7 of the draft CD has summarized the main conclusions derived from the integrated analysis of animal toxicology (CD, Chapter 5), human experimental (CD, Chapter 6) and epidemiological (CD, Chapter 7) studies that evaluated evidence of health effects associated with short-term, repeated, and long-term exposures to O_3 alone or in combination with other pollutants commonly found in the ambient air. This section of the draft Staff Paper integrates conclusions drawn from both sections of the draft CD to provide an overview of health effects of O_3 alone and in mixtures and to identify susceptibility factors associated with exposure to O_3.

3.7.1 Morbidity Health Effects of Acute (Short-term) Exposures to Ozone

In the 1996 CD, it was concluded that short-term O_3 exposures cause: changes in pulmonary function, including tachypnea (rapid, shallow breathing), decreased lung volumes and flows, and increased airway responsiveness to nonspecific stimuli; increased airway resistance; and airway irritation such as cough or chest pain (CD, p. 8-12). Changes in pulmonary function and respiratory symptoms occur as a function of exposure concentration, duration and level of exercise. According to the draft CD, results from the majority of acute exposure studies continue to support the conclusions reported in the 1996 CD.

The 1996 CD concluded that group mean data from numerous controlled human exposure and field studies of healthy subjects (8 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. Also, pulmonary 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 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 draft CD (section 8.7) 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 exercise on pulmonary 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 free air exposures.

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 with heavy and very heavy exercise. 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 exercise 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 exercise, 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 exercise have been observed at 0.08, 0.10 and 0.12 ppm O_3. See Table 3.4 for a summary of short-term health effects of O_3 based on clinical studies.

The 1996 CD concluded that increased O_3 levels are associated with increased hospital admissions and emergency department visits for respiratory causes. Analyses from data in the northeastern U.S. suggest that O_3 air pollution is associated with a substantial portion (on the order of 10 to 20%) of all summertime respiratory hospital visits and admissions. The draft CD concludes that a large multi-city and several single-city studies have indicated a positive

Table 3-4. Summary of Ozone-Induced Respiratory Health Effects from Clinical Studies[5]

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

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

association between increased O_3 levels (especially during the warm season) and increased risk for hospital admissions.

Pulmonary function in children at summer camps in southern Ontario, Canada, in the northeastern U.S., and in southern California is associated with ambient O_3 levels (CD, p. 8-13). 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 hr.

Short-term O_3 exposure of lab animals and humans disrupts the barrier function of the lung epithelium, permitting materials in the airspaces to enter lung tissue, allowing cells and serum proteins to enter the airspaces, and setting off a cascade of responses (CD, p. 8-14). Increased levels of PMNs and protein in lung lavage fluid have been observed following exposure of healthy adults to 0.20, 0.30, and 0.40 ppm O_3 with very heavy exercise and have not been studied at lower concentrations for 1-to 3-hr exposures. Increases in lung lavage protein and PMNs also have been observed at 0.08 and 0.10 ppm O_3 during 6.6 hr exposures with moderate exercise; lower levels have not been tested. Short-term O_3 exposure of lab animals and humans impairs alveolar macrophage (AM) clearance of viable and nonviable particles from the lungs and decreases the effectiveness of host defenses against bacterial lung infections in animals and perhaps humans. The ability of AMs to engulf microorganisms is decreased in humans exposed to 0.08 and 0.10 ppm O_3 for 6.6 hr with moderate exercise.

The draft CD (p. 8-83) concludes that inflammatory responses (PMNs, inflammatory mediators such as cytokines and chemokines) and permeability change (proteins, albumin), typically measured in BAL fluid, also exhibit intersubject variability. Recent meta-analyses on numerous clinical studies indicate interindividual differences in response to short-term O_3 exposures. Also, inflammatory and permeability responses resolve (in some instances complete recovery) and exhibit differential attenuation profiles between normal healthy subjects and people with preexisting respiratory diseases. Some inflammation markers may not resolve readily, and mild persistent inflammation has been reported. It was also concluded that short-term O_3-induced lung function decrements, respiratory symptoms, inflammation, and permeability changes observed in animal toxicology studies are consistent with human studies.

Two health endpoints that were not addressed in the 1996 CD conclusions, but are addressed in the draft CD, are school absenteeism and cardiovascular effects. The draft CD (p. 8-83) concludes that an association between short-term O_3 exposures and school absenteeism (due to respiratory illness) has been suggested. Also, with regard to cardiac outcomes, a limited number of field studies that examined the relationship between short-term O_3 exposures and cardiovascular effects (heart rate variability, myocardial infarction) suggest an association.

3.7.2 Mortality-Related Health 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, the magnitude of the effect was unclear. 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 (CD, p. 7-177, 7-178). The draft 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 risk estimates that are unlikely to be confounded by PM, though the CD observes that future work is needed to better understand the influence of model specifications on the risk coefficient (CD, p. 7-177 to 7-178). For cardiovascular mortality, the draft 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 (CD, p. 7-108). Overall, the draft 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 (CD, p. 8-52).

3.7.3 Health Effects of Repeated Short-term Exposures to Ozone

The 1996 CD drew several conclusions regarding repeated short-term O_3 exposures (CD, p. 8-15). Partial or complete attenuation is observed for some of the O_3-induced responses. After 5 days of exposure, pulmonary 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 draft CD (p. 8-84) 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.

3.7.4 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 months to years causes structural changes in several regions of the respiratory tract (CD, p. 8-15). 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 continue to be extrapolated 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 (CD, p.8-85). Although pathophysiological changes associated with long-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 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 pulmonary function changes observed in children living in cities with high O_3 levels as well as alterations in lung structure alterations reported in an autopsy study in LA support the conclusion that long-term O_3 exposure may play a role in causing irreversible lung damage. Further investigation will be necessary to draw firmer conclusions about chronic health effects of O_3.

3.7.5 Health Effects of Binary 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 (CD, p. 8-16). 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.

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. 8-87). 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 points out the difficulty of trying to link outcomes of epidemiological studies and controlled-exposure studies with binary pollutant mixtures.

3.7.6 Populations at Risk/Susceptibility Factors Associated with Ozone Exposure

The 1996 CD (p. 8-16) 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., exercise level); (4) personal exposure history (e.g., indoor v. outdoor); and (5) personal factors (e.g., age, nutritional status, gender, smoking history, ethnicity). Based on the information assessed in the 1996 CD (p. 8-18), population groups that demonstrated increased responsiveness to ambient concentrations of O_3 consist of exercising, healthy and asthmatic individuals, including children, adolescents, and adults (CD, p. 8-18). 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 draft CD (p. 8-86) concludes that even though the role of ethnic, racial, and nutrition status factors for O_3 susceptibility remains inconclusive, 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) would be considered at greater risk to O_3 exposure.

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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, 2005a) (hereafter cited as "draft Exposure Analysis TSD") presents a more 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. Exposure estimates are developed for current O_3levels, based on 2004 ambient air quality measurements, and for O_3 levels associated with just meeting the current 8-hr O_3 NAAQS, based on adjusting the 2004 air quality data. Exposures to background levels of O_3 are also estimated, based on O_3 concentrations predicted by the GEOS-CHEM atmospheric photochemical model. The model estimated the PRB and total ozone concentrations at each grid point and the grid points selected to represent the 12 urban areas used in the exposure analysis are included in Table 4D-1 in Appendix 4D.

Exposures are modeled for 1) the general population, 2) all school-age children, and 3) active school-age children (defined below). The strong emphasis on children reflects the finding of the last O3 NAAQS-review that children, especially those who are active outdoors, are an important at-risk group. An assessment of exposures of asthmatic school-age children will be presented in the next draft O_3 Staff Paper.

This chapter provides a brief overview of the types of studies that provide data which this analysis is based on, followed by a description of the exposure model used for this analysis, the model input data, and the results of the analysis.

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, 2005b).

The types of 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 measurements, 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" (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. The breathing rate (ventilation rate) at the time of exposure is also an important determinant of the dose received by the individual.

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 (PEM). 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 estimated using physical factors such as air exchange rates, 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 *air exchange rate* (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 *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 air exchange rates account for all of these processes (including "infiltration"), this distinction is not useful in applied modeling of O_3 exposures and will not be discussed further here. Simplistic 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 draft CD reviews O_3 PEMS (draft CD Appendix AX3, p. 163-4) and notes that humidity, wind velocity, badge placement, and interference with other copollutants may result in measurement error. The draft CD reports PEM detection limits ranging from 5 to 23 ppb for averaging times from 24 hours to 1 hour.

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 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. A discussion of monitoring equipment and networks can be found in Chapter 2 of this Staff Paper and in section 2.6 in the draft 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 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, their use must recognize that they may not be representative of the broader population.

The draft CD summarizes results from several personal exposure studies that measured O_3 conducted in the U.S., Canada, and France (draft CD, p. 3-60 to 3-61, Appendix AX3, p. 185-189).

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, air exchange rates, 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 draft CD discusses several studies of microenvironments that contribute to our understanding of the factors and processes that affect exposure to O_3 (draft CD Appendix AX3, p. 190-216).

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 air exchange rate 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.

There are very few sources of O_3 indoors. The draft CD reports on O_3 emissions from photocopiers and from home/office O_3 generators. Some older photocopiers, if run continuously in an enclosed area, can increase O_3 concentrations by as much as 20 ppb. Ozone generators can increase indoor concentrations by more than 200 ppb.

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 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 air concentrations and intake dose 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 staff to estimate O_3 population exposure. Details about the application of the model to estimate O_3 population exposure are provided in sections 4.4 and 4.5 and in the draft Exposure Analysis TSD.

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 air exchange rates and the people's daily activities database. These improvements are described later in this chapter.

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)

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

(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 might 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 dose 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).

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 (e.g., indoor-outdoor air exchange rates). These distributions can depend on the values of other variables calculated in the model or input to APEX. For example, the distribution of air exchange rates in a home, office, or car can depend on the type of heating and air conditioning present, which are 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.

Figure 4-1. Overview of the APEX Model

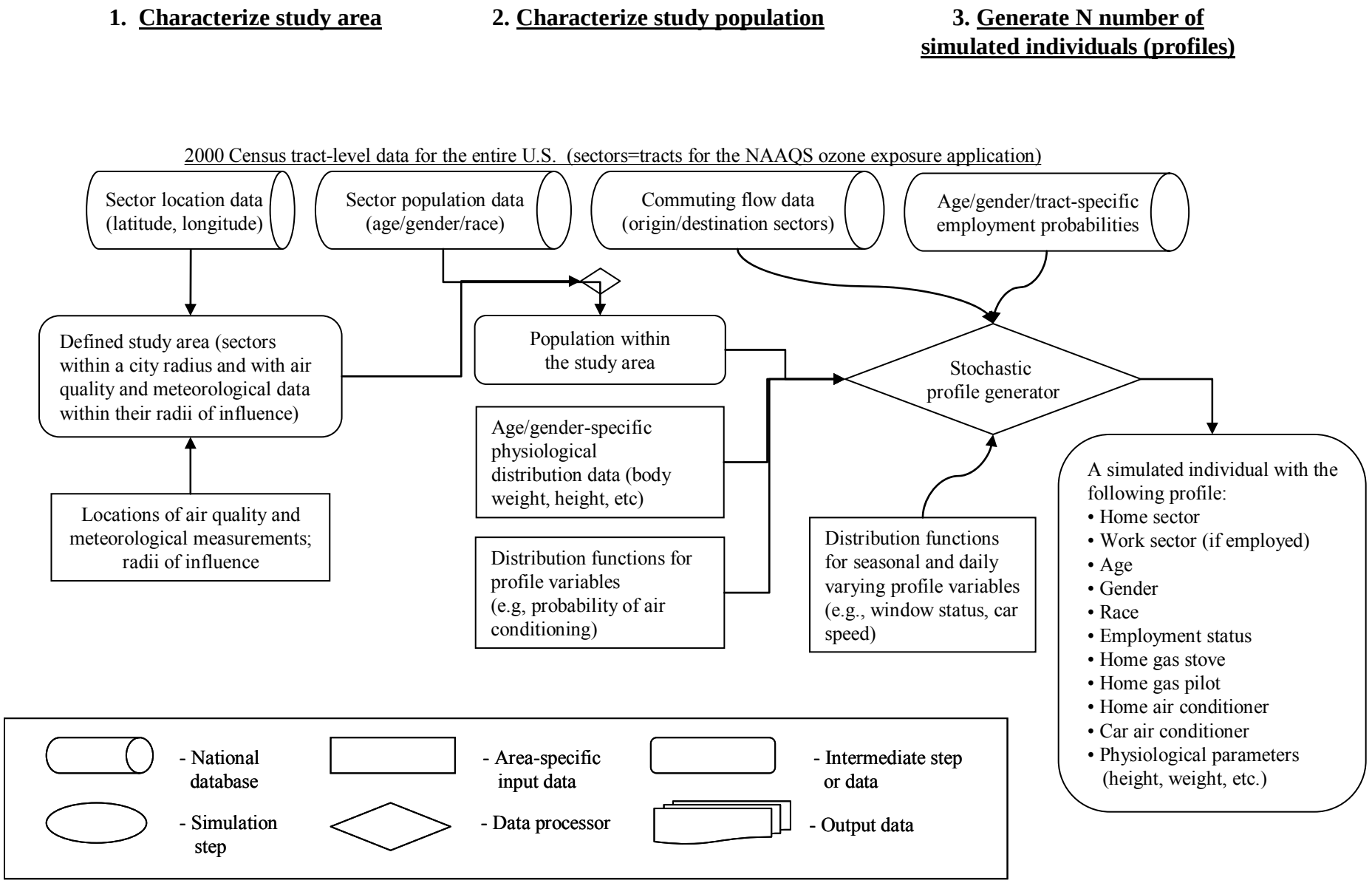


Figure 4-1. Overview of the APEX Model, continued

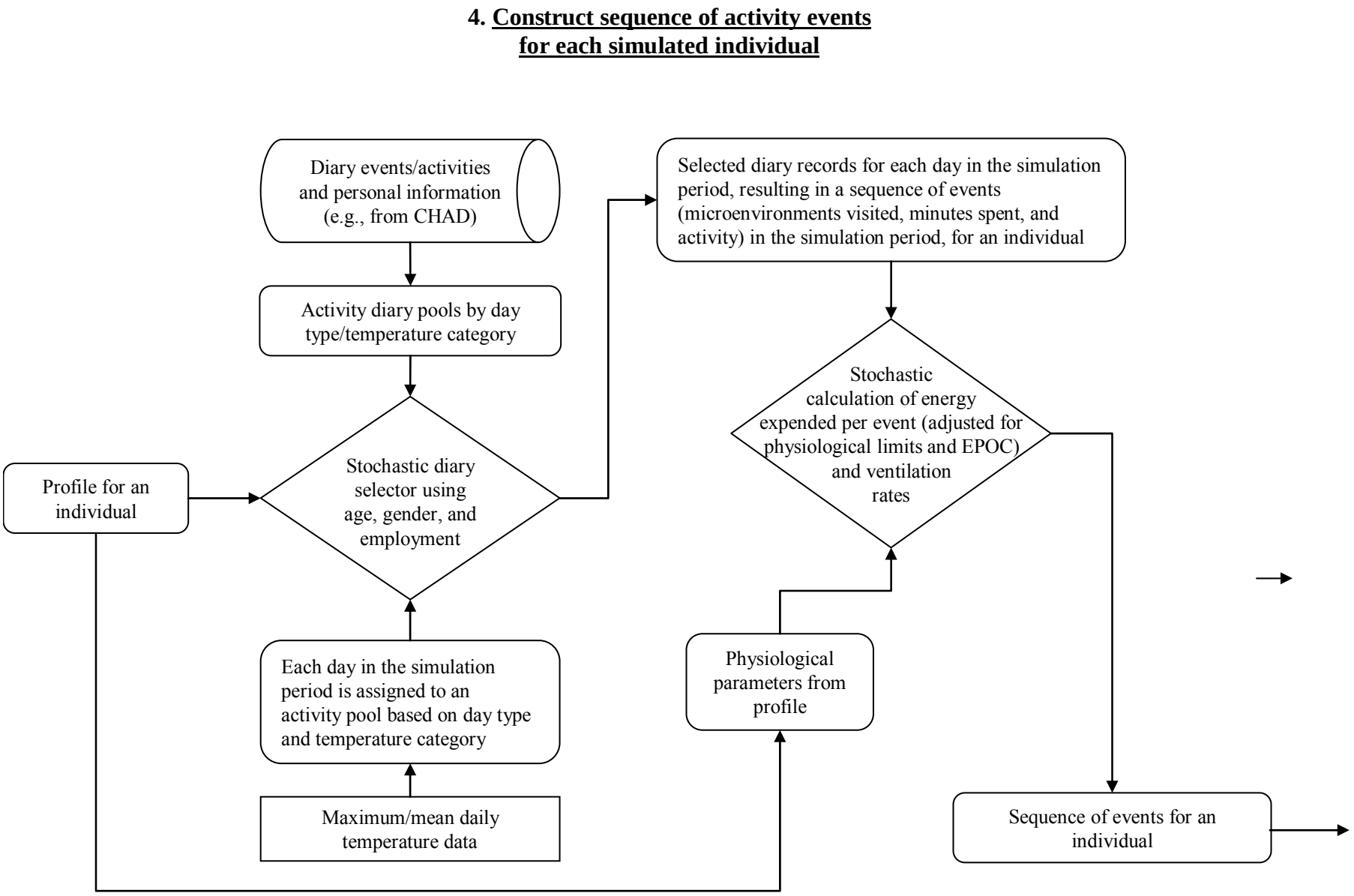
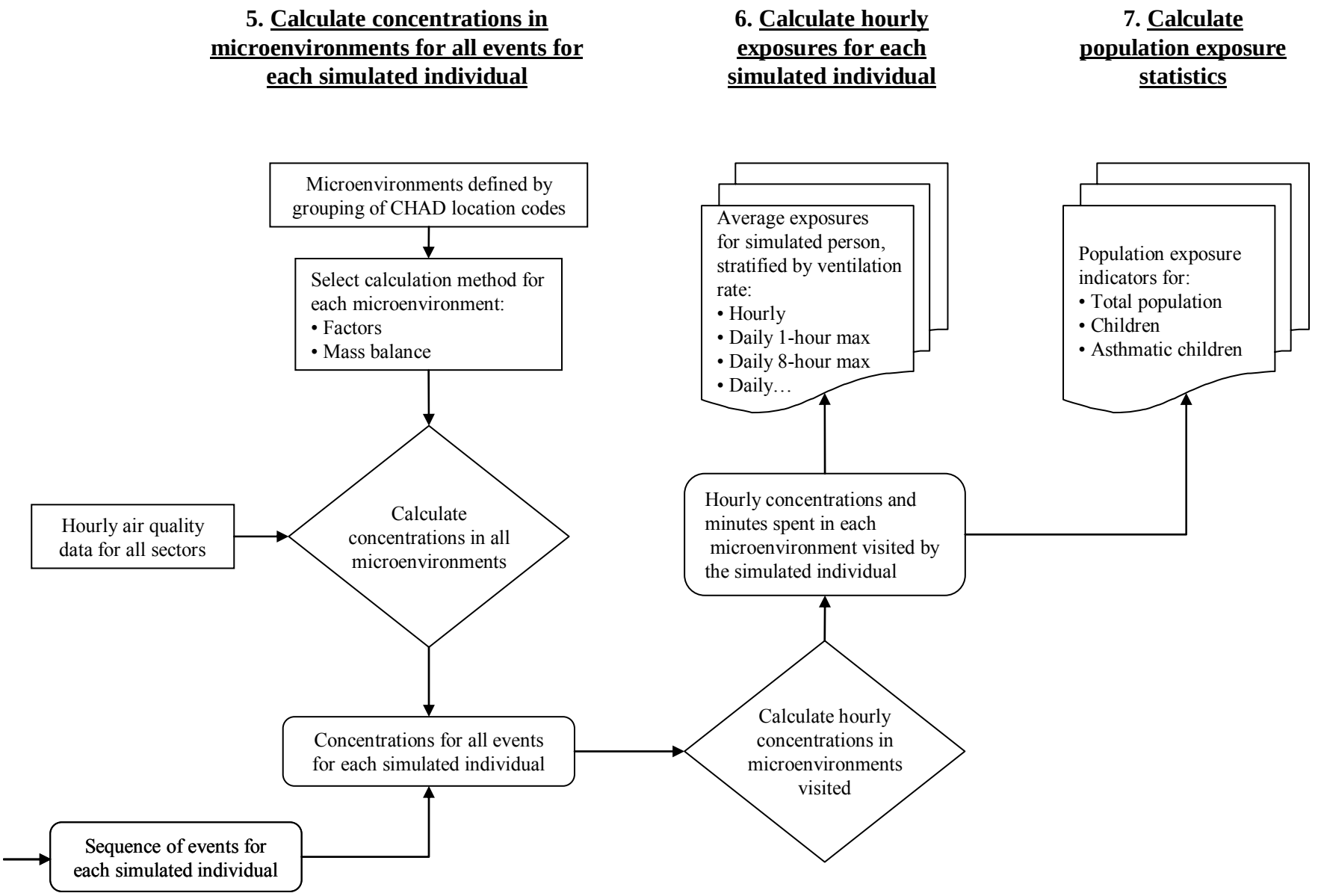


Figure 4-1. Overview of the APEX Model, concluded



The mass balance method 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 exposure concentrations 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 dose rate 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 times 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, which is calculated as Ve/BSA, where Ve is the ventilation rate and BSA is the body surface area of the individual. 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-m2)

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[2] 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 that level of air pollution, or higher, at least once during the modeled period. 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. The latter 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.

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

[2] For purposes of the current exposure analysis, the O_3 season was defined as a fixed period from April 1 through September 30 for all urban areas included in the analysis.

- 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 its predecessor pNEM was used in the last review. However, significant uncertainties in the predictions of APEX remain. In this section we discuss qualitatively some of the limitations of this application of APEX to model population exposures to O_3 pollution. A quantitative uncertainty analysis will be presented in the next draft of this Staff Paper, which will address the impacts of these limitations.

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.

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_2 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. We plan to also model the year 2002 as part of an

analysis of the sensitivity of the exposure modeling results to year-to-year variability of air quality and meteorology, and present these results in the next draft Staff Paper.

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 (draft CD, pages 3-59 to 3-61). However, in some cases, particularly where air exchange rates are high, indoor O_3 concentrations generally closely track outdoor O_3 concentrations (draft CD, Appendix AX3, page 175).

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 variability would not result in uncertainties. However, input data are always a limiting factor. Even if we can accurately characterize the distributions of each individual microenvironmental parameter, we still 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.

4.3.4.2.1 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 seven 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).

4.3.4.2.2 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. This 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.

4.3.4.2.3 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 a minor removal process compared to air exchange and surface removal (Weschler, 2000). Thus the lack of a better treatment of indoor air chemistry is not considered to be a significant limitation of APEX for modeling O_3.

4.3.4.3 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 real people:

- 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. Activity patterns are likely to be affected by many local factors, including topography, land use, traffic patterns, mass transit systems, and recreational opportunities.

4.3.4.4 Modeling Physiological Processes

The modeling of physiological processes that are relevant to the exposure and dose of O_3 is a complicated endeavor. APEX currently has a physiological model for ventilation rates, which is the primary driver of dose of O_3. The limitations of this model have not yet been characterized.

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 epidemiologic 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, staff chose the 12 urban areas listed in Table 4-2 to develop population exposure estimates. 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 period modeled is from April 1 through September 30 for the most recent year. This period encompasses all or most of the O_3 season in 9 of the 12 urban study areas when high ambient O_3 levels are most likely to occur, and for which routine hourly O_3 monitoring data are available. For three of the study areas (Houston, Los Angeles, and Sacramento) the O_3 season is the entire year, but the current exposure analysis only includes the six month period from April through September. The geographic scope and time period modeled are summarized in Table 4-2.

Table 4-2. Urban Areas and Time Periods Modeled

Urban Area (CSA)	Period modeled
Atlanta-Sandy Springs-Gainesville, GA-AL	April 1 to Sept. 30
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 Sept. 30
Detroit-Warren-Flint, MI	April 1 to Sept. 30
Houston-Baytown-Huntsville, TX	April 1 to Sept. 30
Los Angeles-Long Beach-Riverside, CA	April 1 to Sept 30
New York-Newark-Bridgeport, NY-NJ-CT-PA	April 1 to Sept. 30
Philadelphia-Camden-Vineland, PA-NJ-DE-MD	April 1 to Sept. 30
Sacramento--Arden-Arcade--Truckee, CA-NV	April 1 to Sept. 30
St. Louis-St. Charles-Farmington, MO-IL	April 1 to Sept. 30
Washington-Baltimore-N. Virginia, DC-MD-VA-WV	April 1 to Sept. 30

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) and active school-age children. Due to the increased amount of time spent outdoors engaged in relatively high levels of physical activity (which increases dose rates), school-age children as a group are particularly at risk for experiencing O_3-related health effects. The next draft of this Staff Paper will include exposure modeling for asthmatic school-age children.

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" or "active" (McCurdy, 2000).

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

Urban Area (CSA)	Modeled population (thousands)	Modeled children (thousands)	Active children (thousands)
Atlanta	4,548	942	519
Boston	5,714	1,098	529
Chicago	9,311	1,946	933
Cleveland	2,945	582	295
Detroit	5,357	1,110	553
Houston	4,815	1,076	598
Los Angeles	16,349	3,594	1,951
New York	21,357	4,084	2,009
Philadelphia	5,832	1,179	609
Sacramento	1,930	418	226
St. Louis	2,754	572	309
Washington, DC	7,572	1,473	759
Population in all 12 areas	88,484	18,074	9,290

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. 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 the people's daily activities are accurately represented within APEX, it is important to integrate working patterns into the assessment. The APEX commuting data were originally derived from the 2000 Census and were 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).

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:

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

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 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 the version of CHAD used in this modeling analysis.

A key issue in this assessment is the development of an approach for creating O_3-season or year-long activity sequences for individuals based on a cross-sectional activity data base that includes 24-hr 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 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 which reflect the tendency of individuals to repeat activities is 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.

The actual diary construction method targets two statistics, a diversity statistic (***D***) and an 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 construct 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 0.22 for ***D*** and 0.19 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 method for constructing longitudinal diaries from the CHAD data is described in detail in Appendix C of the Exposure Analysis TSD.

4.5.4 Physiological Data

APEX requires values for various physiological parameters for subjects in order to accurately model their pollutant intake via metabolic processes. 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.

Table 4-4. Studies in CHAD

Study name	Geographic coverage	Study time period	Subject ages	Number of persons	Number of person-days	Diary type and study design (random or not)	Reference
Baltimore	A single building in Baltimore	01/1997-02/1997, 07/1998-08/1998	72-93	26	391	Diary	Williams et al, 2000
California Adolescents and Adults (CARB)	California	10/1987-09/1988	12-17 18-94	183 1,579	183 1,579	Recall; Random	Robinson et al. (1989), Wiley et al. (1991a)
California Children (CARB)	California	04/1989-02/1990	0-11	1,200	1,200	Recall; Random	Wiley et al. (1991b)
Cincinnati (EPRI)	Cincinnati metropolitan area	03/1985-04/1985, 08/1985	0-86	888	2,614	Diary; Random	Johnson (1989)
Denver (EPA)	Denver metropolitan area	11/1982-02/1983	18-70	432	805	Diary; Random	Johnson (1984), Akland et al. (1985)
Los Angeles: Elementary School Children	Los Angeles	10/1989	10-12	17	51	Diary	Spier et al. (1992)
Los Angeles: High School Adolescents	Los Angeles	09/1990-10/1990	13-17	19	43	Diary	Spier et al. (1992)

Study name	Geographic coverage	Study time period	Subject ages	Number of persons	Number of person-days	Diary type and study design (random or not)	Reference
National: NHAPS-Air	National	09/1992-10/1994	0-93	4,723	4,723	Recall; Random	Klepeis et al. (1996), Tsang and Klepeis (1996)
National: NHAPS-Water	National	09/1992-10/1994	0-93	4,663	4,663	Recall; Random	Klepeis et al. (1996), Tsang and Klepeis (1996)
University of Michigan children	National	02/1997-12/1997	0-13	2,887	5,616	Recall; Random	Hofferth et al. (1997)
Valdez, AK	Valdez metropolitan area	11/1990-10/1991	11-71	401	401	Recall; Random	Goldstein et al. (1992)
Washington, D.C. (EPA)	Wash., D.C. metropolitan area	11/1982-02/1983	18-98	699	699	Diary; Random	Hartwell et al. (1984), Akland et al. (1985)

1 Adapted from Table 1 in McCurdy et al. (2000).

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 what actual people experience 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 Appendix 4A.

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

4.5.6 Ambient Ozone Concentrations

APEX requires hourly ambient O_3 concentrations at a set of locations in the study area. Data from the EPA AIRS Air Quality Subsystem were used to prepare the ambient air quality input files, using the most recent year (2004) of O_3 measurements. The hourly O_3 concentrations at the AIRS sites in each CSA were interpolated to a 20 by 20 km rectangular grid covering the CSA using a simple inverse squared-distance weighted average for each hour. Grid locations further than 75 km from the closest O_3 monitor were dropped. The hourly gridded and site concentrations 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 a proximity factor. An analysis of the interpolation errors and uncertainty of the O_3 concentrations input to APEX will be presented in the next draft Staff Paper.

In addition to modeling exposures based on 2004 air quality, an analysis was conducted using air quality representative of just meeting the current 8-hr O_3 NAAQS of 0.08 ppm. This was done using a quadratic rollback approach to adjust the hourly O_3 concentrations observed in 2002-2004 to yield a design value of 0.084 ppm (based on rounding conventions, concentrations at or below 0.084 ppm are considered to meet the standard). Design values for the 8-hr O_3 NAAQS are calculated as the 3-year averages of the annual 4th daily maximum 8-hr average concentration based on the maximum monitor within an urban area and are given in Table 4-6 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 rollback approach and evaluation of this approach are described by Johnson (1997), Duff, Horst, and Johnson (1998), and Rizzo (2005).

Table 4-6. 2002-2004 8-Hour 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

The observed concentrations and the concentrations representative of just meeting the current standard are summarized (for 2004 only) in figures in Appendix 4B in terms of the frequencies of daily maximum 8-hr average O_3 concentrations above different concentration levels. These figures also illustrate the percent reduction in exceedances of levels from the 2004 base year to when the current standard is just met.

4.5.7 Meteorological Data

Daily average and maximum 1-hr temperatures are computed from hourly surface temperature measurements obtained from the National Weather Service. These data are not spatially interpolated; 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 air exchange rates for indoor microenvironments, as discussed above.

4.6 EXPOSURE ASSESSMENT RESULTS

The results of the exposure analysis are presented in a series of tables in this section and in graphs in Appendix 4C. The tables summarize exposures to O_3 concentrations above two specific levels, 0.08 and 0.07 ppm, while the graphs in Appendix 4C depict these results over the entire range of observed concentrations. The 0.08 ppm level corresponds to the lowest exposure level used in the controlled human studies (see section 3.6.1). The exposure-response relationships based on these studies are extrapolated down to background levels (section 5.3.1), and the 0.07 ppm level was chosen to illustrate the sensitivity of the exposure modeling results to the selected level. The tables summarize two measures of the extent of population exposures over the modeled period (April 1 through September 30):

- numbers of person-days with daily maximum 8-hr average exposures under moderate exertion above 0.08 and 0.07 ppm (Table 4-77 and Table 4-10),

- numbers of persons who experience one or more daily maximum 8-hr average exposures under moderate exertion above 0.08 and 0.07 ppm (Table 4-8 and Table 4-111), also expressed as percentages of the population (Table 4-9 and Table 4-22) and

Exertion is characterized by equivalent ventilation rates (section 4.3.3). Results are presented for the 2004 base case, "just meeting" the current standard, and the difference between these scenarios (as a percent reduction), for the general population, children (ages 5-18), and for active children. For the tables reporting counts of persons, there are companion tables with the same results expressed as percentages of the population group totals given in Table 4-3.

For example, for Atlanta, Table 4-8 reports an estimated 13.8 thousand active children who experience an 8-hr average exposure above 0.08 ppm under moderate exertion at least once

during the 2004 O_3 season. Under the scenario of just meeting the current 8-hr standard, this number is reduced by 87 percent to 1.8 thousand active children. These correspond to 2.7 and 0.4 percent respectively (Table 4-9) of the population of active children in Atlanta (519 thousand).

The tables in this section have counts of exposures above a level of 0.08 ppm. Appendix 4C shows graphs of counts of person-days of 8-hr exposures above different levels ranging from 0 to 0.16 ppm, concomitant with moderate exertion, for children ages 5 to 18.

These results indicate a significant reduction in 8-hr average exposures above 0.08 ppm under attainment of the current 8-hr O_3 NAAQS. In addition, under the current standard it is rare for an individual to experience more than one 8-hr exposure above 0.08 ppm, as evidenced by the average number of 8-hr exposures above 0.08 for individuals, which is less than 1.01 for each of the three population groups in these tables (compared to 1.2 for historical 2004 air quality).

Table 4-7. Numbers of Person-Days Over the Modeled Periods With Daily Maximum 8-Hour Average Exposures Above 0.08 ppm Under Moderate Exertion (thousands)

	General Population			Children (ages 5-18)			Active Children (ages 5-18)		
City (CSA)	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**
Atlanta	56.4	6.9	88%	20.0	2.3	88%	14.3	1.8	87%
Boston	13.7	0.2	99%	6.9	0.0	100%	4.6	0.0	100%
Chicago	1.6	0.0	100%	1.1	0.0	100%	0.3	0.0	100%
Cleveland	2.9	0.0	100%	1.1	0.0	100%	0.2	0.0	100%
Detroit	0.3	0.0	100%	0.0	0.0	0.0%	0.0	0.0	0.0%
Houston	240.0	21.7	91%	89.0	7.0	92%	58.1	4.4	92%
Los Angeles	1,330.0	0.0	100%	516.0	0.0	100%	302.0	0.0	100%
New York	101.0	1.8	98%	45.8	0.6	99%	24.4	0.6	98%
Philadelphia	32.2	1.3	96%	12.2	0.0	100%	7.7	0.0	100%
Sacramento	12.1	0.0	100%	4.3	0.0	100%	2.4	0.0	100%
St. Louis	0.7	0.0	100%	0.2	0.0	100%	0.1	0.0	100%
Washington DC	144.0	18.6	87%	58.6	6.7	89%	37.9	4.5	88%
All cities	1,934.9	50.5	97%	755.2	16.6	98%	452	11.3	98%

Table 4-8. Numbers of Persons With At Least One Daily Maximum 8-Hour Average Exposure Above 0.08 ppm Under Moderate Exertion Over the Modeled Periods (thousands)

	General Population			Children (ages 5-18)			Active Children (ages 5-18)		
City (CSA)	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**
Atlanta	54.7	6.9	87%	19.2	2.3	88%	13.8	1.8	87%
Boston	13.4	0.2	99%	6.5	0.0	100%	4.2	0.0	100%
Chicago	1.6	0.0	100%	1.1	0.0	100%	0.3	0.0	100%
Cleveland	2.9	0.0	100%	1.1	0.0	100%	0.2	0.0	100%
Detroit	0.3	0.0	100%	0.0	0.0	0.0%	0.0	0.0	0.0%
Houston	220.8	21.3	90%	81.0	7.0	91%	52.8	4.4	92%
Los Angeles	1,019.3	0.0	100%	390.5	0.0	100%	233.6	0.0	100%
New York	101.3	1.8	98%	45.8	0.6	99%	24.4	0.6	98%
Philadelphia	30.8	1.3	96%	11.8	0.0	100%	7.5	0.0	100%
Sacramento	11.6	0.0	100%	4.1	0.0	100%	2.4	0.0	100%
St. Louis	0.7	0.0	100%	0.2	0.0	100%	0.1	0.0	100%
Washington DC	140.8	18.6	87%	57.1	6.7	88%	37.0	4.5	88%
All cities	1,598.2	50.1	97%	618.4	16.6	97%	376.3	11.3	97%

Table 4-9. Numbers of Persons With At Least One Daily Maximum 8-Hour Average Exposure Above 0.08 ppm Under Moderate Exertion Over the Modeled Periods (percent of population group)

	General Population		Children (ages 5-18)		Active Children (ages 5-18)	
City (CSA)	**Base case**	**Current standard**	**Base case**	**Current standard**	**Base case**	**Current standard**
Atlanta	1.2%	0.2%	2.0%	0.2%	2.7%	0.4%
Boston	0.2%	0.0%	0.6%	0.0%	0.8%	0.0%
Chicago	0.0%	0.0%	0.1%	0.0%	0.0%	0.0%
Cleveland	0.1%	0.0%	0.2%	0.0%	0.1%	0.0%
Detroit	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Houston	4.6%	0.4%	7.5%	0.7%	8.8%	0.7%
Los Angeles	6.2%	0.0%	11%	0.0%	12%	0.0%
New York	0.5%	0.0%	1.1%	0.0%	1.2%	0.0%
Philadelphia	0.5%	0.0%	1.0%	0.0%	1.2%	0.0%
Sacramento	0.6%	0.0%	1.0%	0.0%	1.0%	0.0%
St. Louis	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Washington DC	1.9%	0.2%	3.9%	0.5%	4.9%	0.6%

Table 4-10. Numbers of Person-Days Over the Modeled Periods with Daily Maximum 8-Hour Average Exposures Above 0.07 ppm Under Moderate Exertion (thousands)

	General Population			Children (ages 5-18)			Active Children (ages 5-18)		
City (CSA)	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**
Atlanta	323.0	81.2	75%	134.0	30.5	77%	92.0	22.5	76%
Boston	140.0	9.0	94%	59.6	3.9	93%	34.4	2.8	92%
Chicago	21.5	0.5	98%	7.7	0.5	93%	4.3	0.3	94%
Cleveland	40.6	2.6	94%	16.2	1.1	93%	8.5	0.2	98%
Detroit	69.2	0.5	99%	32.8	0.2	100%	21.7	0.0	100%
Houston	765.0	139.0	82%	317.0	49.1	85%	203.0	32.9	84%
Los Angeles	5,870.0	23.4	100%	2,630.0	6.1	100%	1,740.0	2.3	100%
New York	736.0	49.4	93%	312.0	26.2	92%	182.0	15.9	91%
Philadelphia	294.0	23.2	92%	127.0	6.0	95%	80.5	3.3	96%
Sacramento	110.0	2.3	98%	40.9	0.9	98%	22.9	0.4	98%
St. Louis	10.9	2.2	80%	3.1	0.5	85%	2.0	0.3	84%
Washington DC	554.0	193.0	65%	224.0	80.5	64%	140.0	53.2	62%
All cities	8,934.2	526.3	94%	3,904.3	205.5	95%	2,531.3	134.1	95%

Table 4-11. Numbers of Persons With at Least One Daily Maximum 8-hour Average Exposure Above 0.07 ppm Under Moderate Exertion Over the Modeled Period (thousands)

	General Population			Children (ages 5-18)			Active Children (ages 5-18)		
City (CSA)	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**	**Base case**	**Current standard**	**Percent reduction**
Atlanta	289.6	78.2	73%	120.7	29.4	76%	82.0	21.7	74%
Boston	130.9	8.7	93%	54.5	3.8	93%	31.2	2.6	92%
Chicago	21.3	0.5	98%	7.4	0.5	93%	4.0	0.3	93%
Cleveland	38.2	2.6	93%	15.2	1.1	93%	8.1	0.2	98%
Detroit	68.1	0.5	99%	32.4	0.2	100%	21.4	0.0	100%
Houston	614.2	130.3	79%	249.7	45.9	82%	160.3	30.7	81%
Los Angeles	3,405.3	22.0	99%	1,411.2	5.6	100%	914.6	2.3	100%
New York	695.0	49.4	93%	292.9	26.2	91%	170.9	15.9	91%
Philadelphia	269.5	22.3	92%	116.0	5.7	95%	74.5	3.2	96%
Sacramento	94.6	2.2	98%	35.3	0.8	98%	19.7	0.4	98%
St. Louis	10.9	2.2	80%	3.1	0.5	85%	2.0	0.3	84%
Washington DC	503.0	186.3	63%	203.4	77.4	62%	125.3	51.1	59%
All cities	6,140.6	505.2	92%	2,541.8	197.1	92%	1614	128.7	92%

Table 4-22. Numbers of Persons With At Least One Daily Maximum 8-Hour Average Exposure Above 0.07 ppm Under Moderate Exertion Over the Modeled Period (percent of population group)

	General Population		Children (ages 5-18)		Active Children (ages 5-18)	
City (CSA)	**Base case**	**Current standard**	**Base case**	**Current standard**	**Base case**	**Current standard**
Atlanta	6.4%	1.7%	13%	3.1%	16%	4.2%
Boston	2.3%	0.2%	5.0%	0.3%	5.9%	0.5%
Chicago	0.2%	0.0%	0.4%	0.0%	0.4%	0.0%
Cleveland	1.3%	0.1%	2.6%	0.2%	2.7%	0.1%
Detroit	1.3%	0.0%	2.9%	0.0%	3.9%	0.0%
Houston	13%	2.7%	23%	4.3%	27%	5.1%
Los Angeles	21%	0.1%	39%	0.2%	47%	0.1%
New York	3.3%	0.2%	7.2%	0.6%	8.5%	0.8%
Philadelphia	4.6%	0.4%	9.8%	0.5%	12%	0.5%
Sacramento	4.9%	0.1%	8.5%	0.2%	8.7%	0.2%
St. Louis	0.4%	0.1%	0.5%	0.1%	0.6%	0.1%
Washington DC	6.6%	2.5%	14%	5.3%	17%	6.7%

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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, hospital admissions, and mortality associated with recent ambient O_3 levels; and (2) risk reductions associated with just meeting the current 8-hr O_3 NAAQS. The next draft of the Staff Paper will also include risk reductions associated with just meeting various alternative O_3 standards. 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, 2005a; henceforth referred to as the 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 NAAQS and alternative O_3 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. Staff recognizes 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 indications provided by the assessment 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; 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 promulgation 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 second external review draft of the O_3 CD (EPA, 2005c). Some aspects of the current risk assessment may change based on changes that may be incorporated in the final O_3 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.

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, staff is using probabilistic exposure-response relationships developed during the last review which were 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 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 concentration is typically measured as the average of monitor-specific measurements, using population-oriented monitors. Population health responses for O_3 have included population counts of hospital admissions for respiratory and cardiac 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 can be summarized as follows:

- A risk assessment based on controlled human exposure studies uses exposure-response functions, and therefore requires as input (modeled) personal exposures to ambient O_3. A risk assessment based on epidemiological studies uses concentration-response functions, and therefore requires as input (monitored) ambient O_3 concentrations.
- 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 controlled human exposure studies-

based risk assessment 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 controlled human exposure studies-based risk assessment could appropriately be carried out but an epidemiological studies-based risk assessment could not.

- The adequate modeling of hourly personal exposures associated with ambient concentrations 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 could not.
- 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.

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 draft CD concludes that the weight of the evidence supports the general conclusion that O_3, acting alone and/or in combination with other co-pollutants is likely causal. 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).[1] Risks associated with concentrations above this background are judged to be more relevant to policy decisions

[1] 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.

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 (≥ 10, ≥ 15, and ≥ 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 3.3.2.2 and Chapter 6 of the draft CD, there is a significant body of controlled human exposure studies reporting lung function decrements and respiratory symptoms in adults associated with 1- and 6-8-hr exposures to ozone.

Consistent with the approach used in the last review, staff judges that it is reasonable to estimate exposure-response relationships for lung function decrements associated with ozone 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 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 lung function decrements, and since no new information published since the last review suggests any changes that would impact this conclusion, staff has included only the lung function decrements (≥10, 15, and 20% FEV_1) associated with 8-hr moderate exertion exposures in children (age 5 to 18 years old) in the current risk assessment.

Although respiratory symptoms in healthy children were estimated in the last review, staff has 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 draft CD concludes (p.7-48) that "these studies indicate that there is no consistent evidence of an association between O_3 and respiratory symptoms among children."

As discussed in section 3.3.2.2, the draft CD also concludes that collectively, the results of field studies suggest that respiratory symptoms and increased medication use in asthmatic children are associated with acute exposure to O_3. While these recent studies provide strong

evidence that some asthmatic children are likely to experience O_3-related effects, the selective recruitment of inner city asthmatic subjects makes it very difficult to develop quantitative risk estimates for asthmatic children based on these studies.

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 draft 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 draft CD. In selecting health endpoints to be included in the current quantitative risk assessment, staff has focused on health endpoints that are better understood in terms of health consequences (i.e., adversity) 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. Based on these considerations, the following endpoints associated with short-term exposures to O_3 have been included:

- Hospital admissions for respiratory and cardiovascular illness;
- Premature total, respiratory, and cardiovascular mortality.

As noted in the draft CD (p.7-149), "large multi-city studies, as well as many studies from individual cities have reported an association of O_3 concentrations with respiratory and cardiovascular 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 cardiopulmonary hospital admissions." With respect to acute O_3 effects on mortality, the draft CD concludes (p.7-149) 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 draft CD and section 3.3.2, several additional health endpoints including emergency department visits for respiratory illness, increased respiratory symptoms in asthmatic children, 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 emergency department visits. With respect to increased respiratory symptoms in asthmatic children, the evidence is strong that ambient O_3 exposures can lead to these effects, but the design of these epidemiological studies, which focus on subjects recruited in inner-city neighborhoods, pose significant problems since there is a lack of baseline incidence data for this endpoint for asthmatic children residing in urban areas. Further, the staff judges 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 populations 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). In contrast, 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 each of the 12 urban areas.

5.2.3 Air Quality Considerations

Both the controlled human exposure and epidemiolgic-based portions of the risk assessment 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. The year selected to represent recent air quality data is 2004, since this is the most recent year for which complete data are currently available.

In order to estimate health risks associated with just meeting the current 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[2] 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 a single year of data (2004) to estimate risks for a single season (April through September) in a single year. As described in section 4.5.6 and in more detail in Rizzo (2005), after considering several approaches, including proportional rollback and Weibull adjustment procedures, staff 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 to the filled in 2004 O_3 monitoring data, based on the 3-year period (2002-2004) O_3 design value, to generate a new time series of hourly O_3 concentrations that

[2] 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 4th daily maximum 8-hr average concentration based on the maximum monitor within an urban area are the design values.

reflects air quality levels just meeting the current 8-hr O_3 standard for this single year. It should be noted that since compliance with the current standard is based on the 3-year average of the 4th 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. Staff plans to explore the magnitude of this year-to-year variability in the next draft of the assessment by conducting assessments involving adjusting 2002 air quality (a year with generally higher O3 levels in many of the 12 urban study areas) to just meet the current 8-hr standard.

As noted earlier, the risk estimates developed for both the recent air quality scenario and just meeting the current 8-hr standard represent risks in excess of estimated background concentrations. The results of the global tropospheric O_3 model GEOS-CHEM have been used to estimate monthly average background O_3 levels for different geographic regions across the U.S. These GEOS-CHEM simulations include a background simulation in which North American anthropogenic emissions of nitrogen oxides, non-methane volatile organic compounds, and carbon monoxide are set to zero, as described in Fiore et al. (2003). Staff estimated monthly background concentrations for each of the 12 urban areas based on the GEOS-CHEM simulations (Langstaff, 2005a).

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

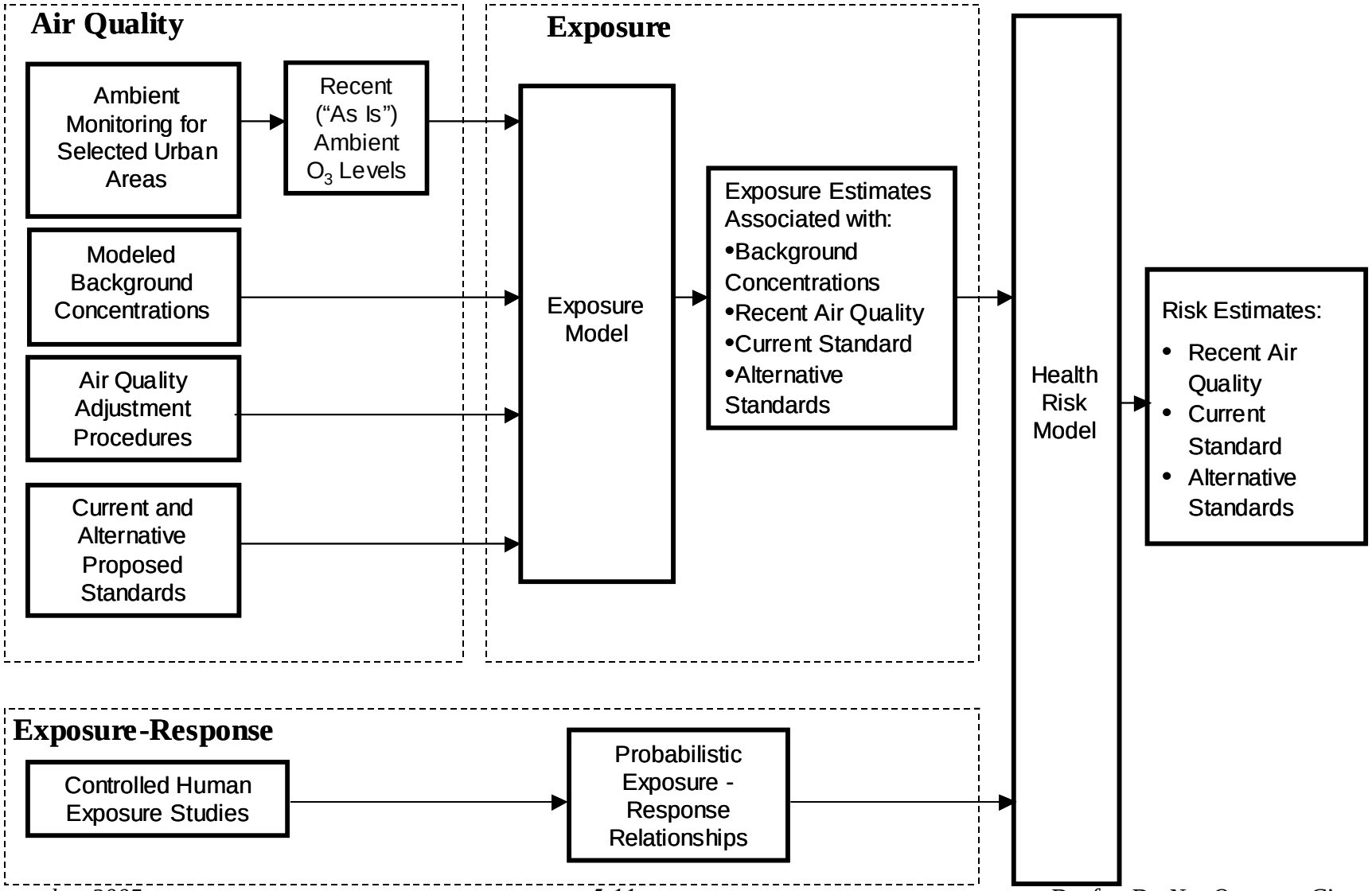
The major components of the portion of the health risk assessment based on data from controlled human exposure studies are illustrated in Figure 5-1. As shown in Figure 5-1, under this portion of the risk assessment, exposure estimates for a number of different air quality scenarios (i.e, recent year 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_1. 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 1 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.

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 staff is interested in risk estimates associated with O_3 concentrations in excess of background concentrations, the following steps were taken: (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.

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



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 ozone, given recent ambient O_3 concentrations;

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

P_j = the fraction of the population having personal exposures to O_3 concentration of e_j ppm, given 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 air quality representing a recent year, for 2004 air quality adjusted to just meet the current 8-hr standard, and for air quality levels representing background based on estimates from the GEOS-CHEM model). Chapter 4 and the draft Exposure Assessment TSD (EPA, 2005d) 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 in the range of 13 to 27 l/min-m^2 were included in the exposure estimates for 8-hr moderate exertion. This range was selected to match the range of 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. As in the prior assessment, the combined data set from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) studies have been used to estimate exposure-response relationships for 8-hr exposures. 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. Regression techniques were then used to fit a function to the data for each of the three measures of lung function decrement. In each case, a linear function provided a good fit.[3]

[3] As noted in Whitfield et al., 1996, the response data point associated with 0.12 ppm for the response measure FEV1 ≥ 15% appeared to be inconsistent with the other data points (see Whitfield et al., 1996, Table 10, footnote c).

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 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 at each of the three O_3 concentrations for which there were data from the underlying studies (0.08, 0.10, and 0.12 ppm). Using diffuse Beta distributions as priors distributions, the resulting posterior distributions are also Beta distributions (see Appendix A in Whitfield et al., 1996). Response rates were calculated for 21 fractiles (for cumulative probabilities from 0.05 to 0.95 in steps of 0.05) plus probabilities of 0.01 and 0.990 using these posterior Beta distributions. For other concentrations, regression techniques were used to fit a linear function through the three points at O_3 concentrations of 0.08, 0.10, and 0.12 ppm and then this function was used to generate response rates for all 21 fractiles at specified O_3 concentrations. If the estimated response rate was less than 0.0, it was set equal to 0.0 and if the response rate was greater than 1.0, it was set to 1.0.

In addition to uncertainties arising from sample size considerations, other uncertainties associated with the use of the exposure-response relationships for lung function responses are briefly summarized below. Additional uncertainties with respect to the exposure inputs to the risk assessment are described in Chapter 4 and the draft Exposure Assessment TSD. 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.

Because of this, we estimated the probability of a response of FEV1 ≥ 15% at an O_3 concentration of 0.12 ppm by interpolating between the FEV1 ≥ 10% and FEV1 ≥ 20% response rates at that O_3 concentration.

- 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., 0.08 ppm). In the prior review the CASAC O_3 Panel supported the staff's decision to use a linear extrapolation approach down to background levels. The same extrapolation has been applied in the current risk assessment.

- 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 draft CD (see section AX6.4) which cites studies by McDonnell et al. (1985b) and Hazucha et al. (2003) as showing significant reproducibility of response.

- 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 (ages 5-18). This approach is supported by evaluation in the draft 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. The draft CD also notes that Hazucha et al. (2003) similarly observed generally reproducible O_3-induced lung function responses in a controlled human exposure study. 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 draft CD, O_3-induced responses can be enhanced or attenuated as a result of recent prior exposures. The possible impact of exposure history on the risk estimates is an additional source of uncertainty that is not quantified in this assessment.

- 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 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 cardiopulmonary-related hospital admissions and total and cardiopulmonary 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

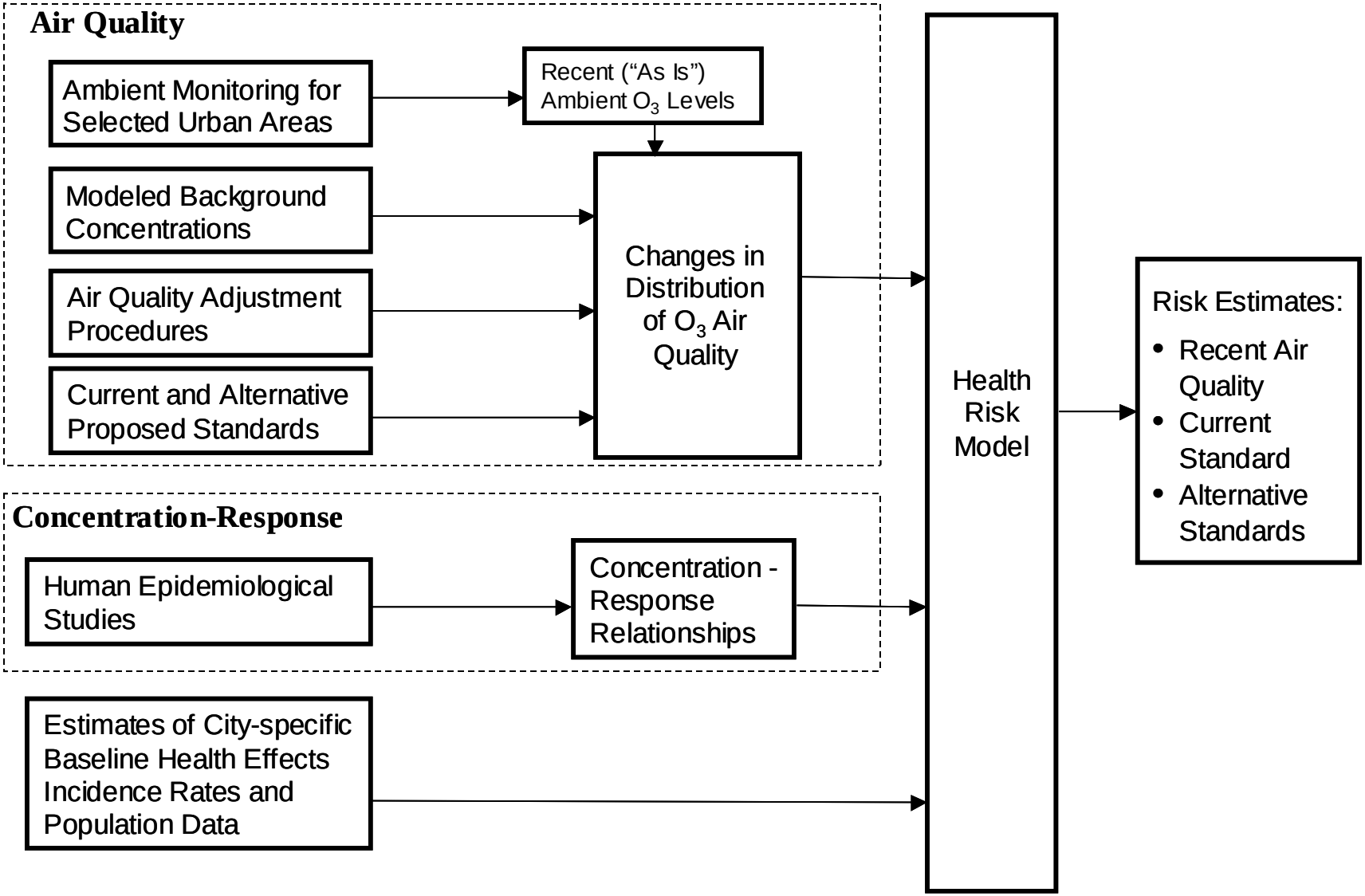
In order to estimate the incidence of a particular health effect associated with recent conditions in a specific county or set of counties attributable to ambient O_3 exposures in excess of background, as well as the change in incidence of the health effect in that county or set of counties corresponding 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, although functions estimated in other locations can be used at the cost of increased 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 5-2 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:

Figure 5-2. Major Components of Ozone Health Risk Assessment Based on Epidemiological Studies



$$y = Be^{\beta x}, \qquad \text{(Equation 5-2)}$$

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 5-2, 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. Staff 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, and (2) hourly background O_3 concentrations. 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. Table 5B-1 (Appendix 5B) provides more detailed information on ambient O_3 concentrations for these locations, including 1-hr and 24-hr average statistics across monitors in each location and the composite monitor values used in this part of the risk assessment.

Different exposure metrics have been used in epidemiological O_3 studies, including the 24-hr average and the daily 1-hr maximum. Therefore, daily changes at the composite monitor in the O_3 exposure metric appropriate to a given concentration-response function were calculated (see Table A-13, Appendix A for summary statistics for the composite monitor O_3 concentrations in the 12 urban locations). 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 the stream of hourly O_3 concentrations from a recent year at the composite monitor, just created, 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 the stream of background hourly O_3 concentrations at the composite monitor, just created, calculate the 1-hr maximum background O_3 concentration for each day at the composite monitor.
- For each day, calculate Δx = (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 standard above background levels were estimated, were done analogously. For this case the monitor-specific series of adjusted hourly concentrations were used rather than the monitor-specific series of recent monitored hourly concentrations. Similarly, calculations for concentration-response functions that used a different exposure metric (e.g., the 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 5-2, another key component in the epidemiological-based risk model 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 mortality and hospital admissions associated with short-term exposures. Once it has been determined that a health endpoint is to be included in the assessment, 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 for the epidemiological studies-based part of the O_3 risk assessment are those locations in which concentration-response functions have been estimated. There are several advantages, however, to using estimates from multi-city studies versus studies carried out in single cities. 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 are presented for both functions.

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;

Table 5-1. Locations and Health Endpoints Included in the O_3 Risk Assessment Based on Epidemiological Studies*

Urban Area	Premature Total Mortality or Cardiorespiratory Mortality	Hospital Admissions for Respiratory and Cardiovascular Illnesses
Atlanta	Bell et al. (2004) Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities	
Boston	Bell et al. (2004) – 95 cities	
Chicago	Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities Schwartz (2004) Schwartz (2004) – 14 cities	
Cleveland	Bell et al. (2004) Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities	Schwartz et al. (1996)
Detroit	Bell et al. (2004) Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities Schwartz (2004) Schwartz (2004) – 14 cities Ito (2003)	It0 (2003)
Houston	Bell et al. (2004) Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities Schwartz (2004) Schwartz (2004) – 14 cities	
Los Angeles	Bell et al. (2004) Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities	Linn et al. (2000)
New York	Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities	Thurston et al. (1992)
Philadelphia	Bell et al. (2004) – 95 cities Huang et al. (2004) Huang et al. (2004) – 19 cities Moolgavkar et al. (1995)	
Sacramento	Bell et al. (2004) Bell et al. (2004) – 95 cities	
St. Louis	Bell et al. (2004) Bell et al. (2004) – 95 cities	
Washington, D.C.	Bell et al. (2004) – 95 cities	

- 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 draft 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 Table 5A-1 (Appendix 5A).

5.3.2.4 Baseline Health Effects Incidence and Population Estimates

As illustrated in Equation 5-4, the most common epidemiological-based health risk model expresses the reduction in health risk (Δy) associated with a given reduction in O_3 concentrations (Δx) as a percentage of the baseline incidence (y). To accurately assess the impact of changes in O_3 air quality on health risk in the selected urban areas, information on the baseline incidence of health effects (i.e., the incidence under recent air quality conditions) in each location is therefore needed. Population sizes, for both total population and various age ranges used in the risk assessment were obtained for the year 2002 (need citation) 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.[4]

County-specific rates for cardiovascular and respiratory hospital discharges, and various subcategories (e.g., asthma, pneumonia, ischemic heart disease), have been obtained, where possible, from state, local, and regional health departments and hospital planning commissions for each of the risk assessment locations.[5] 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.

[4] Since the baseline incidence rates are expressed in terms of cases per 100,000 general population, the general population estimates have been used in combination with these rates to generate the baseline incidence in each location for non-accidental and various types of mortality in calculating the risk estimates.

[5] 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
Atlanta	Fulton, DeKalb	1.5	---	---
Boston	Suffolk	0.7	---	---
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	0.4	---	---
Washington, D.C.	Washington, D.C.	0.6	---	---

* Total population and age-specific population estimates taken from 2000 Census data. Populations are rounded to nearest 0.1 million. The urban areas given in this table are those considered in the studies used in the O_3 risk assessment.

Table 5-3. Baseline Mortality Rates (per 100,000 Population) for 2002 for O_3 Risk Assessment Locations*

City	Counties	Type of Mortality (ICD-9 Codes)			
		Non-accidental (<800)	Cardiovascular and Respiratory (390-448; 490-496; 487; 480-486; 507)	Circulatory (390-459)	Respiratory (460-519)
Atlanta	Fulton, DeKalb	623	131	---	---
Boston	Suffolk	736	---	---	---
Chicago	Cook	781	189	---	---
Cleveland	Cuyahoga	1,058	268	---	---
Detroit	Wayne	913	234	135	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	108	80

* Data 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

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:				
Cardiovascular illness (DRG Codes 103 – 144) – spring	431	---	---	---
Cardiovascular illness (DRG Codes 103 – 144) – summer	421	---	---	---
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	---
COPD (ICD codes 490-496)	---	---	1,593	---
Ischemic heart disease (ICD codes 410-414)	---	---	4,030	---
Heart failure (ICD code 428)	---	---	2,822	---
Dysrhythmias (ICD code 427)	---	---	1,330	---
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.

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 epidemiological-based portion of the risk assessment, 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 the epidemiological-based 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.

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 the most current inputs available – for example, year 2004 air quality data for all of the urban locations, and the most recent available 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 4.19 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. The staff's judgment, as discussed in more detail in Chapter 3, is that for the health effects included in the risk assessment (i.e, total non-accidental mortality, cardiorespiratory mortality, cardiovascular and respiratory

hospital admissions) there is a likely causal relationship with short-term O_3 exposures, 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 draft CD concludes (section 8.4.3.4, p.8-56) 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." The draft CD also concludes (section 8.4.3.2.3, p.8-54) that the U.S. time series studies conducted in multiple cities "provide substantial epidemiological evidence indicating that associations for O_3 with mortality and morbidity are robust to confounding by copollutants."

- 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. The draft CD (section 8.4.3.2.1, p.8-53) states that "ambient concentrations generally overestimate true personal O_3 exposures" and that the "use of ambient concentrations in risk calculations will likely result in effect estimates that are biased towards the null, resulting in biased descriptions of underlying concentration-response relationships." 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, staff believes 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). Staff plans to include additional sensitivity analyses exploring the potential impact of using alternative air quality adjustment procedures on the risk estimates associated with just meeting the current and alternative O_3 standards in the next draft of the Risk Assessment TSD. Staff also plans to develop risk estimates associated with just meeting the current standard based on a different year

within the three-year period on which the design value is based (e.g., 2002, in which O_3 levels were generally higher in most of the locations).

- 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.

The two 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, τ, 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 Appendix B of the draft Risk Assessment TSD for details about the calculation). 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, the available epidemiological studies do not support or refute the existence of thresholds as O_3 levels approach background concentrations.

Several meta-analyses addressing the impact of various factors on estimates of mortality associated with short-term exposures to O_3 were recently published and are discussed in the draft CD. Staff plans to review these analyses and explore whether they provide additional information that can be used to assist in characterizing the uncertainties associated with risk estimates for this health outcome.

5.4 OZONE RISK ESTIMATES

The risk estimates associated with two air quality scenarios, a recent year of air quality as represented by 2004 monitoring data and air quality adjusted to simulate just meeting the current 8-hr standard are presented in this draft Staff Paper in the sections below. The next draft Staff Paper will include risk estimates for alternative 8-hr standards.

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, staff has 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.

Tables 5-5 and 5-6 display the risk estimates for all and "active" school age children (ages 5-18) associated with 2004 O_3 concentrations for two different levels of lung function decrement responses for the 12 urban areas. 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 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 96,000 school age children experienced an FEV_1 decrement $\geq$ 15% during the O_3 season with a median estimate of 738,000 occurrences of this same response in this population. Thus, for this example on average each child is estimated to have over 7 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 all and "active" school age children estimated to experience at least one FEV_1 decrement $\geq$ 15% during the O_3 season are 6.8-12.7 and 7.2-13.5%, respectively. The ranges in median estimates of the percent of all and "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 0.8-4.6% and 0.9-5.1%, respectively.

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 339,000 to over 6.1 million responses during the O_3 season for all school age children and from 202,000 to 3.9 million responses for "active" school age children across the 12 urban areas associated with 2004 O_3 concentrations. For FEV_1 decrement $\geq$ 20% during the O_3 season, Table 5-6 shows a range of median estimates from 13,000 to 670,000 for all school age children and from 9,000 to 440,000 for "active" school age children.

Table 5-5. Comparison of Number and Percent of School Age Children and Active School Age Children Estimated to Experience At Least One Lung Function Response Associated with 8-Hour Ozone Exposures While Engaged in Moderate Exertion*

Location	Health Outcome	All Children (Ages 5-18) Having at Least 1 Lung Function Response Associated with 8-Hour O3 Exposure Under Moderate Exertion**				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		Recent Air Quality (2004)		Just Meeting Current 8-Hour Standard	
		Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent
Atlanta	FEV1>=15%	96 (48 - 164)	10.2% (5.1% - 17.5%)	78 (39 - 138)	8.3% (4.1% - 14.7%)	57 (29 - 96)	10.9% (5.5% - 18.6%)	47 (23 - 82)	9% (4.5% - 15.8%)
	FEV1>=20%	24 (5 - 68)	2.6% (0.6% - 7.2%)	14 (2 - 47)	1.4% (0.2% - 5%)	15 (4 - 42)	2.9% (0.7% - 8.1%)	9 (2 - 29)	1.7% (0.3% - 5.7%)
Boston	FEV1>=15%	88 (44 - 157)	8% (4% - 14.3%)	70 (34 - 131)	6.4% (3.1% - 11.9%)	45 (22 - 79)	8.5% (4.2% - 15%)	36 (18 - 67)	6.9% (3.3% - 12.6%)
	FEV1>=20%	16 (3 - 52)	1.5% (0.3% - 4.8%)	8 (1 - 32)	0.7% (0.1% - 3%)	9 (2 - 28)	1.7% (0.3% - 5.3%)	4 (1 - 18)	0.8% (0.1% - 3.4%)
Chicago	FEV1>=15%	132 (64 - 243)	6.8% (3.3% - 12.5%)	97 (45 - 190)	5% (2.3% - 9.8%)	67 (33 - 123)	7.2% (3.5% - 13.2%)	50 (23 - 96)	5.3% (2.5% - 10.3%)
	FEV1>=20%	15 (1 - 64)	0.8% (0.1% - 3.3%)	4 (0 - 28)	0.2% (0% - 1.4%)	8 (1 - 35)	0.9% (0.1% - 3.7%)	2 (0 - 16)	0.3% (0% - 1.7%)
Cleveland	FEV1>=15%	48 (24 - 85)	8.2% (4.1% - 14.5%)	36 (17 - 67)	6.1% (2.9% - 11.5%)	26 (13 - 45)	8.7% (4.4% - 15.4%)	19 (9 - 36)	6.6% (3.2% - 12.2%)
	FEV1>=20%	9 (1 - 29)	1.5% (0.2% - 5%)	3 (0 - 15)	0.6% (0% - 2.7%)	5 (1 - 16)	1.7% (0.3% - 5.5%)	2 (0 - 9)	0.6% (0% - 3%)
Detroit	FEV1>=15%	87 (43 - 156)	7.9% (3.9% - 14.1%)	68 (33 - 128)	6.2% (3% - 11.6%)	46 (23 - 82)	8.4% (4.2% - 14.9%)	37 (18 - 68)	6.7% (3.2% - 12.3%)
	FEV1>=20%	14 (2 - 50)	1.3% (0.2% - 4.5%)	7 (1 - 30)	0.6% (0.1% - 2.7%)	8 (1 - 28)	1.5% (0.3% - 5.1%)	4 (0 - 17)	0.7% (0.1% - 3.1%)
Houston	FEV1>=15%	119 (61 - 197)	11% (5.7% - 18.3%)	84 (42 - 147)	7.8% (3.9% - 13.7%)	71 (37 - 116)	11.8% (6.1% - 19.4%)	50 (26 - 87)	8.4% (4.3% - 14.5%)
	FEV1>=20%	37 (10 - 93)	3.4% (0.9% - 8.7%)	15 (3 - 52)	1.4% (0.2% - 4.8%)	23 (6 - 57)	3.9% (1.1% - 9.6%)	10 (2 - 32)	1.7% (0.3% - 5.4%)
Los Angeles	FEV1>=15%	456 (239 - 735)	12.7% (6.7% - 20.4%)	208 (103 - 371)	5.8% (2.9% - 10.3%)	264 (139 - 420)	13.5% (7.1% - 21.5%)	123 (62 - 213)	6.3% (3.2% - 10.9%)
	FEV1>=20%	164 (47 - 393)	4.6% (1.3% - 10.9%)	19 (1 - 93)	0.5% (0% - 2.6%)	100 (29 - 235)	5.1% (1.5% - 12%)	12 (1 - 60)	0.6% (0% - 3.1%)
New York	FEV1>=15%	358 (179 - 631)	8.8% (4.4% - 15.4%)	250 (120 - 470)	6.1% (2.9% - 11.5%)	191 (96 - 332)	9.5% (4.8% - 16.5%)	134 (65 - 248)	6.7% (3.2% - 12.3%)
	FEV1>=20%	73 (15 - 229)	1.8% (0.4% - 5.6%)	25 (3 - 108)	0.6% (0.1% - 2.7%)	42 (9 - 127)	2.1% (0.4% - 6.3%)	15 (2 - 61)	0.7% (0.1% - 3.1%)

Location	Health Outcome	All Children (Ages 5-18) Having at Least 1 Lung Function Response Associated with 8-Hour O3 Exposure Under Moderate Exertion**				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		Recent Air Quality (2004)		Just Meeting Current 8-Hour Standard	
		Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent
Philadelphia	FEV1>=15%	112 (57 - 195)	9.5% (4.8% - 16.6%)	84 (41 - 153)	7.1% (3.5% - 13%)	63 (32 - 108)	10.3% (5.2% - 17.7%)	47 (23 - 85)	7.8% (3.8% - 14%)
	FEV1>=20%	26 (6 - 77)	2.2% (0.5% - 6.5%)	11 (1 - 44)	1% (0.1% - 3.7%)	16 (4 - 45)	2.6% (0.6% - 7.4%)	7 (1 - 26)	1.1% (0.1% - 4.3%)
Sacramento	FEV1>=15%	37 (20 - 61)	8.9% (4.7% - 14.5%)	25 (13 - 42)	5.9% (3% - 10.1%)	21 (11 - 34)	9.4% (4.9% - 14.9%)	14 (7 - 23)	6.3% (3.3% - 10.4%)
	FEV1>=20%	9 (2 - 28)	2.3% (0.5% - 6.7%)	3 (0 - 13)	0.7% (0% - 3.2%)	6 (1 - 17)	2.5% (0.5% - 7.3%)	2 (0 - 8)	0.8% (0.1% - 3.6%)
St. Louis	FEV1>=15%	46 (23 - 81)	8% (3.9% - 14.2%)	39 (19 - 72)	6.9% (3.4% - 12.6%)	26 (13 - 47)	8.5% (4.3% - 15.1%)	23 (11 - 41)	7.4% (3.6% - 13.4%)
	FEV1>=20%	7 (1 - 26)	1.3% (0.2% - 4.6%)	4 (0 - 19)	0.8% (0.1% - 3.4%)	5 (1 - 16)	1.5% (0.2% - 5.2%)	3 (0 - 12)	0.9% (0.1% - 3.9%)
Washington, D.C.	FEV1>=15%	149 (75 - 257)	10.1% (5.1% - 17.4%)	117 (58 - 209)	7.9% (3.9% - 14.2%)	82 (42 - 141)	10.8% (5.5% - 18.5%)	66 (33 - 116)	8.7% (4.3% - 15.3%)
	FEV1>=20%	39 (9 - 107)	2.6% (0.6% - 7.3%)	21 (4 - 69)	1.4% (0.3% - 4.7%)	22 (5 - 61)	3% (0.7% - 8%)	13 (3 - 41)	1.7% (0.3% - 5.4%)

*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.

Table 5-6. Comparison of Number and Percent of Occurrences of Lung Function Response Associated with 8-Hour Ozone Exposure

Location	Health Outcome	Occurrences of Lung Function Response Associated with 8-Hour O3 Exposure Among All Children (Ages 5-18) While Engaged in Moderate Exertion**				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		Recent Air Quality (2004)		Just Meeting Current 8-Hour Standard	
		Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent
Atlanta	FEV1>=15%	738 (320 - 1735)	1.1% (0.5% - 2.5%)	528 (220 - 1318)	0.8% (0.3% - 1.9%)	479 (209 - 1113)	1.2% (0.5% - 2.8%)	345 (145 - 851)	0.9% (0.4% - 2.2%)
	FEV1>=20%	52 (8 - 218)	0.1% (0% - 0.3%)	24 (3 - 121)	0% (0% - 0.2%)	35 (5 - 145)	0.1% (0% - 0.4%)	16 (2 - 82)	0% (0% - 0.2%)
Boston	FEV1>=15%	533 (223 - 1350)	0.7% (0.3% - 1.7%)	378 (152 - 1022)	0.5% (0.2% - 1.3%)	296 (124 - 737)	0.8% (0.3% - 2%)	211 (85 - 560)	0.6% (0.2% - 1.5%)
	FEV1>=20%	27 (4 - 126)	0% (0% - 0.2%)	11 (1 - 66)	0% (0% - 0.1%)	15 (2 - 72)	0% (0% - 0.2%)	7 (1 - 38)	0% (0% - 0.1%)
Chicago	FEV1>=15%	847 (340 - 2244)	0.6% (0.2% - 1.6%)	509 (191 - 1493)	0.4% (0.1% - 1.1%)	475 (192 - 1240)	0.7% (0.3% - 1.9%)	288 (109 - 830)	0.4% (0.2% - 1.2%)
	FEV1>=20%	22 (2 - 142)	0% (0% - 0.1%)	5 (0 - 50)	0% (0% - 0%)	13 (1 - 82)	0% (0% - 0.1%)	3 (0 - 30)	0% (0% - 0%)
Cleveland	FEV1>=15%	351 (147 - 875)	0.9% (0.4% - 2.1%)	222 (88 - 606)	0.5% (0.2% - 1.5%)	202 (85 - 496)	1% (0.4% - 2.4%)	129 (51 - 347)	0.6% (0.2% - 1.7%)
	FEV1>=20%	17 (2 - 82)	0% (0% - 0.2%)	5 (0 - 34)	0% (0% - 0.1%)	10 (1 - 49)	0% (0% - 0.2%)	3 (0 - 20)	0% (0% - 0.1%)
Detroit	FEV1>=15%	544 (225 - 1398)	0.7% (0.3% - 1.8%)	371 (146 - 1027)	0.5% (0.2% - 1.3%)	312 (129 - 790)	0.8% (0.3% - 2%)	214 (85 - 584)	0.5% (0.2% - 1.5%)
	FEV1>=20%	24 (3 - 118)	0% (0% - 0.2%)	9 (1 - 57)	0% (0% - 0.1%)	14 (2 - 70)	0% (0% - 0.2%)	6 (0 - 34)	0% (0% - 0.1%)
Houston	FEV1>=15%	853 (382 - 1851)	1.1% (0.5% - 2.4%)	526 (223 - 1233)	0.7% (0.3% - 1.6%)	551 (247 - 1185)	1.2% (0.5% - 2.6%)	342 (146 - 794)	0.8% (0.3% - 1.8%)
	FEV1>=20%	85 (16 - 310)	0.1% (0% - 0.4%)	27 (3 - 130)	0% (0% - 0.2%)	56 (11 - 202)	0.1% (0% - 0.4%)	18 (2 - 86)	0% (0% - 0.2%)
Los Angeles	FEV1>=15%	6171 (2802 - 13306)	2.3% (1.1% - 5.1%)	1974 (778 - 5325)	0.8% (0.3% - 2%)	3935 (1796 - 8387)	2.6% (1.2% - 5.6%)	1293 (513 - 3439)	0.9% (0.3% - 2.3%)
	FEV1>=20%	670 (126 - 2401)	0.3% (0% - 0.9%)	33 (1 - 271)	0% (0% - 0.1%)	440 (83 - 1567)	0.3% (0.1% - 1.1%)	22 (1 - 182)	0% (0% - 0.1%)
New York	FEV1>=15%	2552 (1077 - 6303)	0.9% (0.4% - 2.1%)	1362 (537 - 3760)	0.5% (0.2% - 1.3%)	1464 (621 - 3570)	1% (0.4% - 2.4%)	789 (313 - 2146)	0.5% (0.2% - 1.5%)
	FEV1>=20%	135 (18 - 628)	0% (0% - 0.2%)	33 (3 - 209)	0% (0% - 0.1%)	80 (11 - 369)	0.1% (0% - 0.3%)	20 (2 - 124)	0% (0% - 0.1%)

Location	Health Outcome	Occurrences of Lung Function Response Associated with 8-Hour O3 Exposure Among All Children (Ages 5-18) While Engaged in Moderate Exertion**				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		Recent Air Quality (2004)		Just Meeting Current 8-Hour Standard	
		Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent	Number (1000s)	Percent
Philadelphia	FEV1>=15%	972 (419 - 2307)	1.2% (0.5% - 2.8%)	599 (244 - 1556)	0.7% (0.3% - 1.9%)	588 (255 - 1376)	1.3% (0.6% - 3.1%)	366 (150 - 934)	0.8% (0.3% - 2.1%)
	FEV1>=20%	61 (8 - 269)	0.1% (0% - 0.3%)	20 (2 - 114)	0% (0% - 0.1%)	39 (6 - 169)	0.1% (0% - 0.4%)	13 (1 - 73)	0% (0% - 0.2%)
Sacramento	FEV1>=15%	420 (180 - 990)	1.4% (0.6% - 3.3%)	233 (93 - 615)	0.8% (0.3% - 2.1%)	267 (115 - 622)	1.6% (0.7% - 3.7%)	151 (61 - 392)	0.9% (0.4% - 2.3%)
	FEV1>=20%	24 (3 - 111)	0.1% (0% - 0.4%)	5 (0 - 36)	0% (0% - 0.1%)	15 (2 - 72)	0.1% (0% - 0.4%)	3 (0 - 24)	0% (0% - 0.1%)
St. Louis	FEV1>=15%	339 (142 - 836)	0.8% (0.4% - 2.1%)	267 (108 - 687)	0.7% (0.3% - 1.7%)	216 (91 - 525)	1% (0.4% - 2.4%)	171 (70 - 433)	0.8% (0.3% - 1.9%)
	FEV1>=20%	13 (1 - 75)	0% (0% - 0.2%)	7 (0 - 47)	0% (0% - 0.1%)	9 (1 - 49)	0% (0% - 0.2%)	5 (0 - 32)	0% (0% - 0.1%)
Washington, D.C.	FEV1>=15%	1090 (472 - 2577)	1% (0.4% - 2.4%)	671 (279 - 1698)	0.6% (0.3% - 1.6%)	660 (287 - 1541)	1.2% (0.5% - 2.8%)	410 (171 - 1025)	0.7% (0.3% - 1.9%)
	FEV1>=20%	78 (13 - 320)	0.1% (0% - 0.3%)	32 (5 - 151)	0% (0% - 0.1%)	48 (8 - 198)	0.1% (0% - 0.4%)	20 (3 - 95)	0% (0% - 0.2%)

*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.

The risk estimates associated with 2004 O_3 concentrations for the health endpoints based on epidemiological studies are shown in Figures 5-3 and 5-4 and Table 5-7 for non-accidental mortality and Figures 5-5 and 5-6 and Table 5-8 for cardiovascular and respiratory mortality in all of the urban locations included in the assessment. Table 5-9 presents risk estimates 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 results are for health risks associated with short-term exposures to O_3 concentrations in excess of background levels from April through September 2004. The percent of total incidence that is O_3-related is shown in the top portion of Figures 5-3 through 5-7; the incidence per 100,000 relevant population is shown in the bottom portion of Figures 5-3 through 5-7.

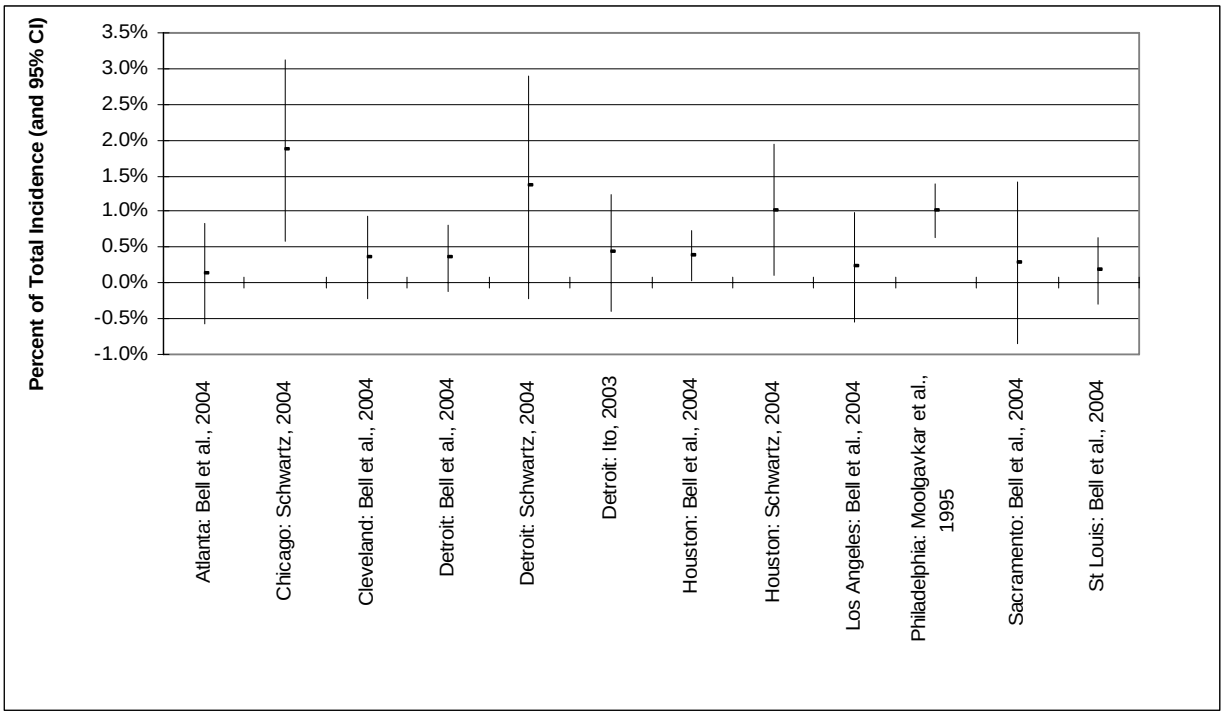
The central tendency estimates in all of the figures and in Tables 5-7 through 5-9 are based on the O_3 coefficients estimated in the studies, or, in the case of the location-specific estimates from Huang et al. (2004) and Bell et al. (2004), on "shrinkage" estimates based on the O_3 coefficients estimated in the study (see section 4.1.9.1.2 of the draft Risk Assessment TSD). The ranges are based either on the 95 percent confidence intervals (CIs) 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).

As discussed previously, assessment locations were chosen in part on the basis of whether an acceptable concentration-response function had been reported for that location. As a result, risks were estimated in a given assessment location only for those health endpoints for which there is at least one acceptable concentration-response function reported for that location. For non-accidental mortality associated with short-term exposure to O_3, Figure 5-3 displays estimates for only nine of the twelve risk assessment locations because acceptable (single-city) concentration-response functions for this health outcome were not available for the other three locations. Figure 5-3 shows estimated percent of non-accidental mortality and cases per 100,000 relevant population related to recent O3 concentrations over background levels, based on single-pollutant, single-city models across all locations for which such models were available.

Table 5-7 shows estimates of incidence, incidence per 100,000 relevant population, and percent of total incidence of non-accidental mortality related to recent O_3 concentrations over background levels in all locations, based on both single-city and multi-city models. Estimates of O_3-related (non-accidental) mortality ranged from 0.4 per 100,000 relevant population in Atlanta (Bell et al., 2004) to 7.3 per 100,000 relevant population in Chicago (Schwartz, 2004). 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 other estimates in those locations in large part because Schwartz

Figure 5-3. Estimated (Non-Accidental) Mortality Associated with Short-Term Exposure to Ozone Above Background: Single-Pollutant, Single-City Models (April – September, 2004)

5-3a. Estimated Percent of Total Incidence that is O_3-Related



5-3b. Estimated O_3-Related Cases per 100,000 Relevant Population

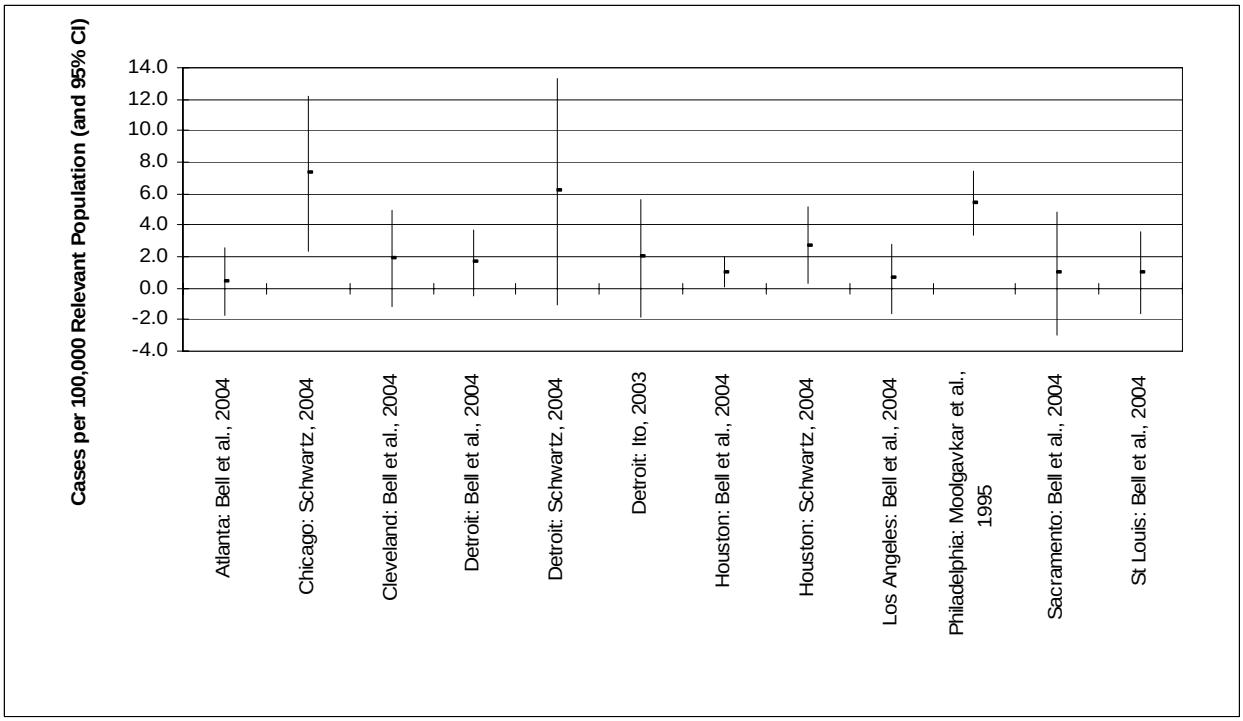


Figure 5-4. Estimated (Non-Accidental) Mortality Associated with Short-Term Exposure to Ozone Above Background (April – September, 2004): Single-City Model (left bar) vs. Multi-City Model (right bar)

5-4a. Estimated Percent of Total Incidence that is O_3-Related

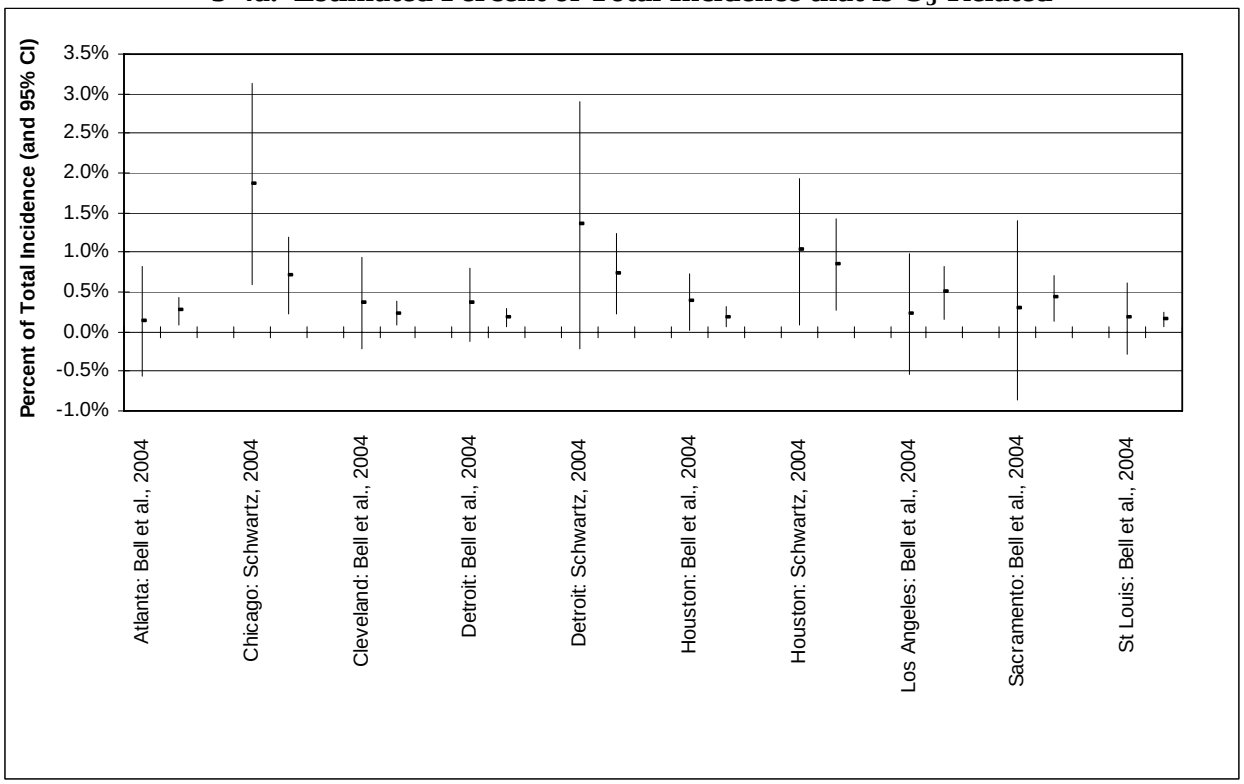


Figure 5-4b. Estimated O_3-Related Cases per 100,000 Relevant Population

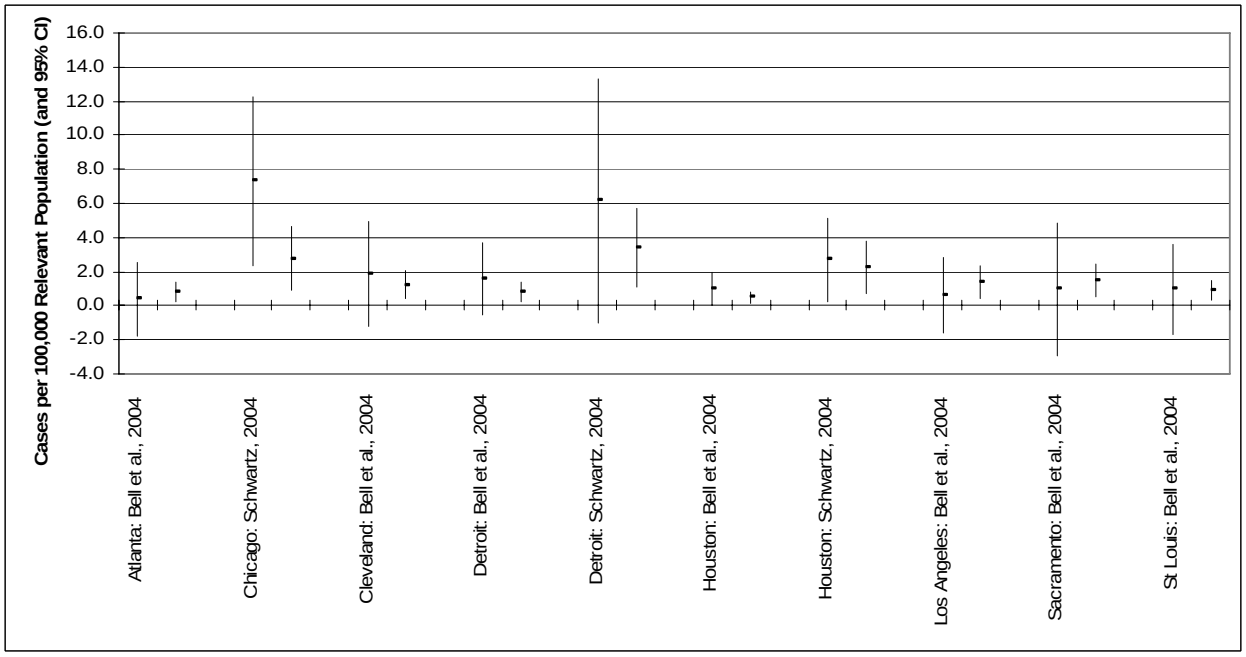


Figure 5-5. Estimated Cardiovascular and Respiratory Mortality Associated with Short-Term Exposure to Ozone Above Background (April – September, 2004): Single-City Model (left bar) vs. Multi-City Model (right bar) – Based on Huang et al. (2004)

5-5a. Estimated Percent of Total Incidence that is O_3-Related

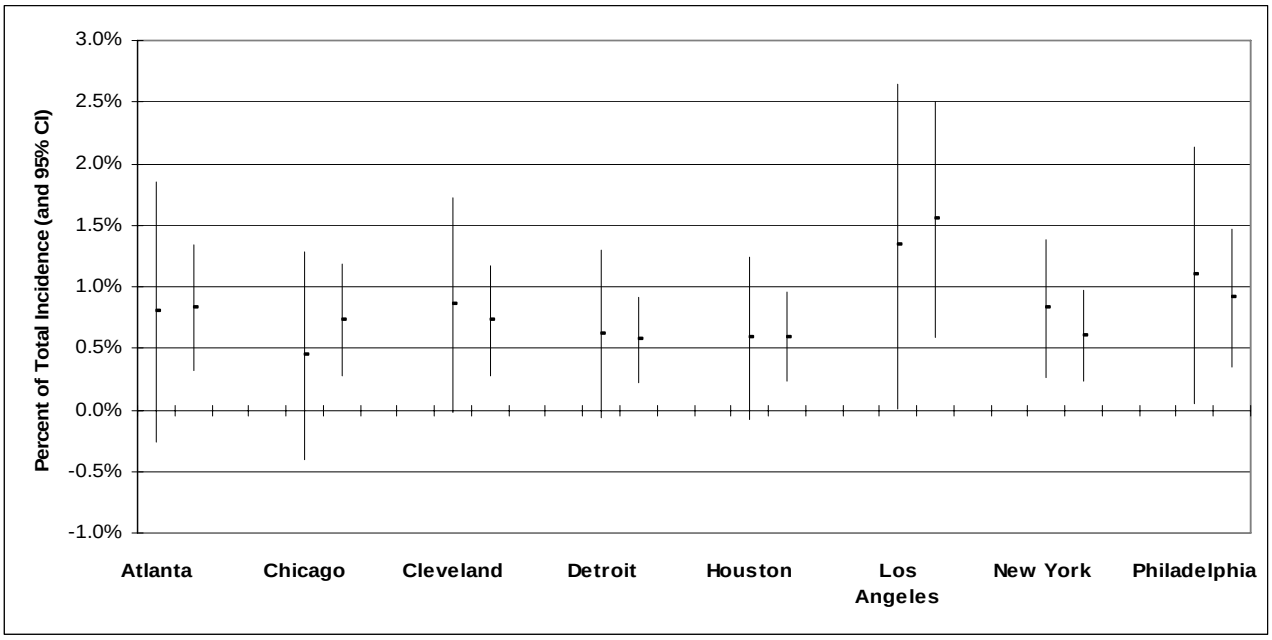


Figure 5-5b. Estimated O_3-Related Cases per 100,000 Relevant Population

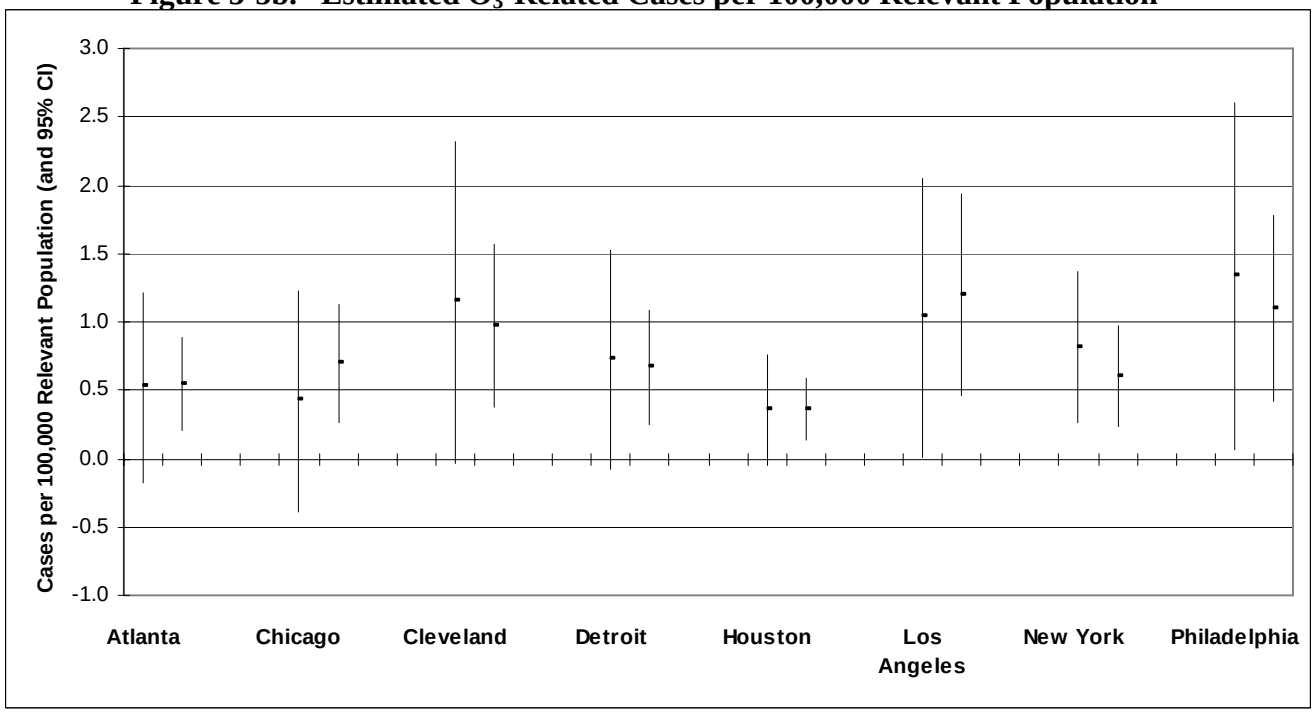


Figure 5-6. Estimated Cardiovascular and Respiratory Mortality Associated with Short-Term Exposure to Ozone Above Background (April – September, 2004): Single-Pollutant vs. Multi-Pollutant Models [Huang et al. (2004) , additional pollutants, from left to right: none, PM10, NO2, SO2, CO]

5-6a. Estimated Percent of Total Incidence that is O_3-Related

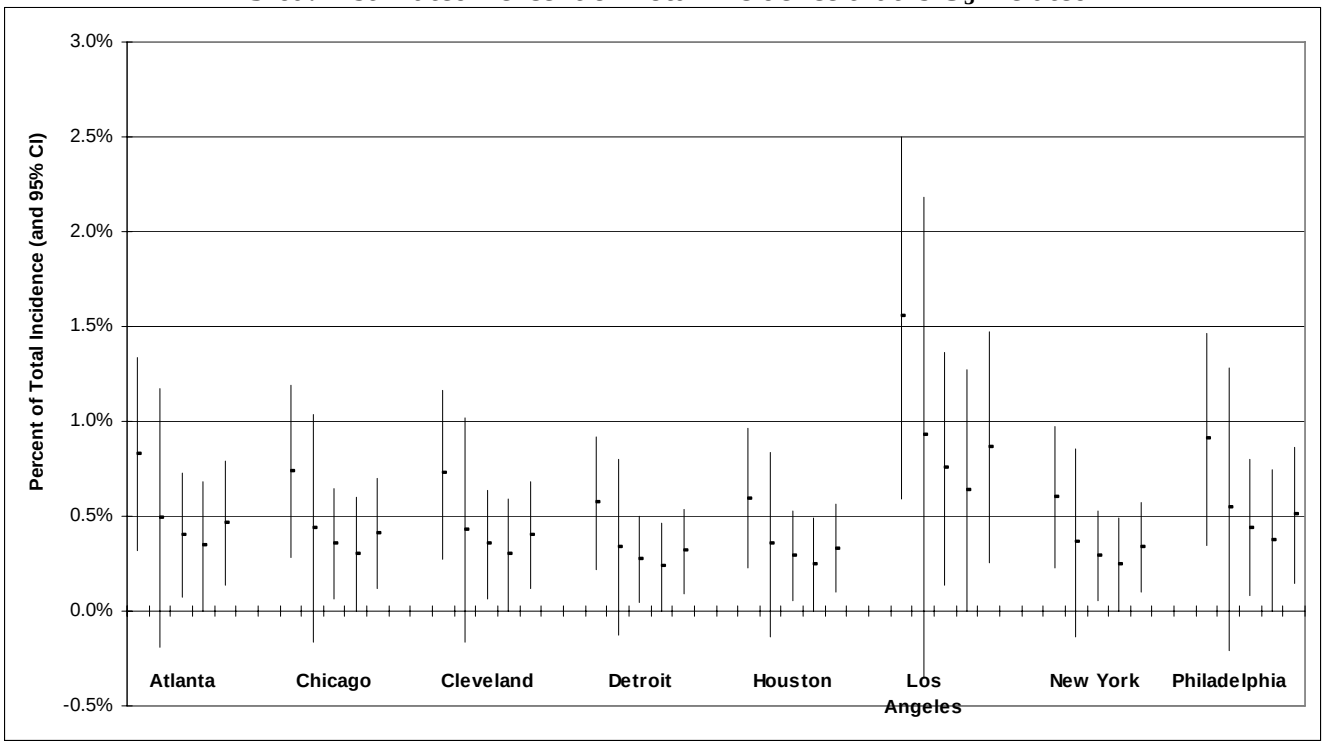


Figure 5-6b. Estimated O_3-Related Cases per 100,000 Relevant Population

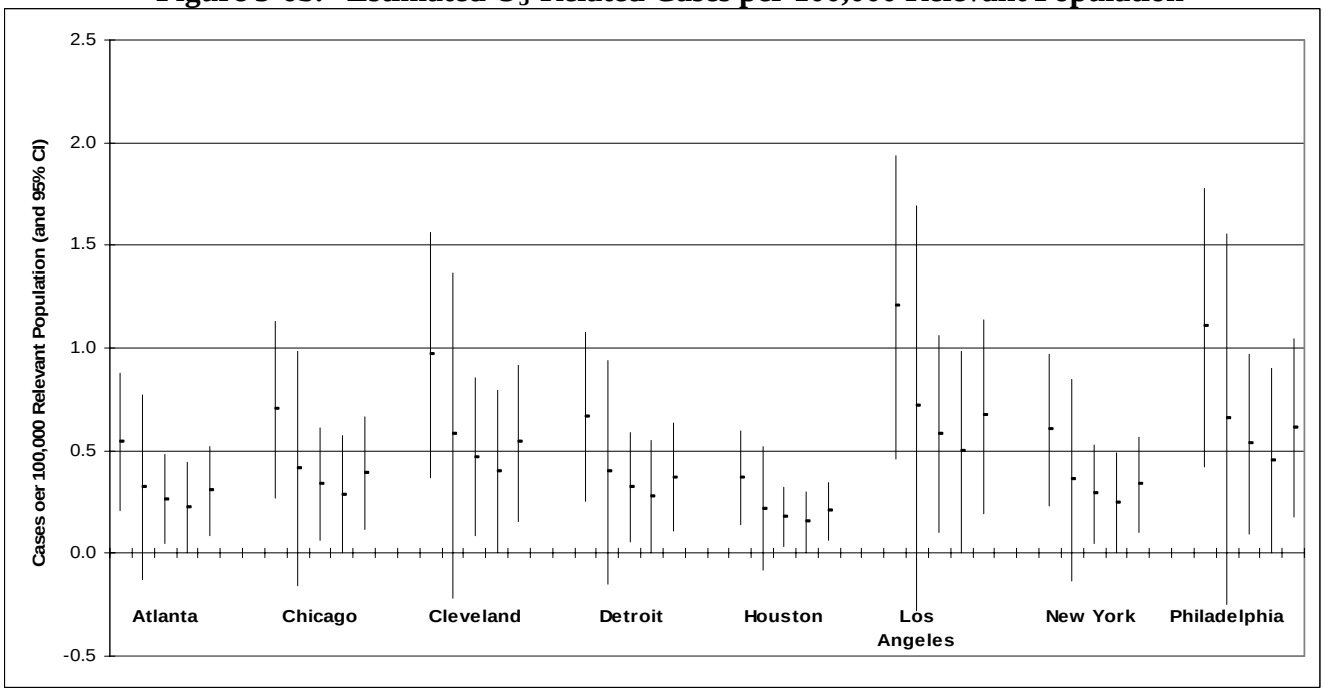


Table 5-7. Estimated Non-Accidental Mortality Associated with Recent Ozone Concentrations (April - September, 2004)

Location	Study	Lag	Exposure Metric	Non-Accidental Mortality Associated with O3 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%)

Location	Study	Lag	Exposure Metric	Non-Accidental Mortality Associated with O3 Above Policy Relevant Background Levels**		
				Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
	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%)
	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	1.4	0.4%

Location	Study	Lag	Exposure Metric	Non-Accidental Mortality Associated with O3 Above Policy Relevant Background Levels**		
				Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
				(6 - 29)	(0.5 - 2.4)	(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 O3. 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 O3 coefficient.

Table 5-8. Estimated Cardiovascular and Respiratory Mortality Associated with Recent Ozone Concentrations (April - September, 2004)

Risk Assessment Location	Study Location	Cardiovascular and Respiratory Mortality Associated with O3 Above Policy Relevant Background Levels**		
		Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
Atlanta	Atlanta	8 (-3 - 18)	0.5 (-0.2 - 1.2)	0.8% (-0.3% - 1.8%)
	19 U.S. Cities	8 (3 - 13)	0.5 (0.2 - 0.9)	0.8% (0.3% - 1.3%)
Chicago	Chicago	23 (-21 - 66)	0.4 (-0.4 - 1.2)	0.4% (-0.4% - 1.3%)
	19 U.S. Cities	38 (14 - 61)	0.7 (0.3 - 1.1)	0.7% (0.3% - 1.2%)
Cleveland	Cleveland	16 (0 - 32)	1.2 (0 - 2.3)	0.9% (0% - 1.7%)
	19 U.S. Cities	14 (5 - 22)	1.0 (0.4 - 1.6)	0.7% (0.3% - 1.2%)
Detroit	Detroit	15 (-2 - 31)	0.7 (-0.1 - 1.5)	0.6% (-0.1% - 1.3%)
	19 U.S. Cities	14 (5 - 22)	0.7 (0.3 - 1.1)	0.6% (0.2% - 0.9%)
Houston	Houston	12 (-2 - 26)	0.4 (0 - 0.8)	0.6% (-0.1% - 1.2%)
	19 U.S. Cities	13 (5 - 20)	0.4 (0.1 - 0.6)	0.6% (0.2% - 1%)
Los Angeles	Los Angeles	99 (1 - 195)	1.0 (0 - 2.1)	1.3% (0% - 2.6%)
	19 U.S. Cities	115 (44 - 185)	1.2 (0.5 - 1.9)	1.6% (0.6% - 2.5%)
New York	New York	73 (23 - 123)	0.8 (0.3 - 1.4)	0.8% (0.3% - 1.4%)

Risk Assessment Location	Study Location	Cardiovascular and Respiratory Mortality Associated with O3 Above Policy Relevant Background Levels**		
		Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
	19 U.S. Cities	54 (21 - 87)	0.6 (0.2 - 1)	0.6% (0.2% - 1%)
Philadelphia	Philadelphia	20 (1 - 39)	1.3 (0.1 - 2.6)	1.1% (0.1% - 2.1%)
	19 U.S. Cities	17 (6 - 27)	1.1 (0.4 - 1.8)	0.9% (0.3% - 1.5%)

*All results are for cardiovascular and respiratory mortality (among all ages) associated with short-term exposures to O3. Results are based on single-pollutant single-city models or a single-pollutant multi-city model estimated in Huang et al. (2004).

**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% credible intervals based on statistical uncertainty surrounding the O3 coefficient.

Table 5-9. Estimated Hospital Admissions Associated with Recent Ozone Concentrations in New York, NY* (April - September, 2004)

Health Effects**	Ages	Lag	Exposure Metric	Health Effects Associated with O3 Above Policy Relevant Background Levels***		
				Incidence (95% CI)	Incidence per 100,000 Relevant Population (95% CI)	Percent of Total Incidence (95% CI)
Respiratory Illness (unscheduled)	All	3-day	1-hr max	447 (108-786)	5.6 (1.4-9.8)	1.3 (0.3-2.2)
Asthma (unscheduled)	All	1-day	1-hr max	382 (81-683)	4.8 (1.0-8.5)	2.9 (0.6-5.2)

*New York in this study is defined as the five boroughs of New York City

**Concentration-response relationships are from Thurston et al. (1992) and are associated with short-term exposures.

***Incidence was quantified down to estimated policy relevant background levels. Incidences per 100,000 relevant population and percent of total incidence are rounded to nearest tenth.

used the 1-hr maximum O_3 concentration, rather than the 24-hr average, as the exposure metric. The changes from recent (2004) 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. As a percent of total incidence, estimated O_3-related (non-accidental) mortality ranged from 0.1 percent in Atlanta (Bell et al., 2004) to 1.9 percent in Chicago (Schwartz, 2004).

Figure 5-4 shows estimated percent of non-accidental mortality that is O_3-related and O_3-related cases per 100,000 relevant population, based on single-city versus multi-city models across all locations for which both types of model were available. Estimates of O_3-related non-accidental mortality based on single-city models tended to have wider confidence or credible intervals than those based on multi-city models, with both multi-city models (from Bell et al., 2004 and Schwartz, 2004) producing statistically significant results. However, the choice of single-city versus multi-city model did not have a uniform effect on the magnitude of the point estimate. In some cases (Atlanta, Los Angeles, and Sacramento), the multi-city models produced larger estimates than the single-city models, while in other cases (Chicago, Cleveland, Detroit, Houston, and St. Louis) the reverse was true.

As shown in Figure 5-5, Bayesian credible intervals around the "shrinkage" estimates (see section 5.3.2.5) of O_3-related cardiovascular and respiratory mortality based on single-city models in Huang et al. (2004) were uniformly larger than the corresponding credible intervals around estimates based on the multi-city model from that study. As noted above, all of the estimates were positive and, with the exception of the single-city estimate for Chicago, all were statistically significant.

Figure 5-6 shows estimated percent of cardiovascular and respiratory mortality and cases per 100,000 relevant population related to recent O_3 concentrations over background levels, based on multi-city models for a single-pollutant versus multi-pollutant models from Huang et al. (2004) across all locations for which such models were available. Table 5-8 shows estimates of incidence, incidence per 100,000 relevant population, and percent of total incidence of cardiovascular and respiratory mortality related to recent O_3 concentrations over background levels in all risk assessment locations covered in Huang et al. (2004), based on both single-city and multi-city single-pollutant models from that study. Estimates of O_3-related cardiovascular and respiratory mortality ranged from 0.4 per 100,000 relevant population in Chicago (using the single-city concentration-response function) and Houston (using both the single-city and the multi-city concentration-response functions) to 1.3 per 100,000 relevant population in Philadelphia (using the single-city concentration-response function). As a percent of total incidence, estimated O_3-related cardiovascular and respiratory mortality ranged from 0.4 percent

in Chicago (using the single-city concentration-response function) to 1.6 percent in Los Angeles (using the multi-city concentration-response function). All of the estimates of O_3-related cardiovascular and respiratory mortality based on Huang et al. (2004), from both single-city and multi-city models, and from both single-pollutant and multi-pollutant models, were positive. The shrinkage-based single-city single-pollutant models for Atlanta, Chicago, Cleveland, Detroit, and Houston for O_3-related cardiovascular and respiratory mortality based on Huang et al. (2004) were not statistically significant. The single city, single pollutant model for the other three locations (Los Angeles, New York, and Philadelphia) and all of the single pollutant, multi-city models were statistically significant for this same health endpoint based on Huang et al. (2004). With respect to the multi-pollutant models for this health endpoint and study, all of the multi-pollutant models were statistically significant, with the exception of the models which included PM_{10}.

Table 5-9 shows estimates of unscheduled hospital admissions for respiratory illness in the New York City area associated with O_3 levels above background of about 450 cases or 5.6 cases per 100,000 relevant population, which represents 1.3% of total incidence for recent (2004) O_3 levels. For asthma-related hospital admissions, the estimates are about 380 cases or 4.8 cases per 100,000 relevant population, which represents about 2.9% of total incidence.

5.4.2 Just Meeting Current 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 a single example year based on adjusting the O_3 levels observed in 2004 to O_3 levels predicted when just meeting the current 0.08 ppm standard, using the 3-year design value from the 2002-2004 time period 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 mortality and hospital admissions, 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). The risk estimates for lung function responses in all and "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. As shown in Table 5-5, across the 12 urban areas, the ranges in median estimates of the percent of all and "active" school age children estimated to experience at least one FEV_1 decrement $\geq$ 15% during the O_3 season are 5.0-8.3% and 5.3-9.0%, respectively. The ranges in median estimates of the percent of all and "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 0.2-1.4% and 0.3-1.7%, respectively.

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 222,000 to over 1.9 million responses during the O_3 season for all school age children and from 129,000 to nearly 1.3 million responses for "active" school age children across the 12 urban areas associated with 2004 O_3 concentrations. For FEV_1 decrement $\geq$ 20% during the O_3 season, Table 5-6 shows a range of median estimates from 5,000 to 33,000 for all school age children and from 3,000 to 22,000 for "active" school age children.

The results of the assessment of the reduced mortality risks associated with O_3 concentrations above background that just meet the current 8-hr daily maximum standard are summarized across urban areas in Figures 5-7 through 5-10, and in Tables 5-10 and 5-11. In addition, Table 5-12 summarizes unscheduled hospital admission risk estimates for respiratory illness and asthma in New York City associated with O_3 concentrations above background and just meeting the current 8-hr standard. Additional hospital admission estimates for three other locations are provided in the draft Risk Assessment TSD. All results for the epidemiological based part of the risk assessment are for health risks associated with short-term exposures to O_3 concentrations in excess of background levels from April through September. The percent of total incidence that is O_3-related is shown in top portion of Figures 5-7 through 5-10; the incidence per 100,000 relevant population is shown in the bottom portion of these same figures.

As described in the previous section, the central tendency estimates in all of the figures and tables are based on the O_3 coefficients estimated in the studies, or, in the case of the location-specific estimates from Huang et al. (2004), on "shrinkage" estimates based on the O_3 coefficients estimated in the study (see section 5.3.2.5). The ranges 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).

The results in this portion of the risk assessment follow the same patterns as the results discussed in section 5.4.2 for risks associated with recent O_3 concentrations, because they are largely driven by the same concentration-response function coefficient estimates and confidence or credible intervals.

Figure 5-7 shows estimated percent of non-accidental mortality and cases per 100,000 relevant population related to O_3 concentrations that just meet the current 8-hr O_3 standard, based on single-pollutant, single-city models across all locations for which such models were available. Table 5-10 shows estimates of incidence, incidence per 100,000 relevant population, and percent of total incidence of non-accidental mortality related to O_3 concentrations that just meet the current 8-hr O_3 standard, based on both single-city and multi-city models. Estimates of O_3-

Figure 5-7. Estimated (Non-Accidental) Mortality Associated with Short-Term Exposure to O3 Above Background When the Current 8-Hour Standard is Just Met: Single-Pollutant, Single-City Models (April – September)

5-7a. Estimated Percent of Total Incidence that is O_3-Related

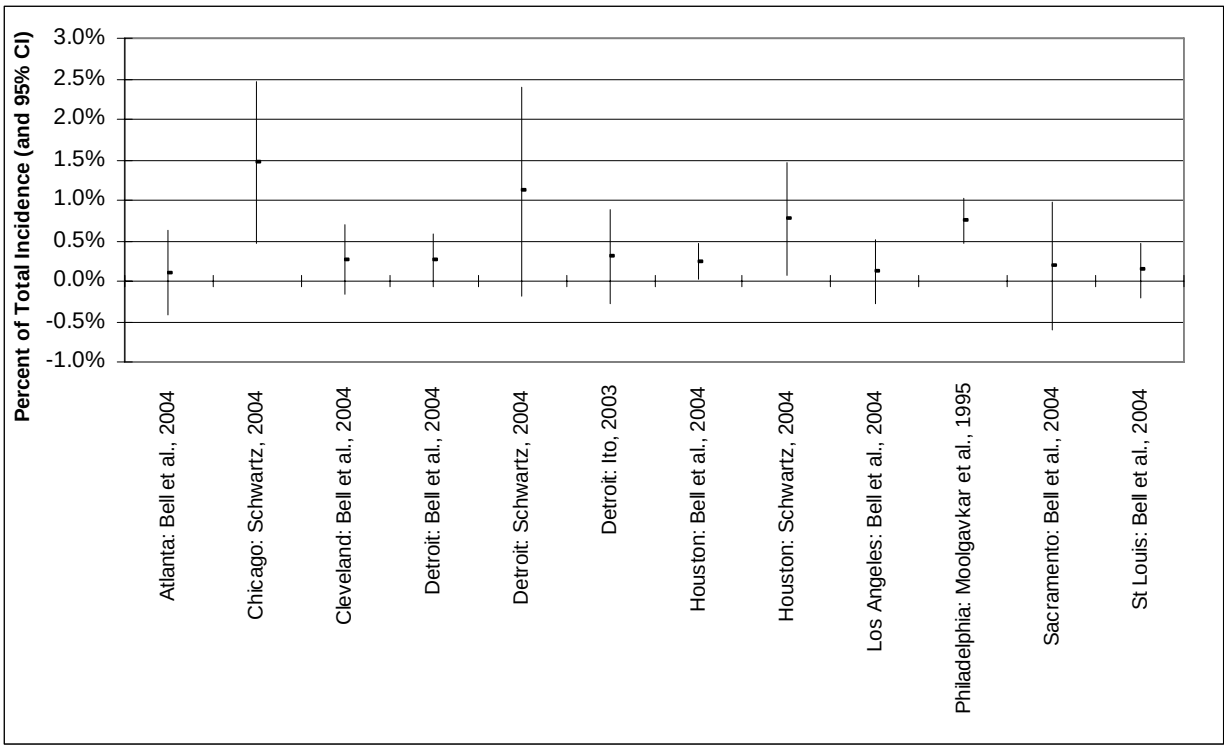


Figure 5-7b. Estimated O_3-Related Cases per 100,000 Relevant Population

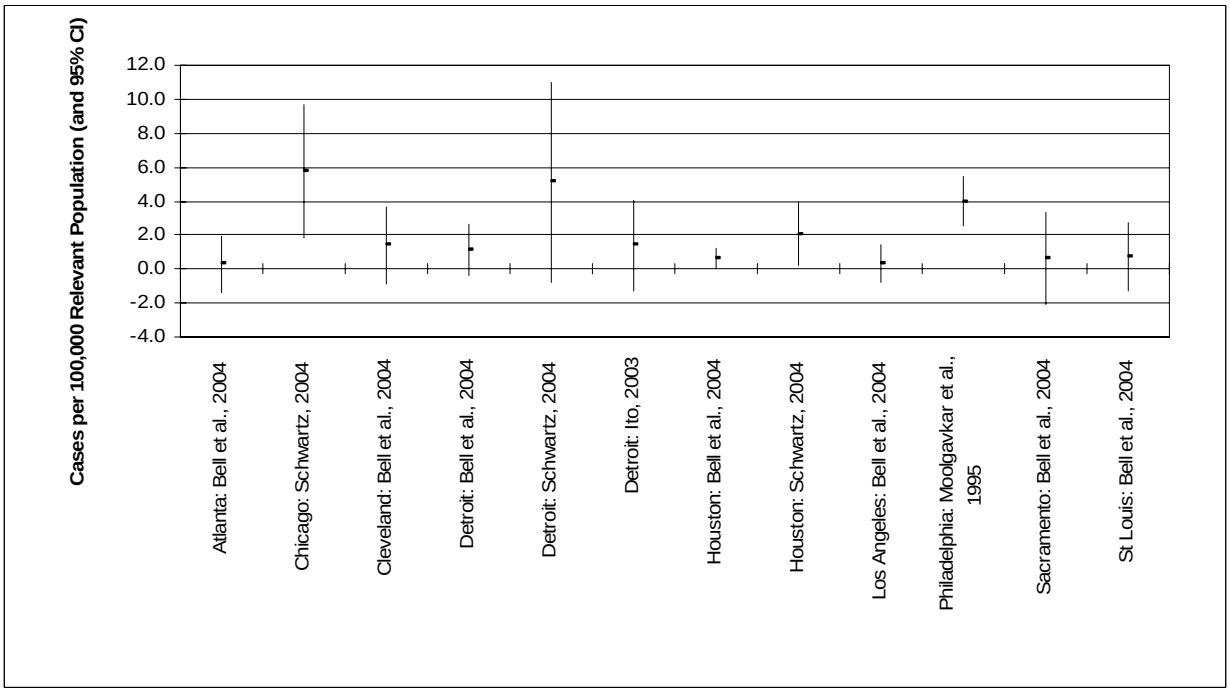


Figure 5-8. Estimated (Non-Accidental) Mortality Associated with Short-Term Exposure to Ozone Above Background When the Current 8-Hour Standard is Just Met (April – September): Single-City Model (left bar) vs. Multi-City Model (right bar)

5-8a. Estimated Percent of Total Incidence that is O_3-Related

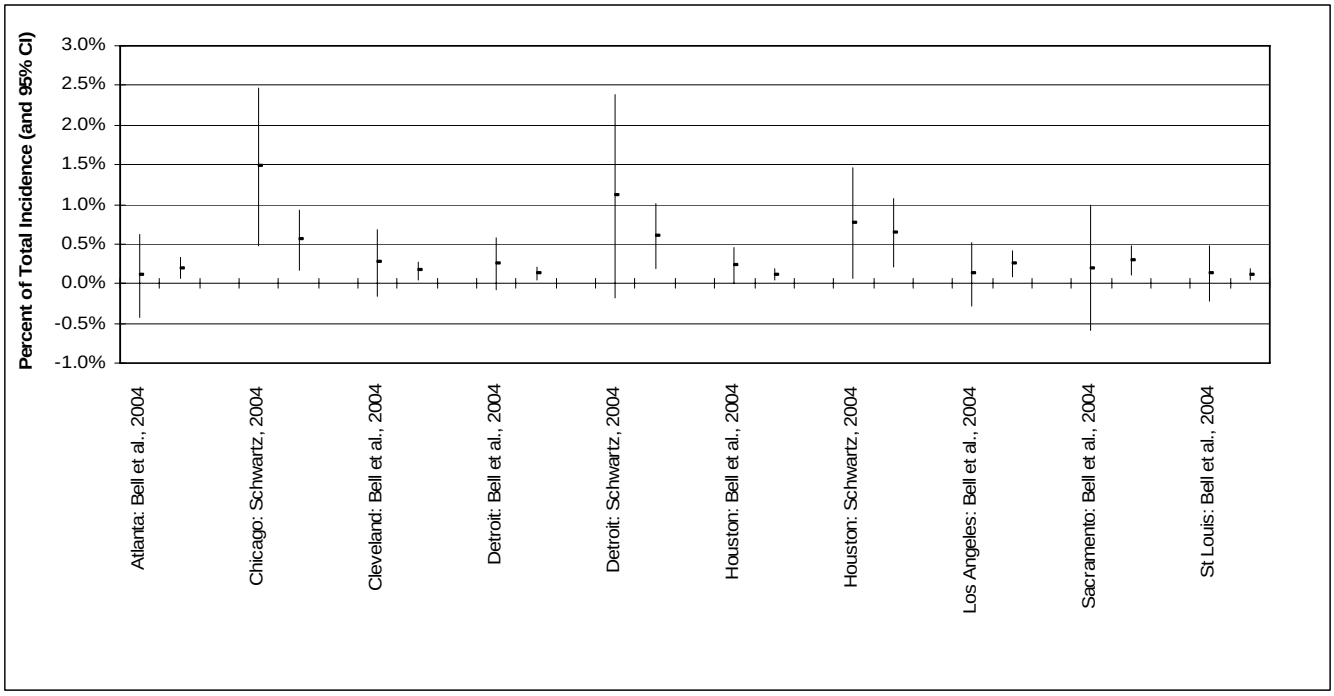


Figure 5-8b. Estimated O_3-Related Cases per 100,000 Relevant Population

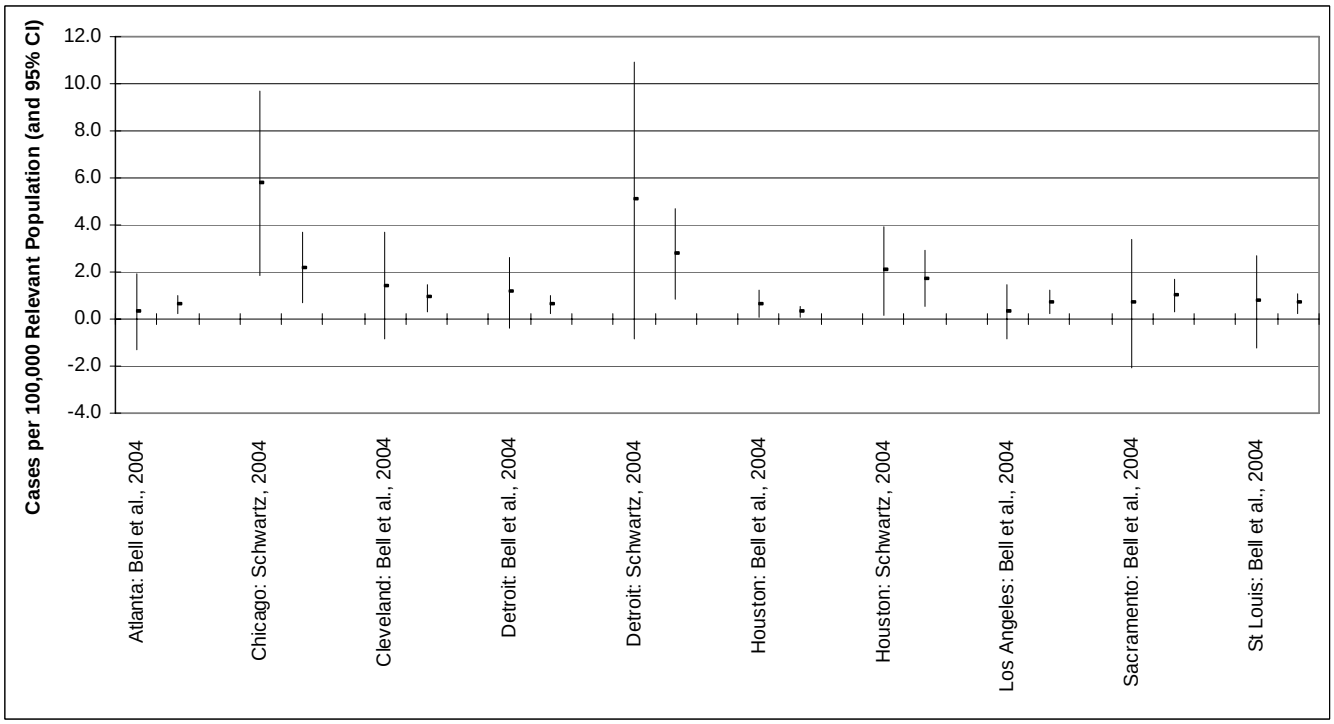


Figure 5-9. Estimated Cardiovascular and Respiratory Mortality Associated with Short-Term Exposure to Ozone Above Background When the Current 8-Hour Standard is Just Met (April – September): Single-City Model (left bar) vs. Multi-City Model (right bar) – Based on Huang et al. (2004)

5-9a. Estimated Percent of Total Incidence that is O_3-Related

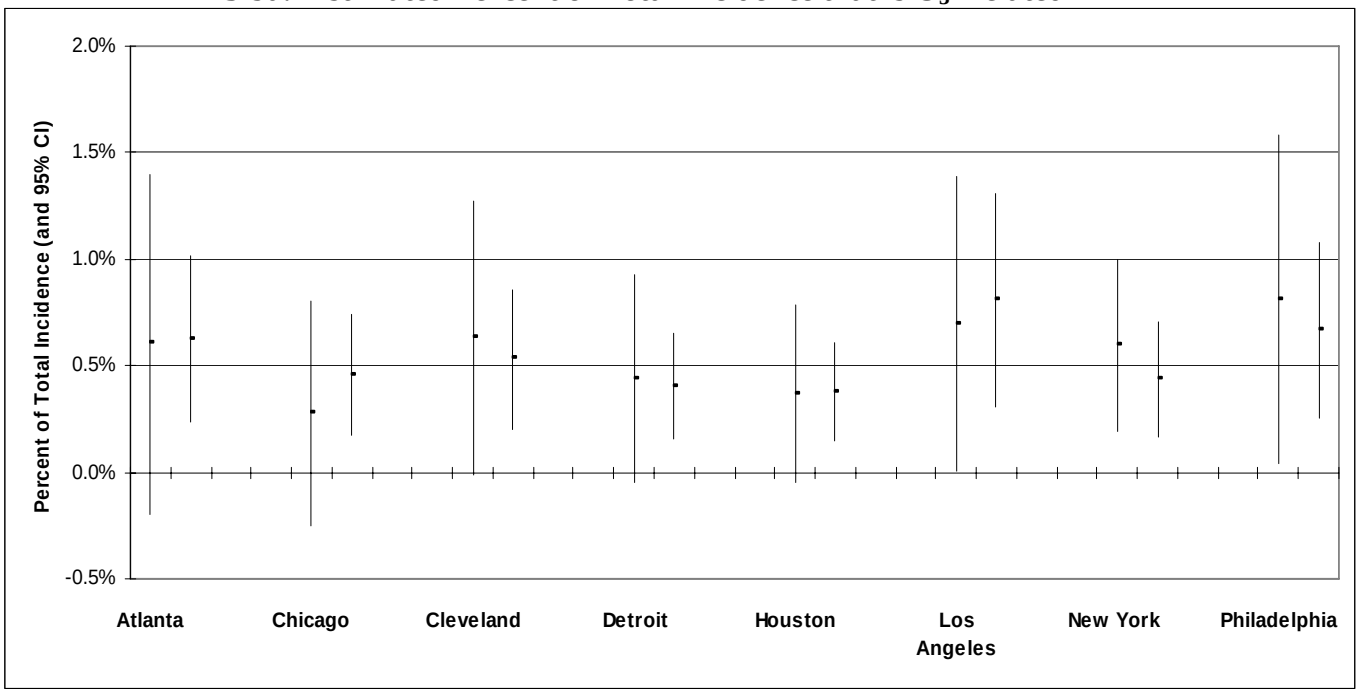


Figure 5-9b. Estimated O_3-Related Cases per 100,000 Relevant Population

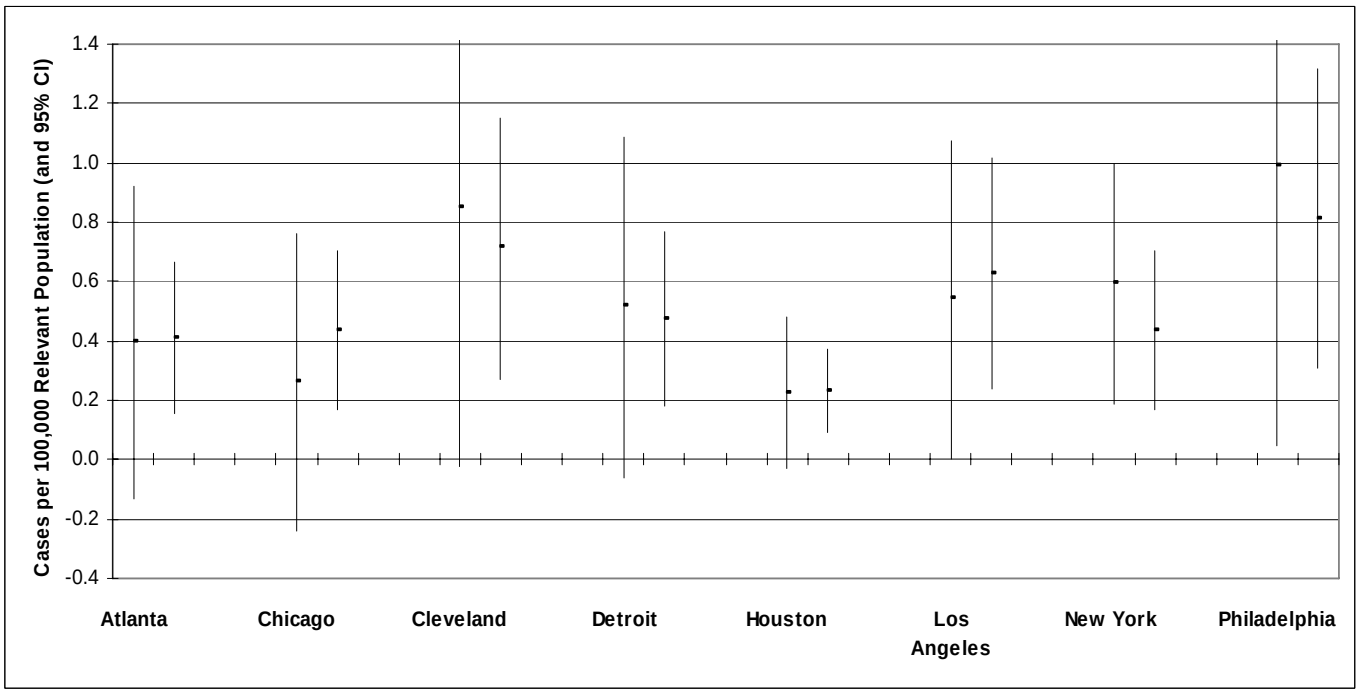


Figure 5-10. Estimated Cardiovascular and Respiratory Mortality Associated with Short-Term Exposure to Ozone Above Background When the Current 8-Hour Standard is Just Met (April – September): Single-Pollutant vs. Multi-Pollutant Models [Huang et al. (2004), additional pollutants, from left to right: none, PM10, NO2, SO2, CO]

5-10a. Estimated Percent of Total Incidence that is O_3-Related

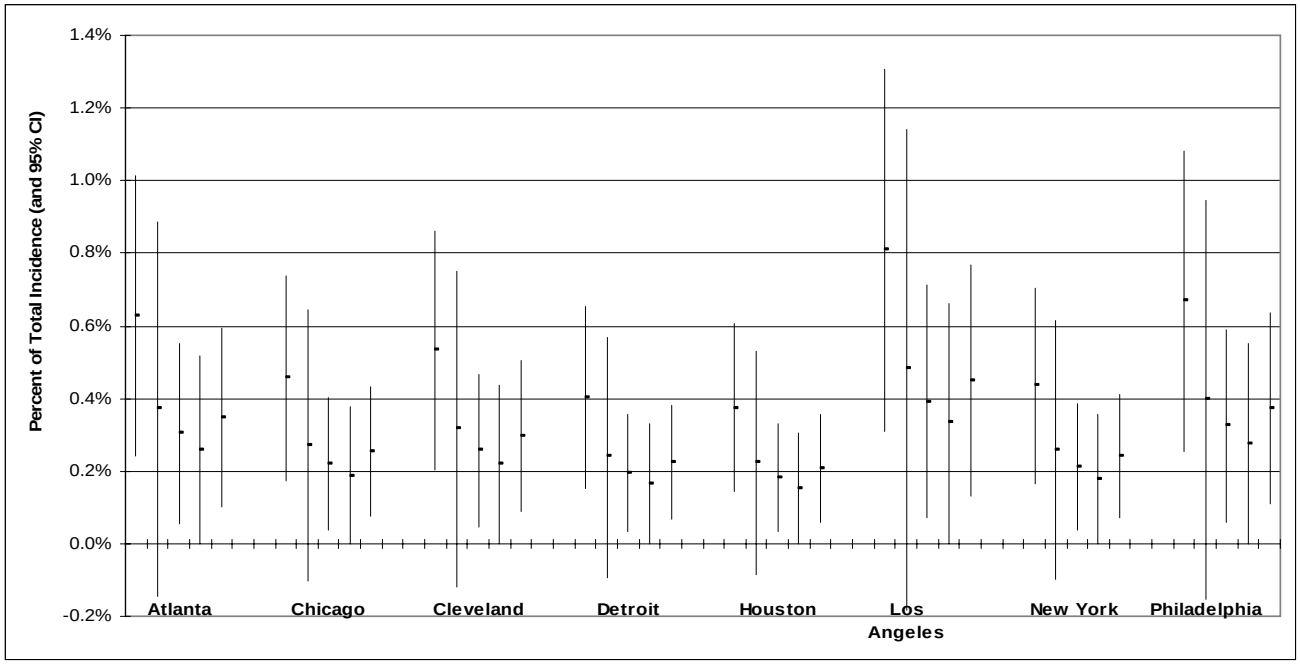


Figure 5-10b. Estimated O_3-Related Cases per 100,000 Relevant Population

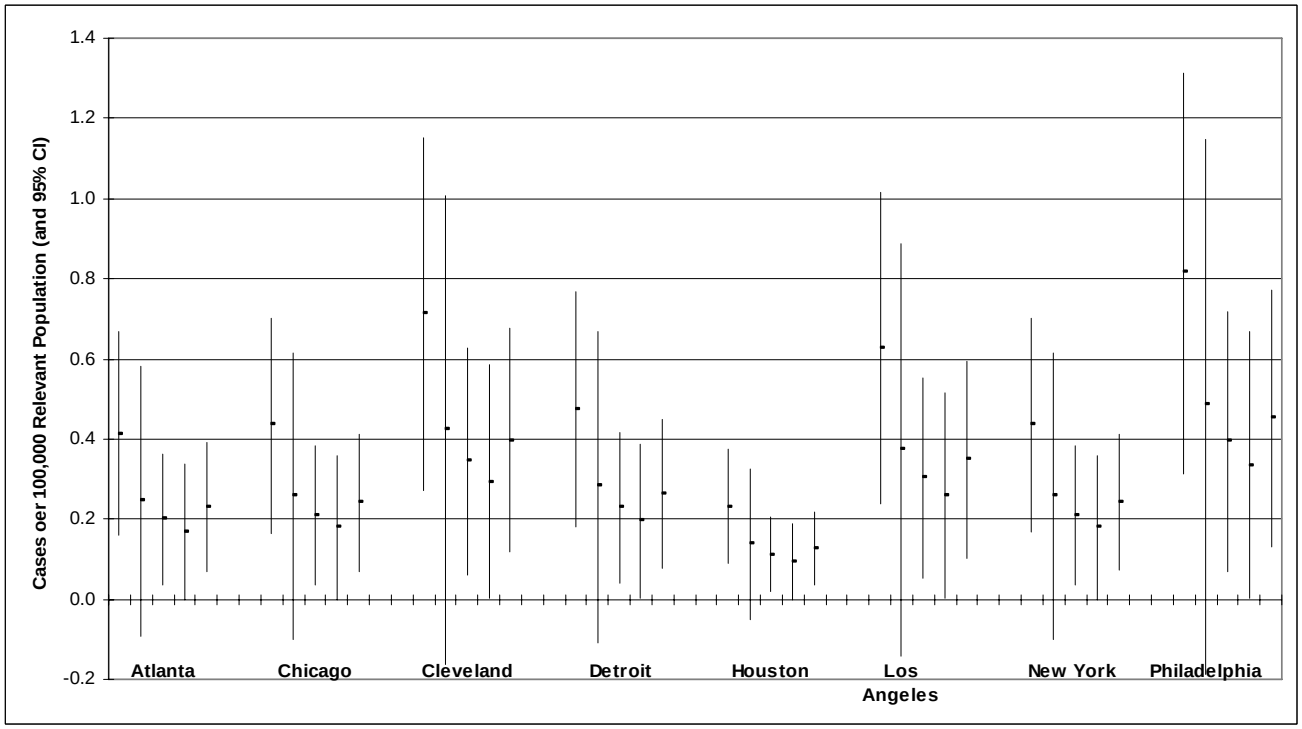


Table 5-10. Estimated Non-Accidental Mortality Associated with Ozone Above Background When the Current 8-Hour Standard is Just Met (April – September)

Location	Study	Lag	Exposure Metric	Non-Accidental Mortality Associated with O_3 Concentrations that Just Meet the Current O_3 Standard**		
				Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
Atlanta	Bell et al. (2004)	distributed lag	24 hr avg.	5 (-20 - 29)	0.3 (-1.3 - 1.9)	0.1% (-0.4% - 0.6%)
	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	9 (3 - 15)	0.6 (0.2 - 1)	0.2% (0.1% - 0.3%)
Boston	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	6 (2 - 9)	0.8 (0.3 - 1.4)	0.2% (0.1% - 0.4%)
Chicago	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	30 (10 - 50)	0.6 (0.2 - 0.9)	0.1% (0% - 0.2%)
	Schwartz (2004)	0-day lag	1 hr max.	310 (98 - 519)	5.8 (1.8 - 9.7)	1.5% (0.5% - 2.5%)
	Schwartz -- 14 US Cities (2004)	0-day lag	1 hr max.	117 (37 - 197)	2.2 (0.7 - 3.7)	0.6% (0.2% - 0.9%)
Cleveland	Bell et al. (2004)	distributed lag	24 hr avg.	20 (-12 - 51)	1.4 (-0.9 - 3.7)	0.3% (-0.2% - 0.7%)
	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	12 (4 - 21)	0.9 (0.3 - 1.5)	0.2% (0.1% - 0.3%)
Detroit	Bell et al. (2004)	distributed lag	24 hr avg.	23 (-8 - 54)	1.1 (-0.4 - 2.6)	0.2% (-0.1% - 0.6%)
	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	12 (4 - 20)	0.6 (0.2 - 1)	0.1% (0% - 0.2%)
	Schwartz (2004)	0-day lag	1 hr max.	105 (-17 - 226)	5.1 (-0.8 - 10.9)	1.1% (-0.2% - 2.4%)

Location	Study	Lag	Exposure Metric	Non-Accidental Mortality Associated with O_3 Concentrations that Just Meet the Current O_3 Standard**		
				Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
	Schwartz -- 14 US Cities (2004)	0-day lag	1 hr max.	57 (18 - 96)	2.8 (0.9 - 4.7)	0.6% (0.2% - 1%)
	Ito (2003)	0-day lag	24 hr avg.	29 (-26 - 83)	1.4 (-1.3 - 4)	0.3% (-0.3% - 0.9%)
Houston	Bell et al. (2004)	distributed lag	24 hr avg.	22 (1 - 42)	0.6 (0 - 1.2)	0.2% (0% - 0.5%)
	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	11 (4 - 18)	0.3 (0.1 - 0.5)	0.1% (0% - 0.2%)
	Schwartz (2004)	0-day lag	1 hr max.	70 (6 - 133)	2.1 (0.2 - 3.9)	0.8% (0.1% - 1.5%)
	Schwartz -- 14 US Cities (2004)	0-day lag	1 hr max.	58 (18 - 98)	1.7 (0.5 - 2.9)	0.6% (0.2% - 1.1%)
Los Angeles	Bell et al. (2004)	distributed lag	24 hr avg.	32 (-77 - 141)	0.3 (-0.8 - 1.5)	0.1% (-0.3% - 0.5%)
	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	69 (23 - 115)	0.7 (0.2 - 1.2)	0.3% (0.1% - 0.4%)
New York	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	43 (15 - 72)	0.5 (0.2 - 0.8)	0.1% (0% - 0.2%)
Philadelphia	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	17 (6 - 28)	1.1 (0.4 - 1.9)	0.2% (0.1% - 0.4%)
	Moolgavkar et al. (1995)	1-day lag	24 hr avg.	61 (38 - 83)	4 (2.5 - 5.5)	0.8% (0.5% - 1%)
Sacramento	Bell et al. (2004)	distributed lag	24 hr avg.	8 (-25 - 41)	0.7 (-2.1 - 3.4)	0.2% (-0.6% - 1%)

Location	Study	Lag	Exposure Metric	Non-Accidental Mortality Associated with O_3 Concentrations that Just Meet the Current O_3 Standard**		
				Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	12 (4 - 20)	1 (0.3 - 1.7)	0.3% (0.1% - 0.5%)
St Louis	Bell et al. (2004)	distributed lag	24 hr avg.	3 (-4 - 9)	0.7 (-1.2 - 2.7)	0.1% (-0.2% - 0.5%)
	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	2 (1 - 4)	0.7 (0.2 - 1.1)	0.1% (0% - 0.2%)
Washington, D.C.	Bell et al. -- 95 US Cities (2004)	distributed lag	24 hr avg.	7 (2 - 12)	1.2 (0.4 - 2.1)	0.3% (0.1% - 0.4%)

*All results are for mortality (among all ages) associated with short-term exposures to O3. 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 O3 coefficient.

Table 5-11. Estimated Cardiovascular and Respiratory Mortality Associated with Ozone Concentrations: that Just Meet the Current 8-Hour Daily Maximum Standard (April – September)

Risk Assessment Location	Study Location	Cardiovascular and Respiratory Mortality Associated with O_3 Concentrations that Just Meet the Current O_3 Standard**		
		Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
Atlanta	Atlanta	6 (-2 - 14)	0.4 (-0.1 - 0.9)	0.6% (-0.2% - 1.4%)
	19 U.S. Cities	6 (2 - 10)	0.4 (0.2 - 0.7)	0.6% (0.2% - 1%)
Chicago	Chicago	14 (-13 - 41)	0.3 (-0.2 - 0.8)	0.3% (-0.3% - 0.8%)
	19 U.S. Cities	23 (9 - 38)	0.4 (0.2 - 0.7)	0.5% (0.2% - 0.7%)
Cleveland	Cleveland	12 (0 - 24)	0.8 (0 - 1.7)	0.6% (0% - 1.3%)
	19 U.S. Cities	10 (4 - 16)	0.7 (0.3 - 1.2)	0.5% (0.2% - 0.9%)
Detroit	Detroit	11 (-1 - 22)	0.5 (-0.1 - 1.1)	0.4% (0% - 0.9%)
	19 U.S. Cities	10 (4 - 16)	0.5 (0.2 - 0.8)	0.4% (0.2% - 0.7%)
Houston	Houston	8 (-1 - 16)	0.2 (0 - 0.5)	0.4% (0% - 0.8%)
	19 U.S. Cities	8 (3 - 13)	0.2 (0.1 - 0.4)	0.4% (0.1% - 0.6%)

Risk Assessment Location	Study Location	Cardiovascular and Respiratory Mortality Associated with O_3 Concentrations that Just Meet the Current O_3 Standard**		
		Incidence	Incidence per 100,000 Relevant Population	Percent of Total Incidence
Los Angeles	Los Angeles	52 (0 - 102)	0.5 (0 - 1.1)	0.7% (0% - 1.4%)
	19 U.S. Cities	60 (23 - 97)	0.6 (0.2 - 1)	0.8% (0.3% - 1.3%)
New York	New York	53 (17 - 89)	0.6 (0.2 - 1)	0.6% (0.2% - 1%)
	19 U.S. Cities	39 (15 - 63)	0.4 (0.2 - 0.7)	0.4% (0.2% - 0.7%)
Philadelphia	Philadelphia	15 (1 - 29)	1 (0 - 1.9)	0.8% (0% - 1.6%)
	19 U.S. Cities	12 (5 - 20)	0.8 (0.3 - 1.3)	0.7% (0.3% - 1.1%)

*All results are for cardiovascular and respiratory mortality (among all ages) associated with short-term exposures to O3. Results are based on single-pollutant single-city models or a single-pollutant multi-city model estimated in Huang et al. (2004).

**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% credible intervals based on statistical uncertainty surrounding the O3 coefficient.

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Table 5-12. Estimated Hospital Admissions Associated with Ozone Above Background In New York, NY* When the Current 8-Hour Standard is Just Met (April – September)

Health Effects**	Ages	Lag	Exposure Metric	Health Effects Associated with O_3 Above Policy Relevant Background Levels***		
				Incidence (95% CI)	Incidence per 100,000 Relevant Population (95% CI)	Percent of Total Incidence (95% CI)
Respiratory Illness (unscheduled)	All	3-day	1-hr max	364 (88-639)	4.5 (1.1-8.0)	1.0 (0.2-1.8)
Asthma (unscheduled)	All	1-day	1-hr max	310 (66-555)	3.9 (0.8-6.9)	2.4 (0.5-4.2)

*New York in this study is defined as the five boroughs of New York City
**Concentration-response relationships are from Thurston et al. (1992) and are associated with short-term exposures.
***Incidence was quantified down to estimated policy relevant background levels. Incidences per 100,000 relevant population and percent of total incidence are rounded to nearest tenth.

related (non-accidental) mortality ranged from 0.3 per 100,000 relevant population in Atlanta (Bell et al., 2004), Houston (Bell et al., 2004 – 95 U.S. Cities), and Los Angeles (Bell et al., 2004) to 5.8 per 100,000 relevant population in Chicago (Schwartz, 2004).

As was the case for the analysis of effects associated with recent O_3 concentrations, 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 other 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 background 1-hr maximum O_3 concentrations were generally larger in the assessment locations than the corresponding changes using the 24-hr average metric.

As a percent of total incidence, estimated non-accidental mortality related to O_3 concentrations that just meet the current 8-hr O_3 standard ranged from 0.1 percent in several locations (Atlanta, Chicago, Detroit, Houston, Los Angeles, New York, and St. Louis) to 1.5 percent in Chicago (Schwartz, 2004). Although 7 of the 12 estimates from single-city single-pollutant models shown in Figure 5-7 were not statistically significant, all 12 were positive. In addition, it should be noted that the multi-city model estimates for non-accidental mortality were statistically significant based on Bell et al. (2004) and Schwartz (2004).

Figure 5-8 shows estimated percent of non-accidental mortality and cases per 100,000 relevant population related to O_3 concentrations that just meet the current 8-hr O_3 standard, based on single-city versus multi-city models across all locations for which both types of model were available. The results followed the same patterns as were observed in the analysis of effects associated with recent O_3 concentrations above background levels, discussed in section 4.2.1 above (see also Figures 4-4a and b). Similarly, the results seen in Figure 5-9, for cardiovascular and respiratory mortality, followed the same patterns as are evident in the corresponding analysis of recent O_3 concentrations (see Figures 5-4 and 5-5).

Figure 5-10 shows estimated percent of cardiovascular and respiratory mortality and cases per 100,000 relevant population related to O_3 concentrations that just meet the current 8-hr O_3 standard, based on multi-city models which include a single-pollutant versus multi-city models with multiple pollutants from Huang et al. (2004) across all locations for which such models were available. Table 5-11 shows estimates of incidence, incidence per 100,000 relevant population, and percent of total incidence of cardiovascular and respiratory mortality related to O_3 concentrations above background that just meet the current 8-hr standard in all risk assessment locations covered in Huang et al. (2004), based on both single-city and multi-city models from that study. Estimates of O_3-related cardiovascular and respiratory mortality ranged from 0.2 per 100,000 relevant population in Houston (using both the single-city and the multi-

city concentration-response functions) to 1.0 per 100,000 relevant population in Philadelphia (using the single-city concentration-response function). As a percent of total incidence, estimated O_3-related cardiovascular and respiratory mortality ranged from 0.3 percent in Chicago (using the single-city function) to 0.8 percent in Los Angeles (using the multi-city function) and Philadelphia (using the single-city function).

The staff notes that all of the estimates of O_3-related cardiovascular and respiratory mortality based on Huang et al. (2004), from both single-pollutant and multi-pollutant models (see Figure 5-10) and from both single-city and multi-city models (see Figure 5-9and Table 5-11) were positive.

Table 5-12 shows estimates of unscheduled hospital admissions for both respiratory illness and asthma in New York City associated with O_3 levels above background for the period from April to September with air quality adjusted to just meet the current 8-hr standard. For total respiratory illness, Table 5-12 shows about 450 cases or 5.6 cases per 100,000 relevant population, which represents 1.3% of total incidence for recent (2004) O_3 levels. For asthma-related hospital admissions, which are a subset of total respiratory illness admissions, the estimates are about 380 cases or 4.8 cases per 100,000 relevant population, which represents about 2.9% of total incidence. The reduction in incidence for both total respiratory illness and asthma admissions from the recent O_3 levels to air quality just meeting the current 8-hr standard is about 19%. Staff also notes that the estimates for this health endpoint for New York City are higher than the estimates in the risk assessment conducted during the prior O_3 NAAQS review which used the same concentration-response function. The main reason for this is the use of a single value of 0.04 ppm for background which is higher than the current modeled values for background in the current assessment and, thus O_3 levels below 0.04 ppm are contributing additional estimated cases in the current assessment.

5.4.3 Just Meeting Alternative Ozone Standards [to be included in next draft of Staff Paper]

5.4.4 Key Observations [to be included in next draft of Staff Paper]

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6. STAFF CONCLUSIONS AND RECOMMENDATIONS ON PRIMARY O_3 NAAQS

6.1 INTRODUCTION

This chapter presents preliminary staff conclusions as to whether consideration should be given to revising the existing primary O_3 standard and, if so, what alternative standards should be considered for additional exposure and risk assessments beyond those presented in Chapters 4 and 5. The results of these additional assessments will then be used to inform the staff recommendations on the primary O_3 NAAQS to be included in the next draft Staff Paper.

The existing O_3 standard is an 8-hour standard set to protect public health from short-term and prolonged exposures to O_3. The standard is defined in terms of four basic elements: indicator, averaging time, level and form. Preliminary staff conclusions on this standard and on alternatives for additional analyses are based on the assessment and integrative synthesis of information presented in the draft CD and on initial staff analyses and evaluations presented in Chapters 2 through 5 herein. As noted in Chapter 1, staff conclusions and recommendations presented in the next draft Staff Paper will be further informed by consideration of the information and analyses in the final CD, additional staff analyses and the results of the completed population exposure and human health risk assessments, and CASAC and public comments received on this draft.

Staff notes that the final decision on retaining or revising the current standard is largely a public health policy judgment. A final decision must draw upon scientific information and analyses about health effects, population exposure, and risks, as well as judgments about how to deal with the range of uncertainties that are inherent in the scientific evidence and analyses. The staff's 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.

6.2 APPROACH

In evaluating whether the current primary standard is adequate or whether consideration of revisions is appropriate, and in developing recommendations on the elements of possible alternative standards for further analyses, staff's approach in this review builds upon the general approach used in the last review by expanding the exposure and risk assessments to reflect the larger body of evidence now available. The 1997 final decision notice (62 FR 38861) outlined the key factors considered in selecting the elements of a standard for O_3: the averaging time; 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). These factors represent 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, informed by air quality, exposure assessment, and quantitative risk assessment when possible, as to the point at which the standards are requisite to protect public health with an adequate margin of safety. This approach to selecting a primary standard was endorsed by CASAC in the last review (Wolff, 1995b), particularly through its advice that "EPA's risk assessments must play a central role in identifying an appropriate level" and recognition that "the selection of a specific level and [form] is a policy judgment."

In developing these preliminary conclusions on the O_3 standard, staff has taken into account evidence-based considerations primarily by assessing the evidence from epidemiological, controlled human exposure, animal toxicological and field studies for a variety of health endpoints. For those endpoints based on epidemiological studies, staff has placed greater weight on associations with health endpoints that the draft 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 is given to evidence of associations that are judged to be only suggestive of possible causal relationships, although we have taken this information into account as part of margin of safety considerations. For the purpose of evaluating the level of the O_3 standard in this review, staff has placed greater weight on U.S. and Canadian studies reporting statistically significant associations. This is because findings of U.S. and Canadian studies are more directly applicable for quantitative considerations in this review, since studies conducted in other countries may well reflect quite different populations and air pollution characteristics.

Staff has also taken into account quantitative exposure- and risk-based considerations, drawn from the results of the exposure and risk assessments conducted in as many as twelve urban areas (discussed in Chapters 4 and 5). More specifically, staff has considered estimates of the magnitude of O_3-related exposures and risks associated with current air quality levels, as well

as the exposure and risk reductions likely to be associated with meeting the current 8-hour primary O_3 NAAQS. Staff recognizes the considerable uncertainties inherent in such estimates, and, as described in Chapters 4 and 5, will take such uncertainties into account by considering the sensitivity of the exposure and risk estimates to alternative assumptions likely to have substantial impact on the estimates.

In this review, as in the previous review, a series of general questions frames staff's approach to reaching conclusions and recommendations, based on the available evidence and information, as to whether consideration should be given to retaining or revising the current primary O_3 standard. Staff's preliminary review of the adequacy of the current standards begins by considering whether the currently available body of evidence assessed in the draft 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, staff then considers 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 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 revised standards, staff then identifies ranges of standards (in terms of indicators, averaging times, levels and forms) that would reflect a range of alternative public health policy judgments, based on the currently available evidence, 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 in the estimated exposure and risk reductions?

In this draft Staff Paper, staff develops preliminary recommendations on alternative standards to be analyzed in additional exposure and risk assessments that will in turn be considered in the next draft Staff Paper to help inform staff conclusions and recommendations as to whether consideration should be given to retaining or revising the primary O_3 NAAQS. The primary standard for O_3 is addressed in section 6.3 below, beginning with staff's consideration of the adequacy of the current primary O_3 standard in subsection 6.3.1. Subsequent subsections address each of the major elements that define the O_3 standard: pollutant indicator, averaging time, form and level. This chapter concludes with a summary of alternative standards to be considered in additional exposure and risk assessments in section 6.3.6. An additional section summarizing key uncertainties and recommendations for additional research related to setting a primary O_3 standard will be included in the next draft Staff Paper.

6.3 PRIMARY O_3 STANDARD

6.3.1 Adequacy of Current O_3 Standard

In the last review, an important input to the primary NAAQS decision was the evidence from human controlled exposure studies of healthy young subjects exposed for 1 to 8 hours. The best documented health endpoints in these studies were decrements in forced expiratory volume (FEV), also known as lung function decrements, and respiratory symptoms, such as cough and chest pain on deep inspiration. For short-term exposures of one to three hours, group mean FEV decrements were statistically significant for O_3 concentrations only at and above 0.12 ppm, but only when subjects engaged in very heavy exercise. By contrast, prolonged exposures of six to eight hours can produce statistically significant FEV decrements at the lowest O_3 concentrations evaluated in studies, 0.08 ppm, even when experimental subjects are engaged in more realistic intermittent moderate exercise levels. The health significance of this newer evidence led to the conclusion in the 1997 final decision (62 FR 38856) that "the 8-hour averaging time is more directly associated with health effects of concern at lower O_3 concentrations than is the 1-hour averaging time."

Also of particular importance in the last review were the following observations: (1) the then-existing 1-hour standard provided little, if any, margin of safety for public health protection;

(2) there was clinical evidence of statistically significant responses at 6- to 8-hour exposures to the lowest concentration evaluated, 0.08 ppm O_3, at moderate exertion, including: lung function decrements, respiratory symptoms (e.g., cough, pain on deep inspiration), nonspecific bronchial responsiveness, and biochemical indicators of pulmonary inflammation; (3) there was epidemiological evidence of associations between ambient O_3 and increased respiratory hospital admissions and emergency room visits; (4) toxicological evidence suggested that repeated long-term exposures to O_3-induced lung tissue damage in experimental animals; however, uncertainty regarding dosimetry and species sensitivity differences limited the quantitative use of these data; and (5) concentration-based forms, within the range considered up to the fifth-highest concentration form, were considered appropriate for a health-based primary O_3 standard. This form of the standard reflected recognition " . . . 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." (62 FR 38856) In making the final decision in the last review, the Administrator recognized that important uncertainties remained with regard to interpreting the role of other pollutants co-occurring with O_3, biological mechanisms of health effects, human exposure, and quantitative risk assessment of the health endpoints analyzed.

6.3.1.1 Evidence-based Considerations

Since the last review, important new information on O_3-related health effects has emerged, including new findings from:

- Dosimetry studies that clarify factors potentially affecting the regional distribution of O_3 in the respiratory tract and that provide improved bases for animal-to-human extrapolation of experimental results.

- Experimental toxicological studies using controlled exposures of humans and laboratory animals to delineate exposure-response relationships and the biochemical mechanisms underlying the toxic effects, pathology and susceptibility.

- Epidemiological studies that provide important information about real-world exposures and the effects of O_3, including premature mortality, hospital admissions, emergency room and doctors visits, on the general population, as well as in susceptible populations, and that address many research needs identified during the last review.

The new evidence about O_3-related effects on respiratory morbidity, cardiovascular morbidity and total, as well as cardiovascular and respiratory, mortality is discussed below.

6.3.1.1.1 Respiratory Morbidity

As described in the draft CD (CD, section 8.4) and in Chapter 3 above, the integrative assessment of these studies continues to support a causal association between short-term O_3

exposures and lung function decrements, respiratory symptoms and pulmonary inflammation that were the most important basis for revising the O_3 NAAQS in 1997. Statistically significant associations between of lung function decrements and respiratory symptoms were found in epidemiological studies even where the $98^{th}/99^{th}$ percentile[1] air quality values are well below the level of the current standard. 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. For all of these health endpoints, there exist considerable inter-individual differences in the magnitude of responses to O_3. Inter-individual differences in lung function and, to a lesser extent, respiratory symptoms are reproducible over a period of time, indicating that some individuals are consistently more responsive than others to O_3. Identification of population groups that are at increased risk to O_3, due to either increased susceptibility or increased potential for exposure, is based on their (1) biological responses to O_3, (2) existing lung disease, (3) activity patterns, and/or (4) personal factors (e.g., age, nutritional status).

Newer information expands understanding of the physiological basis for increased sensitivity in people with asthma. Newer studies continue to indicate that, relative to healthy controls, people with asthma have somewhat larger decreases in pulmonary function in response to O_3. (CD, p. 8-27) New evidence also indicates that people with asthma may have increased occurrence and duration of nonspecific airway responsiveness, and that people with pre-existing allergic asthma may have increased airway responsiveness to allergens following O_3 exposure. (CD, p. 8-29) Newly available human exposure studies suggest that people with asthma may also have increased inflammatory responses relative to non-asthmatic subjects. (CD, p. 8-73) The majority of epidemiological panel studies that evaluated respiratory symptoms and medication use related to O_3 exposures focused on children. (CD, p. 8-44) These studies suggest that O_3 exposure may be associated with increased respiratory symptoms and medication use in children with asthma. Taken together, these findings suggest that O_3 exposure may be a clinically important factor for people with asthma that can exacerbate the response to ambient bronchoconstrictor substances and increase respiratory morbidity and possibly mortality (as discussed further below).

At the time of the last review there was some epidemiological evidence of associations between ambient O_3 and increased respiratory hospital admissions and emergency room visits and only very limited evidence of associations for school absences and premature mortality. Since the last review of the O_3 standard, additional epidemiological studies have evaluated the association between short-term exposures to O_3 and hospital admissions for respiratory causes.

[1] The reason for using percentile values to describe maximum concentrations in the data from ozone studies is discussed more fully in the footnote to Appendix 3A and in the section on the form of the standard below.

Large multi-city studies as well as several individual city studies (CD, Figure 8-5) have reported positive, often statistically significant associations with total respiratory, asthma and COPD hospitalizations, with statistical significance more often found in those studies that analyzed the effect of O_3 during the warm season. The draft CD indicates that despite some inconsistencies noted across the studies, the collective evidence supports the finding of significant and robust effects of O_3 on respiratory hospitalization outcomes.

Although many new studies have evaluated the association between ambient O_3 levels and emergency department visits for respiratory causes, the evidence is still unclear. In general, O_3 effect estimates from summer only analyses tended to be positive and larger, and the estimates were more likely to be statistically significant, compared to results from cool season or all year analyses. (CD, section 7.3.2, Figure 8-5) While several studies observed significant associations between O_3 concentrations and emergency department visits for respiratory causes, inconsistencies were observed which were at least partially attributable to differences in model specifications and differences in the analyses. Because of this, the draft CD concludes that the evidence remains inconclusive regarding effects of O_3 on the risk of emergency department visits.

With regard to school absenteeism, two large U.S. studies and one study from Seoul, Korea have investigated the relationship between ambient O_3 and this effect. All of the studies found statistically significant positive associations between O_3 levels and absences from school. Because of differences in the analyses, the draft CD concludes that results from these three studies suggest that ambient O_3 concentrations may be associated with school absences, especially illness-related absences. Additional studies and analyses using similar lag periods are needed to more clearly delineate quantitative relationships between ambient O_3 and school absences. (CD, p. 8-45)

6.3.1.1.2 Cardiovascular Morbidity

There is limited, new evidence supporting associations between short-term O_3 exposures and a range of effects on the cardiovascular system. An increasing body of animal toxicology evidence suggests that hematological and thermoregulatory alterations (in heart rate variability and/or core body temperature) may mediate acute cardiovascular effects. A few controlled human exposure studies have examined the potential effects of O_3 exposure on cardiovascular functions. These studies have reported impairment of alveolar-arterial oxygen transfer and O_3-induced ventilation-perfusion mismatch, suggesting gas exchange abnormalities that could affect cardiac function. 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.

Based on epidemiological study results, the draft 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. 7-57).

A subset of hospital admission studies examined the effect of O_3 exposure on cardiovascular outcomes. The evidence is inconclusive on the association between O_3 exposure and cardiovascular hospitalizations with regard to year-round data. However, the draft CD concludes that in studies that adjusted for seasonal or meteorological factors, there is suggestive evidence that O_3 is associated with increased risk for cardiovascular hospital admissions in the warm season. (CD, p. 8-48) Studies also report associations between short-term O_3 exposure and mortality from cardiovascular or cardiopulmonary causes (as discussed further below).

6.3.1.1.3 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, the magnitude of the effect was unclear. Since 1996, newly available large multi-city studies designed specifically to examine the effect of O_3 on mortality have provided much more robust and credible information. New data are also available from 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 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. 7-149) Some of the single city studies with positive and statistically significant results have 98^{th} or 99^{th} percentile air quality values well below the level of the current 8-hour O_3 standard. (Appendix 3A) The draft 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 draft 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 have been less consistent, possibly due to lower statistical power in this group. (CD, p. 7-94) Overall, the draft CD concludes that these findings suggest a causal association between short-term O_3 exposure and mortality particularly in the warm season. (CD, p. 8-84)

6.3.1.2 Risk-based Considerations

In discussing risk-based considerations, this section will focus first on the results of the exposure assessment and then on the results of the risk assessments that were based on clinical and epidemiological evidence. As described in Chapter 4, for this review estimates of exposures

were calculated for active people of all ages, school age children (ages 5-18), and "active" school age children.[2] For the initial exposure analyses in this review, an "exposure of concern" was defined the same way as in the previous review. An "exposure of concern," as defined in the 1997 review of the O_3 standard, is an 8-hour average exposure to 0.08 ppm O_3 while intermittently at moderate or greater exertion levels. (62 FR 38860) Exposure results are displayed in Tables 4-7 and 4-8 for daily maximum 8-hour average exposures above 0.08 ppm O_3, in 12 urban areas across the U.S., for two cases (i.e., recent (2004) air quality, and just meeting the 8-hour primary standard), at moderate or greater exertion levels for three groups: active people of all ages; all school age children; and active school age children. Estimates, aggregated across these 12 urban areas of the number of people exposed, in each of the three groups, and the number of person-days (occurrences) of exposures, with daily maximum 8-hour average exposures above 0.08 ppm while at moderate or greater exertion, are shown in Table 6-1 below.[3]

Under the recent (2004) air quality scenario, 1.6 million people, or 2 % of the total population of the 12 urban areas, are estimated to experience one or more exposures of concern. More than 600,000 children, or 3% of the total number of children ages 5-18, and almost 400,000 active children, or 4 % of active children ages 5-18, are estimated to experience one or more exposures of concern. When air quality is adjusted to simulate just meeting the 8-hour standard, the number of people exposed drops substantially. Approximately 50,000 people, or less than 0.1% of the total population of the 12 urban areas, are estimated to experience one or more exposures of concern. Approximately 17,000 children (< 0.1% of all children) and 11,000 active children (0.1% of active children) are estimated to experience exposures of concern when air quality just meets the 8-hour standard. These results suggest a substantial reduction in estimated 8-hour average exposures above 0.08 ppm when the current 8-hour O_3 standard is just met. The estimated reduction in the number of total occurrences of exposures of concern in these 12 urban areas was more than 97% in each of the three population groups. Moreover, a comparison of the number of people exposed with the number of occurrences indicates that very few people are likely to be exposed more than one time during the O_3 season. Under the current standard it is estimated to be rare for individuals to experience more than one 8-hour exposure above 0.08 ppm O_3 while at moderate or greater exertion levels in these 12 urban areas during an O_3 season with air quality similar to 2004.

[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.

[3]For greater discussion of the analyses and a breakdown of exposures by city, see Chapter 4.

As discussed in Chapter 5, risk estimates were calculated for lung function decrements in children, hospital admissions, and mortality. This section focuses first on the risk estimates presented for lung function decrements, then for mortality and hospital admissions. Health risk estimates were calculated for lung function decrements in both all school age children and active school age children, who tend to spend more time outdoors than adults. Tables 5-5 and 5-6 display the risk estimates for all and "active" school age children (ages 5-18) for two different levels of lung function decrement response for the 12 urban areas. These two tables include risk estimates associated with recent (2004) air quality and air quality adjusted to simulate just meeting the current 0.08 ppm, 8-hour O_3 standard. 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 (see Chapter 2 for definition of policy relevant background). Table 5-5 shows the number and percent of children estimated to have at least one moderate or greater lung function response (i.e., FEV_1 decrement $\geq$ 15%) or one large or greater lung function response (i.e., FEV_1 decrement $\geq$ 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. Table 6-2, below, shows this information, the number of children exposed and the number of occurrences, aggregated across all 12 urban areas.

Because O_3 exposures down to policy relevant background levels, rather than exposures just down to a level of 0.08 ppm O_3, contribute to the risk estimates, a more complete picture emerges of the estimated risk remaining after the 8-hour O_3 standard is met for this health endpoint. When the 8-hour standard is met, assuming that the exposure-response relationship extends down to background in a linear fashion among all children 5 to 18 years old, living in these 12 urban areas, it is estimated that more than 1 million children will experience almost 8 million occurrences of moderate or greater lung function responses. Of those children, a smaller number, 134,000 are estimated to experience 211,000 occurrences of large or greater lung function responses. Among active children living in the 12 urban areas, it is estimated that more than 600,000 will experience almost 5 million occurrences of moderate or greater lung function responses, and of those, 83,000 children will experience 136,000 occurrences of large or greater lung function responses.

Table 6-1. Summary of Estimates of Number of People Exposed and Number of Occurrences Associated with 8-Hour Daily Maximum Ozone Concentrations Above 0.08 ppm for 12 Urban Areas in the U.S. (from Tables 4-7 and 4-8)

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) (9.3 million active children)	
		Persons (in thousands and % of population in parentheses)	Person Days (thousands)	Persons (in thousands and % of population in parentheses)	Person Days (thousands)	Persons (in thousands and % of population in parentheses)	Person Days (thousands)
Recent Air Quality (2004)	≥0.08 ppm, moderate exertion*	1598 (2%)	1935	618 (3%)	755	376 (4%)	452
Just Meeting Current 8-hr Standard	≥0.08 ppm, moderate exertion	50 (0.06%)	51 [97% reduction]	17 (0.09%)	17 [98% reduction]	11 (0.1%)	11 [98% reduction]

* Moderate exertion is defined as having an 8-hr average EVR in the range 13-27 l-min/m^2.

Table 6-2. Summary of Comparison of Median Number of Children and Median Number of Occurrences Associated with 8-Hour Ozone Exposure Among All Children and Among Active Children While Engaged in Moderate Exertion* in 12 Urban Areas in the U.S. (from Tables 5-5 and 5-6)

Air Quality Scenario	Level of Lung Function Decrement	All Children (5-18) (18.1 million children)		Active Children (5-18) (9.3 million active children)	
		Persons (in thousands and % of population in parentheses)	Person Days (thousands)	Persons (in thousands and % of population in parentheses)	Person Days (thousands)
Recent Air Quality (2004)	≥ 15%	1728 (10%)	15410	959 (10%)	9445
Just Meeting Current 8-hour Standard	≥ 15%	1156 (6%)	7640 [50% reduction]	646 (7%)	4709 [50% reduction]
Recent Air Quality (2004)	≥ 20%	433 (2%)	1208	259 (3%)	774
Just Meeting Current 8-hour Standard	≥ 20%	134 (1%)	211 [80% reduction]	83 (1%)	136 [80% reduction]

* Moderate exertion is defined as having an 8-hr average EVR in the range 13-27 l-min/m^2.

Several 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 populations. In Table 6-2, the percent of the all children likely to experience one or more moderate or greater lung function responses under recent (2004) air quality and when air quality just meets the current 8-hour standard are 10% and 6%, respectively. The range across the 12 urban areas, from Table 5-5, is about 7% to 13% under the recent (2004) air quality, and about 5% to 8 % when air quality just meets the current 8-hour standard. More than one million children are estimated to experience one or more moderate or greater lung function responses in these 12 urban areas when the current 8-hour primary standard is met. 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, on average, 7 occurrences of moderate or greater lung function responses during an O_3 season.[4] 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 a just 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 7) 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)

For non-accidental mortality associated with "as is" O_3 concentrations (Table 5-7), the estimates of the percent of total mortality attributable to O_3 exposure ranges from 0.1 to 1.9%; with an incidence per 100,000 relevant population ranging from 0.4 to 7.3. Estimated non-accidental mortality associated with O_3 concentrations that just meet the current 8-hour standard (Table 5-10) ranges from 0.1 to 1.5% of total incidence; with an incidence per 100,000 relevant population ranging from 0.3 to 5.7. Estimated cardiovascular and respiratory mortality shows a similar pattern (Tables 5-8, 5-11). For a recent year (2004) of O_3 concentrations, the estimates of the percent of cardiovascular and respiratory mortality attributable to O_3 ranges from 0.4 to 1.6%; the incidence per 100,000 relevant population ranges from 0.4 to 1.3. Estimated cardiovascular and respiratory mortality associated with O_3 concentrations that just meet the

[4] This number is estimated for example for all children, by dividing the estimated number of children (1,156,000) into the estimated number of occurrences (7,640,000) resulting in an average of 7 occurrences per child.

current 8-hour O_3 standard ranges from 0.2 to 0.8% of total incidence; with the incidence per 100,000 relevant population ranging from 0.2 to 0.9.

For unscheduled hospital admissions, risk estimates for the New York City area are shown in Table 5-9 for recent (2004) air quality, and Table 5-12 for just meeting the current 8-hour standard. Table 5-9 shows estimates of unscheduled hospital admissions for respiratory illness in the New York City area associated with O_3 levels above background of about 450 cases or 5.6 cases per 100,000 relevant population, which represents 1.3% of total incidence for recent (2004) O_3 levels. For asthma-related hospital admissions, the estimates are about 380 cases or 4.8 cases per 100,000 relevant population, which represents about 2.9% of total incidence. Table 5-12 shows estimates of unscheduled hospital admissions for both respiratory illness and asthma in New York City associated with O_3 levels above background for the period from April to September with air quality adjusted to just meet the current 8-hr standard. For total respiratory illness, Table 5-12 shows about 450 cases or 5.6 cases per 100,000 relevant population, which represents 1.3% of total incidence for recent (2004) O_3 levels. For asthma-related hospital admissions, which are a subset of total respiratory illness admissions, the estimates are about 380 cases or 4.8 cases per 100,000 relevant population, which represents about 2.9% of total incidence. The reduction in incidence for both total respiratory illness and asthma admissions from the recent O_3 levels to air quality just meeting the current 8-hr standard is about 19%.

6.3.1.3 Summary

These initial analyses suggest that meeting the current 8-hour O_3 standard would likely result in substantial reductions in exposures of concern and associated risks of serious health effects above a level of 0.08 ppm O_3. On the other hand, these analyses also suggest that there is risk of moderate or greater lung function decrements in children, hospital admissions, and mortality from O_3 resulting from exposures across the range of levels allowed by the current standard. Staff concludes that the estimates discussed above are indicative of risk that some might reasonably judge to be important from a public health perspective. Thus, staff believes that it is appropriate to perform additional analyses so as to be able to consider the potential reduction in exposures and risks from alternative standards that may provide more health protection beyond that afforded by the current O_3 primary standard.

6.3.2 Indicator

The staff believes that the conclusions on the appropriate indicator for the primary O_3 NAAQS that were reflected in the 1996 Staff Paper remain 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 raises

concern only for O_3 at levels of photochemical oxidants commonly reported in the ambient air. Thus the staff does not believe that it is appropriate to consider any other indicator for additional analyses.

6.3.3 Averaging Time

6.3.3.1 Short-Term and Prolonged (1 to 8 hours)

The current 8-hour 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 hours was supported by the following key observations and conclusions (62 FR 38861):

(1) The 1-hour averaging time of the previous NAAQS was originally selected on the basis of health effects associated with short-term (i.e., 1- to 3-hour) 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-hour) exposures below the level of the NAAQS.

(3) Results of the quantitative risk analyses showed that the 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 hours.

(4) The 8-hour averaging time is more directly associated with health effects of concern at lower O_3 concentrations than the 1-hour 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, 1995b)

In looking at the new information that is discussed in section 7.6.2 of the draft CD, epidemiological studies have used various averaging periods for O_3 concentrations, most commonly 1-hour, 8-hour and 24-hour averages. As described more specifically below, in general the results presented from U.S. and Canadian studies (Appendix 3A) 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-hour daily maximum O_3 concentrations were somewhat larger than those for longer averaging times, especially 24-hour average O_3. In addition, Gent et al., (2003) reported that associations for 1-hour and 8-hour 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 hours prior to the myocardial infarction was substantially larger than that reported for an association with 24-hour average O_3 (Peters et al., 2001). The draft CD reports results for a number of single-city results that generally reported effect estimate sizes that were larger when comparing 1-hour or 8-hour daily maximum O_3 concentrations with 24-hour 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 draft CD concludes that the epidemiological study results were generally comparable for the three O_3 averaging times (CD, p. 7-120). Given that the 8-hour 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 to continue to base any additional exposure and risk analyses for short-term or prolonged effects on 8-hour average O_3 concentrations.

6.3.3.2 Long-Term

For consideration during the last review, there was a large animal toxicological database providing 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, but there was no corresponding evidence for humans. Furthermore, 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.

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) There is also some new information about the effects of long-term exposures in humans. Epidemiological studies investigating chronic effects in humans following long-term exposures to O_3 previously provided only limited suggestive evidence; however, recent studies of pulmonary function changes observed in children living in cities with high O_3 levels as well as alterations in lung structure reported in an autopsy study in Los Angeles and Miami provide additional evidence that long-term O_3 exposure may play a role in causing irreversible lung damage. However, the strength of the evidence overall does not allow establishment of a likely causal relationship between long-term O_3 exposures and increased respiratory morbidity and mortality. In addition, although there have been recent advancements of dosimetry modeling, providing a better basis for extrapolation, especially of long-term exposures, from animals to humans (CD, p. 8-11), further research must be conducted before quantitative linkages to specific health effects in humans can be established with sufficient certainty to include in a quantitative manner in the review. For these reasons, staff concludes that it is not appropriate at this time to base any exposure or risk assessments on long-term exposures to O_3.

6.3.4 Form

In evaluating alternative forms for the primary standard, the adequacy of the public health protection provided is the foremost consideration. Staff recognizes 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. Instability can have the effect of reducing public health protection, because when areas are subject to shifting in and out of attainment simply because of meteorological conditions it can disrupt ongoing implementation plans and associated control programs. Providing more stability is one of the reasons that in 1997 the primary O_3 NAAQS was changed from a "1-expected-exceedance" form[5] to a less extreme, concentration-based statistic, specifically the 3-year average of the annual fourth-highest daily maximum 8-hour 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.

[5]The 1-expected-exceedance form essentially requires that the fourth-highest air quality value in 3 years, based on adjustments for missing data, to be less than or equal to the level of the standard for the standard to be met at an air quality monitoring site.

During the 1997 review, consideration was given to a range of alternative forms, including the second-, third-, fourth- and fifth-highest daily maximum 8-hour concentrations, recognizing that the public health risks associated with exposure to a pollutant without a clear, discernable threshold are best 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 at the lower end of the range to provide a margin of safety against possible, but uncertain chronic effects, or at the upper end of the range to 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 standard may be exceeded even when attaining a fifth-highest 0.08 ppm concentration standard, argued against choosing that form.

For the purposes of making recommendations of alternative standards for additional exposure and risk analyses, staff considered two concentration-based forms, the nth highest maximum concentration and the percentile-based form of the standard. A percentile-based statistic, as is used in Figure 6-1a and b, 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 do a better job of ensuring that people who live in areas with different length O_3 seasons receive the same degree of public health protection. For this reason, the staff recommends that further analyses be based on a form specified in terms of an nth-highest concentration over a three-year period, with n ranging from 3 to 5. Staff believes that his range is sufficiently broad to allow for consideration of the degree of protection requisite to protect public health and also to ensure stability of the standard.

6.3.5 Level

Since the last review, the body of evidence from animal toxicology and dosimetry studies, controlled human exposure and epidemiological studies has confirmed associations between exposure to O_3 and the effects that were the basis for the 1997 O_3 standard: lung function decrements; symptoms; airway hyper-responsiveness; pulmonary inflammation; and respiratory-related hospital admissions. New evidence has provided a better understanding of

the pathophysiological mechanisms of these effects. This information has also provided new evidence of likely causal associations with more serious effects including associations between increasing O_3 concentrations and hospital admissions for respiratory causes and all cause (non-accidental) mortality. Positive, but inconclusive associations have been found between ambient O_3 concentrations and respiratory symptoms, school absences, emergency department visits, cardiovascular system effects, and cardiovascular and respiratory mortality.

Although it is reasonable to expect that there are biological thresholds for different health effects in individuals or groups of individuals with similar health status, most studies designed to evaluate the existence of a threshold have observed no deviation from a linear function across the range of O_3 measurements from the study, as discussed above in Chapter 3, section 3.4.6. One study found a potential threshold level of about 45 ppb (1-hour maximum concentration) for an association between mortality and short-term O_3 exposure during the summer months. Another found some evidence of a threshold at about 30 ppb (1-hour maximum concentration) for the association between O_3 concentrations and both respiratory and cardiovascular hospital admissions. Other studies, such as ones that have removed days with higher concentrations of O_3 from the data set to test the association between O_3 at lower levels and health outcomes have found that associations remain or are increased in magnitude. In summary, many epidemiological studies have suggested that no threshold levels can be found. In those studies that provide suggestive evidence of threshold, the potential thresholds are at low concentrations, much lower than the current 8-hour standard.

Staff concludes that the results from the initial quantitative exposure and risk assessments done to date suggest that sufficient population exposures and risk of various health endpoints (including pulmonary function decrements, all cause (non-accidental) and respiratory and cardiovascular mortality, and respiratory hospital admissions) remain after meeting the current 8-hour standard that additional analyses for standards below the level of the current 8-hour standard are appropriate. In addition to consideration of exposures and effects that are quantifiable in population exposure and risk assessments, staff believes that it is also appropriate to consider effects that it is not currently possible to quantify, for example the effects of chronic O_3 exposure or the effects on people with asthma, to the extent these considerations would ultimately cause closer examination of the lower end of the range, in developing recommendations about alternative standards for further exposure and risk assessment.

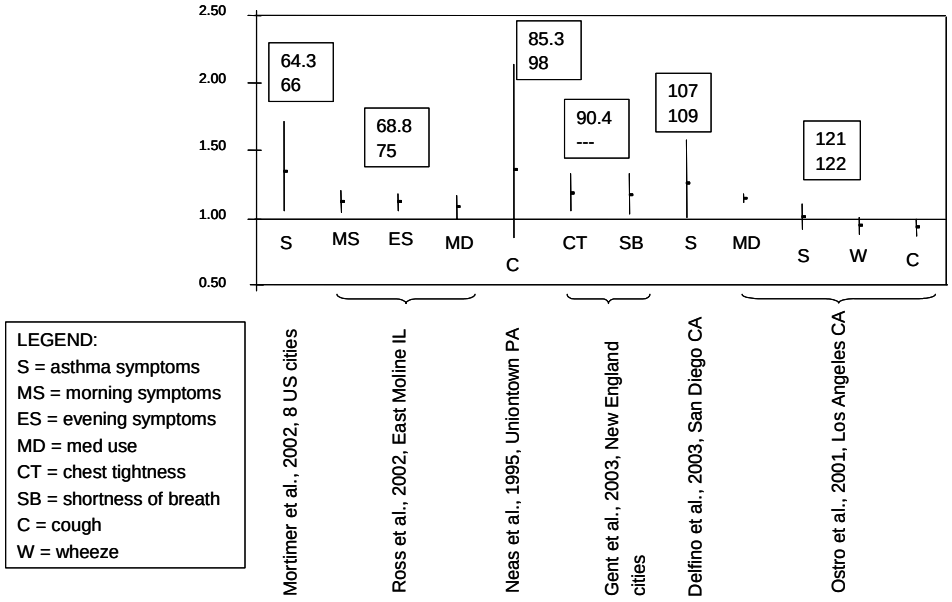
The question then becomes, what level or levels should be evaluated? To answer this question, staff turns to epidemiological studies of associations between O_3 and respiratory symptoms and hospital admissions for respiratory causes from warm season analyses. (Figures 6-1 a and b) Not included in Figure 6-1, but also considered are the reported associations between 8-hour average O_3 levels and daily mortality (Appendix 3A). All of these effects

estimates are consistently positive and many of the reported associations are statistically significant. In this body of evidence, small but statistically significant effects estimates have been reported in studies with $98^{th}/99^{th}$ percentile values as low as approximately 0.06 ppm O_3, 8-hour average. The information is presented in terms of the 98^{th} and 99^{th} percentile values because in the studies being compared, the data spanned widely varying periods of time

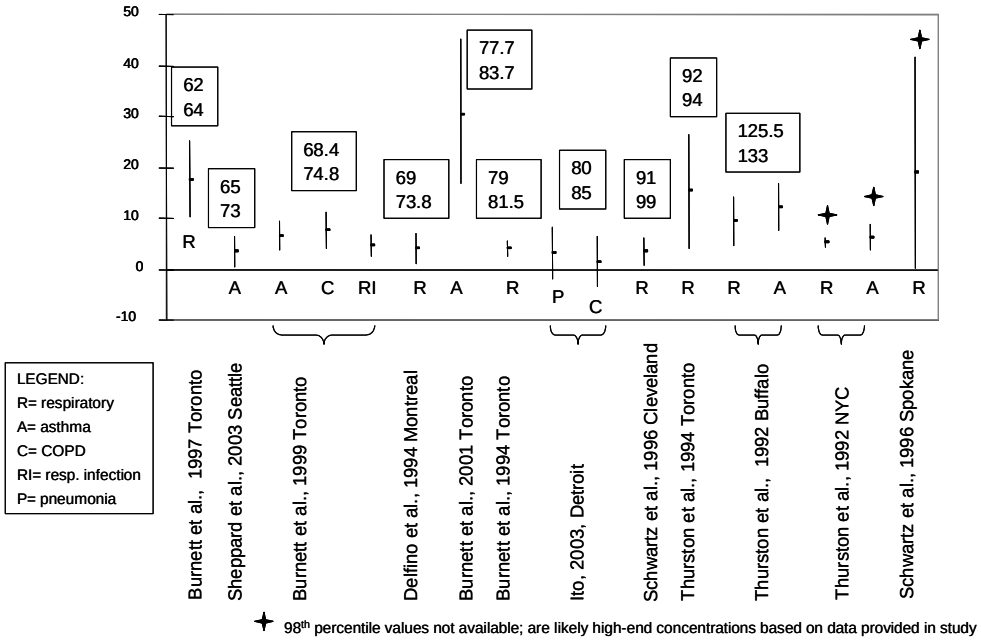
After consideration of the entire body of experimental and epidemiological evidence, the results of exposure and risk assessments and the consideration of non-quantifiable effects, such as the effects of repeated exposures and potentially greater effects on people with asthma, it is staff's view that it is appropriate to conduct additional exposure and risk assessments down to an alternative standard level as low as 0.06 ppm. The level of 0.06 ppm represents the lowest air quality statistic credibly and significantly associated with increased respiratory morbidity effects such as symptoms and hospital admissions, and also with daily mortality.

Figure 6-1 a and b

(a) **Odds Ratios (with 95% confidence intervals) for associations between O_3 and respiratory symptoms, from warm season analyses, in order of increasing 98th and 99th percentile 8-hr O_3 concentrations (in boxes)**



(b) **Effect estimates (with 95% confidence intervals) for associations between O_3 and hospitalization for respiratory diseases, in warm season analyses, in order of increasing 98th and 99th percentile 8-hr O_3 concentrations (in boxes)**



6.3.6 Summary of Alternative Standards to Be Considered in Additional Exposure and Risk Analyses

Staff has considered the evidence from animal toxicology, epidemiological and controlled human exposure studies, estimates of exposures and risk for a recent (2004) year and a year when air quality is estimate to just meet the current 8-hour standard, and the related limitations and uncertainties. For the reasons described above, staff provisionally concludes that it is appropriate to conduct additional assessments of exposure and risk associated with alternative standards that may provide increased protection beyond that afforded by the current 8-hour primary O_3 standard. Staff recommends that additional exposure and risk assessments be conducted for alternative, 8-hour average standards at O_3 levels of 0.08 ppm, third-highest concentration, 0.07 ppm third- through fifth-highest concentration, and if appropriate based on these results, 0.06 ppm, third- through fifth-highest concentration, over a three-year period. This combination of alternative levels and forms will provide a more complete picture of the risk from lower concentrations where the public health risks are relatively small and more uncertain to higher concentrations where the public health risks are greater, but the effects are more certain. The results of these additional assessments will then be used to inform staff recommendations to be included in the next draft Staff Paper on the primary O_3 NAAQS.

6.4 SUMMARY OF KEY UNCERTAINTIES AND RESEARCH RECOMMENDATIONS RELATED TO SETTING A PRIMARY O_3 STANDARD [To be included in the next draft Staff Paper]

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7. POLICY-RELEVANT ASSESSMENT OF WELFARE EFFECTS EVIDENCE

7.1 INTRODUCTION

This chapter presents critical information for 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, 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, 1996).

Ozone can also affect other ecosystem components such as soils, water, animals, and wildlife, 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 7.4). This framework can be used to link ozone 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 ozone related effects would also improve the protection afforded to ecosystems and their related public welfare categories.

Other welfare effects categories affected by O_3 include damage to certain manmade materials (e.g., elastomers, textile fibers, dyes, paints, and pigments) and effects on and by climate. 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, 2005b). Therefore, staff judges that there is insufficient information in

the materials damage literature to inform secondary standard setting and so will not be further discussed. Interested readers are referred to chapter 11 in the draft CD (EPA, 2005b). 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. Though this topic will not be addressed further, its corollary, e.g., climate change impacts on plant response to O_3, will be considered under the discussion of factors that can modify the vegetation responses to O_3 and the implications of these interactions for future field exposure conditions. Thus, this chapter will focus primarily on the well established body of science regarding O_3-related effects on vegetation, as discussed both in the last review and summarized along with relevant new research in the current draft CD (EPA, 2005b).

Included in this discussion are plans for a number of analyses that update the exposure, risk and benefits assessments conducted in the last review (EPA, 1996b). The EPA held a consultation with the CASAC O_3 Panel on October 3, 2005 on the scope and methods being considered in the planned assessments. The planned assessments described in this chapter take into account the range of comments received from individual Panel members and the discussion that occurred during the consultation. Staff recognizes that while these updated assessments incorporate newer data, models, and approaches, and take into account current and alternative ozone air quality scenarios under consideration, they are still limited by important data gaps and uncertainties in currently available models and approaches. Due to the limitations of time and staff resources, this first draft Staff Paper includes only descriptions of the planned assessments. The second draft Staff Paper will contain results from the assessments, a more complete discussion of the associated uncertainties and limitations, and staff conclusions and recommendations with regard to the secondary O_3 NAAQS.

7.2 EFFECTS ON VEGETATION

Science published since the conclusion of the 1996 review has not fundamentally altered the understanding and conclusions regarding ozone effects on vegetation and ecosystems found in the previous CD, though in some cases, recent work has expanded or clarified our understanding, especially at the level of plant cell and tissue response (EPA, 2005b). In addition, only a few new studies focus on addressing the data gaps or uncertainties identified in the last review. Some notable exceptions within the U.S. include a shift and slight increase in research

designed to examine the joint interaction of elevated CO_2 and O_3 on the productivity of U.S. vegetation, and the expansion of data collection and analysis of O_3-induced visible foliar injury occurrences at United States Department of Agriculture Forest Service Forest Inventory and Analysis (USDA FS FIA) biomonitoring sites. In Europe, O_3 vegetation research has continued, though with a shift in focus from the use of ambient exposure measures to modeled O_3 uptake by vegetation in the context of developing an exposure index that can be used as a planning tool (i.e., critical levels).

Significantly, however, a number of recent advances in the development and use of mechanistic process models, leaf and canopy flux models, and improved understanding of the relationships between impacts to vegetation and impacts to ecosystem structure and function, can be linked to this expanded and further elucidated scientific base underpinning these developments. Specifically, the expanded understanding regarding O_3 impacts at the genetic, physiological, and mechanistic levels informs the interpretation of risk associated with vegetation response at current O_3 levels. For example, staff is increasingly aware that O_3 impacts at the genetic and cellular level may hold the key to understanding the more subtle but equally important implications of rising CO_2 levels, temperature, and O_3 levels on plant adaptability under conditions of climate change. Therefore, this section reviews the key scientific conclusions identified in 1996 O_3 CD (EPA, 1996a), and incorporates new information from the current draft CD where it expands or changes our understanding of the O_3-plant interactions.

7.2.1 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). Most OTC's consist of a cylindrical aluminum frame covered with transparent film and are approximately 3m in diameter with 2.5-m-high walls. Charcoal filtered air, non-filtered air or O_3-supplemented air is blown through a perforated panel at the bottom of the chamber, into the plant canopy and then escapes through the top of the chamber. Hogsett et al. (1987a) described in detail many of the various modifications to the original OTC designs that appeared subsequently, e.g., the use of larger chambers to permit exposing small trees (Kats et al., 1985) and grapevines (Mandl et al., 1989). Several other modifications were made over the years to improve ventilation reduce ambient air incursions, and a plastic rain-cap to exclude precipitation (Hogsett et al., 1985).

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. OTCs can

provide a consistent, definable exposure because of the constant wind speed and delivery systems. From a policy prospective, the statistically robust 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 unrealistic exposures. First, the 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 the cause-effect relationships (Krupa et al., 1995; Legge et al., 1995). However, in at least one case where canopy resistances were quantified in OTCs and in the field, it was determined that gaseous pollutant exposure to crops in OTCs was similar to that which would have occurred at the same concentration in the field (Unsworth et al., 1984a, 1984b). A second concern is that the introduction of the O_3-enriched air into the lower part of chambers as described by Heagle et al. (1973) and Mandl et al. (1973) results in a O_3 concentration gradient that decreases with increasing height, the converse of the situation observed in ambient air in which the O_3 concentration decreases from above a plant canopy to ground level (Grünhage and Jäger, 1994; Pleijel et al., 1995, 1996). Finally, as with all methods that expose vegetation to modified O_3 concentrations in the field, OTCs create internal environments that differ from ambient air. For OTC's the 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 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, in general, essentially the same regardless of exposure system used and chamber effects did not significantly affect response. A recent example is the 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.

Though the OTC method has remained a widely used technique in the U.S. and Europe for exposing plants to varying levels of O_3 (EPA, 2005b), in recent years, a few studies have

employed a modified Free Air CO_2 Enrichment (FACE) method to expose vegetation to elevated O_3. This is an exposure methodology originally developed to expose vegetation without chambers to elevated levels of CO_2. FACE has been modified in Illinois and Wisconsin to include exposure of soybean and deciduous trees to O_3, 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 tree/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. Specifically, it is not possible to produce a number of replicated treatment levels, including O_3 concentrations below ambient, or a control where ambient O_3 levels are already at phytotoxic levels. Thus, FACE sites cannot be used to build the statistically robust C-R functions like those produced with OTCs and is of limited value in developing empirical models for predicting O_3 effects. In addition, FACE systems are relatively expensive to operate, likely limiting the number of new sites that will employ these systems and the variety of species studied.

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. Specifically, 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, supporting the previously observed variation among trembling aspen clones (*Populus tremuloides* L.) using OTCs (Karnosky et al., 1999). The FACE study also evaluated the effects of 3 years of exposure to combinations of elevated CO_2 and O_3 on growth responses in mixtures of five trembling aspen clones (Isebrands et al., 2000, 2001). Height, diameter, and stem volume (diameter^2 × height) were decreased by elevated O_3. On average for all clones, stem volume was decreased by 20% over the 3 years in the elevated O_3 treatment as compared with the 1x-ambient treatment. These results also appear to show similar response patterns reported previously with the same clones grown in soil in pots or the ground in OTCs without the alterations of microclimate induced by chambers (EPA, 2005b). As more FACE data become available, a more quantitative comparison of findings from these two systems would be useful.

Staff recognizes there are other exposure methods described both in the 1996 CD and in the current draft CD that have and can provide useful information on plant responses to O_3 exposure including , chemical protectants, exclusion, passive monitors and naturally occurring gradients. However, based on the considerations described above, especially the policy need for

robust C-R functions, staff concludes that the OTC methodology is currently the most useful in a policy context.

7.2.2 Species (Intra-Plant) Response/Mode of Action

This section emphasizes reactions of O_3 with the plant cell and tissue, rather than the whole plant, to describe the fundamental mechanisms known to govern the response of the plant to O_3 exposure. This section discusses the movement of O_3 into plant leaves and their biochemical and physiological responses to O_3. 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 regarding the fundamental hypotheses concerning O_3-induced changes in physiology continues to be valid. However, during the last decade, this understanding of the cellular processes within plants has been further clarified and enhanced. This section describes: (1) the regulation of O_3 entry into the leaf, (2) reactions of O_3 or its reaction products at the cell surface, (3) movement and/or transformation of reaction products into the cell, (4) O_3 -triggered wound or pathogen attack response, (5) plant defense and compensation mechanisms, (6) O_3–induced changes to plant metabolism, and (7) delayed expression of plant response.

7.2.2.1 Entry of Ozone into the Leaf

To cause injury, O_3 must first enter the plant. Ozone-induced changes to a leaf's cuticle (the outer layer of the leaf surface) are minimal, and O_3 does not penetrate the cuticle (Kerstiens and Lendzian, 1989). Thus, only the O_3 that diffuses into a plant through the stomata (which exert some control on O_3 uptake) to the active sites within a leaf has the potential to impair plant processes or performance. Once inside the leaf, a phytotoxic effect will occur only if sufficient amounts of O_3 reach sensitive cellular sites that are subject to the various physiological and biochemical controls within the leaf cells. 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, 1996).

For O_3 to be absorbed into a leaf, it must first reach the stomatal openings in the leaf. Foliar absorption is controlled by the leaf boundary layer and stomatal conductances, which together determine leaf conductance. Although the movement of pollutants through a boundary layer into the stomata region is known to be important, and even rate limiting in many cases of low wind velocity, its description has been defined from aeronautical concepts and usually relates to smooth surfaces that are not typical of leaf-surface morphology; however, it is nearly the only treatment available (Gates, 1968). Once through the boundary layer, the gas must enter the leaf through the stomata.

The entry or flux of gases through the stomata into a leaf is dependent upon the physical and chemical processes of gas phase and surfaces and has been well-defined. In the past, the internal concentration of O_3 has been assumed to be zero (Laisk et al., 1989), due to early studies that found that virtually no O_3 could pass through a leaf. That was expected because O_3 is extremely reactive with cellular biochemicals. However, a recent study by Moldau and Bichele (2002) indicated that the internal O_3 concentration may not be zero as previous assumed. However, because O_3 has no easily measured isotope, virtually no measurements have been done on an actual dose of O_3, i.e., the amount of O_3 which reacts with individual biochemicals inside the leaf. In addition, only a limited number of studies have measured O_3 concentration or its reaction products within the leaf (e.g., Moldau and Bichele (2002)), and only a few instances of direct measures of O_3 flux to foliage in the field are reported.

Several factors complicate estimates of flux into leaves and at the whole plant and canopy scales. First, in some species, O_3 modifies the opening of the stomata, usually closing it partially, so that the flux rate will change (see next section for more discussion). Secondly, leaves exist as part of a three dimensional canopy. Thus, the relationship of any given leaf to the ambient air is unique so that the amount of O_3 absorbed can vary from leaf to leaf, making it difficult to extrapolate uptake from the level of an individual leaf to that of a whole plant or canopy. Thirdly, O_3 uptake in a plant canopy is a complex process involving O_3 adsorption to surfaces e.g., leaf cuticles, stems, and soil (termed non-stomatal deposition) and scavenging reactions of O_3 with intra-canopy biogenic VOCs and naturally occurring NOx emissions from soils, so that less O_3 is ultimately available for absorption into leaves.

Not surprisingly, as understanding of these complicating factors has grown, the issue of how to characterize and define uptake or flux has received more attention. Specifically, interest has been increasing in recent years, particularly in Europe, in using mathematically tractable flux models for O_3 assessments at the regional and national scale (Emberson et al., 2000a,b). Uptake or flux models have to distinguish between stomatal and non-stomatal components of O_3 deposition to adequately estimate actual concentration reaching the interior of a leaf. Determining this O_3 uptake via canopy and stomatal conductance by necessity relies on models to predict total flux and ultimately the "effective" flux (Grünhage et al., 2004; Massman et al., 2000; Massman, 2004). "Effective flux" has been defined as the balance between the O_3 flux and the detoxification process (Dämmgen et al., 1993; Grünhage and Haenel, 1997; Musselman and Massman, 1999). The time-integrated "effective flux" is termed "effective dose". As described more fully below, and in the CD, scientific understanding of the detoxification mechanisms is not yet complete so that the ability to model this component of flux would require an intensive research effort.

The current state of the science with respect to flux models and their relevance to the standard setting process will be revisited in greater detail in section 7.2.4, on Indices.

7.2.2.2 Reactions of O_3 and possible reaction product(s) at cell surfaces

Ozone diffuses into the leaf air spaces and reacts either 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). Each reaction has the possibility of transforming O_3 into another chemical species (a toxicant) which, in turn, may react with other chemical species and lead to a cascade of reactions.

Within the stomata, gases react with the water at the cell's surface and generate new species with the components within the cell wall region. Although these chemical reactions are poorly understood, some of the fundamentals are known (Heath, 1987, 1988; Wellburn, 1990). Ozone reacts with organic molecules at the double bonds to form carbonyl groups and, under certain circumstances, generates peroxides, including hydrogen peroxides (H_2O_2). The role of hydrogen peroxide as a signaling molecule in plants, is now better understood. One example is its link to the hormone ABA-induced closure of the stomata (Pel et al., 2000). Pel et al. (2000) also found that ABA induced the production of H_2O_2 through Reactive Oxidative Species (ROS) accumulation. This complex interaction between H_2O_2 and ABA could help explain why O_3 would often decrease conductance in some cases, but not always (Heath, 1994b). Other chemicals present in the water phase can lead to many other oxygenated moieties. Each of the steps is generally pH dependent (Jans and Hoigne, 2000; Walcek et al., 1997. Effective detoxification reactions can occur here via antioxidant metabolites and enzymes if they are present at high enough concentrations (Castillo et al., 1987; Matters and Scandalios, 1987).

7.2.2.3 Movement of an O_3 reaction product(s) into the cell with enzymatic or chemical transformation of those products in the cell

It is believed that the initial site of O_3 injury is near or within the plasma membrane. Ozone is soluble in water and once 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. A toxic product of O_3 may migrate through the cytoplast to react with photosynthetic processes, or a spurious signal generated at the membrane may affect some control process or signal transduction pathway (Schraudner et al., 1998; Overmyer et al., 2000, 2003; DeCaria et al., 2000; Rao et al., 2002; Booker et al., 2004; Leitao et al., 2003; Rao and Davis, 2001; Sandermann, 2000; Vahala et al., 2003). Certainly, membrane functions, such as membrane fluidity (Pauls and Thompson, 1980), permeability (Elkiey and Ormrod, 1979), K+-exchange via ATPase reactions (Dominy and Heath, 1985), and Ca^{2+} exclusion (Castillo and Heath, 1990), are changed. The initial sites of membrane reactions seem to involve transport

properties and, possibly, the external signal transducer molecules. It would seem that one of the primary triggers of O_3-induced cell responses is a change in internal Ca^{2+} levels (CD, 2005). The presence of an internal antioxidant would be critical to reduce the concentration of most oxidants.

7.2.2.4 Ozone Initiated Wounding and Pathogen Attack Response

The primary set of metabolic reactions that O_3 triggers now clearly includes those typical of "wounding" responses generated by cutting of the leaf or by pathogen/insect attack. The similarity of wounding responses (Langebartels et al., 1991) and O_3-induced membrane disruption suggests the induction of normal wound-regulated genes (Mehlhorn et al., 1991; Sandermann, 1998). The sequence of the plant response to a pathogen is (1) recognition of the gene products of the pathogen by the plant (elicitor), (2) generation of an immediate phytoresponse to attempt to localize the attack and its products, and (3) generation of a systemic acquired resistance (SAR) to subsequent attack by the pathogen. One aspect of this total response is the production of O_2 and H_2O_2 by the cell (Lamb and Dixon, 1997).

Ozone per se does not generate the H_2O_2, but rather triggers stress-related H_2O_2 formation similar to what occurs in a pathogen attack (ROS reaction). 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. SAR has been heavily investigated, and DNA probes have existed for some time for a series of expressed genes. Several enzyme classes are associated with O_3 injury, including glucanases and peroxidases and others. Thus, strong evidence exists from enzyme function and genetic material that O_3 induces an activation of a SAR-like response.

Ethylene (ET) is another compound produced when plants are subjected to biotic stressors, e.g., attacks by insects, fungi, and bacteria or abiotic stressors such as wounding or environmental stressors such as heat, cold, or oxidative stress and O_3. Increased ET 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-ET correlated well with the degree of foliar injury that developed within hours or days after O_3 exposure. The amount of ET released was exponentially related to the O_3 exposure, with peaks of high O_3 (rather than accumulated dose) generating a higher rate of ET release, at least for a single O_3 exposure under an acute dose. Furthermore, the amount of O_3-induced ET declined with repeated exposure, indicating an acclimatization to O_3. This acclimatization effect associated with repeated wounding has not yet been well described. Thus, one could postulate that O_3 generates a wounding response with a production of ET, which would, in turn, generate a change in stomatal conductance and photosynthesis. Clearly, these multiple events may have confounded some earlier studies.

7.2.2.5 Defense and Compensation Mechanisms

The first line of defense against O_3 is a closure of the stomata to exclude its uptake. This is counterproductive for efficient photosynthesis, but some amount of closure limits the rate of O_3 deposition into the leaf tissue to allow for a secondary line of defense to detoxify the O_3. The secondary line of defense involves a range of antioxidants, including ascorbate, glutathione peroxidase (GSH-Px), and sulfuroxide dimutase (SOD) which are highly reactive to the types of chemicals that can be generated by O_3. The timescales for changes in their levels vary: some rise rapidly, while others rise more slowly. The pattern of changes in these particular proteins varies greatly among different species and conditions.

Since 1996, the role of detoxification in providing a level of resistance to O_3 has been further investigated. For example, most recent reports indicate that ascorbate within the cell wall is the real first line of all defense. Ascorbate is water soluble, present in the solution where O_3 can dissolve, and is highly reactive. Ascorbate concentration declines when the tissue is exposed to O_3 (Luwe et al.,1993; Moldau, 1998), and appears to be closely linked to the amount of O_3 penetrating the leaf tissue. Ascorbate is present within the cell wall, cytoplasm, and chloroplasts (Burkey, 1999; Moldau, 1998); and can move between the cytoplasm and the cell wall with relative ease (Bichele et al., 2000. It is likely that ascorbate is in higher concentration than ET, and that the rate reaction of ascorbate with O_3 would therefore greatly dominate any possible reaction of O_3 with ET.

In spite of the new research, however, it is still not clear as to what extent detoxification can protect against O_3 injury. 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. Although these detoxification and compensation processes divert resources away from other sinks and expend energy, they may counteract the reduction in canopy carbon fixation caused by O_3. The quantitative importance of these processes requires further investigation.

7.2.2.6 Changes to Plant Metabolism

Ozone-related physiological effects within the leaves can 1) inhibit photosynthesis; 2) alter the assimilation of photosynthate and shift its allocation patterns; and 3) can lead to reduced biomass production, growth, and yield (EPA, 1986, 1996a). The working hypothesis is that O_3 which is not eliminated by antioxidants in the cell wall alters the properties of the plasma membrane. Once this membrane disruption occurs, the cell must mobilize repair systems to

overcome the injury. Thus, carbon and energy sources once destined for productivity, must be used in repair processes. Some of these repairs are thought to result from the induction of specific genes.

Photosynthesis is inhibited by exposure to O_3. A large body of literature published since 1996 has further elucidated the mechanism of this effect. Pell et al., 1997 show 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 loss of 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 results of these studies and others suggest that alterations to the dark reactions are much more common than to light reactions (Farage et al., 1991; Farage and Long, 1999).

The rate of leaf senescence has been shown to increase as a function of increasing O_3 exposure. The loss of Rubisco and its messenger RNA is linked to an early senescence or a speeding up of normal development leading to senescence. However, the mechanism of the increased senescence is not known, and, hence, deserves further study. Most studies have shown that O_3 decreases allocation of photosynthate to roots. In some cases, allocation to leaf production has increased. Whether these changes are driven entirely by changes in carbohydrate availability or are controlled by other factors (e.g., hormones) is not known. The loss of productivity is not yet clearly explained. However, several studies provide some insight into possible mechanisms. A study by Grantz and Yang (2000) suggests that O_3 can trigger a plant-wide response that may be linked to alterations in signal transduction and the generation of whole plant signals. Stitt (1996) suggested that "…allocation is regulated by long-distance signals that act to influence growth of selected sinks and to modify the delivery of resources to these sinks in parallel." In addition, Cooley and Manning (1987), citing McLaughlin and McConathy (1983), suggested three possible ways that O_3 fumigation might alter translocation: (1) malfunction of the phloem loading process, (2) increased translocation to leaf injury repair, and (3) an altered balance between the leaf and sinks caused by reduced carbon fixation and a greater demand for assimilate in the leaf. Alternatively, ethylene appears to be able to repress the expression of extracellular invertase, which is critical for control and downloading of sucrose derived from the translocational stream (Roitsch, 1999). More work is needed on the interactions between assimilation, translocation, and source/sink relations with O_3 exposure. In these interactions, one must be aware of the developmental age of the plants and their phytohormonal status.

7.2.2.7 Relationships Between Age and Size and Ozone Response

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 in one year will affect the response of that tree in the next year. This has been called "memory effect", although the term "carry-over" is preferred. 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. 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; U.S. Environmental Protection Agency, 1996) and in roots (Andersen et al., 1991; EPA, 1996a). Accumulation of carry-over effects over time will affect survival and reproduction.

It is important to note that while understanding of how O_3 interacts with the plant at a cellular level has dramatically improved in recent years, the translation of those mechanisms into how O_3 is involved with altered cell metabolism, with whole plant productivity, and with other physiological facts remain to be more fully elucidated.

7.2.3 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.

The 1996 O_3 CD (EPA, 1996) 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, rigorous, systematic investigations of interactions have been rare, and most of the new information is as fragmented as before. This is inevitable, partly in view of the vast scope of the possible interactions between

O_3 and other environmental variables and partly due to the overall lack of funding for research in these areas (EPA, 2005b). Therefore, only a brief overview of the current understanding from this research is provided. The reader is referred to the 1996 O_3 CD and the current draft CD for further information.

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.

7.2.3.1 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. 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.

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. salicylic acid, ethylene and jasmonic acid) and the signaling of these molecules determines in some cases the O_3 susceptibility of plants (CD, 2005). It is unlikely that single genes are responsible to O_3 tolerance responses, except in rare cases (Engle and Gabelman, 1966).

7.2.3.2 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 higher 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. Most of the large number of such interactions that may affect crops, forest trees, and other natural vegetation have yet to be studied. The trend suggested previously that O_3 increases the likelihood and success of insect attack has received some support from recent studies, but only with respect to chewing insects. With the economically important group of sucking insects such as the aphids, no clear trends have been revealed by the latest studies. We are still far from being able to predict the nature of any particular O_3 plant insect interaction, its likelihood, or its severity.

The situation is a little clearer with respect to interactions involving facultative necrotrophic plant pathogens with O_3, generally leading to increased disease. With obligate biotrophic fungal, bacterial, and nematode diseases, there are twice as many reports indicating O_3-induced inhibitions than enhancements. The frequent reports that infection by obligate biotrophs reduces the severity of O_3-induced foliar injury should not be interpreted as "protection", because of the negative effects on the host plant of the disease per se. With obligate biotrophs, the nature of any interaction with O_3 is probably dictated by the unique, highly specific biochemical relationships between pathogen and host plant. 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.

Several studies have indicated that the functioning of tree root symbioses with mycorrhizae may be adversely affected by O_3, but there is also evidence that the presence of mycorrhizae may overcome root diseases stimulated by O_3 and that O_3 may encourage the spread of mycorrhizae to the roots of uninfected trees. The latest studies, therefore, present no clearer picture of the likely nature of simple interactions of O_3 and root symbionts.

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. And the suppression of Ponderosa pine seedling growth by blue wild-rye grass was markedly increased by O_3. However, we are far from being able to predict the outcome of the impact of O_3 on specific competitive situations, such as successional plant communities or crop-weed interactions.

7.2.3.3 Physical Factors

Light, a component of the plant's physical environment, 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 to O_3 of light-tolerant species while decreasing that 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.

Although the 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, abundant evidence indicates that the ready availability of soil moisture results in greater sensitivity to O_3. The partial "protection" against the adverse effects of O_3 afforded by drought has been observed in field experiments and modeled in computer simulations. 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, but, even though the nature of the response is largely species-specific, successful applications of model simulations will lead to larger-scale predictions of the consequences of $O_3 \times$ drought interactions. However, it must be recognized that regardless of the interaction, the net result 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, affects 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.

7.2.3.4 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 contradictory. Some experimental evidence indicates that low general fertility increases sensitivity to O_3, while simulation modeling of trees suggests that nutrient deficiency and O_3 act less than additively; however there are too many examples of contrary trends 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 examime 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 (as discussed in 7.2.3 above) 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, although such interactions cannot be predicted from the component two-way interactions. 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. Although many regions are predicted to experience severe, possibly irreversible, adverse effects due to climate change, beneficial changes may also take place. Findings from the U.S. Global Change Research Program (USGCRP) (NAST, 2000) and related reports illustrate the considerable uncertainties and difficulties in projecting likely

climate change impacts at the regional or local scale. The USGCRP findings also reflect the mixed nature of projected potential climate change impacts, i.e., combinations of deleterious and beneficial effects, for U.S. regions and the variation of projected impacts across different regions. 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.

7.2.4 Effects-Based Air Quality Exposure Indices

The language in sections 108 and 109 of the Clean Air Act indicates that the secondary NAAQS is to specify a level of ambient air quality that when met, will protect the public welfare from any known or anticipated adverse effects associated with the presence of such air pollutant in the ambient air. Since those words were written, the vegetation and ecosystem science has evolved to demonstrate that the presence of a pollutant (O_3) in ambient air is only one of a multitude of factors influencing the likelihood of an adverse vegetation and/or ecosystem effect occurring as a result of exposure to a pollutant. However, since most of the other factors that play a role in regulating the potential impact of an air pollutant on vegetation are outside of human control, except in controlled experiments or heavily managed agricultural settings, it seems reasonable to continue to focus on the potential contribution of anthropogenically derived ambient air concentrations of O_3 in producing adverse effects to vegetation, recognizing that it is not possible to predict for all plants occurring in the U.S. at any given time and ambient pollutant concentration, which and to what degree modifying factors are influencing either the rate of that pollutant uptake from the ambient air or the plant's response to that uptake. Thus, any ambient air quality exposure index will by necessity be a simplification of the actual relationship between pollutant concentrations in the ambient air and plant response. That said, there may be ways to improve upon or more carefully focus the application of existing air quality exposure indices to improve their predictive power.

Most of what is known about vegetation response to O_3 is a result of controlled experiments that sought to minimize the influence of other confounding variables so that a clear O_3 signal could be measured. Experimental exposure profiles were typified by the episodic occurrence of a large number of higher O_3 concentrations. Though not atypical, growth or yield effects may be over- or underestimated in regions of the country where a different type of temporal pattern is prevalent. Therefore, it should be recognized that the conclusions drawn about the importance of different exposure features are heavily influenced by the nature of the experiments conducted.

In the last review, the aspects of exposure known to affect plant response included a) exposure duration (i.e., O_3 effects are cumulative); b) higher concentrations appear to be more important than lower; c) plant sensitivity to O_3 varies with time of day and crop development stage. Exposure indices that accumulate the hourly O_3 concentrations and preferentially weight the higher concentrations had better statistical fits to growth/yield response than did the mean and peak indices. No experiments were conducted to test the performance of these indices in the field. Instead, the testing of adequacy of available indices was accomplished through regression analyses of earlier studies. Therefore, indices selected for further consideration based on the regression analysis were those that could best quantify growth and yield effects in crops, perennials and trees (primarily seedlings) and were cumulative and peak weighted (e.g., SUM06, W126, and AOT40). These indices are also known as "concentration based" as they only consider ambient concentrations in deriving the value of the index.

Other issues raised during the last review regarding the most relevant aspects of exposure for inclusion in an air quality exposure index included the question of the relative importance of cumulative peak (>0.10 ppm) versus mid-range (0.05-0.099 ppm) concentrations, given the concern that higher concentrations do not always occur at the time of maximum plant uptake in the field. This coincidence was considered to be the critical factor in determining peak concentration impacts on plants. Based on evidence at that time, it was not possible to resolve this issue and no experimental studies had addressed this question. A multicomponent index was suggested that combined a concentration-weighted, cumulative index with the number of occurrences of hourly averaged concentrations >=0.10 ppm but no direct experimental studies have been conducted to address the usefulness of this approach in reducing uncertainty. Another element considered was the appropriate diurnal window (e.g., 7, 12 or 24 hours) over which to cumulate exposures. At that time, staff concluded that the 12 hour, daylight period was the most appropriate, and widely applicable based on the information available at that time that the majority of plants, although not all, have significantly reduced stomatal conductance at night, so that the potential for significant impacts from nighttime O_3 exposures was considered low.

7.2.4.1 Concentration-based Forms

Concentration-based air quality exposure indices focus on a particular feature or features (e.g., concentration, duration, and exposure patterns) of the ambient pollutant profile that has been experimentally shown to be predictive of plant response. A few recent studies have focused on the role of these different components of O_3 exposure and have substantiated the earlier conclusions in the 1996 CD and Staff Paper of the importance of higher concentration, shape of the peak, and the episodicity of peak occurrence in eliciting the plant response to O_3 exposure. A few studies have also further clarified the role of nocturnal conductance. Because it has

implications for selecting the appropriate diurnal timeframe over which to cumulate exposures, this latter topic is reviewed in more detail below.

Musselman and Minnick (2000) performed an extensive review of the literature and reported that a large number of species had varying degrees of nocturnal stomatal conductance (Musselman and Minnick, 2000). Although stomatal conductance was lower at night than during the day for most plants, nocturnal conductance could result in some measurable O_3 flux into the plants. In addition, plants might be more susceptible to O_3 exposure at night than during the daytime, because of possibly lower plant defenses at night (Musselman and Minnick, 2000). Nocturnal O_3 flux also depends on the level of turbulence that intermittently occurs at night. Based on their review, Musselman and Minnick (2000) recommended that any O_3 exposure index used to relate air quality to plant response should use the 24-h cumulative exposure period for both exposure-response and effective flux models.

The role of nighttime stomatal conductance and O_3 exposure was demonstrated experimentally as well. Grulke et al. (2003) showed that the stomatal conductance at night for Ponderosa pine in the San Bernardino NF (CA) ranged from 10% to 25% that of maximum daytime gas exchange. In June, at the high-elevation site, 11% of the total daily O_3 uptake of pole-sized trees occurred at night. In late summer, however, O_3 uptake at night was negligible. Birch seedlings exposed to O_3 at night show greater reductions in growth than those exposed to O_3 in daylight (Matyssek et al., 1995). Massman (2004) suggested that nocturnal stomatal O_3 uptake accounted for about 15% of the cumulative daily effective O_3 dose that was related to predicted injury.

A number of findings, however, confound the generalization of the importance of nocturnal exposures. For example, field mustard (Brassica rapa L.) plants exposed to O_3 during the day or night showed little significant difference in the amounts of injury or reduced growth response to O_3 treatment, and the stomatal conductance was 70 to 80% lower at night (Winner et al., 1989). Tissue biomass of Ponderosa pine seedlings was significantly reduced when seedlings were exposed to either daytime or nighttime episodic profiles (Lee and Hogsett, 1999) and the biomass reductions were much greater with daytime peak concentrations than with nighttime peak concentrations. In an evaluation of a very large number of indices that described the O_3 impact on spring wheat, Finnan et al. (1997) did not find any improvement in performance of the cumulative concentration-weighted indices by weighting those concentrations occurring during sunlight hours. Thus, it would appear that the importance of nocturnal conductance is species specific.

7.2.4.2 Flux-based forms

A large number of recent studies have focused on the development of a flux-based index to better relate ambient O_3 to observed vegetation effects. Though a few such studies were published prior to 1996 and reviewed in the 1996 O_3 CD (U.S. Environmental Protection Agency, 1996b), a large body of recent literature has further highlighted and elucidated the multiple controlling factors and complexities (outlined below) that are associated with linking ambient ozone concentrations to observed plant response. Specific factors that influence stomatal uptake and subsequent plant response to O_3 include:

(1) The potential for maximum flux of O_3 into a leaf depends on synchronicity between the timing of peak exposure events and maximal stomatal conductance. In cases where there is disconnect between these two diunal patterns, the predicted effect of the exposure for that species/individual is an overestimation. This concern is especially apparent when assessing the impact of O_3 across all the varied climatic regions and species occurring within the U.S..

(2) Multiple meteorological, species- and site-specific factors influence O_3 uptake. In order to integrate those factors that drive the patterns of stomatal conductance and exposure, some studies use stomatal (Ashmore et al., 2004a) or physiological process-based models (Laurence et al., 2001). However, the species- and site-specific scope of these models limits their usefulness in national or regional scale risk assessments.

(3) Not all O_3 stomatal uptake results in a reduction in yield. This nonlinear relationship between O_3 uptake and plant injury (not growth alteration) response depends to some degree on the amount of internal detoxification occurring with each particular species; species having high amounts of detoxification potential may show less of a relationship between O_3 stomatal uptake and plant response. Because detoxification potential is genetically determined, it cannot be generalized across species. Much more needs to be learned about the detoxification processes available to plants and to what extent they modify the potentially phytotoxic dose in the leaf interior before this factor can be meaningfully considered in a biologically-relevant index.

It is anticipated that, as the overlapping mathematical relationships of conductance, concentration, and defense mechanisms are better defined, O_3-flux-based models may be able to predict vegetation injury and/or damage at least for some categories of canopy-types with more accuracy than the currently available exposure-response models. The results of these studies and reviews indicate the need to continue to develop indices that are more physiologically and meteorologically connected to the actual dose of O_3 the plant receives. The flux approach should

provide an opportunity to improve upon the concentration-based exposure index in the future, recognizing that a concerted research effort is needed to develop the necessary experimental data and modeling tools that will provide the scientific basis for such critical levels for O_3 (Dämmgen et al., 1994; Fuhrer et al., 1997; Grünhage et al., 2004).

7.2.4.3 The Critical Level Approach

Both the concentration-based and flux-based exposure index forms can be used to establish a "critical level" for plant exposure to O_3. One definition of a critical level is "the concentration of pollutant in the atmosphere above which direct adverse effects on receptors, such as plants, ecosystems, or materials may occur according to present knowledge" (UNECE, 1988). As used by the United Nations Economic Commission for Europe International Cooperative Programme (UNECE ICP), the critical levels are not air quality regulatory standards in the U.S. sense, but rather planning targets for reductions in pollutant emissions to protect ecological resources. Critical levels for O_3 are intended to prevent long-term deleterious effects on the most sensitive plant species under the most sensitive environmental conditions, but not to quantify O_3 effects. The nature of the "adverse effects" was not specified in the original definition, which provided for different levels for different types of harmful effect (e.g., visible injury or loss of crop yield). There are also different levels for crops, forests, and seminatural vegetation. The caveat, "according to present knowledge," is important because critical levels are not rigid; they are revised periodically as new scientific information becomes available. To date, critical levels (Level I) have been set for agricultural crops, for foliar injury symptoms in the field and for forest trees (see section 7.2.5 and EPA, 2005b). Level I critical levels are currently used to map and identify areas in Europe in which the levels are exceeded, and that information is then used to plan optimized and effects-based abatement strategies.

In the 1990s, however, many exposure studies demonstrated that the simple, exposure-based approach led to the overestimation of effects in some regions and underestimation in others (Fuhrer et al., 1997; Kärenlampi and Skärby, 1996) because it did not differentiate between plant species, and it did not include modifying site and micrometeorological factors of O_3 uptake such vapor pressure deficit (VPD), water stress, temperature, and light and variation in canopy height. At that time, a decision was made by the UNECE ICP to work towards a flux-based approach for the critical levels ("Level II"), with the goal of modeling O_3 flux-effect relationships for three vegetation types: crops, forests, and seminatural vegetation (Grünhage and Jäger, 2003). Progress has been made in modeling flux (Ashmore et al., 2004a,b) and the Mapping Manual is being revised (Ashmore et al., 2004a,b; Grennfelt, 2004; Karlsson et al., 2003). The revisions may include a flux-based approach for three crops: wheat, potatoes, and cotton. However, because of a lack of flux-response data, a cumulative, cutoff concentration-

based (AOTx) exposure index will remain in use for the near future for most crops and for forests and seminatural herbaceous vegetation (Ashmore et al., 2004a).

7.2.4.4 Summary

From the above discussion, several cautionary statements emerge that must be kept in mind when considering the most appropriate and useful concentration- or flux-based forms for characterizing the air quality that is associated with adverse vegetation effects (e.g., when defining a critical level). First, current understanding of the important components of exposure in eliciting plant response are based on exposure regimes that favored O_3 uptake, contained large numbers of peak concentrations, and closely controlled other environmental factors. In the absence of further study, it is unclear how well indices selected on this basis perform under different exposure and growth scenarios. Second, flux-based models are currently limited by the species-specific information required and by the observed nonlinearity between total flux and plant response. Better understanding of the detoxification and compensation processes would be required to account for this nonlinearity in future models. In some cases, O_3 exposure has been shown to explain O_3 effects as well or better than calculated internal O_3 dose (Grulke, et al. 2002; Hanson et al., 1994).

Other relevant information that should be evaluated include the extent to which: (1) nighttime exposures represent a significant percentage of total diurnal exposures, and whether their impact on growth or foliar injury effects are proportional; (2) elevation and nocturnal turbulence effects may alter actual nocturnal uptake; and (3) plant defense mechanisms and other processes may differ at night, leading to either more or less susceptibility than that associated with daytime exposures. Staff will take into account the expanded evidence on the importance of nocturnal conductance/exposures that has become available since the last review, along with the associated caveats, in its consideration of appropriate averaging time windows.

Until such research can be done, the current draft CD concludes that, at this time, based on the current state of knowledge, exposure indices that differentially weight the higher hourly average O_3 concentrations but include the mid-level values still represent the best approach for relating vegetation effects to O_3 exposure in the U.S.. This is due in part to the existence of a large database that has been used for establishing exposure-response relationships. Such a database does not yet exist for relating O_3 flux to growth response. The draft CD further concludes that the disconnects between period of maximum uptake and peak O_3 occurrence, as well as the potential for nocturnal uptake, should be considered by adding some weighting functions into the currently used exposure indices. Of particular consideration would be their inclusion in regional-to-national estimations of O_3 impacts on vegetation. In evaluating the information now available and described in the current CD, staff will consider whether and how

additional flux/uptake-related factors could be combined with existing cumulative, peak weighted indices in order to develop an air quality index that is a better surrogate predictor of vegetation risk.

7.2.5 Ozone Exposure-Plant Response Relationships

Much of what is 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). These earlier conclusions were derived from basically two types of studies: (1) studies that developed predictive equations relating O_3 exposure to plant response, and (2) studies that compared the effects of discrete treatment level(s) to a control. The advantage of the regression approach is that exposure-response models can be used to interpolate results between treatment levels. During the 1980s, the most commonly used indices for expressing O_3 exposure were 7-, 8-, or 12-h daytime average values over the duration of O_3 exposure, which was often 3 months or somewhat less for experimental studies with crops. Studies into the 1990's also began to use cumulative, peak weighted forms.

(1) Ozone can cause a range of effects, beginning with individual cells, leaves, and plants, and proceeding to plant populations and communities. These effects may be classified as either "injury" or "damage". Injury encompasses 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 yield or the intended use or value of the plant (Guderian, 1977). In contrast, damage includes all effects that 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.

(2) Research results since 1978 did not invalidate EPA conclusions (EPA, 1978, 1986) that foliar symptoms due to O_3 exposures reduce the market value of certain crops and ornamentals where leaves are the product (such as spinach, petunia, geranium, and poinsettia) and that such damage occurs at ambient O_3 concentrations observed in the U.S.. In addition, the results of OTC studies that compared yields at ambient O_3 exposures with those in filtered air and retrospective analyses of crop data also established that ambient O_3 concentrations were sufficient to reduce the yield of major crops in the U.S..

(3) A 3-month SUM06 exposure of 24.4 ppm h, corresponding to a 7-h mean of 49 ppb and a 2HDM of 94 ppb O_3 may prevent a 10% loss in 50% of the 49 experimental cases analyzed by Tingey et al. (1991). A 12-h growing season mean of 0.045 ppb should restrict yield losses to 10% in major crop species (Lesser et al., 1990).

(4) Depending on duration, concentrations of O_3 and SUM06 exposures currently in the United States are sufficient to affect the growth of a number of tree species. Given the fact that multiple-year exposures may cause a cumulative effect on the growth of some trees (Simini et al., 1992; Temple et al., 1992), it is likely that a number of species currently are being impacted, even at ambient O_3 exposures.

(5) Exposure-response functions for 51 cases of seedling response to O_3 (Hogsett et al., 1995), including 11 species representing deciduous and evergreen growth habits, suggest that a SUM06 exposure for 5 months of 31.5 ppm h would protect hardwoods from a 10% growth loss in 50% of the cases studied. A SUM06 exposure of 42.6 ppm h should provide the same level of protection for evergreen seedlings. These conclusions do not take into the account the possibility of effects on growth in subsequent years, an important consideration in the case of long-lived species.

(6) Studies of the response of trees to O_3 have established that, in some cases (for instance, poplars and black cherry), trees are as sensitive to O_3 as are annual plants, in spite of the fact that trees are longer-lived and generally have lower gas exchange rates, and, therefore, lower O_3 uptake.

(7) Use of the chemical protectant, EDU, is of value in estimating O_3-related losses in crop yield and tree growth, provided that care is exercised in establishing appropriate EDU dosages to protect the plants without affecting growth.

Studies conducted since the conclusion of the last review have not fundamentally altered the conclusions stated above. Unfortunately, no single exposure index has been used consistently in the recent literature. Of the cumulative indices that preferentially weight higher concentrations, the SUM06 index has been used most commonly in the U.S. literature, while the use of the AOT40 index has become quite common in Europe. This lack of consistency makes it difficult to compare experimentally derived exposure-response data expressed as AOT40 to ambient U.S. O_3 exposures. The paragraphs below touch on areas where new research has confirmed or expanded the knowledge base that existed in the last review.

(1) Much of the research on the effects of O_3 on growth, biomass, and yield effects in annual and biennial species during the last decade has been conducted in Europe. Substantial effort has gone into developing a Level-I critical level for crops. Based on regression analysis of 15 OTC studies of spring wheat, an AOT40 value of 2.8 ppm·h corresponded to a 5% yield loss (Fuhrer et al., 1997). Because a 4 to 5% decrease could be detected with a 99% confidence level, a critical level of an AOT40 value of 3 ppm·h was selected in 1996 (Kärenlampi and Skärby, 1996).

(2) Several studies during recent decades have 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). Reproductive effects will culminate for seed-bearing plants 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. and that there may be economically important effects of ambient O_3 on the quality of crop and forage species. For example, the yield reductions for soybean are generally similar to those reported previously (EPA, 2005b). Ozone may also reduce the quality or nutritive value of annual species. Foliar symptoms are important if they reduce the marketability of the crop. In Europe, Level I critical levels have been determined for such effects.

(3) During the past 10 years, much of the research in the U.S. has focused on perennial species, including forage crops. 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 for ruminant animal feed at O_3 exposures that occur in some years over large areas of the U.S.. 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 Europe, a provisional critical level for perennials of an AOT40 value of 7 ppm·h over 6 months has been proposed to protect sensitive plant species from the adverse effects of O_3.

(4) A few investigations reported since the last review have examined saplings or mature trees, notably of oak species in the southern Appalachian Mountains and pine species in California. Most of these studies have been of natural (uncontrolled) O_3 exposures. Additional studies have examined foliar symptoms on mature trees, and in recent years such surveys have become more common and with greater attention to the standardization of methods and the use of reliable indicator species (Campbell et al., 2000; Smith et al., 2003). Previous CDs have

noted the difficulty in relating foliar symptoms to effects on individual tree growth, stand growth, or ecosystem characteristics (EPA, 1996a). This difficulty remains to the present day.

(5) Some investigators have suggested that a comprehensive risk assessment of the effects of O_3 on mature tree species might best be accomplished by extrapolating measured effects of O_3 on seedlings to effects on forests using models based on tree physiology and forest stand dynamics (Chappelka and Samuelson, 1998; Laurence et al., 2000, 2001).

(6) An ongoing study was undertaken using a FACE carbon dioxide and O_3 enrichment facility in Rhinelander, WI (Isebrands et al., 2000, 2001). These studies showed that O_3-symptom expression was generally similar in OTCs, FACE, and gradient sites, supporting the previously observed variation among aspen clones (Karnosky et al., 1999).

(7) Many studies have demonstrated that root growth is more sensitive to O_3 exposure than is stem growth. In Finland, reduced root growth was found for a number of clones of silver birch (Oksanen and Saleem, 1999). After 5 years, root growth was decreased by 33%, but shoot growth was not affected by O_3 exposures of a 7-h mean of 15 ppm-h over 5 years in a FACE system (Oksanen, 2001). Data from a long-studied pollution gradient in the San Bernardino Mountains of southern California suggests 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). 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.

(8) European beech was selected for development of a Level I critical level, because data from several studies were available for this species and because deciduous tree species were judged to be more sensitive to O_3 compared to evergreen tree species (Fuhrer et al., 1997; Kärenlampi and Skärby, 1996). A critical level was defined as an AOT40 value of 10 ppm h for daylight hours for a 6-month growing season (Kärenlampi and Skärby, 1996). However, other studies have shown that other species such as silver birch may be more sensitive to O_3 than beech (Pääkkönen et al., 1996).

(9) Recent results support the conclusions of the 1996 CD (EPA, 1996) 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. However, the data suggest that ambient exposures that occur in different regions of the U.S. can sometimes reduce the growth of seedlings of deciduous species. 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.

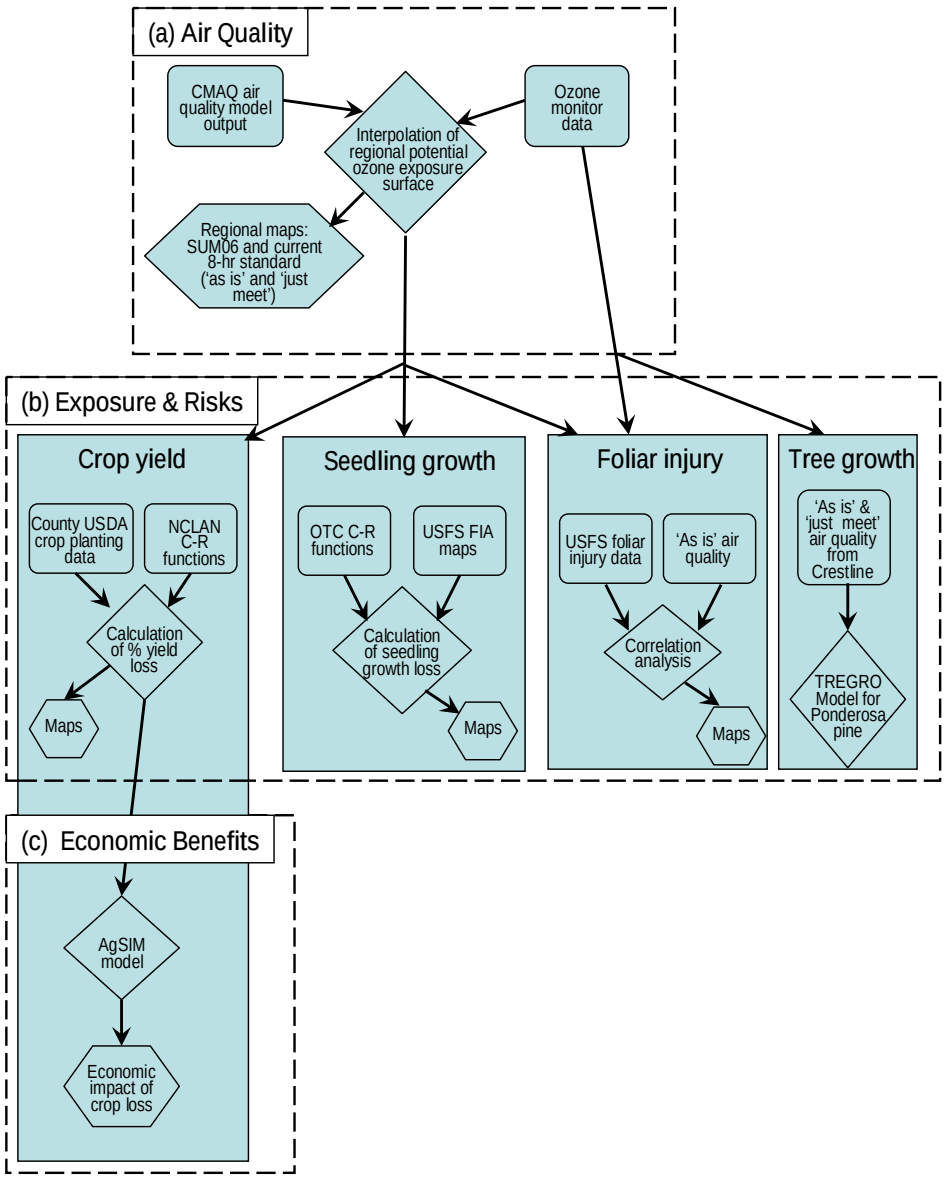
7.3 VEGETATION IMPACT ASSESSMENT

7.3.1 Overview

The planned assessments for the current review are outlined in Figure 7.1(a-c). These assessments build upon the 1996 review and ozone response relationships contained in that review. This section is organized based on each of the main components of the assessment. First, the air quality data, modeling and interpolation analyses that will be input into the rest of the vegetation assessment are discussed. A description then follows of the four areas in which O_3 exposures and impacts will be assessed. The vegetation exposure and risk discussion is divided between the crop and tree analyses. The crop part of the analysis will focus on the estimated effect of current O_3 on crop yield and how this, in turn, affects modeled economic parameters for the agriculture sector. The tree analyses have three parts: (1) seedling growth will be updated to estimate growth loss under estimated 2001 O_3 conditions; 2.) foliar injury will be linked to current monitored and estimated air quality levels; and (3) the TREGRO model will be used to model ponderosa pine growth under recent air quality data and under scenarios where alternative standards are just met. The plans discussed in the following sections take into account the range of views that were expressed during the recent consultation with the CASAC O_3 Panel. Differing views were expressed in some areas by Panel members and the description of the assessments has addressed the comments to the extent possible. Generally the comments were concerned with better characterization of uncertainties in the O_3 exposure interpolation for 2001, O_3 concentration measurements at the height of monitor inlets relative to the actual O_3 concentration at the vegetation height, the continued relevance of C-R functions from NCLAN studies and their incorporation into the agricultural model used in the crop analysis. This first draft Staff Paper acknowledges and seeks to identify all the potentially relevant sources of uncertainty that will be more fully quantitatively and qualitatively characterized in the second draft Staff Paper.

1 Figure 7.1(a-c). Major Components of Planned Environmental Assessment

2



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7.3.2 Air Quality Analysis

To accomplish an assessment of the effects of ambient O_3 exposures on vegetation and ecosystems, it is important to characterize recent O_3 air quality over broad geographical areas of concern. This presents a great challenge since vast rural areas of the U.S., where important crops and natural vegetation occur, do not have O_3 monitors. Thus, staff is currently evaluating a variety of approaches for estimating potential O_3 exposures in these non-monitored areas. Three main approaches available for characterizing ozone exposures in non-monitored areas are: (1) use of sophisticated models of air quality to model the entire U.S.; (2) use of data collected from monitors to interpolate non-monitored areas; and (3) combining monitored and modeled information into an interpolated surface. The section below describes the main approach staff plans to use to combine monitored observations and modeled O_3 predictions from CMAQ to estimate O_3 exposures in many areas as possible. Staff also intends to evaluate a whether interpolation without modeled data would be adequate in areas with relatively dense monitoring coverage. As suggested during the CASAC consultation, staff will also interpolate across smaller, more homogeneous regions rather than across the entire contiguous U.S. The staff also plans to rely on monitoring data where possible (see sections 7.2.4)

7.3.2.1 Monitor coverage

EPA monitored data is currently available through 2004. The monitored hourly O_3 data is available from two 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 7.2a-b and are described in section 2.3.1 and 2.3.2 of Chapter 2. The AQS monitoring network currently has over 3000 monitors measuring O_3 concentrations and monitors are generally sited near population centers. However, there are approximately 36 monitored 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. (see Figure 7-2b).

During the recent CASAC consultation, the question was raised about how O_3 concentrations measured by the monitoring network compare to concentrations occurring at the surface of vegetation. 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 other surfaces on the ground and can create vertical gradient of decreasing O_3 concentration from the inlet height of the monitors to the surface of vegetation and crops (Regener, 1957). The magnitude of the gradient is determined by the intensity of turbulent mixing in the surface layer. During the daytime hours the vertical O_3 gradient is relatively small because turbulent mixing maintains the downward flux of O_3. For

example, Hovath 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 Germany. This is compared to a 20% decrease during stable conditions which usually occur during the night. While staff acknowledges there is likely to be bias in using O_3 data from inlets of ambient monitors to characterize O_3 exposures close to the surface, this bias is likely to be relatively small under typical turbulent mixing during the day. The day-time versus the night-time bias is an important distinction considering the assessments outlined below will rely heavily on daytime metrics such as the12hr SUM06.

7.3.2.2 Modeling tools

Staff plans to use O_3 outputs from the EPA/NOAA CMAQ model system (http://www.epa.gov/asmdnerl/CMAQ, Byun and Ching, 1999; Arnold et al. 2003; Hogrefe et al. 2004; Eder and Yu, 2005) to spatially scale an interpolation of O_3 monitoring data for different regions of the U.S.. The CMAQ modeling system has undergone two external peer reviews through the Community Modeling and Analysis System (CMAS) based at the University of North Carolina at Chapel Hill (UNC) Carolina Environmental Program (Amar et al. 2005, 2004). 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, PM, and nutrient deposition) holistically. The CMAQ model incorporates output fields from emissions and meteorological modeling systems and several other data sources through special interface processors into the CMAQ Chemical Transport Model (CCTM). Currently, the Sparse Matrix Operator Kernel Emissions (SMOKE) System produces the emissions factors and the Fifth Generation Penn State University/ National Center for Atmospheric Research Mesoscale Model (MM5) provides the meteorological fields. CCTM then performs chemical transport modeling for multiple pollutants on multiple scales.

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 currently only available for limited years. Currently, 2001 outputs from CMAQ version 4.5 are 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. Emission inventories of SO_2, CO, NOx, and VOCs are based on EPA's 2001 National Emission Inventory (NEI) and are consistent with inventories

used for the analysis of the Clean Air Interstate Rule (CAIR) rule (EPA, 2005c). Biogenic emissions were processed using the Biogenic Emissions Inventory System (BEIS) version 3.13. The staff recognizes that O_3 exposures vary between years depending on meteorology and other factors. Therefore, staff will add additional years for comparison if more CMAQ outputs become available.

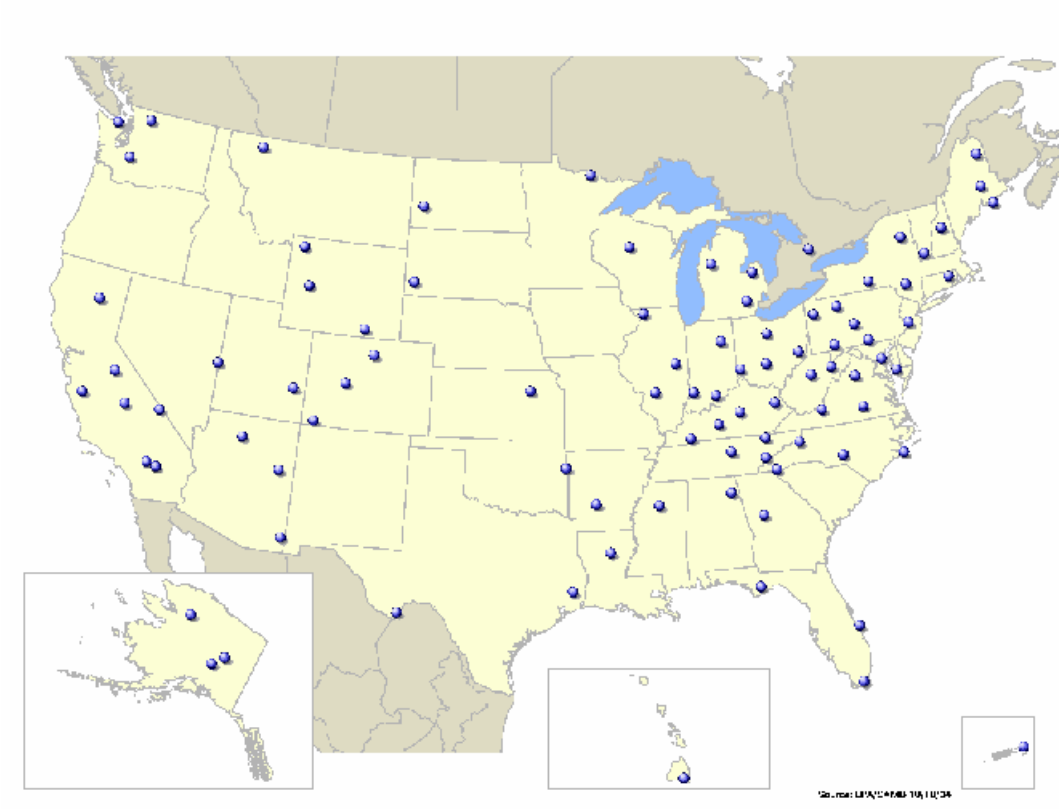
Recently EPA/NOAA conducted an initial evaluation of the eastern U.S. domain of CMAQ version 4.5 (Appel et al., 2005; http://www.cmascenter.org/docs/CMAQ/v4.5/CMAQv4.5_EvaluationDocument-Final2005.pdf). This evaluation used the same metrics published by Eder and Yu (2005) for the CMAQ version 4.4 model release. For the modeled summer months of June, July and August of 2001, CMAQ version 4.5 predictions were compared to AQS monitor sites. The prediction of daily 8hr-max O_3 was relatively good, showing a slight positive normalized mean bias of 1.62% and a normalized mean error of 17.4%. Hourly ozone patterns are predicted well during the daytime. However, the CMAQ consistently over-predicted hourly O_3 at night. Nighttime over-predictions in O_3 have been improved over CMAQ version 4.4 by modifications to the minimum K_z approximation in CMAQ version 4.5, but additional investigations are needed. Again, since many of the assessments outlined below rely daytime O_3 accumulated in the 12hr SUM06 (8AM-8PM), the night-time over-prediction is less of an issue. Overall, CMAQ predictions of daily 8hr O_3 averages were improved in the 12km x 12km grid size when compared to the 36km x 36km grid size.

Since CMAQ output is averaged over large square blocks and monitor observations are effectively averages over much smaller regions, CMAQ output and monitor observations have a mismatch in spatial resolution. (Fuentes and Rafferty 2005). The problem is well known, but is often ignored since there are not standard operational methods that can be applied to the CMAQ model output to deal with this problem. The CMAQ version 4.5 evaluation described above ignores the mismatch of spatial resolution and treats CMAQ output as a point-value. The staff believes this simplification is reasonable because O_3 is a secondary pollutant and its concentration generally varies fairly smoothly in flat rural areas where important crops and vegetation grow. However, O_3 is notably variable in complex terrain, across in urban/rural gradients and along coastal areas. In these cases significant differences in O_3 concentration could occur with a 12x12km call and the uncertainties associated with areas are unknown. The current assessment is most concerned with rural areas and it is recognized that any estimates of O_3 exposure in complex terrain are very uncertain.

Figure 7.2 Locations of AQS monitors (top) and CASTNET monitoring stations

a.

b.



7.3.2.3 Generation of Potential Ozone Exposure Surfaces

Staff will interpolate O_3 exposures on a regional basis rather than a continuous surface for the US. The result of these interpolations will be the creation of regional Potential Ozone Exposure Surfaces (rPOES). First staff will separate the eastern and western regions of the U.S. based on the 12km and 36km CMAQ model domains. The eastern domain will be partitioned into homogeneous sub-regions as defined by Eder et al. (1993). For the western domain, staff will follow the subregions as defined by Lee et al (2001).

To estimate a rPOES for different regions of the contiguous U.S., staff plans to primarily use the interpolation module in BenMAP, which uses the enhanced Voronoi Neighbor Averaging (eVNA) interpolation method to combine monitored data with spatial scaling from CMAQ model outputs (see appendix C.3.2 of http://www.epa.gov/ttn/ecas/models/modeldoc.pdf). This method employs inverse-distance weighting of monitoring data scaled by the CMAQ model. This method makes the implicit assumption that CMAQ adequately characterizes the general spatial pattern of O_3 exposures. It also retains the true monitored values at monitored sites. Exceptions to this approach might be warranted in certain cases. For example, in areas with fairly dense monitor coverage (e.g., northeastern U.S.) staff will investigate whether interpolation without spatial scaling would be a satisfactory. Likewise, in areas of the country with little or no monitor coverage, where an interpolation would depend on data from distant monitors that may have very little correlation with the true O_3 exposure at the unmonitored cell, staff is evaluating the benefit of identifying criteria that could be used to define the appropriate spatial "window" within which monitored sites can be used to interpolate values for the non-monitored area and/or whether it is more suitable in these cases to use CMAQ modeled O_3 exposures only, instead of relying on interpolated O_3 values. At a minimum, staff plans to generate the rPOES in terms of both the 12-hr (8 am to 8 pm), maximum 3-month SUM06 index and the 8-hr average index that reflects the form of the current secondary standard.

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 ozone exposure estimate. This limitation will be noted when results are presented in the second draft of the staff paper. It is expected that this eVNA with spatial scaling from CMAQ approach will be an improvement over a simple interpolation between monitors that does not use spatial scaling from an air quality model. The interpolation technique will be run without spatial scaling to test this expectation and to determine if interpolation without CMAQ scaling could be used to characterize O_3 exposures in regions with relatively dense monitoring coverage. This will allow for characterization of ozone exposures in other years besides 2001. Finally, the uncertainties associated with estimating exposures at non-

monitored areas will be quantified by removing a subset of monitors and interpolating the missing monitors with the remaining data.

During the recent CASAC consultation, the question was raised as to whether other approaches, such as kriging, would be appropriate for the interpolation of O_3 exposures in non-monitored areas. The eVNA approach outlined above is simple, but does not allow for calculation of the model error in the same way kriging does. While staff agrees that kriging may be an appropriate interpolation method in general, it is not available as an option in the BenMAP model that will be used for this assessment.

7.3.2.4 Alternative Air quality scenarios

The following air quality scenarios will be generated:

- "As is" air quality (using base year 2001)
- Meeting the current standard: 4th highest daily maximum 8-hr average of 0.084 ppm
- Meeting alternative O_3 standards

In conjunction with work being done as part of the health risk assessment, the quadratic air quality adjustment that was used in the last review will be used to simulate just meeting the current and alternative standards (Johnson, 1997). 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. EPA has recently evaluated the implementation of this method on a subset of monitors and found that when this method is used to roll-back O_3 values from "high" years, it yields a similar distribution of hourly O_3 values to that of "low" O_3 years (Rizzo, 2005). Further, the quadratic method performs better than proportional and peak-shaving methods when compared to monitor data. In addition, EPA NHEERL-WED lab is conducting an evaluation of the quadratic method for the rural Crestline monitor in the San Bernardino Mountains of Southern California. Results of that evaluation will be included in the next draft Staff Paper.

7.3.3 Crop Risk/Benefits Assessments

In light of a number of developments since the last review, including the potential to better characterize O_3 exposures in crop growing regions using the CMAQ model, changes in air quality, updated crop planting information, and an alternative agricultural economic model that reflects the most up-to-date market forces, staff plans to update the previous review's crop risk and economic benefits assessments in order to better evaluate the adequacy of the level of protection afforded by the current standard.

One element of the analysis that has not changed since the last review is the source of the crop yield loss concentration response (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 and were studied under a variety of unique combinations of sites, water regimes, and exposure conditions, producing a total of 54 separate cases. According to the most recent USDA National Agricultural Statistical Survey (NASS) data, these 12 species 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 61% of principal crops acreage planted.

Since the NCLAN studies were performed in 1980-1988 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 ozone tolerance under natural conditions. Since the last review there has been little evidence that crops are becoming more tolerant or more sensitive to ozone (EPA, 2005b). Crops are bred for higher yield and this may even make them more susceptible to O_3 through higher stomatal conductance. In cotton, some newer varieties have been found to have higher yield loss to ozone 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). Given the limited amount of information available on the O_3 sensitivity of current cultivars of different crops, staff plans to focus this analysis most heavily on crops (such as soybean, cotton, and wheat) with information on O_3 sensitivity of different cultivars.

[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)

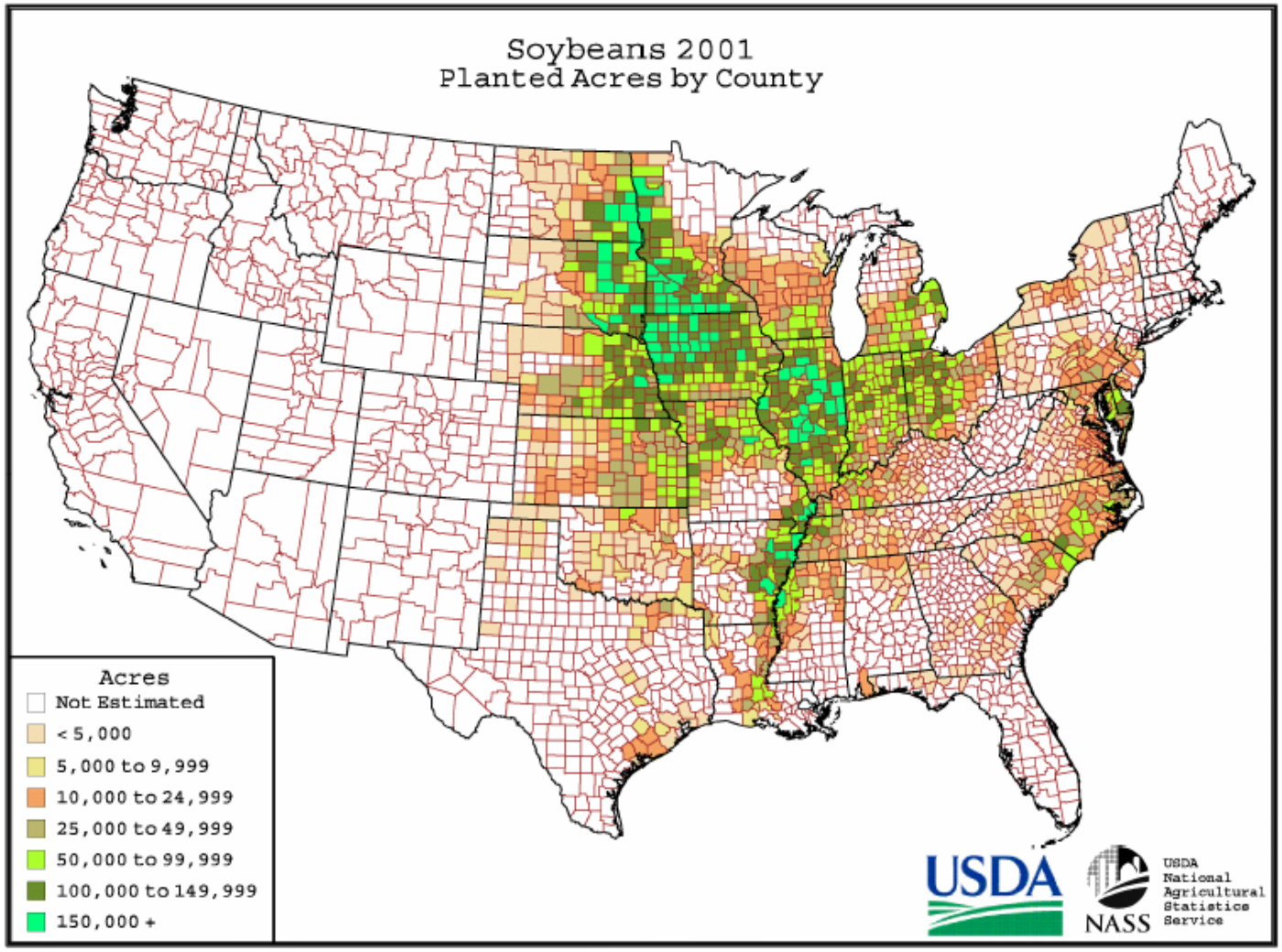
7.3.3.1 Exposure Assessment

In the last review, C-R functions were developed in terms of the SUM06 and W126 indices for most NCLAN crops (Lee and Hogsett, 1996). Currently, work is underway to re-analyze the NCLAN database to recalculate the C-R functions in terms of an 8-hr average index. Specifically, staff plans to plot relative crop yield loss against an 8-hr average index calculated from the 1-hr averages contained in the NCLAN database. The benefits of this re-analysis are two-fold: (1) it permits evaluation of the appropriateness of the 8-hr average index for predicting growth effects of the NCLAN studies as compared to a SUM06 index, and (2) it permits direct evaluation of estimated yield effects expected to occur under air quality scenarios expressed in terms of the current 8-hr, 0.08 ppm standard level.

7.3.3.2 Crop yield loss Assessment

County-level crop planting data will be obtained from USDA-NASS (National Agricultural Statistics Service; http://www.usda.gov/nass) for 2001 for each NCLAN crop as available (Figure 7-3). This information will be used to create GIS maps containing the planting data for each species/cultivar of commodity crop. Staff plans to overlay the rPOES (as discussed in section 7.3.2) with GIS maps of the crop growing regions and then calculate yield loss using the relevant C-R functions. This combination of data will result in an estimate of county-level percent yield loss for each selected NCLAN crop. Staff plans to create GIS maps of percent yield loss of each crop for the counties in which they were planted in 2001. This analysis will also be performed for just meeting the current standard and other alternative standards. The change in crop county-level percent yield loss estimates between 'as is' 2001 air quality and meeting various standards will serve as inputs to the AGSIM agricultural economic benefits model.

Figure 7.3 Range of planted soybean for the year 2001



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7.3.3.3 Economic Benefits Assessment – AGSIM

The Agriculture Simulation Model (AGSIM) model (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 will be performed before running the 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. Initially, AGSIM will be used to calculate the economic benefits of yield changes between the 'as is' and 'just meet' scenarios for base year 2001. This approach will also be used to calculate benefits from any alternative standards under consideration. If data are available, the same analysis will be performed using air quality data from other years. Information will be used from a range of crop cultivars as they are available for each crop. This will allow for some bounding of possible effects of tolerant and sensitive cultivars.

7.3.4 Tree Seedling/Mature Tree/Forest Species Quantitative/Qualitative Risk Assessments

In the last review, 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, 2005b). Section 7.2.4.1 outlines plans to re-analyze the OTC C-R functions in terms of an 8-hr average index. Section 7.2.4.2 describes how staff plans to update the tree seedling risk analysis performed in the last review. Section 7.2.4.4 discusses the planned approach for modeling O_3 impacts on mature trees. Section 7.2.4.3 discusses the planned approach for assessing O_3 effects on vegetation in natural settings using visible foliar injury data. 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.

[2] For example, AGSIM© has been used in EPA's prospective study of the benefits deriving 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.

7.3.4.1 Selected Species Exposure Assessment

Similar to crops (section 7.3.3), C-R functions for tree seedling biomass loss due to O_3 exposures have not been reported in terms of an 8-hr average index. Staff plans to re-analyze the 11 OTC tree seedling C-R functions described in the 1996 O_3 Staff Paper in terms of the current 8-hr exposure metric. This re-analysis will enable staff to evaluate the appropriateness of using an 8-hr average index as a predictor of tree seedling growth/biomass losses and to directly evaluate estimated seedling biomass loss values expected to occur under air quality exposure scenarios expressed in terms of the current 8-hr, 0.08 ppm secondary standard.

7.3.4.2 Selected Tree Seedling Biomass Loss

In the 1996 O_3 Staff Paper, information on tree species growing regions was derived from the USDA Atlas of United States Trees (Little, 1971). Staff plans to use more recent information from the USDA Forest Service FIA database in order to update tree growing ranges for the 11 tree species studied by NHEERL-WED. In a process similar to that used for crops staff plans to combine the POES with the C-R function for each of the tree seedling species and information on each tree species growing region to produce estimates of biomass loss for each of the 11 tree seedling species. From this information, staff plans to generate GIS maps depicting these results for each POES scenario.

7.3.4.3 Foliar Injury Incidence/Epidemiology – FIA Data

Since the last review, there have been large amounts of data generated regarding visible foliar injury to native plant species resulting from ozone exposure. The current draft CD discusses the breadth of this new information.

Foliar injury is a valuable indicator of phytotoxic concentrations of ozone in ambient air which, at high enough concentrations, can have wide ranging effects from altering plant fitness and aesthetics, possibly altering species composition of natural systems, and reducing the marketability and yield of commercially valuable species. The degree of visible foliar injury is dependent on a range of environmental and genetic factors and may vary widely even among co-members of a population at similar exposure levels. While sensitivity to ozone may vary considerably between and within taxonomic groups, common patterns of injury have been discovered. There are generally four types of lesions that form on leaves and needles as a result of ozone exposure in sensitive species: pigmented lesions (stippling), surface bleaching, bifacial necrosis, and chlorosis.

The Unites States Forest Service, first as the Forest Health Monitoring Program (FHM) and then as the Forest Inventory and Analysis (FIA) Program, has been collecting data since 1990 regarding the incidence and severity of visible foliar injury to several plants throughout the U.S. shown to be sensitive to ozone (Coulston et al. 2003, 2004; Smith et al. 2003). This injury

has been well documented as an effect of ozone on these species and is as such a useful indicator of elevated ozone concentrations. Biomonitoring sites are located throughout the country and analysis of foliar injury within these sites follows an established and rigorous protocol which records the incidence of characteristic stippling on the leaves of species known to exhibit sensitivity to ozone. The relative severity of injury is calculated based on the percentage of leaves showing characteristic injury for multiple individual plants of several species per site. These values are then used to give Biotic Index values for each site and each species for each year (Smith et al., 2002).

Staff intends to compare the incidence and severity of visible foliar injury attributable to ozone with available EPA maps of counties considered to fall below the level of the current 8hr., 0.08 ppm secondary ozone standard (See Figure 7.4) for the same period to determine the extent to which foliar injury continues to occur at levels below the current standard. Because the EPA definition of attainment for these counties incorporates a three-year average of ambient air concentration that does not capture year-to-year changes in ozone concentrations, this analysis will compare year-to-year data to account for anomalous years in the ambient average. Similarly, staff will also compare yearly county-level 12-hour SUM06 to incidence of foliar injury (See Figure 7.5). Particular attention will be paid to visible foliar injury in national parks (Class I areas) and other areas of aesthetic interest since the perception of visible injury in these areas may be more valued by the public.

Interpolation of ozone monitors for 2001will be done using the CMAQ model for spatial scaling. This potential ozone exposure surface (rPOES), as described in section 7.2.2, will then be used to determine the amount of correlation between modeled O_3 exposures, interpolated FIA O_3 exposures, and visible foliar injury as measured in the FIA data for that year. If a close correlation exists, further analysis of foliar injury for additional years using FIA interpolated ozone values may be possible using site or species specific data to determine the extent of impacts under the current ambient air quality. An analysis of this exposure surface will also compare the degree to which the POES generated by EPA predicts relative changes in the severity of foliar injury.

Important uncertainties associated with this approach of comparing O_3 exposures to foliar injury data include the following:

- The monitoring protocol used by the FIA changed significantly between the 2001 and 2002 data collection seasons. These changes added to the robustness of the data set and increased the number of sites and species for which visible foliar injury is collected. Due to the availability of CMAQ data, EPA must use 2001 data to generate the POES. Since the FIA data for 2001 is concentrated in the northeast and north-central regions of the US, those are the regions for which a comparison can be made.

- The geographical locations of the FIA biomonitoring sites are considered confidential by the Forest Service. The data provided to EPA may have the coordinates "fuzzed" up to 8.5 miles to maintain this confidentiality. This introduces some error in determining the actual location of the foliar injury with relation to county boundaries and relative elevations.
- The SUM06 values calculated by the FIA program include all air quality monitors in the AQS but do not include CASTNET monitors. In addition, the elevation of the monitors has not been considered.

Figure 7.4 County-level 4ht highest maximum 8-hour averages for 2001

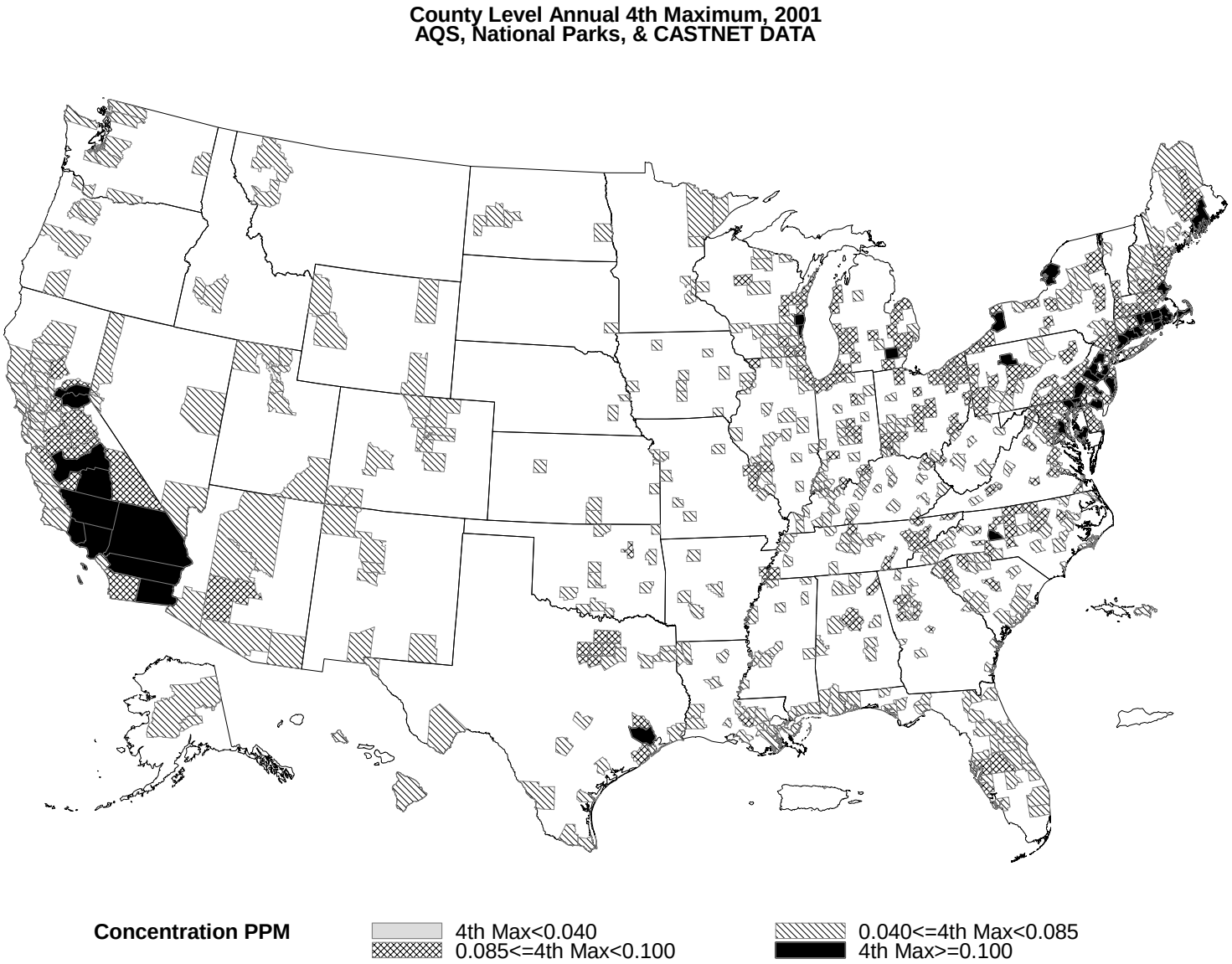
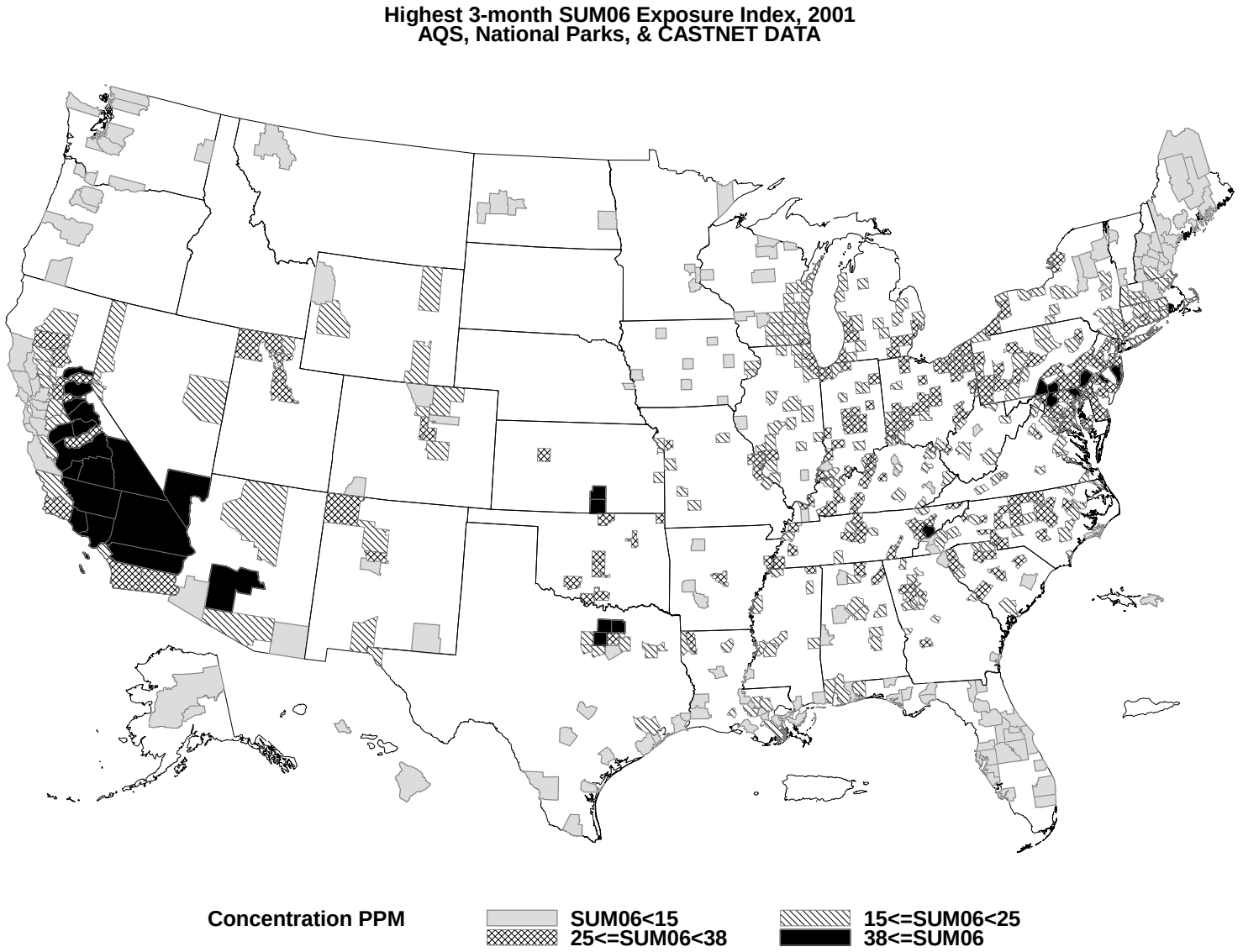


Figure 7.5 County-level max 3month 12-hour SUM06 for 2001



7.3.4.4 Ponderosa Pine case study for mature tree

In the 1996 O_3 Staff Paper, analyses on trees were limited to the seedling growth stage. 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. Therefore, in order to go beyond the seedling stage, staff is planning to use a tree growth model 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 ponderosa pine. This method offers a means to evaluate effects on mature trees capturing the interaction of O_3 uptake climate and meteorology.

A tree growth simulation model, TREGRO (Weinstein et al, 1990) 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/metorology interactions on several species of trees in different regions of the US (Tingey et al., 2001; Weinstein et al., 1991; Retzlaff et al., 2000; Laurence et al., 1993; Laurence et al., 2001; Weinstein et al., 2005). Staff is collaborating with the EPA NHEERL-WED lab to use the TREGRO to assess long-term ponderosa pine growth at the Crestline site in the San Bernardino Mountains of California associated with 'as is' air quality, and air quality adjusted to just meet alternative O_3 standards. 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 this site to simulate ponderosa pine growth over time with the improving air quality using TREGRO (Tingey et al., 2004).

Staff and NHEERL-WED scientists plan to use Crestline air quality and climate data from the years 1995 to 2000 and 1980 to1985. The years 1980 to 1985 will be used to represent "bad" air quality years and 1995 to 2000 will represent recent improved air quality. Air quality from each year will be rolled back using the quadratic method to 'just meet' the current 8-hr secondary standard (4^{th} highest maximum average = 0.08ppm). TREGRO will be 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. The differences between growth under 'just meet' air quality and "as is" air quality will be compared and allow for the evaluation of the potential effectiveness of the current secondary standard in protecting ponderosa pine as an ecological resource. The comparisons between the annual average biomass change under the two different 6 year periods (1980-1985 and 1995-2000) will allow staff to evaluate the additional potential benefits from the current 8-hour standard compared to the indicated improved growth achieved with the previous secondary standard put into place in the late 1970s.

7.4 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, 2005b). 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 the 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. Ecosystems 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 mankind, 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.

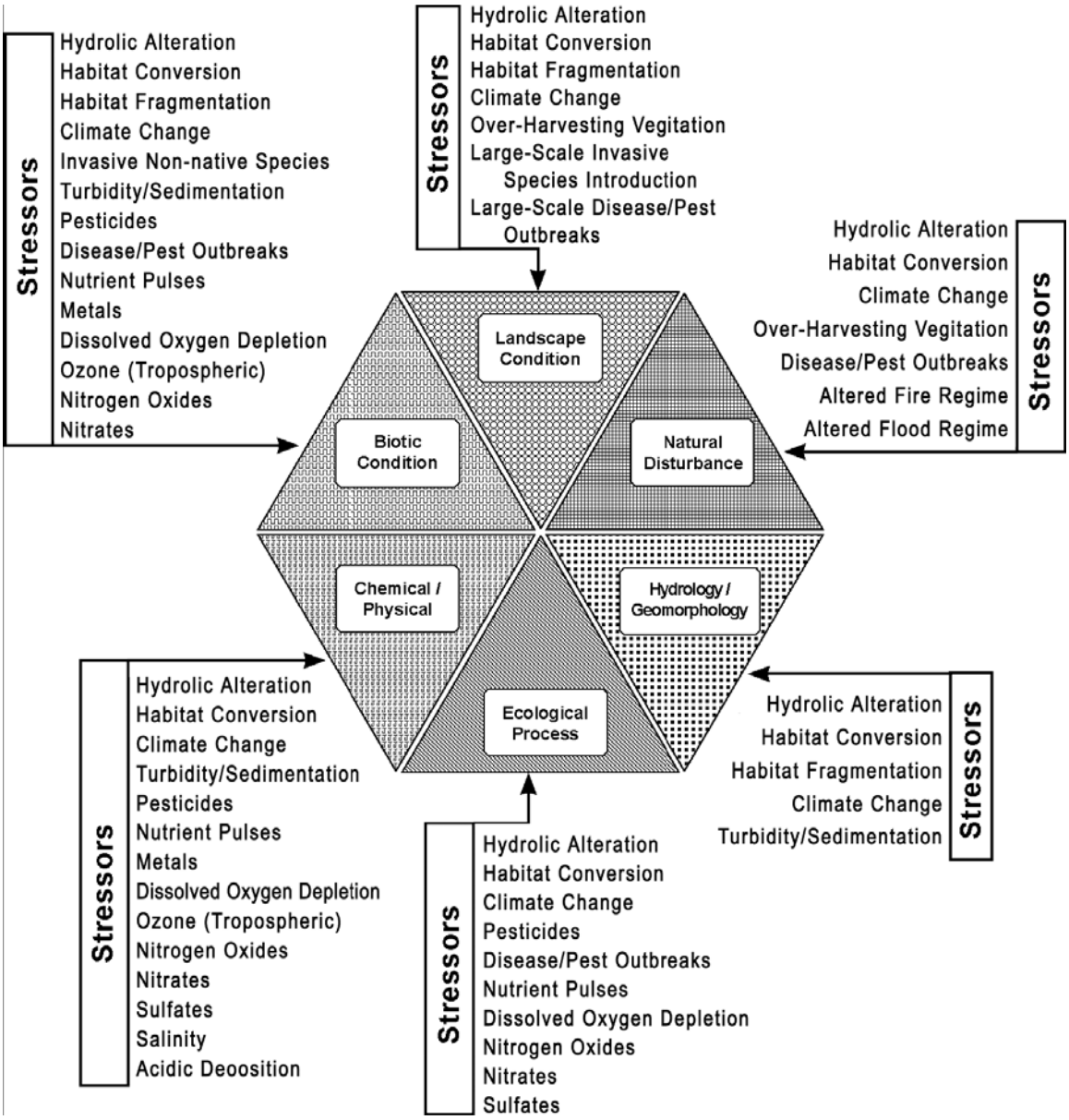
Figure 7.6 outlines the how common anthropogenic stressors, including tropospheric O_3, might affect the essential ecological attributes outlined by the SAB.

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, 2005b). 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 7.3.4.3 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, 2005b) 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 7.6 Common anthropogenic stressors and the essential ecological attributes they affect. Modified from Young and Sanzone (2002)



7.4.1 Evidence Demonstrating the Potential for Ozone to Alter Ecosystem Structure and Function

The seven case studies listed in the draft CD demonstrate the potential for O_3 to alter ecosystem structure and function. The oldest and best 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). 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 most well-documented studies of population and community response to O_3 effects are the long-term studies of sunflower (*Plantago major*) in native plant communities in the United Kingdom (Davison and Reiling, 1995; Lyons et al., 1997; Reiling and Davison, 1992c). Sensitive populations of sunflower had significant growth decreases in elevated O_3 (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 sunflower 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 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.

7.4.2 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 two important ecological services.

7.4.2.1 Carbon Sequestration

Terrestrial ecosystems are important in the Earth's carbon (C) balance and potentially have a role in offsetting emissions of CO_2 by humans. 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). CO_2 enters vegetation through stomates and is used in photosynthesis to produce carbohydrates that form plant tissues. 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 amount of net productivity and C sequestration of the individual plants and entire ecosystems. One issue in the O_3 effects on C sequestration is the interaction of rising O_3 pollution and rising CO_2 concentrations in the coming decades. Models generally predict that in the future C sequestration will increase with increasing CO_2, but often there is not an accounting of the decrease in productivity due to the local effects of tropospheric O_3. In some cases, 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). Another issue, separate from the stimulation of productivity by CO_2, is how O_3 is currently affecting C sequestration. In a study including all ecosystem types, Felzer et al. (2004), estimated that US Net Primary Production (NPP) 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. 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).

7.4.2.2 Water Resources

At present, there are no publications on the effects of O_3 exposure that are carried through at the ecosystem level to changes in mass water flow, channel morphology, riparian habitat complexity, or sediment movement. It is possible that processes occurring at smaller scales are affecting geomorphological processes in ecosystems; however, difficulties in scaling these responses spatially and temporally have made this challenging to show experimentally. It is possible that O_3 exposure affects water quality through changes in energy and material flows. One mechanism for how the amount of water quantity may be affected by O_3 exposure at the landscape level is through loss of tight stomatal control. Moderately high O_3 exposure may affect the mechanism of stomatal opening (McAinsh et al., 2002), resulting in sluggish stomatal opening and closing (Reich and Lassoie, 1984). During moderately high O_3 exposure in a drought year, canopy transpiration was greater for yellow poplar than on adjacent days with lower O_3 exposure, which could alter water use at the landscape level. Oxidant exposure (O_3 and NOx) may decrease the ability of exposed plants to close stomata at night (Grulke et al., 2004), thus increasing water loss from the landscape. Ecosystem models should aid in interpreting O_3-exposure effects at the landscape level.

7.4.3 Research needs

The knowledge base for examining the range of ecological effects of O_3 on natural ecosystems has changed little from the last review, however there is currently greater recognition that ecosystem response to ozone needs to be examined in a more holistic way that include recognition of important ecosystem services and how to quantify and value changes to these services. Below are listed areas of research that would improve our understanding of the role of ozone, and how important ecosystem attributes may be protected. For example, there is a need for information on the following ecosystem-level responses***:***

- *Ecosystem Processes*. Little is known about the effects of O_3 on water, C, and nutrient cycling, particularly at the stand and community levels. Effects on below-ground ecosystem processes in response to O_3 exposure alone and in combination with other stressors are critical to projections at the watershed and landscape scales. Little is yet known about the effects of O_3 on structural or functional components of soil food webs, or how these impacts could affect plant species diversity (Andersen, 2003).
- *Biodiversity and Genetic Diversity*. The study of genetic aspects of O_3 impacts on natural ecosystems has been largely correlational in nature and it remains to be shown conclusively whether O_3 affects biodiversity or genetic diversity (Davison and Barnes, 1998; Pitelka, 1988; Winner et al., 1991). Studies of competitive interactions under

elevated O_3 levels are needed (Laurence and Andersen, 2003), and reexamination via new sampling of population studies to bring in a time component to previous studies showing spatial variability in population responses to O_3 are needed. These studies could be strengthened by modern molecular methods to quantify impacts on diversity.

- *Natural Ecosystem Interactions with the Atmosphere*. Little is known about feedbacks between O_3 and climate change on VOC production, which in turn, could affect O_3 production (Fuentes et al., 2001). At moderate-to-high O_3 exposure sites, aberrations in stomatal behavior could significantly affect individual tree water balance of sensitive trees, and if the sensitive tree species is dominant, hydrologic balance at the watershed and landscape level could be affected. This has not been addressed in any model because O_3 exposure effects, if included in the modeling effort have assumed a linear relationship between assimilation and stomatal conductance.

- *Below-Ground Interactions*. While the negative effects of O_3 on below-ground growth are well characterized, interactions of roots with the soil or microorganisms are not.

- *Other Interactive Effects*. Interaction studies with other components of global change (e.g., warming, increasing atmospheric CO_2, N deposition) or with various biotic stressors are needed to better predict complex interactions likely in the future (Laurence and Andersen, 2003). Whether O_3 will negate the positive effects of an elevated CO_2 environment on plant carbon and water balances is not yet known; nor is it known if these effects will scale up through the ecosystem. How O_3 might affect the progress of pest epidemics and insect outbreaks as concentrations increase is unclear (Ball et al., 1998).

- *Reproduction Effects*. Information concerning the impact of O_3 on reproductive processes and reproductive development under realistic field or forest conditions are needed, as well as examination of reproductive effects under interacting pollutants (Black et al., 2000).

- *Comparative Extrapolation*. The vast majority of O_3 studies of trees have been conducted with young, immature trees and in trees that have not yet formed a closed canopy. Questions remain as to the comparability of O_3 effects on juvenile and mature trees and on trees grown in the open versus those in a closed forest canopy in a competitive environment (Chappelka and Samuelson, 1998; Kolb and Matyssek, 2001; Samuelson and Kelly, 2001).

- *Scaling-Up Issues*. Scaling the effects of O_3 from the responses of single or a few plants to effects on communities and ecosystems is a complicated matter that will 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. Linking these various studies via impacts on common research quantification across various scales using measures of such factors as leaf area index or spectral reflective data, which could eventually be remotely sensed (Kraft et al., 1996; Panek et al., 2003), would provide powerful new tools for ecologists.

- *Comparative Risk Assessment Methodologies*. Methodologies to determine the important values of services and benefits derived from natural ecosystems such that

these could be used in comprehensive risk assessment for O_3 effects on natural ecosystems (Heck et al., 1998).

- *Economic Valuation*. There is a critical need for research to support the development of methods to value ecosystem services affected by O_3 in order to estimate the potential economic and non-monetized benefits accruing from O_3 reductions.

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Appendix 3A. Ozone Epidemiological Study Results: Summary of effect estimates and air quality data reported in studies, distribution statistics for 8-hr daily maximum ozone concentrations for the study period and location, and information about monitoring data used in study.

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Respiratory Symptoms:							
Mortimer et al., 2002 8 U.S. cities morning symptoms	1.35 (1.06, 1.71)	8h	48	64.3	66	28.8-66	6/1/93 - 8/31/93 AQS, all monitors in corresponding county, averaged for 10am to 6pm
Gent et al., 2003 New England cities chest tightness	1.19 (1.05, 1.34)	8h 1d	51.3	95.2	91.8	27.1-99.6	4/1/01 - 9/30/01 10 sites in CT and 4 in Springfield MA
Gent et al., 2003 New England cities shortness of breath	1.17 (1.03, 1.33)	8h 1d	51.3	95.2	91.8	27.1-99.6	4/1/01 - 9/30/01 10 sites in CT and 4 in Springfield MA
Ostro et al., 2001 2 S Cal counties Asthma med use	1.15 (1.12, 1.19)	1h	59.5/ 95.8 (57.2)	121	122	14-122	Aug-Nov 1993 2 sites - downtown LA and Pasadena, individuals matched to closest site
Ostro et al., 2001 2 S Cal counties shortness of breath	1.01 (0.92, 1.10)	1h 3d	59.5/ 95.8 (57.2)	121	122	14-122	Aug-Nov 1993 2 sites - downtown LA and Pasadena, individuals matched to closest site
Ostro et al., 2001 2 S Cal counties Wheeze	0.94 (0.88, 1.00)	1h 3d	59.5/ 95.8 (57.2)	121	122	14-122	Aug-Nov 1993 2 sites - downtown LA and Pasadena, individuals matched to closest site
Ostro et al., 2001 2 S Cal counties Cough	0.93 (0.87, 0.99)	1h 3d	59.5/ 95.8 (57.2)	121	122	14-122	Aug-Nov 1993 2 sites - downtown LA and Pasadena, individuals matched to closest site
Neas et al., 1995 Uniontown PA pm cough	1.36 (0.86, 2.14)	12h 0d	37.2 (56.1)	85.3	98	15-98	6/10/90 - 8/23/90 1 site near Laurel Highlands HS

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Delfino et al., 2003 San Diego, CA Symptom score>1	0.75 (0.24, 2.33)	8h 0d	17.1	34.8	35.2	5.8-35.2	Nov 99 - Jan 00 Huntington Park central site
Delfino et al., 2003 San Diego, CA Symptom score>1	1.55 (0.52, 4.63)	8h 1d	17.1	34.8	35.2	5.8-35.2	Nov 99 - Jan 00 Huntington Park central site
Delfino et al., 2003 San Diego, CA Symptom score>2	6.67 (1.09, 40.88)	8h 0d	17.1	34.8	35.2	5.8-35.2	Nov 99 - Jan 00 Huntington Park central site
Delfino et al., 2003 San Diego, CA Symptom score>2	1.15 (0.41, 3.17)	8h 1d	17.1	34.8	35.2	5.8-35.2	Nov 99 - Jan 00 Huntington Park central site
Delfino et al., 1998 San Diego, CA Asthma symptoms	1.26 (1.00, 1.58)	8h 0d	73	107	109	43-109	8/1/95 - 10/30/95 SDAPCD site
Schwartz et al., 1994 6 US cities Cough	1.15 (0.99, 1.33)	24h 1d	36.9				Harvard 6 cities sites; school year period for each, from 1985/6 to 1987/8
Schwartz et al., 1994 6 U.S. cities lower respiratory symptoms	1.22 (1.00, 1.50)	24h 1d	36.9				Harvard 6 cities sites; school year period for each, from 1985/6 to 1987/8
Ross et al., 2002 East Moline, IL morning symptoms	1.12 (1.05, 1.20)	8h 3d ave	41.5	68.8	75	8.9-78.3	Apr-Oct 1994 AQS data - East Moline sites
Ross et al., 2002 East Moline, IL Evening symptoms	1.12 (1.06, 1.19)	8h 3d ave	41.5	68.8	75	8.9-78.3	Apr-Oct 1994 AQS data - East Moline sites

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Ross et al., 2002 East Moline, IL Asthma med use	1.08 (0.99, 1.17)	8h 3d ave	41.5	68.8	75	8.9-78.3	Apr-Oct 1994 AQS data - East Moline sites
Thurston et al., 1997 Connecticut chest symptoms	1.21 (1.12, 1.31)	1h 0d	83.6	NA	NA	NA	last wk of June 1991-93 on-site monitor
Thurston 1997 Connecticut Asthma med use	1.19 (1.08, 1.32)	1h 0d	83.6	NA	NA	NA	last wk of June 1991-93 on-site monitor
Lung Function Changes:							
Mortimer et al., 2002 8 U.S. cities am PEF (%)	-0.59% (-1.05, -0.13)	8h	48	64.3	66	28.8-66	6/1/93 - 8/31/93 AQS, all monitors in corresponding county, averaged for 10am to 6pm
Linn et al., 1996 Los Angeles FEV1 (ml)	-0.26 (SE 0.25) (am) -0.18 (SE 0.20) (pm)	24h 0d	23	150	164	2.5-192.5	Jan 91-Dec 92 SCAQMD sites in 3 communities: Upland, Rubidoux, Torrance
Newhouse et al., 2004 Tulsa, OK am PEF (L/min)	-0.274 ($p<0.05$) (mean O_3) -0.289 ($p<0.05$) (max O_3)	24h 1d	30	92.7	104.7	17.3-104.7	9/1/00 - 10/31/00 OK DEQ site about 1 km from U Tulsa
Ross et al., 2002 East Moline, IL PEF (L/min)	-2.29 (-4.26, -0.33) (am) -2.58 (-4.26, -0.89) (pm)	8h 0-1d 1d	41.5	68.8	75	8.9-78.3	Apr-Oct 1994 AQS data - East Moline sites
Neas et al., 1995 Uniontown PA PEF (L/min)	-2.79 (-6.7, -1.1) (pm)	12h 0d	37.2 (56.1)	85.3	98	15-98	6/10/90 - 8/23/90 1 site near Laurel Highlands HS

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Neas et al., 1999 Philadelphia PA PEF (L/min)	-1.38 (-2.81, 0.04) (am) -2.58 (-4.91, -0.35) (pm)	12h 0d 1-5d ave	56	96.9	104.5	17.7-104.5	7/8/93 - 9/3/93 2 sites: Airport and Presbyterian Nursing Home (58th and Greenway)
Korrick et al., 1998 Mt. Washington NH FEV1 (%)	-2.6 (-4.1, -0.4)	1h 0d	40	87	89	24 – 91	summers 1991, 92 2 sites: Mt. Washington Observatory and mountain base at Auto Rd
Thurston et al., 1997 Connecticut summer camp PEF (L/min)	-0.096 (p<0.05)	1h 0d	83.6	NA	NA	NA	last wk of June, 1991-1993 on-site monitor
Naeher et al., 1999 SW Virginia PEF (L/min)	-7.65 (-13.0, -2.25) (pm)	24h 1-5d ave	34.87	74	79	13-87	summers 1995-1996 1 site in Vinton VA
Brauer et al., 1996 Fraser Valley, BC FEV1 (mL)	-3.8 (SE 0.4) (end shift) -4.5 (SE 0.6) (next day)	1h 0d	40.3	55	55	3-55	June-August 1993 BC Ministry of Environment sites
Emergency Department Visits: Respiratory Diseases							
Peel et al., 2005 Atlanta	2.89 (1.03, 4.77)	8h 3d ave	55.6	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Delfino et al., 1997 Montreal (>64yo)	28.93 (11.98, 45.88)	8h 1d	34.7	57.5	64.9	7-64.9	May-Aug 1988 and 1989 AQS data, 5 sites
Delfino et al., 1997 Montreal (>64yo)	31.61 (12.91, 50.31)	1h 1d	34.7 (28.9)	57.5	64.9	7-64.9	May-Aug 1988 and 1989 AQS data, 5 sites
Jones et al., 1995 Baton Rouge, LA (1-17 yo)	-13.00 (-32.82, 12.66)	24h 0d	28.2 (56.4)	111.8	118	21-119	6/1/90 - 8/31/90 DEQ 3 sites

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Jones et al., 1995 Baton Rouge, LA (18-60 yo)	20.00 (2.29, 40.78)	24h 0d	28.2 (56.4)	111.8	118	21-119	6/1/90 - 8/31/90 DEQ 3 sites
Jones et al., 1995 Baton Rouge, LA (>60 yo)	27.00 (-3.48, 67.10)	24h 0d	28.2 (56.4)	111.8	118	21-119	6/1/90 - 8/31/90 DEQ 3 sites
Wilson et al., 2005 Portland NH,	-3.00 (-8.49, 2.82)	8h 0d	43.1	108	121	15-142	Apr-Oct 1998-2000 AQS data, single monitor in each city
Wilson et al., 2005 Manchester NH	-3.00 (-8.53, 2.87)	8h 0d		85	93	5-121	Apr-Oct 1998-2000 AQS data, single monitor in each city
Stieb et al., 1996 St. John, Canada	9.33 (-0.07, 18.74)	1h 2d	41.6 (36.1)	83	91	5-140.5	May-Sept 1984-1992 EC data averaged across sites
Emergency Department Visits: Asthma							
Peel et al., 2005 Atlanta, GA	2.65 (-0.50, 5.89)	8h 3d ave	55.6	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Wilson et al., 2005 Manchester NH	-3.00 (-8.91, 3.29)	8h 0d	NA	108	121	15-142	Apr-Oct 1998-2000 AQS data, single monitor in each city
Wilson et al., 2005 Portland NH	9.40 (10.26, 8.55)	8h 0d	NA	85	93	5-121	Apr-Oct 1998-2000 AQS data, single monitor in each city
Friedman et al., 2001 Atlanta GA (1-16 yo)	30.89 (5.34, 62.64)	1h 0-1d	77.2 (60.7)	85.8	85.8	20-85.8	7/19/96 - 8/4/96 3 sites in Atlanta
Tolbert et al., 2000 Atlanta, GA	6.37 (2.53, 10.34)	8h 1d	59.3 (60.7)	92.4	112.6	16.2-135.8	AQS, GA and Fulton Co., SOS, USGS; 7 sites in Atlanta MSA
Zhu et al., 2003 Atlanta, GA (0-16 yo)	2.41 (-2.39, 7.44)	8h 0d					

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Jaffe et al., 2003 3 Ohio cities	9.27 (0.13, 19.25)	8h 2-3d	(66.1)	104	108	24-124	7/1/91 to 6/30/96 all data from active monitors
Jaffe et al., 2003 Cincinnati	15.76 (-1.01, 35.38)	8h 2d	60	106	116	24-124	7/1/91 to 6/30/96 all data from active monitors
Jaffe et al., 2003 Cleveland	3.03 (-8.52, 16.04)	8h 2d	50	104	107	27-111	7/1/91 to 6/30/96 all data from active monitors
Jaffe et al., 2003 Columbus	15.76 (-2.49, 37.44)	8h 3d	57	98	106	25-117	7/1/91 to 6/30/96 all data from active monitors
Cassino et al., 1999 NYC (in heavy smokers)	-5.42 (-8.38, -2.36)	24h 0d	17.5 (32.6)	83.3	88.8	3-114.6	1/1/89 - 12/31/93 data from sites throughout NYC
Cassino et al., 1999 NYC (in heavy smokers)	2.74 (-3.00, 8.83)	24h 1d	17.5 (32.6)	83.3	88.8	3-114.6	1/1/89 - 12/31/93 data from sites throughout NYC
Cassino et al., 1999 NYC (in heavy smokers)	9.69 (3.93, 15.76)	24h 2d	17.5 (32.6)	83.3	88.8	3-114.6	1/1/89 - 12/31/93 data from sites throughout NYCl
Cassino et al., 1999 NYC (in heavy smokers)	-1.62 (-7.01, 4.08)	24h 3d	17.5 (32.6)	83.3	88.8	3-114.6	1/1/89 - 12/31/93 data from sites throughout NYC
Emergency Department Visits: Other respiratory diseases:							
Peel et al., 2005 Atlanta, GA Pneumonia	1.80 (-2.27, 6.04)	8h 3d ave	55.6	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Peel et al., 2005 Atlanta, GA COPD	3.49 (-2.77,10.15)	8h 3d ave	55.6	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Peel et al., 2005 Atlanta, GA upper respiratory infection	3.25 (1.10, 5.44)	8h 3d ave	55.6	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Cardiovascular outcomes, biomarkers, and physiological changes:							
Liao et al., 2004 3 US cities HRV (high frequency power)	-0.010 (SE 0.016)	8h 1d	41				1996-1998 AQS data
Liao et al., 2004 3 US cities SD of normal RR intervals	-0.336 (SE 0.290)	8h 1d	41				1996-1998 AQS data
Peters et al., 2000 Boston Defibrillator discharge	OR 0.96 (0.47, 1.98) (patients with 1+ event) OR 1.23 (0.53, 2.87) (patients with 10+ events)	24h 0d	18.6	75.2	78.1	15.7-102.7	Jan 95 - Dec 97 1 site
Peters et al., 2001 Boston Myocardial infarction	OR 1.31 (0.85, 2.03) (2h O_3) OR 0.94 (0.60, 1.49) (24h O_3)	24h and 2h 1d and 1h	19.9	75.8	81.5	17.7-102.7	Jan 95 - May 96 1 site (case-crossover)
Park et al., 2004 Boston HRV (low frequency power)	-11.5% (-21.3, -0.4)	4h	23	81.8	92	10-122.6	Nov 2000- Oct 2003 Mass Dept. Environ. Protection sites

Study; Location	Effect Estimate (lower CL, upper CL)	Air Quality Data from Study *		Statistics for 8-hr daily max air quality data **			Study period; Monitoring information
		Ave time; Lag	Mean	98th %	99th %	Range	
Gold et al., 2000 Boston HRV (r-MSSD) (ms)	-3.0 (SE 1.9) (first rest period) -5.8 (SE 2.4) (slow breathing period)	1h	34	77.3	92.5	21.8-100	June-Sept 1997 1 site, MA Dept. Environ. Protection
Dockery et al., 2005 Boston Ventricular arrhythmia	OR 1.09 (0.93, 1.29) (all events)	48h	22.9	75	82.1	2–102.7	7/11/95 - 7/11/02 6 sites, Mass Dept. Envir. Protection
Rich et al., 2005 Boston Ventricular arrhythmia	OR 1.21 (1.00, 1.45) (all events)	24h	22.6	74	81.5	2-102.7	Aug 1995 - June 2002 6 sites, Mass Dept. Envir. Protection
Emergency Department Visits: Cardiovascular Diseases							
Metzger et al., 2004 Atlanta, GA all CV	0.96 (-1.59, 3.58)	8h 3dave	53.9	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Metzger et al., 2004 Atlanta, GA Dysrrhythmia	0.96 (-3.96, 6.13)	8h 3dave	53.9	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Metzger et al., 2004 Atlanta, GA CHF	-4.19 (-9.74, 1.71)	8h 3dave	53.9	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Metzger et al., 2004 Atlanta, GA IHD	2.28 (-2.30, 7.09)	8h 3dave	53.9	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor
Metzger et al., 2004 Atlanta, GA peripheral vascular	1.68 (-1.57, 5.05)	8h 3dave	53.9	127	140	3-152	1/1/93 to 12/21/02 AQS Confederate Ave monitor

Hospital Admissions: Cardiovascular Diseases							
Linn et al., 2000 Los Angeles CA (summer)	2.02 (-16.14, 24.11)	24h 0d	32.9 (98.7)	175	180	188	Los Angeles basin - averaged from monitors across basin
Fung et al., 2003 Windsor CV <65 yo	-0.14 (-11.79, 13.06)	1h 0d	39.3 (31.6)	78	85	0-106	4/1/95 - 12/31/00 4 sites in Winsdor
Fung et al., 2003 Windsor CV <65 yo	5.84 (-10.50, 25.16)	1h 0-2d ave	39.3 (31.6)	78	85	0-106	4/1/95 - 12/31/00 4 sites in Winsdor
Fung et al., 2003 Windsor CV 65+ yo	-3.57 (-10.35, 3.72)	1h 0d	39.3 (31.6)	78	85	0-106	4/1/95 - 12/31/00 4 sites in Winsdor
Fung et al., 2003 Windsor CV 65+ yo	1.94 (-8.01, 12.95)	1h 0-2d ave	39.3 (31.6)	78	85	0 -106	4/1/95 - 12/31/00 4 sites in Winsdor
Burnett et al., 1997 Toronto CV	20.47 (9.32, 32.76)	1h 2-4d ave	41.2 (31.6)	62	64	0-79	summers 1992, 93, 94 7-9 sites in metro Toronto
Gwynn et al., 2000 Buffalo circulatory	0.23 (-1.27, 1.74)	24h 1d	26.2 (38.7)	92.5	104	4.5-123	1988-1990 AQS data from multiple sites in Buffalo/Rochester area
Hospital Admissions: Specific Cardiovascular Diseases							
Koken et al., 2003 Denver CO myocardial infarction	-32.91 (-47.16, -14.82)	24h 0d	25 (44.2)	64.5	65.5	11-76	July-August 1993-1997 AQS sites in Denver County (2 sites)
Koken et al., 2003 Denver Coronary Atheroschlerosis	27.02 (8.30, 48.98)	24h 2d	25 (44.2)	64.5	65.5	11-76	July-August 1993-1997 AQS sites in Denver County (2 sites)
Koken et al., 2003 Denver Pulm Heart Disease	49.16 (8.35, 105.22)	24h 1d	25 (44.2)	64.5	65.5	11-76	July-August 1993-1997 AQS sites in Denver County (2 sites

Ito, 2003 Detroit MI ischemic heart disease	0.52 (-2.27, 3.39)	24h 3d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data, 4 ozone sites
Ito, 2003 Detroit MI dysrrhythmia	-1.04 (-5.87, 4.04)	24h 3d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data, 4 ozone sites
Ito, 2003 Detroit MI heart failure	0.76 (-2.47, 4.09)	24h 3d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data 4 ozone sites
Ito, 2003 Detroit MI stroke	0.50 (-3.03, 4.15)	24h 3d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data 4 ozone sites
Hospital Admissions: Respiratory Diseases							
Luginaah et al., 2003 Windsor (males)	5.56 (-10.57, 24.59)	1h 0d	39.3 (31.6)	78	85	0-106	4/1/95 - 12/31/00 4 sites in Winsdor
Luginaah et al., 2003 Windsor (females)	-6.83 (-23.92, 14.09)	1h 0d	39.3 (31.6)	78	85	0-106	4/1/95 - 12/31/00 4 sites in Winsdor
Thurston et al., 1992 Buffalo NY	4.94 (-0.23, 10.12)	1h 2d	60 (58.9)	125.5	133	24-133	June-Aug 1988-1989 NYDEC monitors
Delfino et al., 1994 Montreal	4.05 (1.00, 7.11)	8h 4d	32.1	69	73.8	8.6-82.3	Jul-Aug 1984-1988 7 sites in Montreal; 2 sites near heavy traffic areas not used
Burnett et al., 1994 Toronto	3.95 (2.50, 5.43)	1h 1d	(41.7)	79	81.5	15-104.3	1983-1988 Ont Min Environ 22 sites May-August
Burnett et al., 1997 16 Canadian city	6.72 (3.52, 10.02)	1h 1d	32.9 (25.3)	47.1	51.3	6.2-68.4	4/1/81 - 12/31/91 used Apr-Dec data, all stations in each city
Burnett et al., 1997 Toronto	17.57 (10.44, 25.15)	1h 1-3d ave	41.2 (31.6)	62	64	0-79	summers 1992, 93, 94 7-9 sites in metro Toronto
Yang et al., 2003 Vancouver (<3 yo)	50.43 (32.64, 70.61)	24h 4d	13.41 (21.3)	42.7	47.3	1.1-71.9	1/1/86 - 12/31/98 25 sites, Great Vancouver Regional District

Yang et al., 2003 Vancouver (65+yo)	28.53 (18.47, 39.43)	24h 4d	13.41 (21.3)	42.7	47.3	1.1-71.9	1/1/86 - 12/31/98 25 sites, Great Vancouver Regional District
Schwartz et al., 1996 Cleveland	3.51 (0.88, 6.20)	1h 1-2d ave	56 (55.1)	91	99	5-120.3	1988-1990 Cuyahoga county warm season only
Moolgavkar et al., 1997 Minneapolis/St. Paul	8.08 (4.47, 11.81)	24h 1d	26.2 (45.1)	83.2	87.7	4.6-101.8	1/1/86 - 12/31/91 AQS data from all monitoring stations
Gwynn et al., 2001 NYC (white)	1.08 (-0.44, 2.63)	24h 1d	22.1 (34.2)	90.6	106	6-125	1988-1990 AQS data
Gwynn et al., 2001 NYC (nonwhite)	4.01 (2.47, 5.57)	24h 1d	22.1 (34.2)	90.6	106	6-125	1988-1990 AQS data
Gwynn et al., 2001 NYC (uninsured)	4.51 (2.80, 6.25)	24h 1d	22.1 (34.2)	90.6	106	6-125	1988-1990 AQS data
Thurston et al., 1992 NYC	0.42 (0.10, 0.74)	1h 3d	29.1				June-Aug 1988-1989 NYDEC monitors
Gwynn et al., 2000 Buffalo	3.94 (1.78, 6.15)	24h 1d	26.2 (38.7)	92.5	104	4.5-123	1988-1990 AQS data from multiple sites in Buffalo/Rochester area
Schwartz et al., 1996 Spokane	19.08 (0.17, 41.57)	1h 2d	79	NA	NA	NA	1988-1990 1 residential site
Thurston et al., 1994 Toronto	15.30 (4.11, 26.50)	1hr 0d	57.47 (45.8)	92	94	8-125	July-Aug, 1986-1988 Breadalbane site
Hospital Admissions: Asthma							
Sheppard et al., 2003 Seattle, WA	3.44 (0.58, 6.39)	8h 2d	30.4	65	73	2-100	1987-1994 1 site at Lake Sammamish
Nauenberg et al., 1999 Los Angeles (all insurance)	1.00 (-6.28, 8.84)	24h 0d	19.88 (19.1)	46.5	50.5	2-67	(11/15-3/1)1991-1994 2 SCAQMD sites in zip codes 90025 and 90012
Burnett et al., 2001 Toronto (<2 yo)	30.25 (16.87, 45.15)	1h 5d ave	45.2 (38.6)	77.7	83.7	9-110.8	1/1/80 - 12/31/94 4 sites

Thurston et al., 1992 Buffalo NY	6.59 (1.29, 11.89)	1h 3d	60 (58.9)	125.5	133	24-133	June-Aug 1988-1989 NYDEC monitors
Burnett et al., 1999 Toronto	6.47 (3.68, 9.33)	24h 1-3d ave	19.5 (26.7)	68.4	74.8	0.1-110.8	summers 1992, 93, 94 7-9 sites in metro Toronto
Lin et al., 2003 Toronto, 6-12 yo	-7.84 (-22.02, 8.92) (female) -26.04 (-44.53, -1.39) (male)	1h 0d	28.2	68.4	74.8	0.14-110.8	1981-1993 4 sites, Ontario Ministry of Environment and Energy (case-crossover)
Thurston et al., 1992 New York City	0.95 (0.20, 1.69)	1h 1d	29.1				June-Aug 1988-1989 NYDEC monitors
Schwartz et al., 1994 Detroit	10.81 (5.13, 16.80)	24h 1d	21 (37.6)	82.8	88.5	10-122.7	1986-1989 AQS data 9 sites in 86 and 89, 8 sites in 87 and 88
Hospital Admissions: Other respiratory diseases							
Moolgavkar et al., 1997 Minneapolis/St. Paul pneumonia	8.90 (4.62, 13.34)	24h 1d	26.2 (45.1)	83.2	87.7	4.6-101.8	1/1/86 - 12/31/91 AQS data from all monitoring stations
Ito, 2003 Detroit MI pneumonia	3.10 (-1.84, 8.28)	24h 3d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data, 4 ozone sites
Ito, 2003 Detroit MI COPD	1.25 (-3.55, 6.28)	24h 3d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data 4 ozone sites
Burnett et al., 1999 Toronto COPD	7.49 (4.00, 11.10)	24h 2-4d ave	19.5 (26.7)	68.4	74.8	0.1-110.8	summers 1992, 93, 94 7-9 sites in metro Toronto
Schwartz et al., 1994 Detroit COPD	11.68 (2.92, 21.19)	24h 1d	21 (37.6)	82.8	88.5	10-122.7	1986-1989 AQS data 9 sites in 86 and 89, 8 sites in 87 and 88
Moolgavkar et al., 1997 Minneapolis/St. Paul COPD	6.04 (1.22, 11.10)	24h 1d	26.2 (45.1)	83.2	87.7	4.6-101.8	1/1/86 - 12/31/91 AQS data from all monitoring stations

Burnett et al., 1999 Toronto Respiratory Infection	4.52 (2.43, 6.64)	24h 1-2d ave	19.5	68.4	74.8	0.1-110.8	summers 1992, 93, 94 7-9 sites in metro Toronto
Mortality: Total nonaccidental							
Bell et al., 2004 95 U.S. cities (warm)	0.44 (0.14, 0.74)	24h 0d	26.84				1987-2000 AQS data, 10% trimmed mean to average across monitors after correction for each monitor
Bell et al., 2004 95 U.S. cities (warm)	0.78 (0.26, 1.30)	24h 0-6d dl	26.84				1987-2000 AQS data, 10% trimmed mean to average across monitors after correction for each monitor
Schwartz et al., 2004 14 U.S. cities (warm)	1.04 (0.30, 1.79)	1h 0d	45.9				1986-1993 AQS data, May-September (case-crossover)
Ostro et al., 2003 Coachella Valley CA	-1 (-4.42, 2.55)	1h	62				1/1/89 – 12/20/98 sites in Palm Springs and Indio
Ostro et al., 1995 2 Southern CA counties	0.80 (-0.18, 1.78)	1h 0d	140				1980-1986 4 sites in San Bernardino and Riverside counties: Upland, Rubidoux, Redlands, Perris
Moolgavkar et al., 1995 Philadelphia (summer)	2.82 (1.33, 4.33)	24h 1d	35.5				1973-1988 AQS data
Ito, 2003 Detroit MI	0.86 (-0.36, 2.09)	24h 0d	20.9 (34.3)	81.5	88.7	2-123.5	1985-1990 AQS data, 4 ozone sites
Ito, 2003 Detroit MI	1.88 (-1.69, 5.58)	24h 0d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data, 4 ozone sites
Fairley, 2003 San Jose CA	2.81 (-0.27, 5.99)	8-h 0d	29	67	74	2-105	1989-1996 San Jose 4th St. site
Chock et al., 2000 Pittsburg PA (<75 yo)	-1.48 (-5.63, 2.85)	1h 0d	(35.4)	80	88.9	2.3-92.5	1989-1991 1 site with daily obs, used only data between 1200 and 2000 hours

Chock et al., 2000 Pittsburg PA (75+)	-1.82 (-6.03, 2.59)	1h 0d	(35.4)	80	88.9	2.3-92.5	1989-1991 1 site with daily obs, used only data between 1200 and 2000 hours
Kinney et al., 1995 Los Angeles	0.00 (-4.90, 5.15)	1h 1d	70 (53.4)	115.3	130	5.4-156.1	1985-1990 8 ozone sites
Gamble et al., 1998 Dallas TX	3.69 (0.85, 6.62)	24h 1-2d	22 (37.9)	81	86.3	2-98.7	1990-1994 TNRCC data, 2-3 sites in Dallas Co.
Dockery et al., 1992 St. Louis	0.60 (-2.46, 3.750	24h 1d	22.5				Sept 1985-August 1986 Harvard site on S side of city
Dockery et al., 1992 E Tennesse	-1.30 (-7.91, 5.78)	24h 1d	23				Sept 1985-August 1986 Harvard site, ~50 km SW of Knoxville
Ito et al., 1996 Cook County	3.89 (2.21, 5.59)	1h 0-1d	38.1 (31.8)	76	85.6	2.7-124	1985-1990 AQS sites with at least 4 y data, 5 O3 sites
Klemm et al., 2004 Atlanta quartknot **	2.40 (-3.39, 8.54)	8h 0-1d	47.03			6.63- 124.41	ARIES database, as described in Klemm 2000
Klemm et al., 2004 Atlanta monthknot **	4.16 (-2.42, 11.19)	8h 0-1d	47.03			6.63- 124.41	ARIES database, as described in Klemm 2000
Goldberg et al., 2003 Montreal (CHFunderlying)	4.26 (-5.30, 14.78)	24h 0-2d	29				1984-1993 Environment Canada data, 9 sites
Vedal et al., 2003 Vancouver	16.63 (5.54, 28.88)	1h 0d	27.4 (21.4)	53.3	47.3	1.1-58.7	Jan 94 - Dec 96 19 sites in Greater Vancouver Regional District and EC
Villeneuve et al., 2003 Vancouver	1.31 (-0.78, 3.45)	24h 0d	13.4 (21.3)	69.3	47.3	3.1-71.9	1/1/86 - 12/31/98 13 census subdivisions
Mortality: Cardiovascular or Cardiorespiratory diseases							
Bell et al., 2004 95 U.S. cities	1.28 (0.61, 1.96)	24h 0-6d dl	26.84				1987-2000 AQS data, 10% trimmed mean to average across monitors after correction for each monitor

Huang et al., 2004 19 U.S. cities	1.47 (0.54, 2.40)	24h 0d	18-56				June 1- Sept 30, 1987-1994 AQS data
Lipfert, et al., 2000 Philadelphia	30.19 (p<0.055)	1h 0-1dave	44.76 (39.7)	88.8	93.6	2.3-116.6	May 92 - Sept 95 1 Camden and 1 Phila site
Lipfert, et al., 2000 Philadelphia	-2.00 (p<0.055)	1h 0-1dave	44.76 (39.7)	88.8	93.6	2.3-116.6	May 92 - Sept 95 1 Camden and 1 Phila site
Ostro et al., 2003 Coachella Valley	-4 (-8.88, 1.14)	1h	62				1/1/89 – 12/20/98 sites in Palm Springs and Indio
Ito, 2003 Detroit MI	1.45 (-0.29, 3.21)	24h 0d	20.9 (34.3)	81.5	88.7	2-123.5	1985-1990 AQS data, 4 ozone sites
Ito, 2003 Detroit MI	1.79 (-3.38, 7.24)	24h 0d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data, 4 ozone sites
Fairley, 2003 San Jose CA	2.36 (-2.12, 7.04)	8h 0d	29	67	74	2-105	1989-1996, San Jose 4th St. site
Gamble et al., 1998 Dallas TX	3.28 (-1.48, 8.27)	24h 1-2d	22 (37.9)	81	86.3	2-98.7	1990-1994 TNRCC data, 2-3 sites in Dallas Co.
Ito et al., 1996 Cook County	4.64 (2.07, 7.27)	1h 0-1d	38.1 (31.8)	76	85.6	2.7-124	1985-1990, AQS sites with at least 4 y data, 5 O3 sites
Moolgavkar et al., 2003 Cook County	0.30 (0.16, 0.44)	24h 0d	18				1987-1995 AQS data
Villeneuve et al., 2003 Vancouver	0.66 (-2.57, 3.99)	24h 0d	13.4 (21.3)	69.3	47.3	3.1-71.9	1/1/86 - 12/31/98 13 census subdivisions
Goldberg et al., 2001 Montreal	2.81 (1.35, 4.30)	24h 0-2d	29				1984-1993 Environment Canada data, 9 sites
Vedal et al., 2003 Vancouver	16.19 (-0.67, 35.91)	1h 0d	27.4 (21.4)	53.3	47.3	1.1-58.7	Jan 94 - Dec 96 19 sites in Greater Vancouver Regional District and EC

Mortality: Respiratory Diseases							
Ostro et al., 2003 Coachella Valley	3 (-8.77, 16.29)	1h	62				1/1/89 – 12/20/98 sites in Palm Springs and Indio
Ito, 2003 Detroit MI	0.07 (-4.34, 4.68)	24h 0d	20.9 (34.3)	81.5	88.7	2-123.5	1985-1990 AQS data, 4 ozone sites
Ito, 2003 Detroit MI	7.44 (-5.37, 21.99)	24h 0d	25 (38.7)	80	85	4.3-101.3	1992-1994 AQS data, 4 ozone sites
Vedal et al., 2003 Vancouver	6.01 (-22.53, 45.06)	1h 0d	27.4 (21.4)	53.3	47.3	1.1-58.7	Jan 94 - Dec 96 19 sites in Greater Vancouver Regional District and EC
Villeneuve et al., 2003 Vancouver	1.50 (-4.24, 7.58)	24h 0d	13.4 (21.3)	69.3	47.3	3.1-71.9	1/1/86 - 12/31/98 13 census subdivisions
Moolgavkar et al., 2003 Cook County (COPD)	0.30 (-0.10, 0.71)	24h 0d	18				1987-1995 AQS data

* Includes ozone averaging period and lag period for effect estimate calculation; for example, 1h represents 1-hour maximum concentration and 0d represents a 0-day lag period. Mean values taken from study publications, for the ozone averaging period used in the study (e.g., 1h, 8h, 24h). Where 8-hour daily max ozone concentrations were used, the mean 8-hour daily max concentration is presented in parentheses.

** Using ozone data obtained for the study period in the location of the study, 8-hour daily maximum concentrations were derived and statistics calculated. The 98th and 99th percentile values for the full study period distribution are presented here, along with the range (minimum-maximum) of concentrations. Since the time periods of the studies vary in length, from several weeks to over 10 years, the 98th and 99th percentile values were selected for presentation here as a high study period concentration that roughly approximates a 4th maximum concentration, depending on the study period length. NA= data not available

APPENDIX 4A. MICROENVIRONMENT MODELING PARAMETERS

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 between 10 and 20 ºC to 2.29 for New York 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 and 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 (Table A-1). The final AER distributions used for the exposure modeling are given in Table A-2.

Table .A-1. City-specific air conditioning prevalence rates (percentage of residences with central or room A/C)

City	Survey Area and Year	Percentage
Atlanta	Atlanta, 2003	97
Boston	Boston, 2003	75
Chicago	Chicago, 2003	87
Cleveland	Cleveland, 2003	75
Detroit	Detroit, 2003	81
Houston	Houston, 2003	99
Los Angeles	Los Angeles, 2003	55
New York	New York, 2003	82
Philadelphia	Philadelphia, 2003	91
Sacramento	Sacramento, 2003	95
St. Louis	St. Louis, 2003	96
Washington DC	Washington DC, 2003	96

Table A-2. Lognormal distributions used for residential air exchange rates

City	Air Conditioner in residence (Yes/No)	Temperature Range (Celsius)	Scale	Shape	Geometric Mean	Geometric Standard Deviation
Houston	Yes	≤ 20	-0.898	0.748	0.407	2.113
		20-25	-0.760	0.662	0.467	1.938
		25-30	-0.862	0.814	0.422	2.258
		> 30	-0.695	0.541	0.499	1.717
	No	≤ 10	-0.422	0.518	0.656	1.679
		10-20	-0.469	1.070	0.625	2.916
		> 20	-0.088	0.897	0.916	2.451
	Yes	≤ 20	-0.529	0.639	0.589	1.894

Los Angeles	Yes	≤ 20	-0.529	0.639	0.589	1.894
		20-25	0.096	0.861	1.100	2.365
		25-30	-0.207	0.882	0.813	2.415
		> 30	-1.323	1.026	0.266	2.790
	No	≤ 10	-0.611	1.127	0.543	3.087
		10-20	-0.292	0.735	0.747	2.085
		20-25	0.316	0.825	1.372	2.283
		> 25	-0.012	0.676	0.988	1.967
Boston, Chicago, Cleveland, Detroit, New York City, Philadelphia	Yes	≤ 10	-0.341	0.702	0.711	2.018
		10-25	0.130	0.985	1.139	2.677
		> 25	0.218	0.778	1.244	2.177
	No	≤ 10	0.016	0.760	1.016	2.138
		10-20	-0.235	0.714	0.791	2.042
		> 20	0.474	0.751	1.606	2.119
Atlanta, Washington D.C.	Yes	≤ 10	-0.045	0.674	0.956	1.962
		10-20	-0.660	0.702	0.517	2.017
		20-25	-0.646	0.783	0.524	2.189
		> 25	-0.937	0.730	0.392	2.076
	No	≤ 10	-0.283	0.840	0.754	2.317
		10-20	-0.359	0.779	0.698	2.180
		20-25	0.313	0.829	1.367	2.292
		> 25	0.065	0.687	1.067	1.989
Sacramento	Yes	≤ 25	-0.687	0.653	0.503	1.921
		> 25	-0.186	0.856	0.830	2.353
	No	≤ 10	-0.643	1.161	0.526	3.192
		10-20	-0.408	0.777	0.665	2.174
		20-25	0.052	0.537	1.054	1.711
		> 25	-0.190	0.817	0.827	2.265
St. Louis	Yes	≤ 10	-0.153	0.703	0.858	2.020
		10-20	-0.642	0.739	0.526	2.094
		20-25	-0.405	0.923	0.667	2.517
		25-30	-0.770	0.850	0.463	2.339
		> 30	-0.466	0.729	0.627	2.073
	No	≤ 10	-0.077	0.734	0.926	2.084

		10-20	-0.310	0.846	0.733	2.330
		> 20	0.321	0.822	1.378	2.276

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 (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. Table A-3 gives the fitted parameters for this distribution, which is used for AER distributions for the indoor, non-residential microenvironments.

Table A-3. Lognormal distributions used for all non-residential indoor air exchange rates for all cities

Scale	Shape	Geometric Mean	Geometric Standard Deviation	Lower Bound	Upper Bound
0.1038	0.1036	1.1094	3.0150	0.07	13.8

Proximity and Penetration Factors For Outdoors, In-vehicle, and Mass Transit

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 rationale for the selection of distributions of penetration and proximity factors for outdoors and in-vehicle microenvironments used in this modeling analysis, which are listed in Table A4.

Table A-4. Distributions of penetration and proximity factors for outdoors and in-vehicle microenvironments

Microenvironment	Parameter	Road Type	Distribution	Mean	Standard Deviation	Lower Bound	Upper Bound
Outdoors near road; outdoors, public garage / parking lot	Penetration factor	All	Constant	1.0			
	Proximity factor	All	Normal	0.755	0.203	0.422	1.0
Other outdoors microenvironments	Penetration factor	All	Constant	1.0			
	Proximity factor	All	Constant	1.0			
In-vehicle	Penetration factor	All	Normal	0.300	0.232	0	1
	Proximity factor	Local Roads	Normal	0.755	0.203	0.422	1
		Urban Roads	Normal	0.754	0.243	0.355	1
		Interstates	Normal	0.364	0.165	0.093	1

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.

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APPENDIX 4B. FREQUENCY DISTRIBUTIONS OF DAILY MAXIMUM 8-HOUR AVERAGE OZONE CONCENTRATIONS

The measured concentrations and the concentrations representing just meeting the current 8-hour standard, for 2004 only, are summarized in the graphs in this Appendix in terms of the frequencies of daily maximum 8-hour average O_3 concentrations above various concentration levels. Since these are summations of "exceedances" for all monitors in an urban area, having more monitors will lead to higher counts in these figures. These graphs also show the percent reduction in exceedances of levels from the 2004 base year to when the current 8-hour standard is just met.

The lines in these graphs with hollow triangles and squares indicate frequencies for the 2004 base and current standard respectively, and their values can be read off the left axis. The lines with solid circles give the percent reduction from the base to current standard, and correspond to the scale of the axis on the right side of the figures.

Figure 4B-1

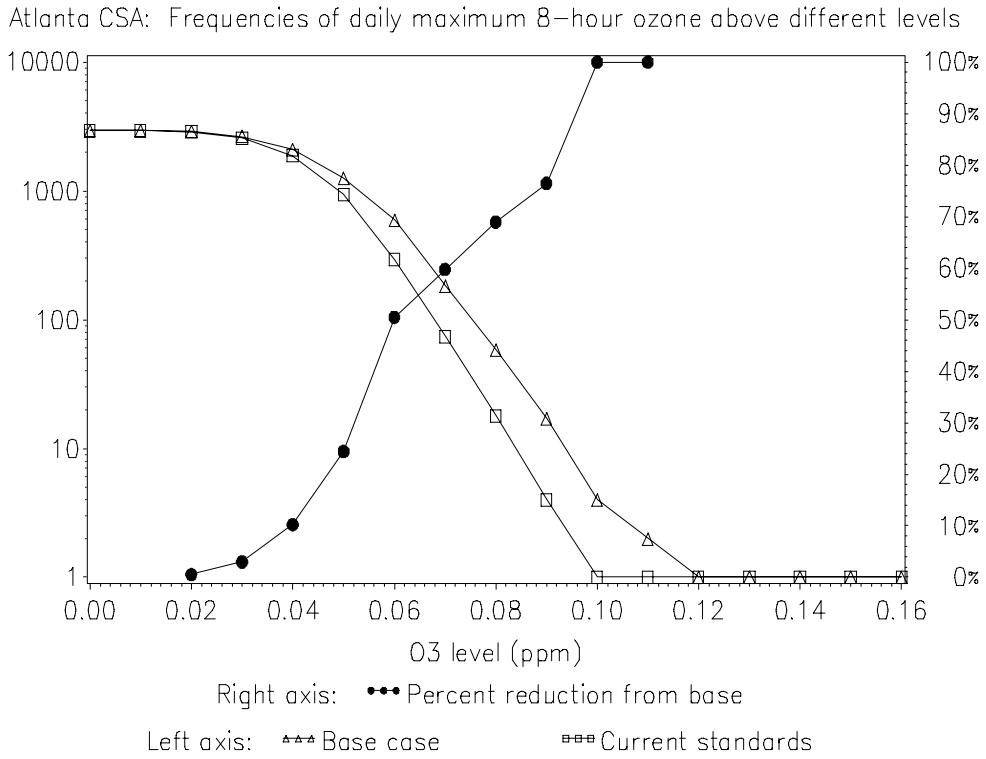


Figure 4B- 2

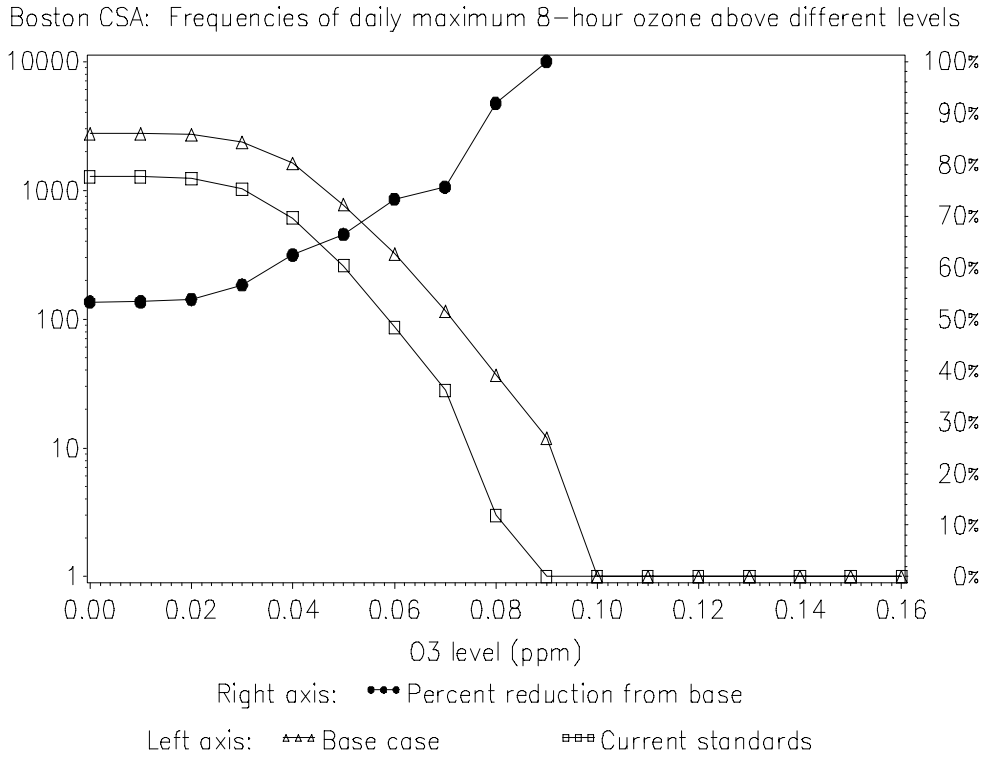


Figure 4B-3

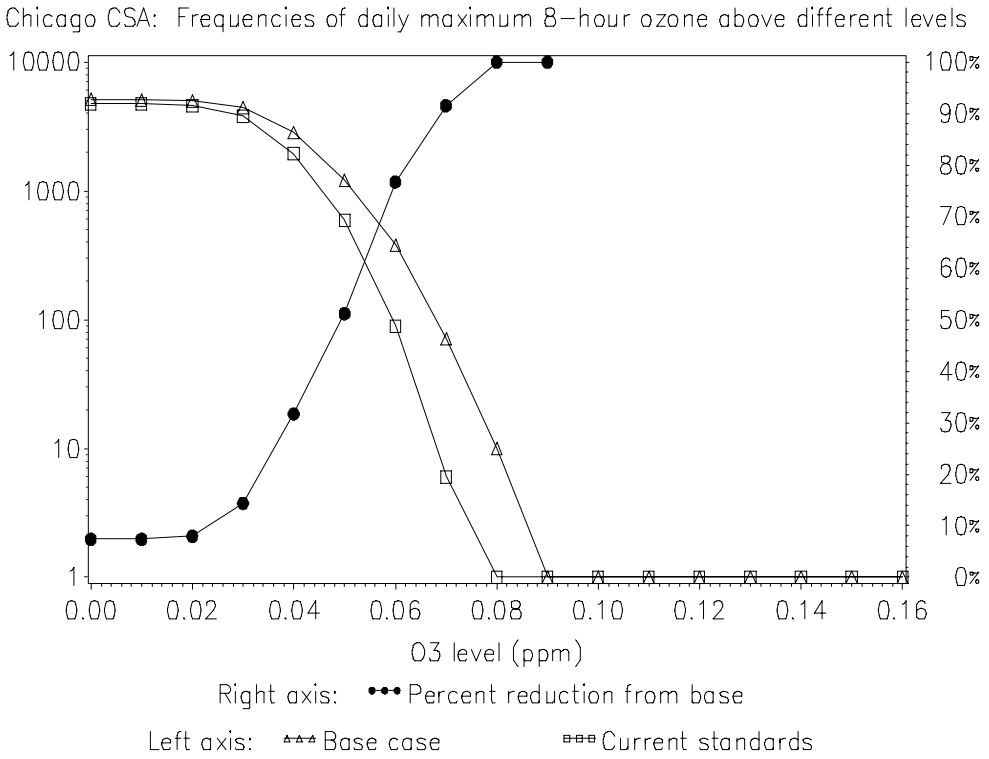


Figure 4B-4

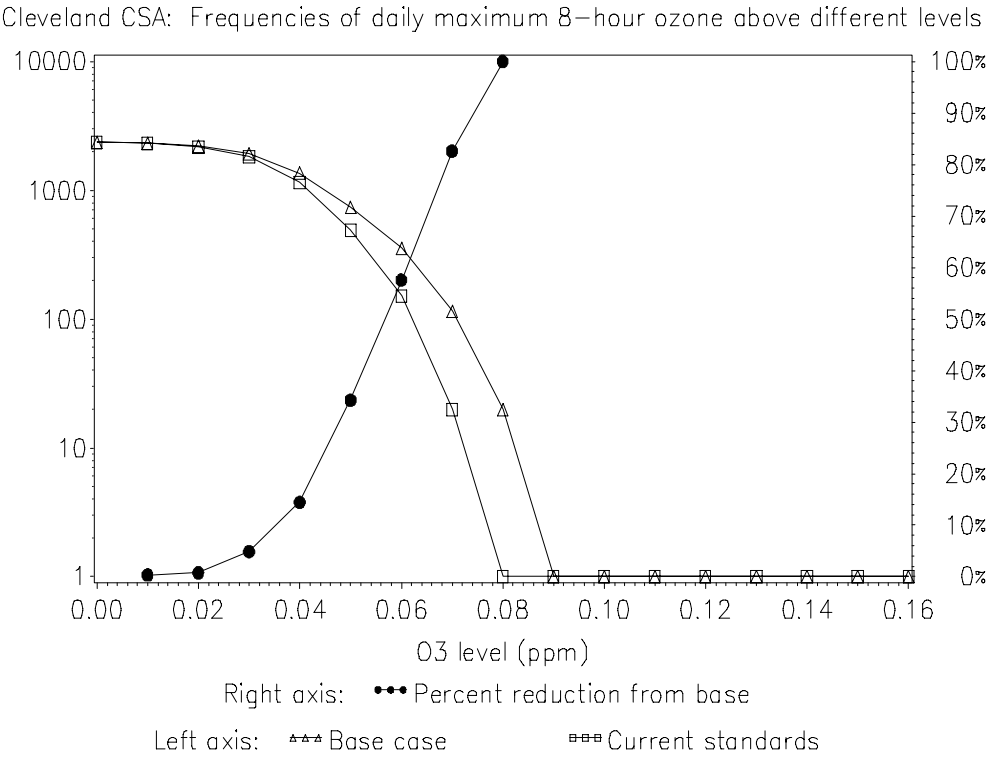


Figure 4B-5

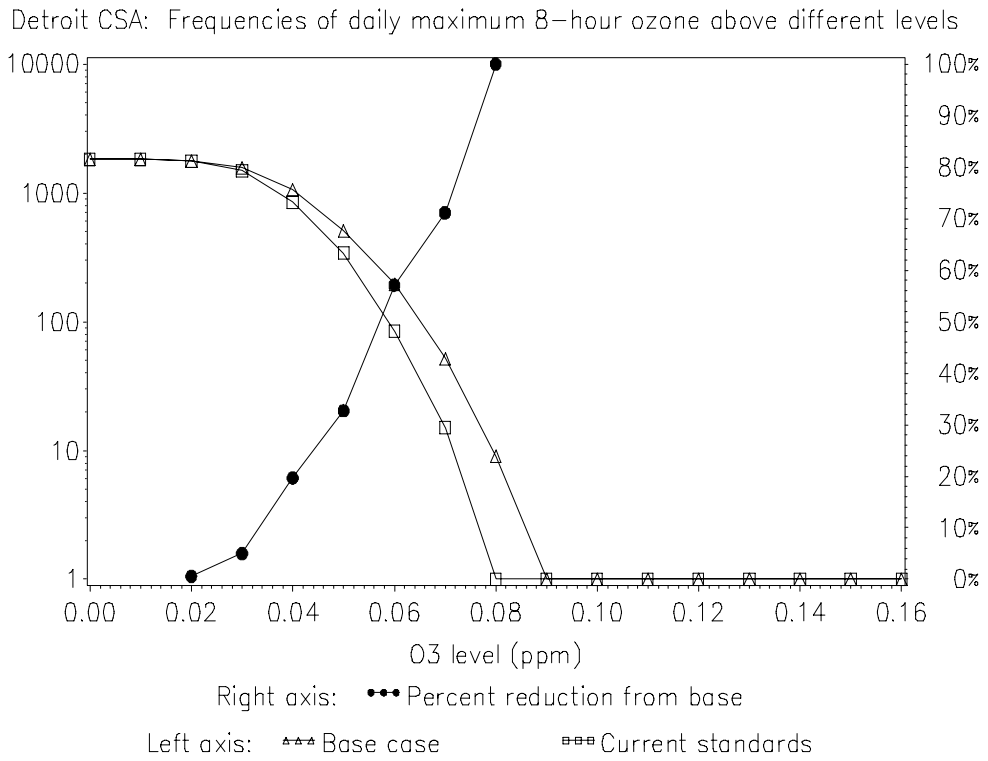


Figure 4B-6

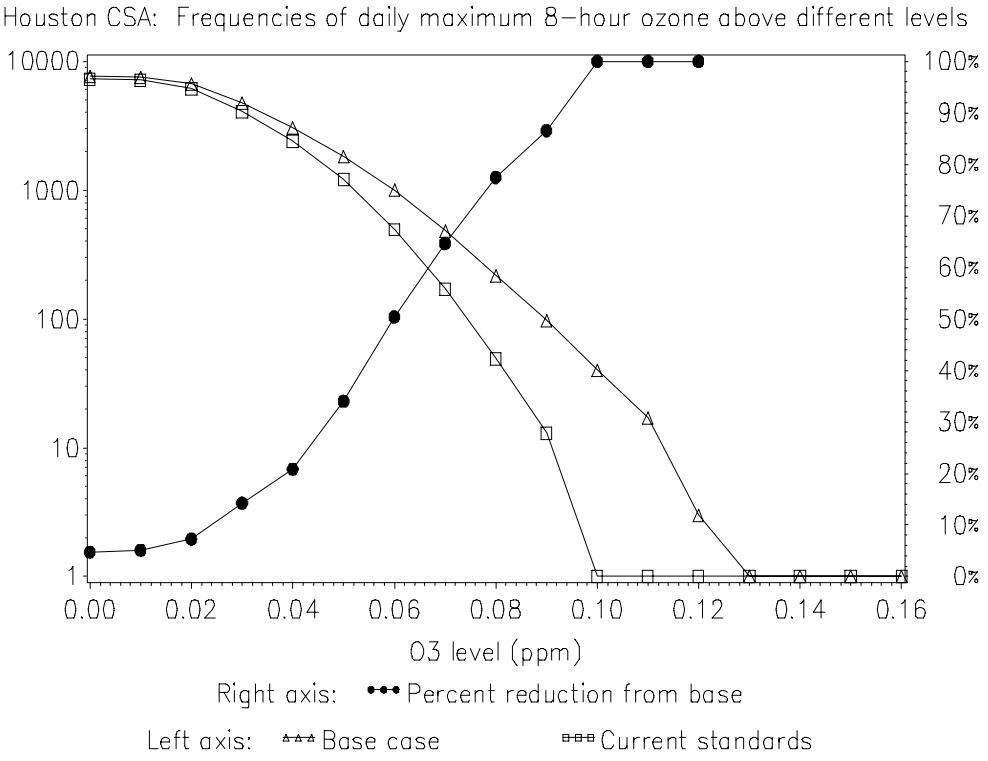


Figure 4B-7

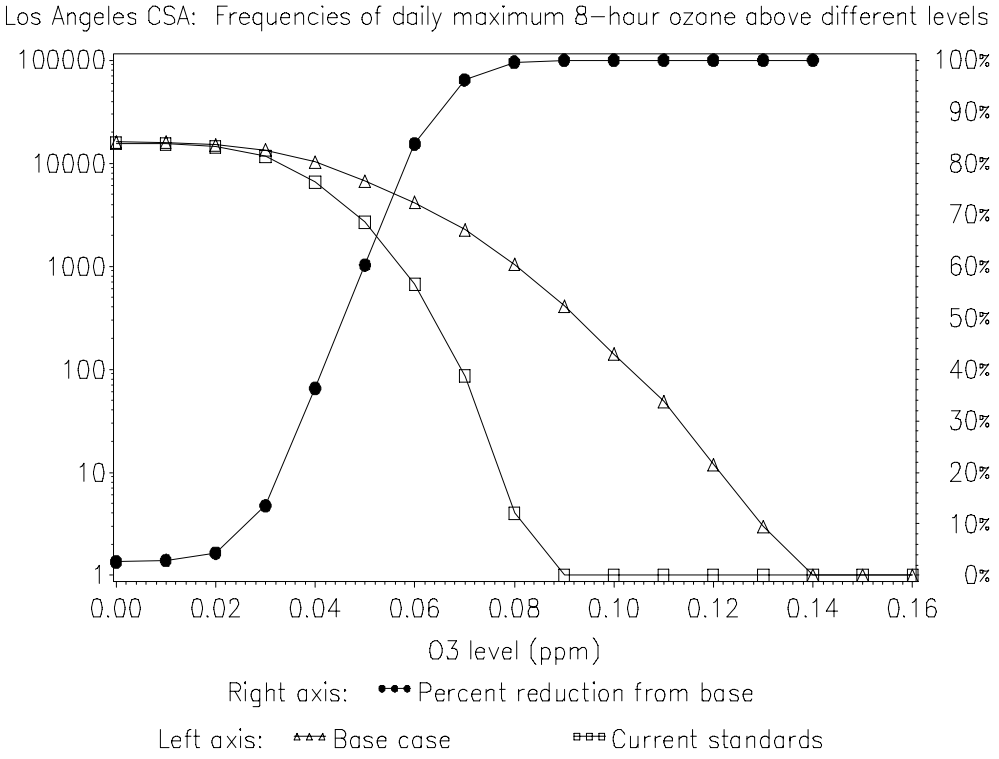


Figure 4B-8

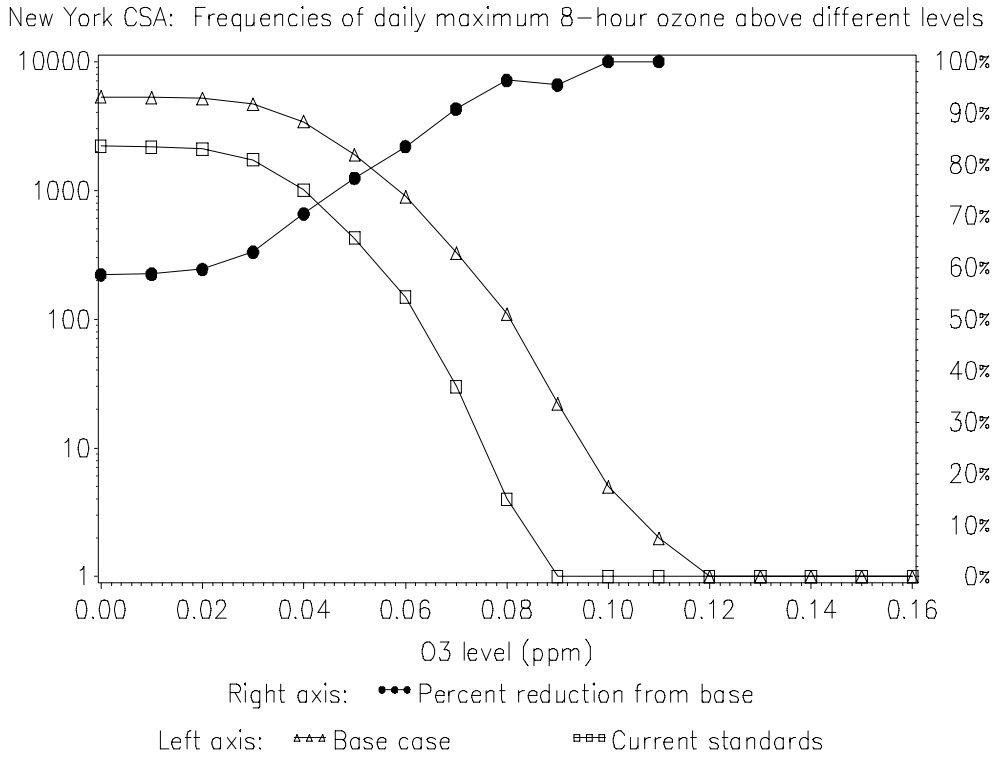


Figure 4B-9

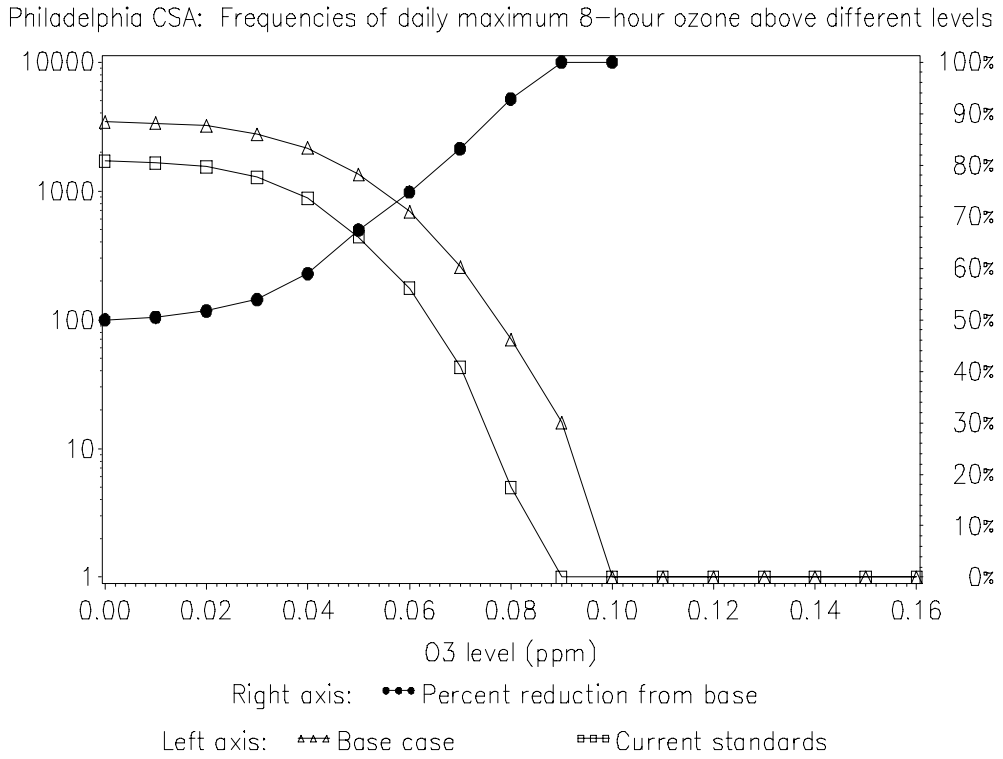


Figure 4B-10

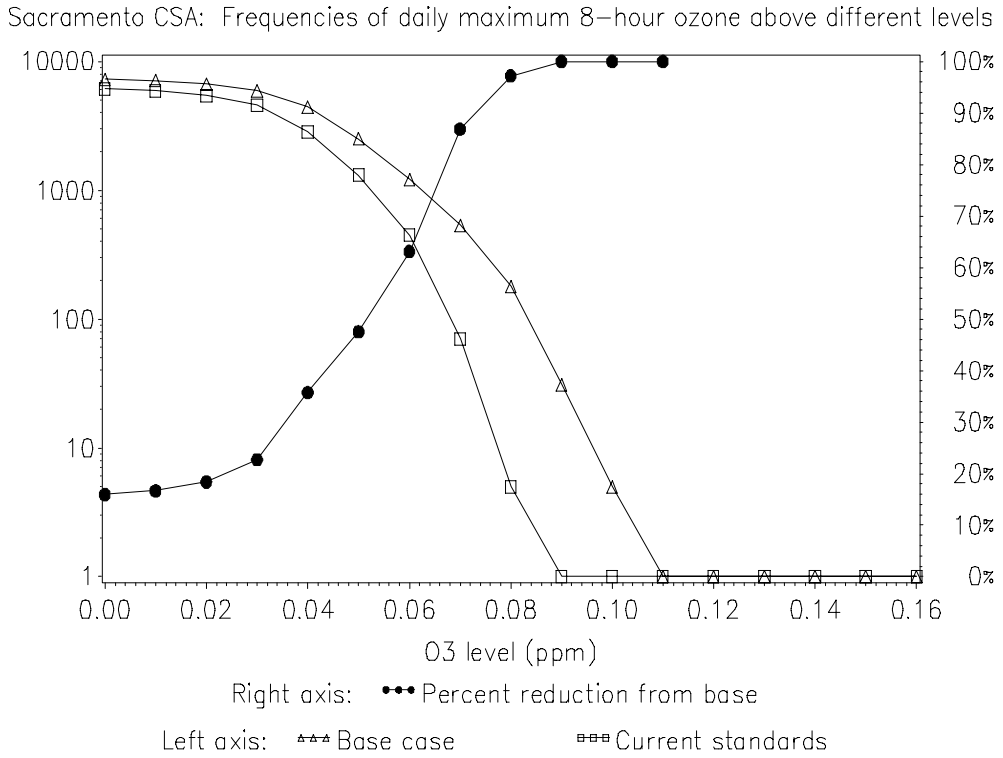


Figure 4B-10 1

Figure 4B-11

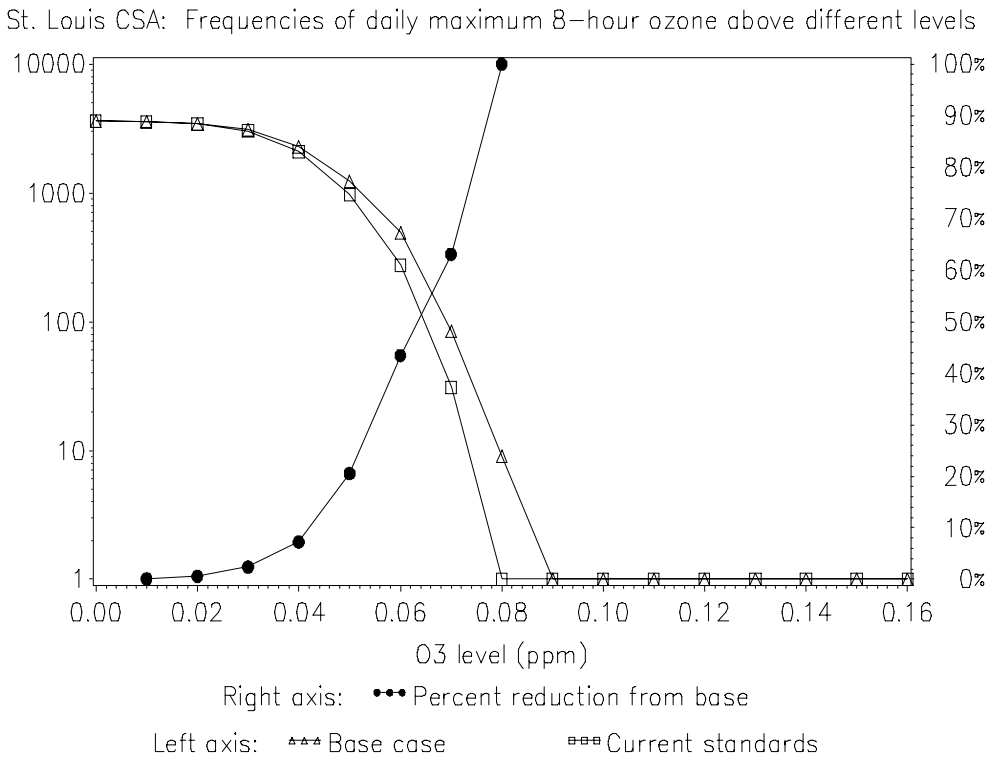
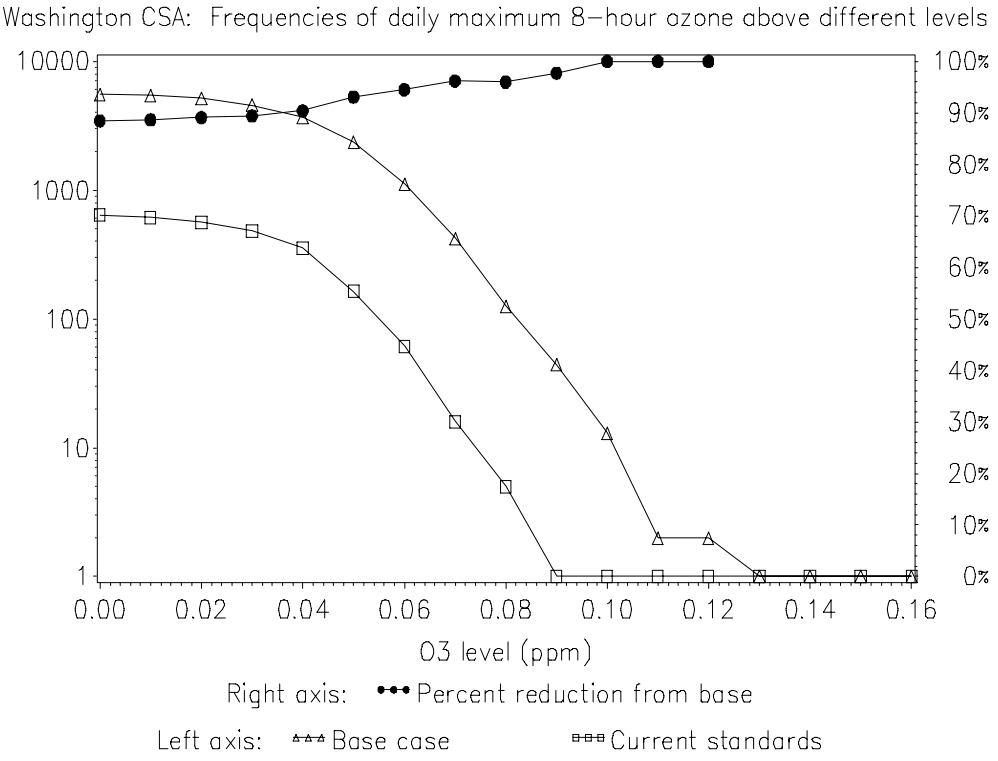


Figure 4B-12



APPENDIX 4C. EXPOSURES FOR EXERCISING CHILDREN

This appendix presents graphs for each modeled city of counts of person-days of daily maxima 8-hour average exposures above different levels, concomitant with moderate exertion, for children ages 5 to 18. The lines with hollow triangles and squares indicate counts for the 2004 base and current standard respectively, and their values can be read off the left axis. The lines with solid circles give the percent reduction from the base to current standard counts, and correspond to the axis on the right.

Figure 4C-1

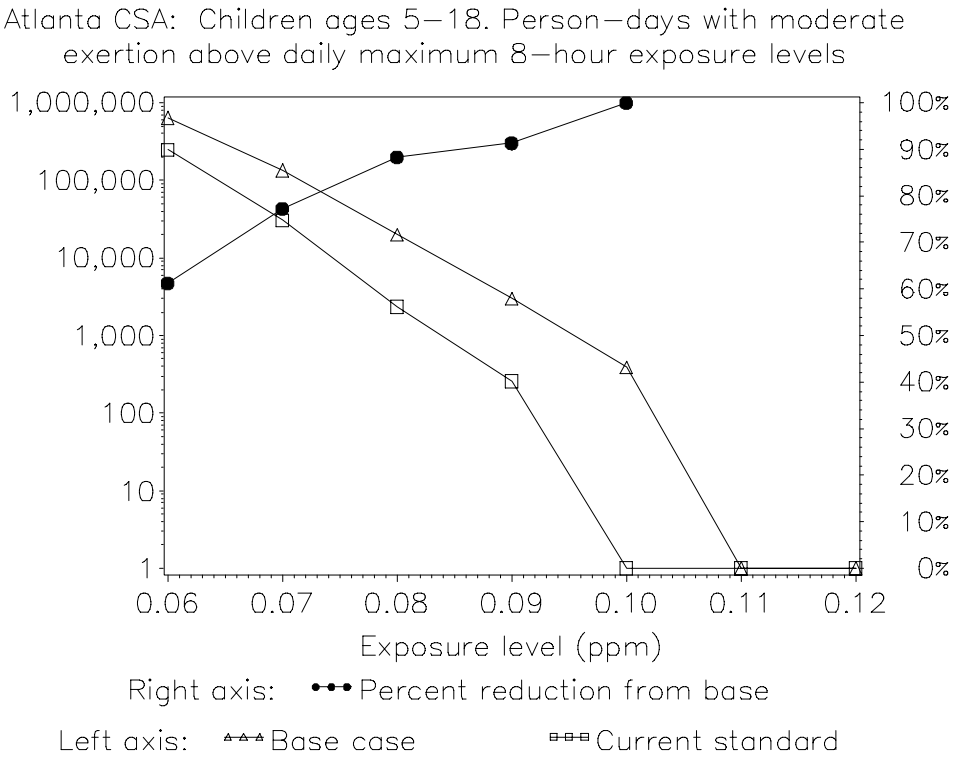


Figure 4C-2 1

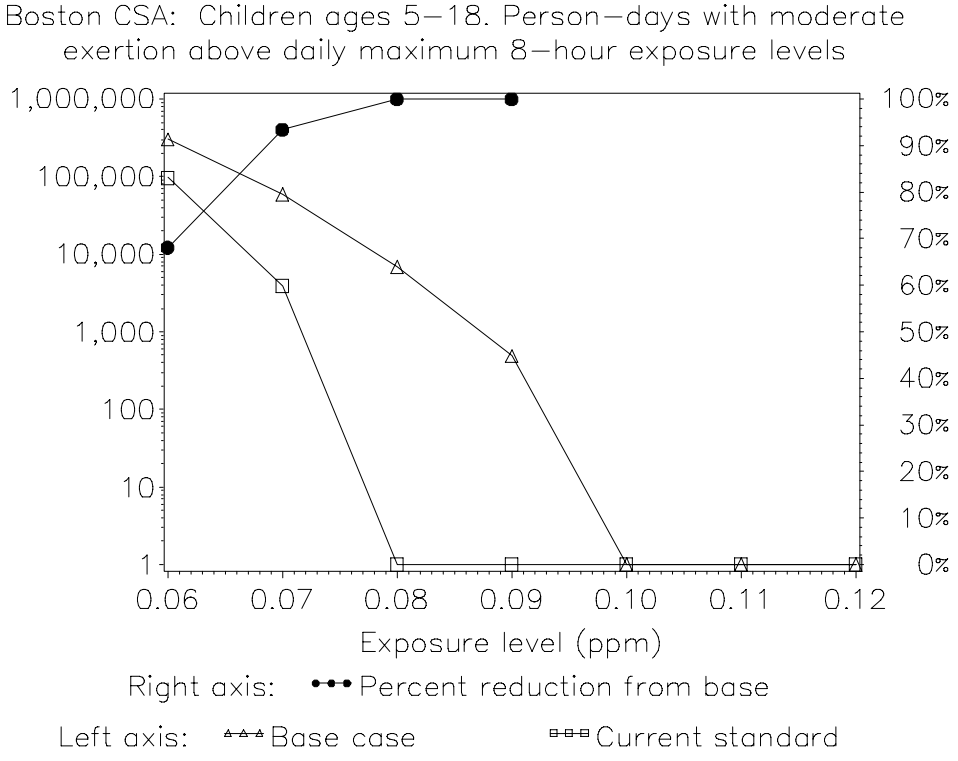


Figure 4C-3

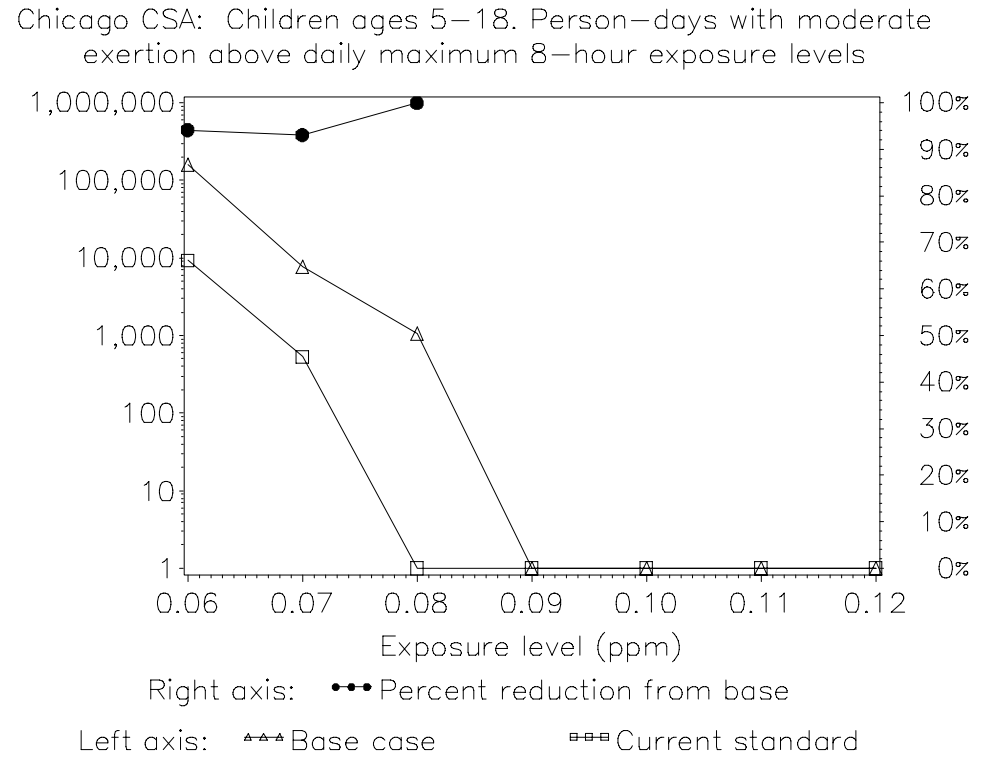


Figure 4C-4

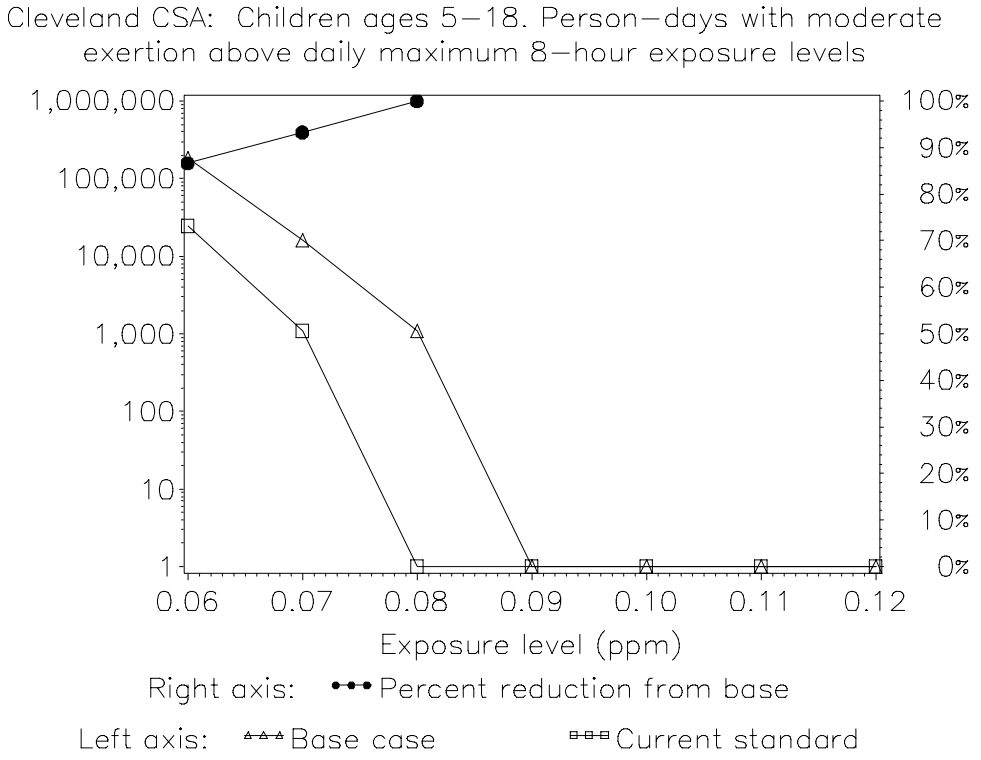


Figure 4C-5

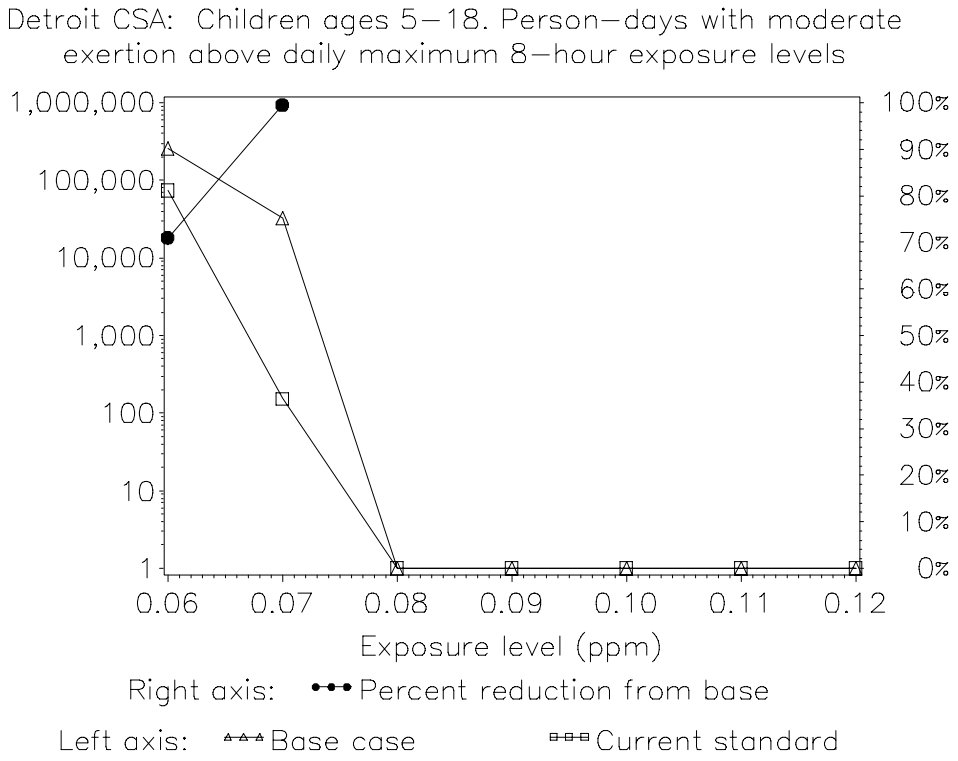


Figure 4C-6

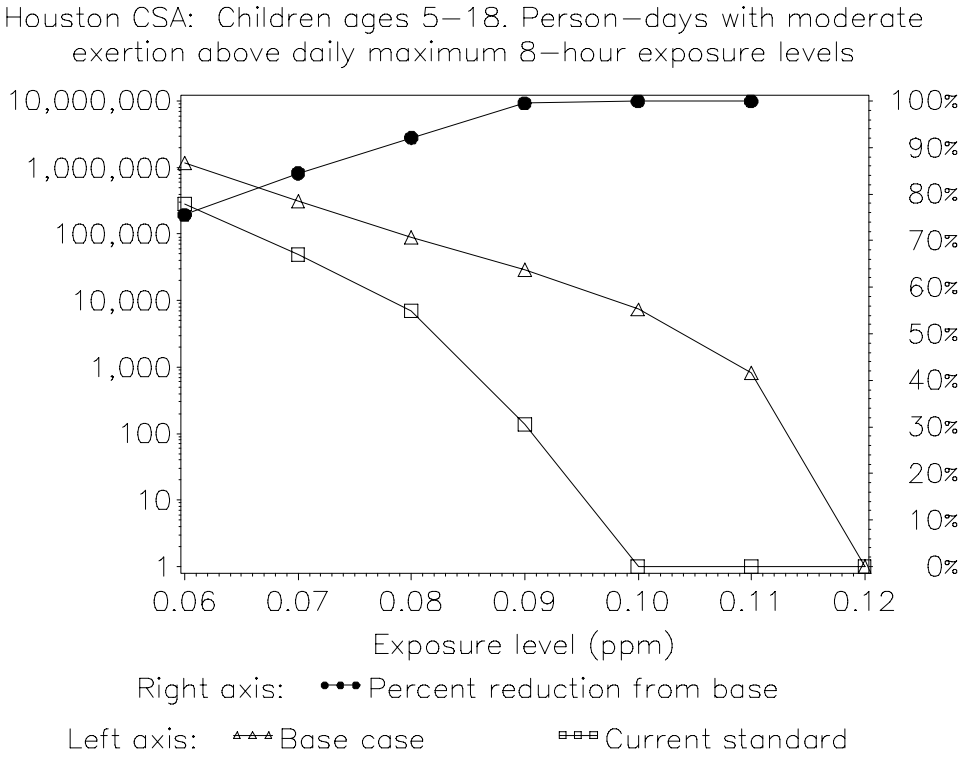


Figure 4C-7

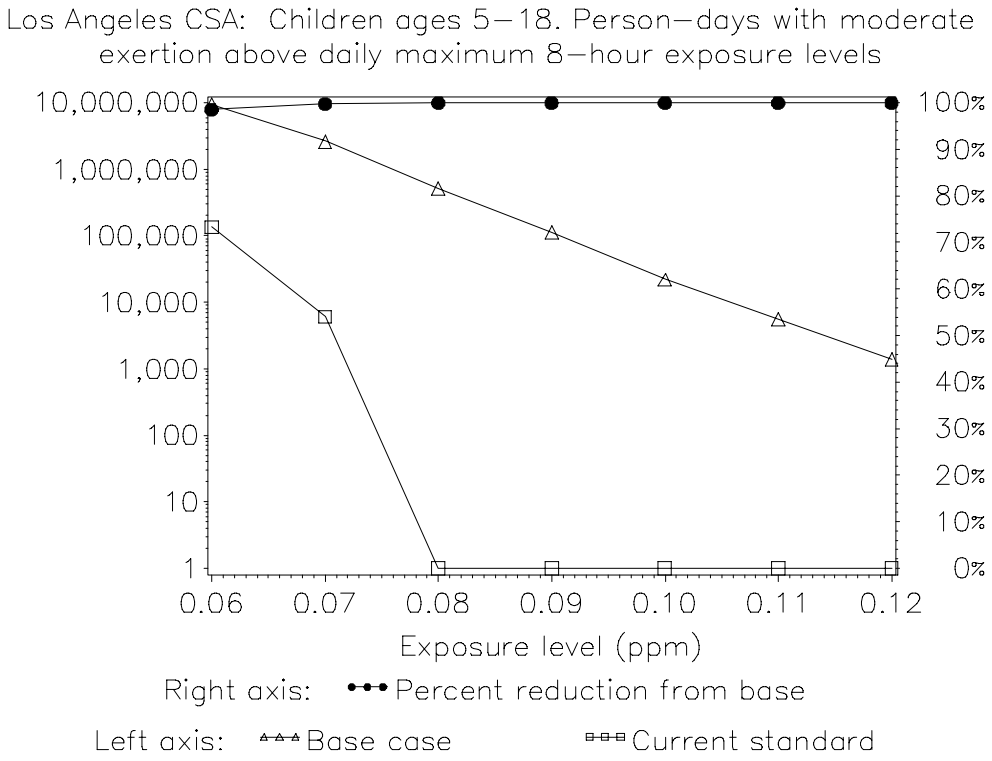


Figure 4C-8

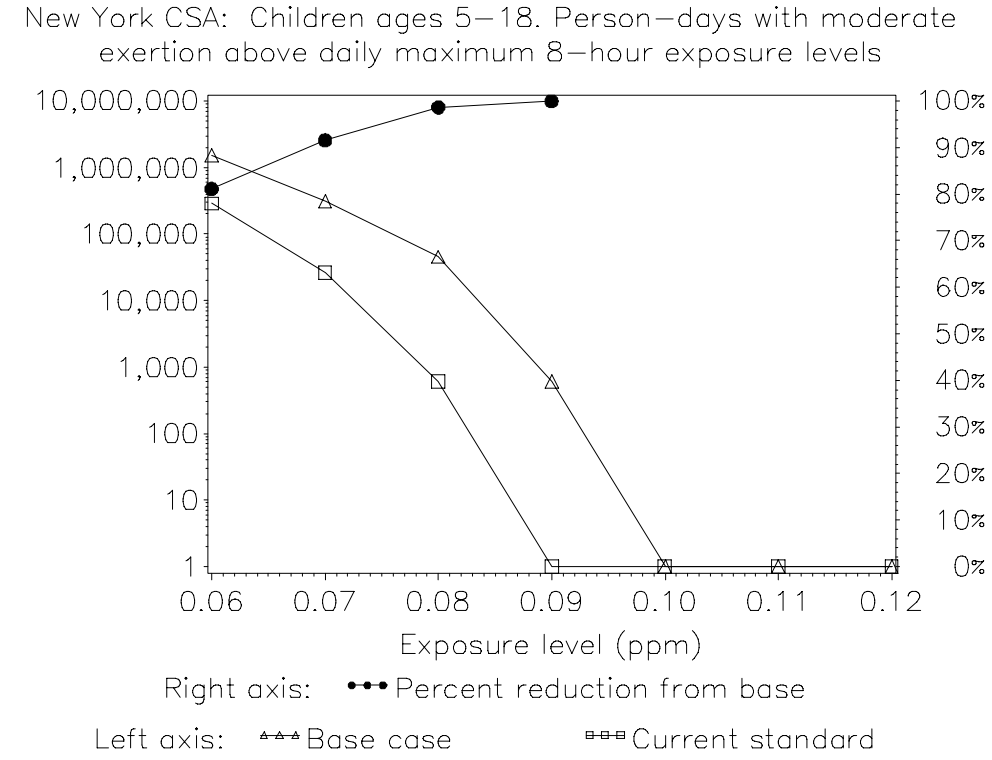


Figure 4C-9

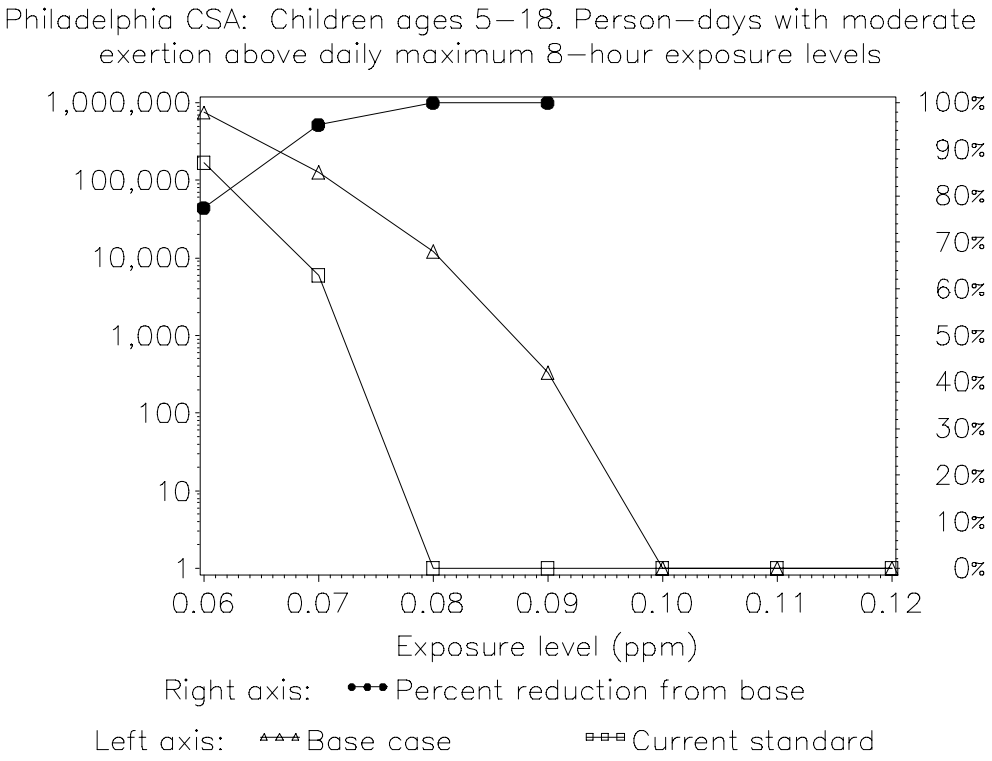


Figure 4C-10

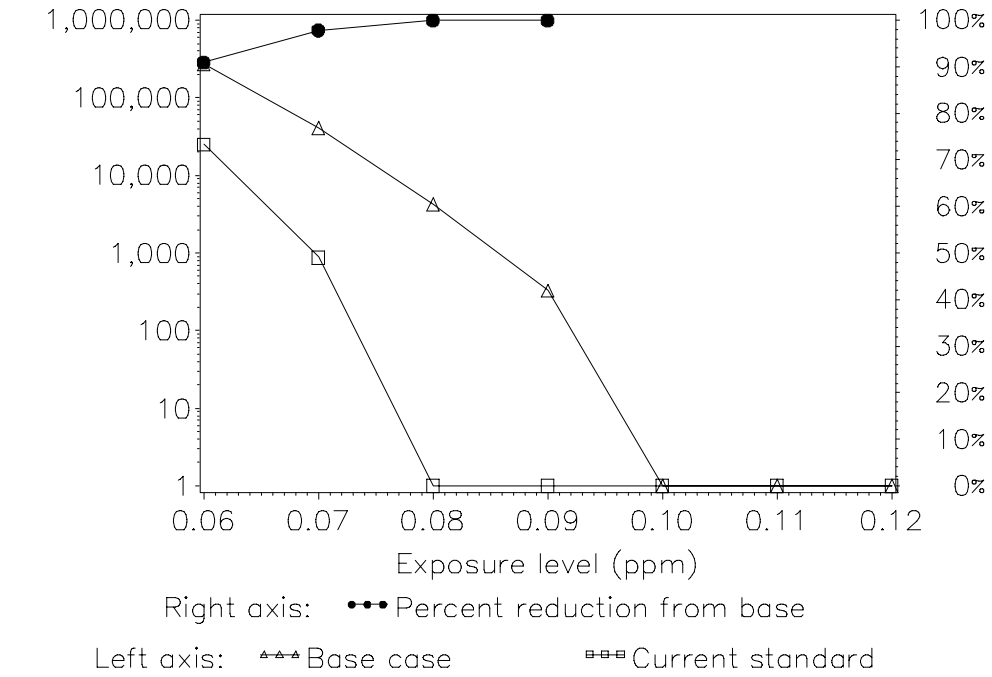


Figure 4C-11

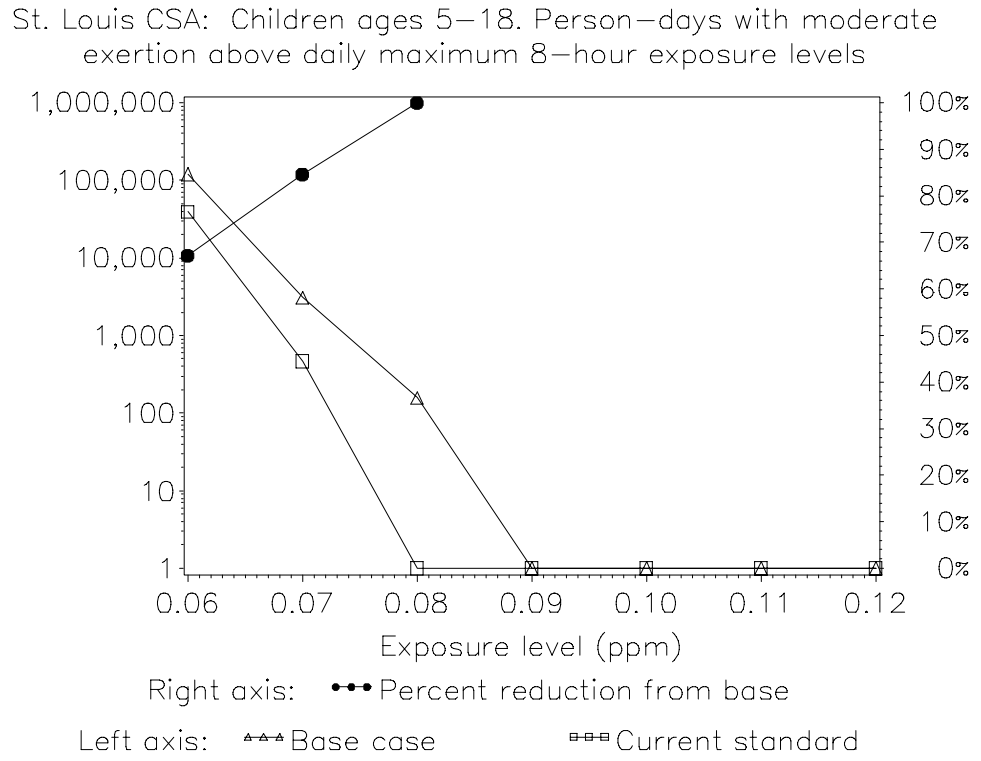
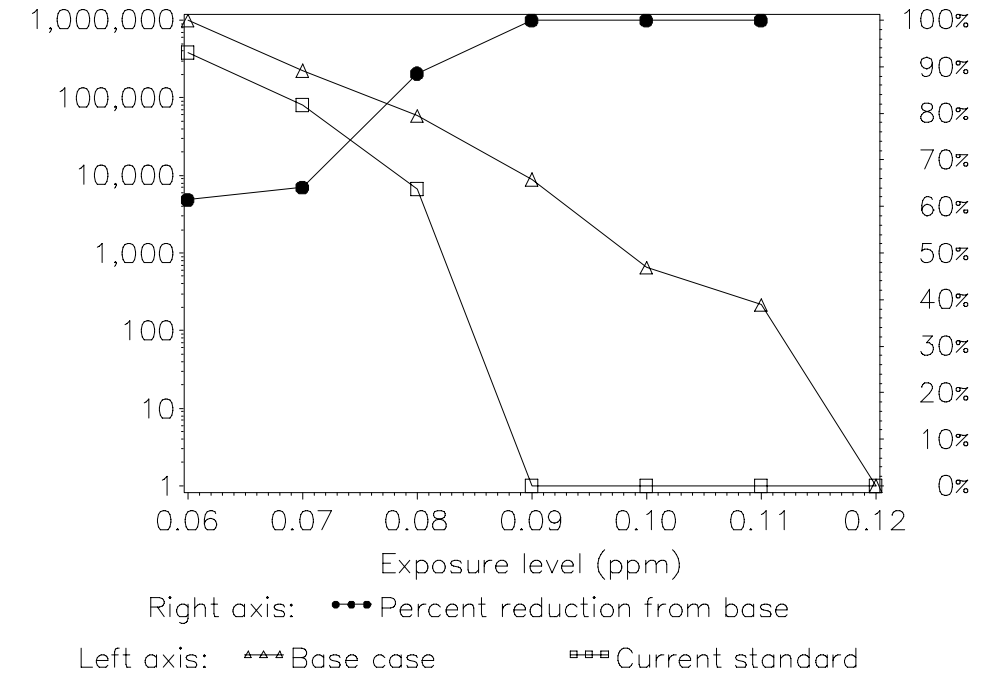


Figure 4C-12



Appendix 4D. Table 4D-1. GEOS-CHEM Grids Used for 12 Urban Locations

City	I	J	latitude	longitude
Atlanta	38	12	34	-85
Boston	43	16	42	-72.5
Chicago	37	16	42	-87.5
Cleveland	39	16	42	-82.5
Detroit	39	16	42	-82.5
Houston	34	10	30	-95
Los Angeles	25	12	34	-117.5
New York	42	15	40	-75
Philadelphia	42	15	40	-75
Sacramento	23	14	38	-122.5
St. Louis	36	14	38	-90
Washington, DC	41	14	38	-77.5

APPENDICES FOR CHAPTER 5

Table 5A-1. Monitor-Specific O_3 Air Quality Information: Atlanta, GA

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
1305700011	0.089			
1306700031	0.100	0.084	0.073	0.085
1307700021	0.099	0.077	0.083	0.086
1308500012	0.088	0.077	0.068	0.077
1308900021	0.095	0.080	0.084	0.086
1308930011	0.090	0.091	0.088	0.089
1309700041	0.098	0.085	0.080	0.087
1311300011	0.088	0.077	0.084	0.083
1312100551	0.100	0.091	0.089	0.093
1313500021	0.089	0.088	0.092	0.089
1315100021	0.099	0.082	0.085	0.088
1322300031	0.099	0.083	0.073	0.085
1324700011	0.099	0.078	0.087	0.088
Average:	0.095	0.083	0.082	
			Design Value*:	0.093

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-2. Monitor-Specific O_3 Air Quality Information: Boston, MA

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
2500900051	0.088			
2500920061	0.100	0.079	0.081	0.086
2500940041	0.094	0.080	0.077	0.083
2501711021	0.096	0.073	0.070	0.079
2502130031	0.107	0.088	0.078	0.091
2502500411	0.102	0.078	0.079	0.086
2502500421	0.074	0.074	0.064	0.07
2502700151	0.091	0.080	0.074	0.081
Average:	0.094	0.079	0.075	
			Design Value*:	0.091

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-3. Monitor-Specific O_3 Air Quality Information: Chicago, IL

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
1703100011	0.094	0.077	0.065	0.078
1703100321	0.096	0.080	0.067	0.081
1703100422	0.103			
1703100501	0.084	0.069		
1703100641	0.085	0.067	0.054	0.068
1703100721	0.085	0.075	0.060	0.073
1703100761			0.068	
1703110032	0.092	0.071	0.067	0.076
1703116011	0.081	0.075	0.067	0.074
1703140021	0.084	0.070	0.059	0.071
1703140071	0.093	0.073	0.064	0.076
1703142011	0.087	0.080	0.067	0.078
1703142012	0.067		0.051	
1703170021	0.091	0.082	0.071	0.081
1703180031	0.074			
1704360011	0.084	0.066	0.065	0.071
1708900051	0.082	0.076	0.069	0.075
1709710021	0.090	0.074	0.068	0.077
1709710071	0.100	0.078	0.071	0.083
1709730011	0.087			
1711100011	0.090	0.079	0.068	0.079
1719710081	0.086	0.077	0.063	0.075
1719710111	0.087	0.073	0.068	0.076
1808900221	0.094	0.076	0.064	0.078
1808900241	0.086	0.081		
1808900301			0.064	
1808920081	0.101	0.081	0.067	0.083
1809100051	0.107	0.082	0.070	0.086
1809100101	0.100	0.084		
1812700202	0.097	0.079		
1812700241	0.101	0.077	0.069	0.082
1812700261	0.100	0.082	0.072	0.084
5505900021	0.110	0.085		
5505900191	0.116	0.088	0.078	0.094
5505900221	0.096	0.088		
Average:	0.092	0.077	0.066	
			Design Value*:	0.094

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-4. Monitor-Specific O_3 Air Quality Information: Cleveland, OH

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
3900710011	0.103	0.099	0.081	0.094
3903500341	0.090	0.076	0.057	0.074
3903500641	0.090	0.079	0.063	0.077
3903550021	0.098	0.089	0.077	0.088
3905500041	0.115	0.097	0.075	0.095
3908500031	0.104	0.092	0.079	0.091
3908530021	0.088	0.080	0.076	0.081
3909300171	0.099	0.085	0.074	0.086
3910300031	0.091	0.086	0.077	0.084
3913310011	0.097	0.091	0.081	0.089
3915300201	0.103	0.089	0.077	0.089
Average:	0.098	0.088	0.074	
			Design Value*:	0.095

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-5. Monitor-Specific O_3 Air Quality Information: Detroit, MI

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
2604900211	0.088	0.087	0.075	0.083
2604920011	0.089	0.091	0.077	0.085
2609900091	0.095	0.102	0.081	0.092
2609910031	0.092	0.101	0.071	0.088
2612500012	0.093	0.090	0.075	0.086
2614700051	0.100	0.086	0.074	0.086
2616100081	0.091	0.091	0.071	0.084
2616300012	0.088	0.085	0.065	0.079
2616300161	0.092	0.084	0.066	0.08
2616300192	0.083	0.098	0.066	0.082
Average:	0.091	0.092	0.072	
			Design Value*:	0.092

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-6. Monitor-Specific O_3 Air Quality Information: Houston, TX

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
4803910032	0.095			
4803910041	0.092	0.097	0.103	0.097
4803910161			0.081	
4816700141	0.093	0.092	0.088	0.091
4816710022	0.083	0.082		
4820100242	0.096	0.095	0.096	0.095
4820100263	0.088	0.098	0.085	0.09
4820100292	0.098	0.096	0.090	0.094
4820100461	0.078	0.093	0.084	0.085
4820100472	0.072	0.082	0.083	0.079
4820100512	0.101	0.103	0.095	0.099
4820100551	0.094	0.107	0.104	0.101
4820100621	0.095	0.094	0.097	0.095
4820100661	0.084	0.081	0.097	0.087
4820100701	0.088	0.100	0.078	0.088
4820100751	0.078	0.096	0.093	0.089
4820110151		0.108	0.093	
4820110342	0.093	0.102	0.091	0.095
4820110353	0.092	0.105	0.092	0.096
4820110391	0.095	0.113	0.097	0.101
4820110411	0.090			
4820110501	0.094	0.092	0.097	0.094
4833900781	0.082	0.094	0.080	0.085
Average:	0.090	0.097	0.091	
			Design Value*:	0.101

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-7. Monitor-Specific O_3 Air Quality Information: Los Angeles, CA

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
0603700021	0.097	0.104	0.092	0.097
0603700161	0.111	0.123	0.095	0.109
0603701131	0.073	0.083	0.076	0.077
0603710021	0.091	0.096	0.089	0.092
0603711031	0.077	0.082	0.078	0.079
0603712011	0.111	0.119	0.101	0.11
0603713011	0.049	0.057	0.065	0.057
0603716011	0.074	0.082	0.079	0.078
0603717011	0.099	0.109	0.095	0.101
0603720051	0.095	0.101	0.093	0.096
0603740021	0.059	0.063	0.070	0.064
0603750011	0.064	0.070		
0603750051			0.085	
0603760121	0.131	0.137	0.107	0.125
0603790331	0.102	0.103	0.095	0.1
0605900071	0.069	0.080	0.088	0.079
0605910031	0.066	0.079	0.076	0.073
0605920221	0.081	0.095	0.085	0.087
0605950011	0.071	0.080	0.075	0.075
0606500121	0.113	0.127	0.112	0.117
0606520021	0.097	0.100	0.094	0.097
0606550011	0.109	0.105	0.099	0.104
0606560011	0.107	0.116	0.095	0.106
0606580011	0.109	0.120	0.111	0.113
0606590011	0.104	0.112	0.100	0.105
0606590031			0.060	
0607100011	0.092	0.088	0.082	0.087
0607100051	0.131	0.130	0.122	0.127
0607100121	0.115	0.103	0.097	0.105
0607100171	0.087	0.084	0.087	0.086
0607103061	0.106	0.104	0.085	0.098
0607110042	0.105	0.114	0.102	0.107
0607112341	0.089	0.087	0.082	0.086
0607120021	0.114	0.132	0.111	0.119
0607140011	0.113	0.110	0.099	0.107
0607140031	0.117	0.137	0.119	0.124
0607190021	0.101	0.111	0.102	0.104
0607190041	0.105	0.123	0.112	0.113
0611100051	0.076			
0611100071	0.080	0.087	0.086	0.084
0611100091	0.087	0.093	0.086	0.088
0611110041	0.097	0.093	0.092	0.094
0611120021	0.092	0.093	0.092	0.092
0611120031	0.064	0.074	0.069	0.069
0611130011	0.064	0.069	0.065	0.066
Average:	0.093	0.099	0.091	
			Design Value*:	0.127

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-8. Monitor-Specific O_3 Air Quality Information: New York, NY

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
3600500831	0.096	0.079	0.074	0.083
3600501101	0.089	0.082	0.069	0.08
3602700071	0.111	0.081	0.076	0.089
3607150011	0.082	0.087	0.078	0.082
3607900051	0.102	0.082	0.082	0.088
3608100981	0.082	0.072	0.064	0.072
3608101241	0.089	0.086	0.075	0.083
3608500671	0.099	0.086	0.083	0.089
3610300021	0.108	0.094	0.081	0.094
3610300041	0.090	0.082		
3610300092	0.103	0.102	0.079	0.094
3611110051	0.084	0.082	0.076	0.08
3611920041	0.102	0.091	0.078	0.09
Average:	0.095	0.085	0.076	
			Design Value*:	0.094

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-9. Monitor-Specific O_3 Air Quality Information: Philadelphia, PA

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
4201700121	0.111	0.087	0.082	0.093
4202900501	0.104	0.085		
4202901001	0.112	0.085	0.085	0.094
4204500021	0.106	0.080	0.081	0.089
4209100131	0.101	0.085	0.083	0.089
4210100041	0.082	0.069	0.054	0.068
4210100141	0.098	0.083	0.077	0.086
4210100241	0.110	0.082	0.091	0.094
4210101361	0.094	0.070	0.073	0.079
Average:	0.102	0.081	0.078	
			Design Value*:	0.094

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-10. Monitor-Specific O_3 Air Quality Information: Sacramento, CA

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
0601700101	0.098	0.096	0.089	0.094
0601700111	0.067	0.065		
0601700121	0.077	0.075	0.073	0.075
0601700201	0.111	0.106	0.089	0.102
0605700051	0.099	0.098	0.093	0.096
0605700071	0.093	0.090	0.085	0.089
0605710011	0.065			
0606100021	0.101	0.094	0.092	0.095
0606100041	0.101	0.089	0.087	0.092
0606100061	0.095	0.085	0.082	0.087
0606100071		0.068		
0606130011	0.097			
0606700021	0.095	0.086	0.076	0.085
0606700061	0.105	0.097	0.083	0.095
0606700101	0.083	0.076	0.067	0.075
0606700111	0.069	0.087	0.077	0.077
0606700121	0.104	0.098	0.087	0.096
0606700131	0.079	0.075	0.067	0.073
0606750031	0.097	0.097	0.089	0.094
0611300041	0.076	0.077	0.071	0.074
0611310031	0.088	0.082	0.069	0.079
Average:	0.090	0.086	0.081	
			Design Value*:	0.102

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-11. Monitor-Specific O_3 Air Quality Information: St. Louis, MO

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
1708310011	0.100	0.083	0.073	0.085
1711700021	0.085	0.077	0.068	0.076
1711900081	0.094	0.089	0.074	0.085
1711910091	0.090	0.088	0.078	0.085
1711920072	0.090	0.082	0.068	0.08
1711930071	0.084	0.083	0.073	0.08
1716300102	0.093	0.079	0.073	0.081
2909900121	0.093	0.082	0.070	0.081
2918310021	0.099	0.091	0.077	0.089
2918310041	0.098	0.090	0.076	0.088
2918900041	0.098	0.088	0.070	0.085
2918900061	0.094	0.086	0.067	0.082
2918930011	0.094	0.082	0.067	0.081
2918950011	0.095	0.088	0.068	0.083
2918970031	0.093	0.088	0.069	0.083
2951000071	0.090	0.084		
2951000721	0.081	0.071	0.058	0.07
2951000861	0.098	0.090	0.072	0.086
Average:	0.093	0.085	0.071	
			Design Value*:	0.089

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5A-12. Monitor-Specific O_3 Air Quality Information: Washington, D.C.

AIRS Monitor ID	Fourth Daily Maximum 8-Hour Average (ppm)			Average of the 3 Year-Specific Values (ppm)
	2002	2003	2004	
1100100251	0.097	0.079	0.080	0.085
1100100411	0.102	0.082	0.070	0.084
1100100431	0.106	0.081	0.081	0.089
Average:	0.102	0.081	0.077	
			Design Value*:	0.089

*The design value is the maximum of the monitor-specific averages of the annual fourth daily maximum 8-hour average over the 3 year period.

Table 5B-1. Summary of Locations, Concentration-Response Functions, Months Included and Counties Included

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
Atlanta	March - October	Bell et al. (2004) - 95 cities	non-accidental mortality	none[2]	24-hr avg.	April - October	---
		Bell et al. (2004) - Atlanta	non-accidental mortality	none	24-hr avg.	April - October	Fulton, De Kalb [3]
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - Atlanta	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Fulton, De Kalb
Boston	April - September	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
Chicago	April - September	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - Chicago	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Cook
		Schwartz (2004) - 14-city	non-accidental mortality	none	1-hr max.	May - September	---
		Schwartz (2004) - Chicago	non-accidental mortality	none	1-hr max.	May - September	Cook [4]
Cleveland	April - October	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Bell et al. (2004) - Cleveland	non-accidental mortality	none	24-hr avg.	April - October	Cuyahoga
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - Cleveland	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Cuyahoga
		Schwartz et al. (1996)	hosp. adms. for resp. illness	none	1-hr max.	"warm season"	Cuyahoga
Detroit	April - October	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---
		Bell et al. (2004) - Detroit	non-accidental mortality	none	24-hr avg.	April - October	Wayne

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - Detroit	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Wayne
		Schwartz (2004) - 14-city	non-accidental mortality	none	1-hr max.	May - September	---
		Schwartz (2004) - Detroit	non-accidental mortality	none	1-hr max.	May - September	Wayne [4]
		Ito (2003) – GAM stringent[5]	non-accidental mortality	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GAM stringent	circulatory mortality	none	24-hr avg.	April - October	Wayne

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Ito (2003) – GAM stringent	respiratory mortality	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GAM stringent	unscheduled hospital adms. For pnuemonia	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GAM stringent	unscheduled hospital adms. For COPD	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GAM stringent	unscheduled hospital adms. for ischemic heart disease	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GAM stringent	unscheduled hospital adms. For heart failure	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GAM stringent	unscheduled hospital adms. For dysrhythmias	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GLM[6]	unscheduled hospital adms. For pnuemonia	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GLM	unscheduled hospital adms. For COPD	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GLM	unscheduled hospital adms. for ischemic heart disease	none	24-hr avg.	April - October	Wayne

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Ito (2003) – GLM	unscheduled hospital adms. For heart failure	none	24-hr avg.	April - October	Wayne
		Ito (2003) – GLM	unscheduled hospital adms. For dysrhythmias	none	24-hr avg.	April - October	Wayne
Houston	All year	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---
		Bell et al. (2004) - Houston	non-accidental mortality	none	24-hr avg.	All year	Harris
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - Houston	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Harris

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Schwartz (2004) - 14-city	non-accidental mortality	none	1-hr max.	May - September	---
		Schwartz (2004) - Houston	non-accidental mortality	none	1-hr max.	May - September	Harris [4]
Los Angeles	All year	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---
		Bell et al. (2004) - Los Angeles	non-accidental mortality	none	24-hr avg.	All year	Los Angeles
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - Los Angeles	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Los Angeles

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Linn et al. (2000)	unscheduled hosp. adms. for cardiovascular illness	none	24-hr avg.	All year; separately by season	Los Angeles, Riverside, San Bernardino, Orange[7]
		Linn et al. (2000)	unscheduled hosp. adms. for pulmonary illness	none	24-hr avg.	All year; separately by season	Los Angeles, Riverside, San Bernardino, Orange[7]
		Linn et al. (2000)	unscheduled hosp. adms. for cerebrovascular illness	none	24-hr avg.	All year; separately by season	Los Angeles, Riverside, San Bernardino, Orange[7]
New York	April - September	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - New York	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Bronx, Kings, New York, Richmond, Queens, Westchester
		Thurston et al. (1992)	unscheduled hosp. adms. for respiratory illness	none	1-hr max.	June - August	Bronx, Kings, New York, Richmond, Queens[8]
		Thurston et al. (1992)	unscheduled hosp. adms. for asthma	none	1-hr max.	June - August	Bronx, Kings, New York, Richmond, Queens
Philadelphia	April - October	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	---

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	PM_{10}	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	NO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	SO_2	24-hr avg.	June - September	---
		Huang et al. (2004) - 19 cities	cardiovascular and respiratory mortality	CO	24-hr avg.	June - September	---
		Huang et al. (2004) - Phila.	cardiovascular and respiratory mortality	none	24-hr avg.	June - September	Philadelphia
		Moolgavkar et al. (1995)	non-accidental mortality	none	24-hr avg.	June - August	Philadelphia
		Moolgavkar et al. (1995)	non-accidental mortality	TSP, SO_2	24-hr avg.	June - August	Philadelphia
Sacramento	All year	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---
		Bell et al. (2004) - Sacramento	non-accidental mortality	none	24-hr avg.	All year	Sacramento
St. Louis	April - October	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---

Risk Assessment Location	Ozone Season in Risk Assessment Location	Study/C-R Function	Health Endpoint	Other Pollutants in Model	Exposure Metric	Months Included for C-R Functions[1]	Counties Included for C-R Functions
		Bell et al. (2004) - St. Louis	non-accidental mortality	none	24-hr avg.		St. Louis city (FIPS 29510)
Washington, D.C.	April - October	Bell et al. (2004) - 95 cities	non-accidental mortality	none	24-hr avg.	April - October	---

[1] The months listed here are the months for which the concentration-response function was estimated. However, all concentration-response functions were *applied* in the risk assessment to April – Sept.

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

[3] Counties used by Bell et al. and Huang et al. are provided at http://www.ihapss.jhsph.edu/data/NMMAPS/documentation/counties.htm and in the June 2000 NMMAPS report (Number 94, Part II) are given in Appendix A, Table A.1.

[4] Personal communication via email (6-12-05) from J. Schwartz.

[5] Generalized Additive Model, using a stringent convergence criterion.

[6] Generalized Linear Model.

[7] Excluding mountain and desert regions of the first three counties.

[8] The paper doesn't list the counties, but notes that, in the case of New York City, surrounding counties were not included; this implies that only the five counties of which New York City is comprised are included in the analysis. This was confirmed in a personal communication from the author (G. Thurston).

5C.1 Tables of Study-Specific Information

Table 5C-1. Study-Specific Information for O_3 Studies in Atlanta, GA

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	0	71	0.00020	-0.00084	0.00123
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Huang et al. (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	0	71	0.00120	-0.00039	0.00279
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

Table 5C-2. Study-Specific Information for O_3 Studies in Boston, MA

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	-3	86	0.00028	-0.00079	0.00136

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

Table 5C-3. Study-Specific Information for O_3 Studies in Chicago, IL

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Schwartz (2004)	Mortality, non-accidental	< 800	all	0-day lag	1 hr max.	logistic	none	NA	NA	0.00099	0.00031	0.00166
Schwartz -- 14 US Cities (2004)	Mortality, non-accidental	< 800	all	0-day lag	1 hr max.	logistic	none	NA	NA	0.00037	0.00012	0.00062
Huang et al. (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	0	65	0.00075	-0.00067	0.00218
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

Table 5C-4. Study-Specific Information for O_3 Studies in Cleveland, OH

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	2	75	0.00061	-0.00038	0.00161
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Huang et al. (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	2	75	0.00148	-0.00004	0.00299
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117
Schwartz et al. (1996)	Hospital admissions, respiratory illness	460-519	65+	avg of 1-day and 2-day lags	1 hr max.	log-linear	none	NA	NA	0.00086	0.00020	0.00148

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

Table 5C-5. Study-Specific Information for O_3 Studies in Detroit, MI

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	2	75	0.00076	-0.00024	0.00177
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Schwartz (2004)	Mortality, non-accidental	< 800	all	0-day lag	1 hr max.	logistic	none	NA	NA	0.00068	-0.00011	0.00148
Schwartz -- 14 US Cities (2004)	Mortality, non-accidental	< 800	all	0-day lag	1 hr max.	logistic	none	NA	NA	0.00037	0.00012	0.00062
Ito (2003)	Mortality, non-accidental	< 800	all	0-day lag	24 hr avg.	log-linear	none	NA	NA	0.00093	-0.00085	0.00271
Ito (2003)	Mortality, respiratory	460-519	all	0-day lag	24 hr avg.	log-linear	none	NA	55	0.00359	-0.00276	0.00993
Ito (2003)	Mortality, circulatory	390-459	all	0-day lag	24 hr avg.	log-linear	none	NA	55	0.00089	-0.00172	0.00349
Huang et al. (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	2	75	0.00135	-0.00015	0.00286
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117
Ito (2003)	Hospital admissions (unscheduled), pneumonia	480-486	65+	0-day lag	24 hr avg.	log-linear (GAM str. estimation)***	none	NA	55	-0.00218	-0.00621	0.00186
Ito (2003)	Hospital admissions (unscheduled), pneumonia	480-486	65+	1-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	-0.00054	-0.00459	0.00352
Ito (2003)	Hospital admissions (unscheduled), pneumonia	480-486	65+	2-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00066	-0.00342	0.00473
Ito (2003)	Hospital admissions (unscheduled), pneumonia	480-486	65+	3-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00190	-0.00216	0.00595
Ito (2003)	Hospital admissions (unscheduled), ischemic heart disease	410-414	65+	0-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00054	-0.00221	0.00328
Ito (2003)	Hospital admissions (unscheduled), ischemic heart disease	410-414	65+	1-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	-0.00047	-0.00325	0.00231
Ito (2003)	Hospital admissions (unscheduled), ischemic heart disease	410-414	65+	2-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00071	-0.00211	0.00354
Ito (2003)	Hospital admissions (unscheduled), ischemic heart disease	410-414	65+	3-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00140	-0.00139	0.00418
Ito (2003)	Hospital admissions (unscheduled), heart failure	428	65+	0-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00065	-0.00252	0.00383

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Ito (2003)	Hospital admissions (unscheduled), heart failure	428	65+	1-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00323	0.00002	0.00645
Ito (2003)	Hospital admissions (unscheduled), heart failure	428	65+	2-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00223	-0.00104	0.00550
Ito (2003)	Hospital admissions (unscheduled), heart failure	428	65+	3-day lag	24 hr avg.	log-linear (GAM str. estimation)	none	NA	55	0.00178	-0.00145	0.00501

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

***"GAM str. estimation" denotes that estimation of the log-linear C-R function used a generalized additive model with a stringent convergence criterion. This study also estimated log-linear C-R functions using generalized linear models (GLM).

NA denotes "not available."

Table 5C-6. Study-Specific Information for O_3 Studies in Houston, TX

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	1	76	0.00079	0.00005	0.00154
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Schwartz (2004)	Mortality, non-accidental	< 800	all	0-day lag	1 hr max.	logistic	none	NA	NA	0.00044	0.00004	0.00084
Schwartz -- 14 US Cities (2004)	Mortality, non-accidental	< 800	all	0-day lag	1 hr max.	logistic	none	NA	NA	0.00037	0.00012	0.00062
Huang et al. (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	1	76	0.00122	-0.00016	0.00261
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

Table 5C-7. Study-Specific Information for O_3 Studies in Los Angeles, CA

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. (2004)***	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	0	68	0.00018	-0.00043	0.00079
Bell et al. -- 95 US Cities (2004)***	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Huang et al. (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	0	68	0.00107	0.00001	0.00213
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117
Linn et al. (2000)****	Hospital admissions (unscheduled), pulmonary illness -- spring	75-101*****	30+	0-day lag	24 hr avg.	log-linear	none	1	70	0.00110	-0.00047	0.00267
Linn et al. (2000)****	Hospital admissions (unscheduled), pulmonary illness -- summer	75-101*****	30+	0-day lag	24 hr avg.	log-linear	none	1	70	0.00060	-0.00077	0.00197
Linn et al. (2000)****	Hospital admissions (unscheduled), cardiovascular illness -- spring	103-144*****	30+	0-day lag	24 hr avg.	log-linear	none	1	70	0.00030	-0.00068	0.00128
Linn et al. (2000)****	Hospital admissions (unscheduled), cardiovascular illness -- summer	103-144*****	30+	0-day lag	24 hr avg.	log-linear	none	1	70	0.00010	-0.00088	0.00108

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

***Los Angeles is defined in this study as Los Angeles County.

****Los Angeles is defined in this study as Los Angeles, Riverside, San Bernardino, and Orange Counties.

*****Linn et al. (2000) used DRG codes instead of ICD codes.

Table 5C-8. Study-Specific Information for O_3 Studies in New York, NY

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. -- 95 US Cities (2004)***	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Huang et al. (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	-2	81	0.00170	0.00054	0.00286
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)***	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117
Thurston et al. (1992)****	Hospital admissions (unscheduled), respiratory	466, 480-486, 490, 491, 492, 493	all	3-day lag	1 hr max.	linear	none	NA	206	1.370E-08	3.312E-09	2.409E-08
Thurston et al. (1992)****	Hospital admissions (unscheduled), asthma	493	all	1-day lag	1 hr max.	linear	none	NA	206	1.170E-08	2.488E-09	2.091E-08

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

***New York in this study is defined as the five boroughs of New York City plus Westchester County.

****New York in this study is defined as the five boroughs of New York City.

NA denotes "not available."

Table 5C-9. Study-Specific Information for O_3 Studies in Philadelphia, PA

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065
Moolgavkar et al. (1995)	Mortality, non-accidental	< 800	all	1-day lag	24 hr avg.	log-linear	none	1	159	0.00140	0.00086	0.00191
Moolgavkar et al. (1995)	Mortality, non-accidental	< 800	all	1-day lag	24 hr avg.	log-linear	TSP, SO2	1	159	0.00139	0.00066	0.00212
Huang et al. (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	-3	84	0.00151	0.00007	0.00296
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00124	0.00047	0.00201
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	PM10	NA	NA	0.00074	-0.00033	0.00171
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	NO2	NA	NA	0.00060	0.00011	0.00109
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	SO2	NA	NA	0.00051	0.00001	0.00102
Huang et al. -- 19 US Cities (2004)	Mortality, cardiovascular and respiratory	390-448; 490-496; 487; 480-486; 507.	all	distributed lag	24 hr avg.	log-linear	CO	NA	NA	0.00069	0.00020	0.00117

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

Table 5C-10. Study-Specific Information for O_3 Studies in Sacramento, CA

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations** (ppb)		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	0	71	0.00026	-0.00079	0.00131
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

Table 5C-11. Study-Specific Information for O_3 Studies in St. Louis, MO

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations**		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	0	118	0.00044	-0.00072	0.00159
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

Table 5C-12. Study-Specific Information for O_3 Studies in Washington, D.C.

Study	Health Effects*	ICD-9 Codes	Ages	Lag	Exposure Metric	Model	Other Pollutants in Model	Observed Concentrations**		O_3 Coefficient	Lower Bound	Upper Bound
								min.	max.			
Bell et al. -- 95 US Cities (2004)	Mortality, non-accidental	< 800	all	distributed lag	24 hr avg.	log-linear	none	NA	NA	0.00039	0.00013	0.00065

*Health effects are associated with short-term exposures to O_3.

**Rounded to the nearest ppb.

NA denotes "not available."

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