

OZONE
MAAS

PHOTOCOPY
PRESERVATION



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Brian Burke,

4/8/94

Sorry you did not
get these materials
regarding our 4/6 Interagency
meeting on the ozone air
quality standard. (We had
intended you to get them
well in advance !)

I'll keep you posted
about next steps.

— Chris Woltz



EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
WASHINGTON, D.C. 20503

MAR 30 1994

MEMORANDUM FOR INTERAGENCY GROUP ON OZONE NAAQS REVIEW
(DISTRIBUTION LIST)

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FROM: Art Fraas *AF* Chris Wolz *CW*
Office of Information and Regulatory Affairs,
Office of Management and Budget

SUBJECT: Meeting of an Interagency Group on the
Environmental Protection Agency's Review of the
"National Ambient Air Quality Standard" for Ozone,
Wednesday, April 6, 1994

The Environmental Protection Agency (EPA) has asked the Office of Management and Budget (OMB) to assist in coordinating an interagency group to consult with EPA in its review of the National Ambient Air Quality Standard (NAAQS) for ozone. The interagency group would, as a first step, discuss with EPA methodological issues underlying the NAAQS review, such as the human exposure analysis and the health risk assessment that EPA is conducting for its "Staff Paper." Additional issues that might be covered later in this process could include the assessment of welfare effects and the form of the standard.

We have scheduled a meeting for the interagency group with EPA for **Wednesday, April 6, 1994**, from 9:30 a.m. to 11:30 a.m., to discuss the NAAQS review in general, and specifically the human exposure and health risk analysis. We hope you can attend this meeting.

EPA should already have sent to you several documents for discussion at this meeting, including: "Estimation of Ozone Exposures Experienced by Urban Residents Using a Probabilistic Version of NEM and 1990 Population Data," September 1993; "A Probabilistic Assessment of Health Risks Associated with Short-term and Long-term Exposure to Tropospheric ozone," February, 1994; and "Ozone NAAQS Development Project Plan," December 16, 1993.

The meeting will be held in Room 472 of the Old Executive Office Building, 17th and Pennsylvania Avenue N.W., Washington, D.C. For security clearance, please call our office on (202) 395-3084 by Monday, April 4, and leave your name and date-of-birth with our support staff.

Attached is a brief background note on the NAAQS and the review process.

Attachment

cc: Official File - NRB
Chron File - NRB
Jim MacRae
Art Fraas
NRB:CWolz:mrn:3/29/94 - Ozone.Memo

Background Information on the National Ambient Air Quality Standard for Ozone

The Clean Air Act (CAA) requires that the Environmental Protection Agency (EPA) establish standards for levels of air pollutants in the ambient air to protect the public health and welfare. (Sections 108 and 109 of the Clean Air Act) Ozone is a highly reactive gas which, in the troposphere, can produce a wide variety of harmful effects on human health and vegetation, and materials, and EPA has maintained a NAAQS for ozone (or its precursors) since 1971. The ozone NAAQS is the driving force behind a broad array of emissions control regulations both at the State and Federal level. Despite two decades of pollution control regulations and a trend towards lower nationwide ozone concentrations over the past decade, efforts to attain the NAAQS have not succeeded. EPA estimated that in 1988, about 120 million people lived in urban areas in which the current ozone NAAQS was exceeded.

Setting of the NAAQS and Statutory Constraints: The CAA requires EPA to list pollutants that cause or contribute to air pollution and "which may reasonably be anticipated to endanger public health and welfare[.]" (Section 108) Once a pollutant has been listed, EPA must review the relevant scientific literature on the effects of a pollutants and develop both primary and secondary ambient air quality standards. (Section 109) Currently, EPA has NAAQS for six pollutants: carbon monoxide (CO), sulfur dioxide, (SO₂), particulate matter (PM-10), nitrogen dioxide (NO₂), lead (Pb), and ozone (O₃).

The primary ambient air quality standard must be set at levels which with an adequate margin of safety, "are requisite to protect the public health" and the Courts have held that the CAA does not allow the consideration of economic or technical factors. EPA must also issue secondary standards, to "protect the public welfare from any known or anticipated adverse effects associated with" the pollutant. In setting secondary standards, EPA must consider a range of factors, e.g., crop damage, damage to buildings and materials and visibility impairment. In 1979, EPA revised the existing NAAQS and established the current primary and secondary NAAQS for ozone. The current ozone secondary NAAQS is set at the level of the primary NAAQS, which is 0.12 ppm averaged over one hour, not to be exceeded more than one hour per year.

Health and Welfare Effects of Ozone: At elevated concentrations, ozone can adversely affect human health, impairing normal functioning of the lungs and reducing the ability to perform physical exercise. These effects may be aggravated in sensitive individuals and those with preexisting lung disease. Symptoms associated with exposure to ozone at elevated levels include cough, chest pain, and throat irritation. There is recent data

showing some adverse health effects from exposure to ozone for six to eight hour periods at levels below the current NAAQS of 0.12 ppm; in its current review of the NAAQS, EPA will assess this information and the need for a standard (e.g., an 8-hour standard) to replace or supplement the current 1-hour standard. The chronic health effects of repeated exposure to elevated levels of ozone have been raised as a health concern, although in its 1993 review of the NAAQS, EPA concluded that the preliminary information available on chronic effects (often based on animal studies) was not sufficient to support the establishment of a chronic standard for ozone.

With regard to welfare effects, estimates based on experimental studies of major cash crops in the U.S. indicate that elevated ozone levels are responsible for several billion dollars in agricultural crop yield losses each year. Exposure to elevated levels of ozone also can cause foliar damage in many crops, as well as damage to forests and ecosystems. In its current NAAQS review, EPA will consider options to protect the public welfare, such as a standard with an averaging period that extends over a growing season.

The Ozone NAAQS and Air Pollution Control Measures: The NAAQS are the driving force behind both a number of Federal regulations to limit the emissions of air pollutants and "State Implementation Plans" (SIPs) that establish control measures for sources within each nonattainment area. SIPs must include both mandatory control measures listed in the Clean Air Act and enough additional controls as are necessary--as shown by computer modeling done to the satisfaction of EPA--to achieve attainment of the NAAQS on schedule. Billions of dollars per year are spent on air pollutant emissions control measures in the ninety-seven areas that are designated as non-attainment for the ozone NAAQS. The mandatory control measures under the Clean Air Act vary according to the severity of the ozone level in the nonattainment area, and may include:

- Control of emissions of volatile organic compounds and nitrogen oxides from **major stationary sources** under New Source Review, and Reasonable Available Control Technology requirements;
- **Transportation planning and controls**, including the Employer Trip Reduction Program, and HOV highway lanes;
- And **mobile source** (i.e., cars and trucks) emissions control requirements, including tailpipe standards, clean fuels requirements, and inspection and maintenance programs.

EPA's Review Schedule: EPA's Administrator Carol Browner has committed EPA to conduct an accelerated review of the ozone NAAQS. The CAA requires EPA to review the NAAQS every five years but after a revision in 1979, EPA completed its first review of the 1979 standard under a Court deadline on March 1, 1993. In EPA's 1993 action, EPA concluded that "revisions of the primary and secondary NAAQS are not appropriate at this time" due to a

large body of recent scientific literature that EPA had not been able to rigorously review within the time provided under the Court order. (Federal Register, March 9, 1993) EPA did commit, however, to proceed with the next review "as rapidly as possible to assess the more recent health and welfare effects information" and to publish a proposed decision in 1996, followed by promulgation of a final decision by 1997. EPA's schedule is:

MAJOR MILESTONES

TENTATIVE DATES*

CASAC subcommittee meeting on exposure assessment methods:

* December 1993

CASAC and public comment period for Criteria Document (CD)
(90 days)

* February-May 1994

CASAC subcommittee meeting on risk assessment methods

* March 1994

CASAC meeting on CD

* July 1994

Comment period on Staff Paper (SP)

* September-October 1994

CASAC meeting on SP

* October 1994

Public comment period on revised CD (90 days)

* Early 1995

CASAC meeting on revised CD and SP

* Mid-1995

Agency development of regulatory decision/proposal; package draft

* Mid-1995 to late 1995

OMB review of proposal package

* Early 1996

Publication of proposal in the Federal Register

* Mid-1996

Public comment on proposal (90 days)

* Mid-1996

CASAC meeting to discuss review proposal

* Late 1996

Regulatory decision and final package draft completed

* Early 1997

OMB review of promulgation package

* Early 1997 to mid-1997

Publication of promulgation notice in the Federal Register

* Mid-1997

Interagency Group on EPA's Review of the Ozone NAAQS

Meeting Agenda
April 6, 1994

Introduction and Purpose

OMB, EPA

History and Overview of NAAQS Process

Karen Martin, EPA

- Statutory Requirements
- Components of Review Process
- EPA Management of Review Process

Schedule and Status of Major Elements

Karen Martin, EPA

Overview of Key Issues

Harvey Richmond/Allen Basala, EPA

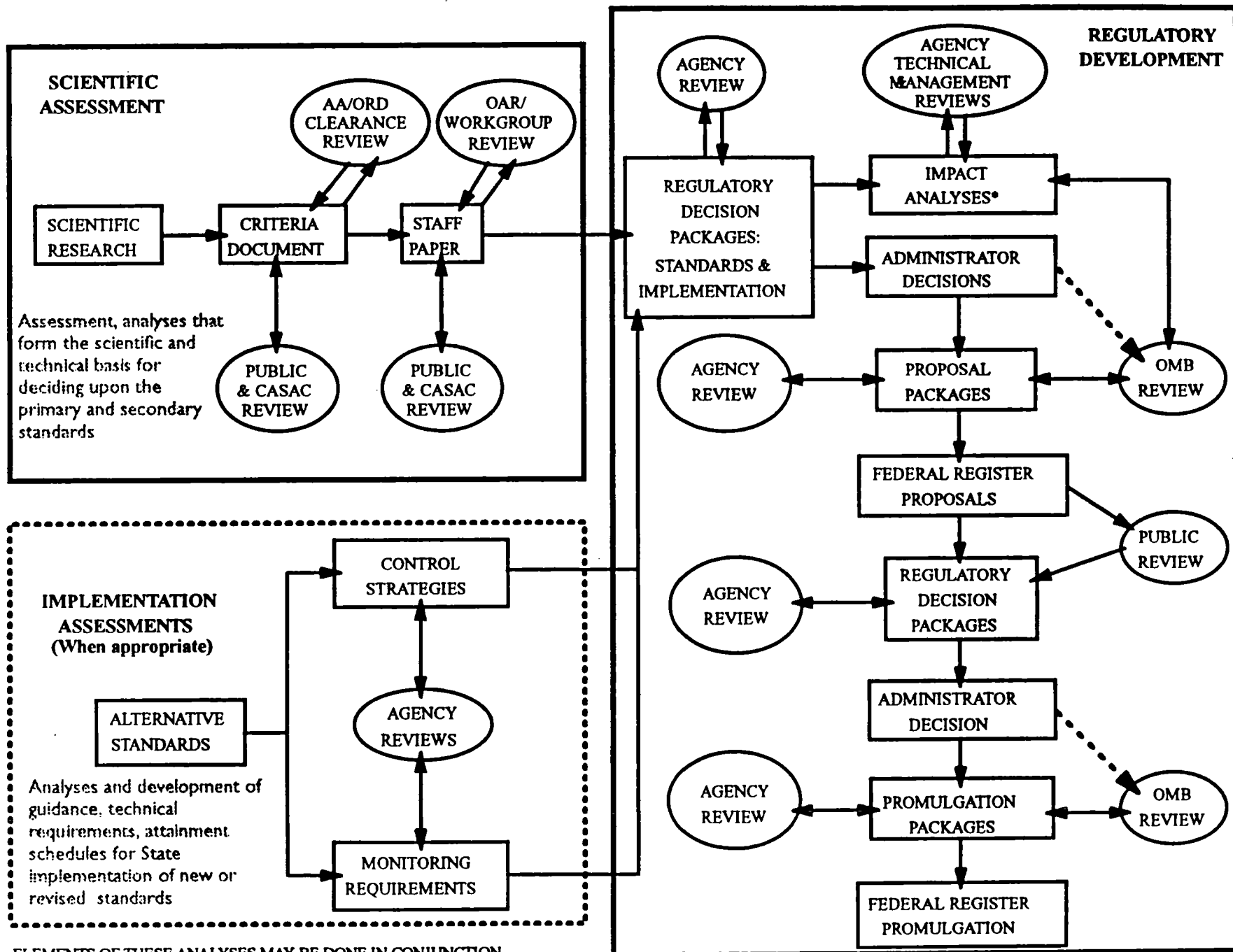
- Adverse Health Effects
- Sensitive Sub-populations
- Margin of Safety
- Welfare Effects
- Form of Current Standard
- Alternative Standards
- Cost/Benefit Assessments

Human Exposure and Health Risk Assessments

Harvey Richmond, EPA

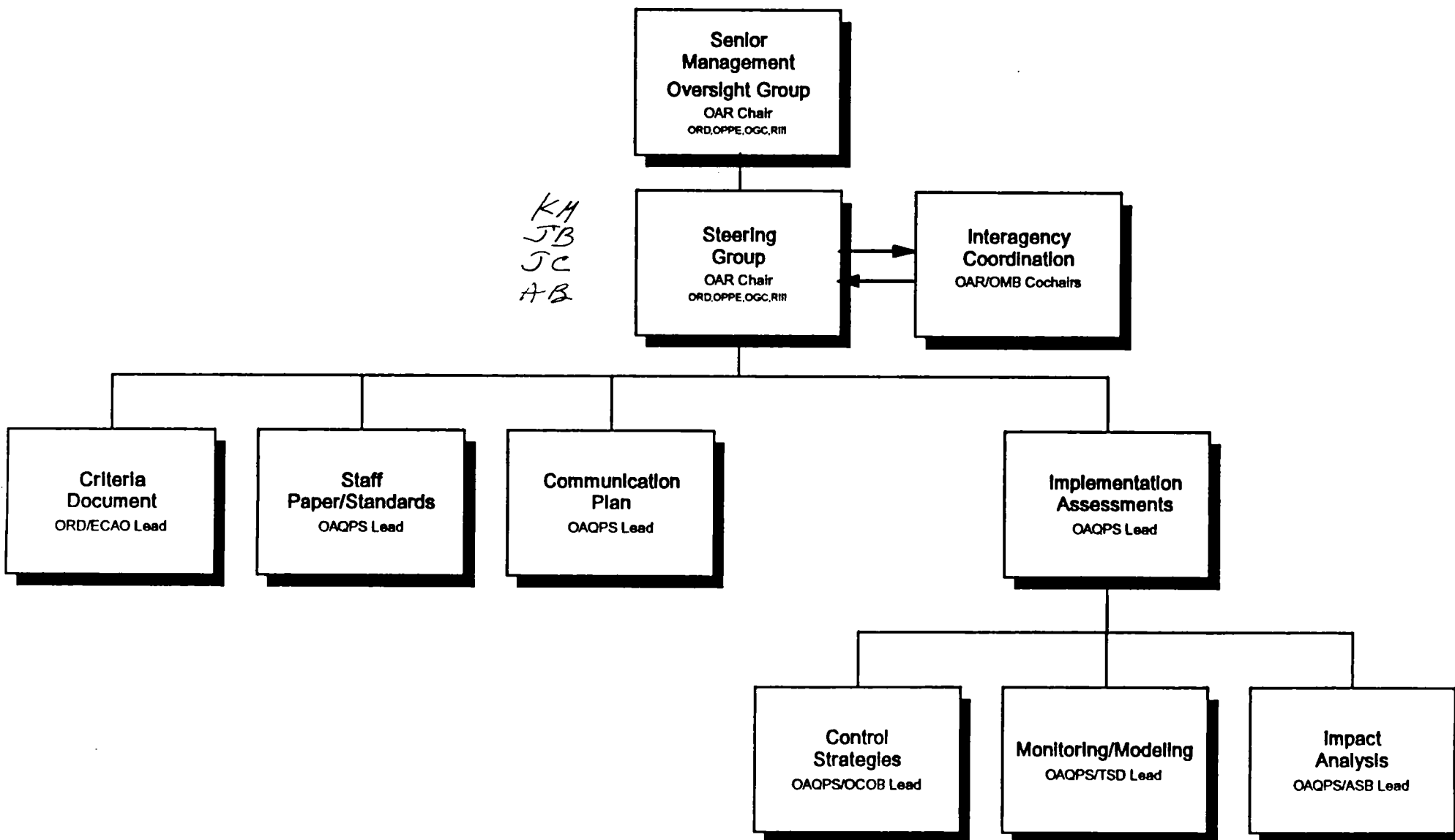
Next Steps

NAAQS REVIEW PROCESS COMPONENTS

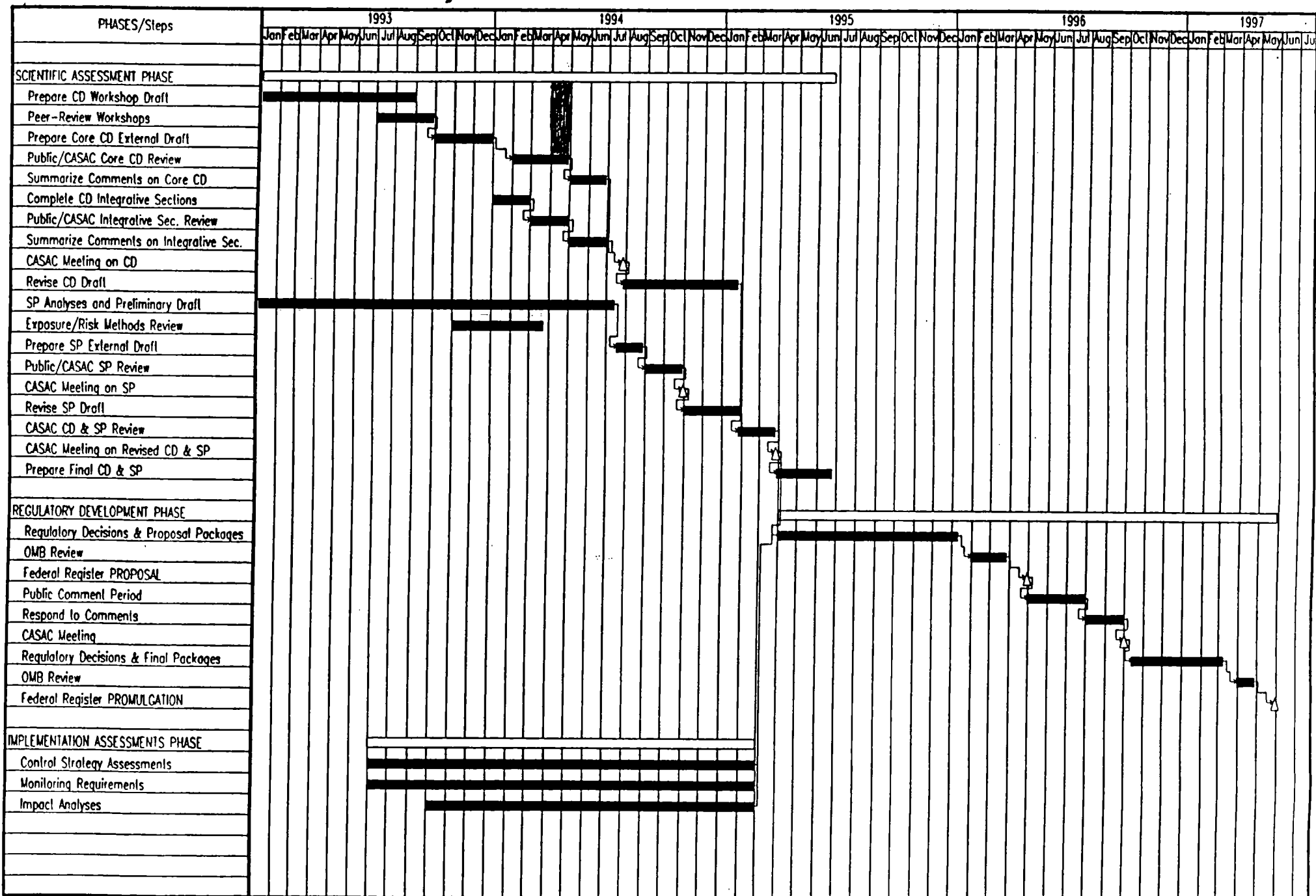


ELEMENTS OF THESE ANALYSES MAY BE DONE IN CONJUNCTION WITH THE SCIENTIFIC AND TECHNICAL ASSESSMENTS.

Ozone NAAQS Review Process Management Structure



Projected Ozone NAAQS Review Schedule



WHAT HEALTH EFFECTS HAVE BEEN IDENTIFIED IN THE OZONE CRITERIA DOCUMENT?

ACUTE (1- TO 3-HOUR) EFFECTS

(The first two effects categories formed much of the basis for the last decision on the ozone primary NAAQS.)

- CHANGES IN LUNG FUNCTION (E.G., REDUCED LUNG VOLUMES AND FLOWS; RAPID, SHALLOW BREATHING)
- RESPIRATORY SYMPTOMS (E.G., COUGH; CHEST PAIN ON DEEP INSPIRATION; THROAT & NOSE IRRITATION)
- INCREASES IN AIRWAY RESPONSIVENESS (I.E., TENDENCY FOR LUNGS TO BECOME REACTIVE TO ALLERGENS OR OTHER BRONCHOCONSTRICTORS)
- INCREASE IN INDICATORS OF LUNG INFLAMMATION, BUT ONLY AT VERY HIGH OZONE LEVELS
- ALL OF THE ABOVE EFFECTS ARE A FUNCTION OF EXPOSURE DURATION, EXPOSURE CONCENTRATION, AND LEVEL OF EXERCISE

MULTI-HOUR (6- TO 8-HOUR) EFFECTS

- LARGER CHANGES IN LUNG FUNCTION FOR ANY GIVEN EXPOSURE LEVEL THAN ACUTE EXPOSURES
- RESPIRATORY SYMPTOMS
- INCREASES IN AIRWAY RESPONSIVENESS
- INDICATORS OF LUNG INFLAMMATION
- INCREASED RESPIRATORY HOSPITAL ADMISSIONS IN MANY CITIES
- INCREASED MORTALITY (STILL VERY UNCERTAIN)

CHRONIC (MONTHS TO YEARS) EFFECTS

- STRUCTURAL CHANGES IN THE LUNGS, PARTICULARLY IN THE CENTRIACINAR REGIONS, WHICH IS WHERE THE ALVEOLI AND CONDUCTING AIRWAYS MEET (I.E., AIR EXCHANGE AREA)
- EXPERIMENTAL CHRONIC STUDIES HAVE BEEN CONDUCTED ONLY WITH ANIMALS; EPIDEMIOLOGICAL STUDIES WHICH HAVE TRIED TO ASSOCIATE CHRONIC HEALTH EFFECTS IN HUMANS TO OZONE EXPOSURE AS YET HAVE PROVIDED ONLY UNCERTAIN EVIDENCE
- GENOTOXICITY DATA ARE NEGATIVE OR WEAK

WHAT WE 'FARE EFFECTS HAVE BEEN DEMONSTRATED IN THE DRAFT OZONE CRITERIA DOCUMENT?

- **ANNUAL SPECIES**

- Effects include foliar injury, reduced growth or yield, reduced fruit or seed production. Yield loss may also include changes in crop quality (physical appearance, ability to withstand storage, etc.)
- Ambient O₃ levels are sufficiently elevated in several parts of the U.S. to impair the growth and yield of annuals.

- **PERENNIAL SPECIES AND ECOSYSTEMS**
(crops, deciduous trees and shrubs, evergreens)

- Carry-over effects have been observed in multiple-year studies including: altered bud elongation (i.e., ponderosa pine) and altered root regrowth and carbohydrate storage.
- Yields of multiple-year forage crops (i.e., alfalfa) are reduced at concentrations at or near ambient in many parts of the country.
- Growth reductions (stem diameter and # of shoots) have been reported for some fruit and nut trees (almond, pear, plum and apricot).

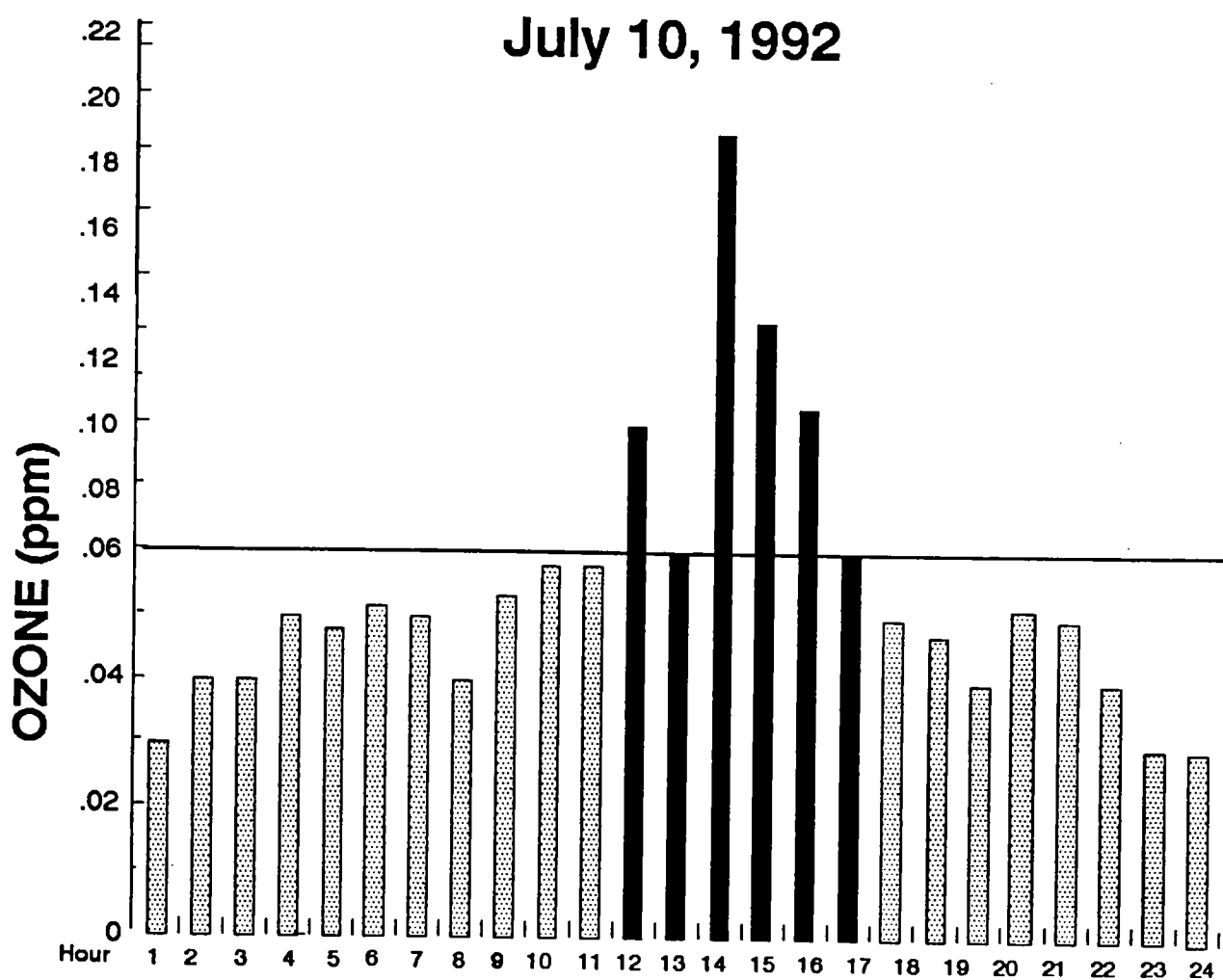
- **MATERIALS**

- Natural rubber and synthetic polymers are susceptible to damage from ozone. However, antioxidants and other protective measures have been incorporated into much of the materials produced today.
- Several artists' pigments are subject to fading or other color changes. Newer paints are more resistant but older works of art may be at risk of permanent damage.

How SUM06 is calculated

All values $\geq .06$ which occurred in each 24-hr. period are summed:

$$.10 + .06 + .19 + .13 + .10 + .06 = .64$$



.08 for a SUM08 standard.

*See Corvallis work
.06 + .08 "performed well"*

**OZONE NAAQS
DEVELOPMENT PROJECT PLAN**

**OFFICE OF AIR QUALITY
PLANNING AND STANDARDS**

**RESEARCH TRIANGLE PARK
NORTH CAROLINA**

December 16, 1993

Ozone NAAQS Development Project Plan

I. Introduction/Background

A. Purpose of Project Plan

There are two major purposes for this ozone (O₃) national ambient air quality standards (NAAQS) development project plan. They are:

- (1) To describe the proposed process for coordinating and implementing the scientific assessments, standards development, implementation assessments, Office of Management and Budget (OMB) coordination, and communication plan within the Administrator's accelerated schedule (final action by mid-1997).
- (2) To identify key issues in scientific assessment and standards development for the NAAQS review and lay out plans for preparing scientific and technical assessments related to decisions on the appropriate primary and secondary NAAQS.

B. Background

On April 30, 1971, the EPA promulgated primary and secondary NAAQS for photochemical oxidants under section 109 of the Act (36 FR 8186). These were set at an hourly average of 0.08 parts per million (ppm) total photochemical oxidants not to be exceeded more than 1 hour per year. On April 20, 1977, the EPA announced (42 FR 20493) the first review and updating of the 1970 Air Quality Criteria Document for Photochemical Oxidants in accordance with section 109(d)(1) of the Act. The EPA published the final revised Air Quality Criteria for Ozone and Other Photochemical Oxidants on June 22, 1978.

Based on the 1978 revised Air Quality Criteria Document (U.S. EPA, 1978) and taking into account public comments on revisions proposed to the primary and secondary NAAQS on June 22, 1978, (43 FR 16962), the EPA announced its final decision on the proposed revisions to the 1971 standards (44 FR 8202, February 8, 1979). The final rulemaking revised the level of the primary standard from 0.08 ppm to 0.12 ppm, set the secondary standard identical to the primary standard, changed the chemical designation of the standards from photochemical oxidants to O₃, and revised the definition of the point at which the standard is attained to when the expected number of days per calendar year with maximum hourly average concentrations above 0.12 ppm is equal to or less than one as determined by Appendix H.

On March 17, 1982 (47 FR 11561), the EPA announced that it was undertaking plans to revise the existing 1978 "Air Quality Criteria Document for Ozone and Other Photochemical Oxidants" and on August 22, 1983, announced (48 FR 38009) that review of primary and secondary standards for O₃ had been initiated. The EPA subsequently provided a number of opportunities for public review and comment on drafts of the Criteria Document and OAQPS Staff Paper ("Review of the National Ambient Air Quality Standards for Ozone: Assessment of Scientific and Technical Information--OAQPS Staff Paper"). The Clean Air Scientific Advisory Committee (CASAC), after reviewing the draft Criteria Document in 1985 and 1986, sent to the Administrator on October 22, 1986, a "closure letter," outlining key issues and recommendations and indicating that it was satisfied with the final draft of the 1986 Criteria Document.

Following closure, a number of new scientific findings were made that appeared to be of sufficient importance concerning potential health and welfare effects of O₃ to warrant preparation of a supplement to the Criteria Document. The CASAC, having already reviewed two drafts of the OAQPS Staff Paper in 1986 and 1987, concluded that sufficient new information existed to recommend incorporation of relevant new information into a third draft of the OAQPS Staff Paper.

The CASAC held a public meeting on December 14-15, 1988 to review the draft Supplement and draft OAQPS Staff Paper. Major issues included: the definition of adverse health effects of O₃, the significance of health studies suggesting that exercising individuals exposed for 6 to 8 hours to O₃ levels at or below 0.12 ppm may experience inflammation and transient decreases in pulmonary function, the possibility that chronic irreversible effects may result from long-term exposures to elevated levels of O₃, and the importance of analyses which indicate agricultural crop damage may be better defined by a cumulative seasonal average than by a 1-hour peak level of O₃. In its "closure letter" of May 1, 1989, the CASAC indicated that the draft Supplement and draft OAQPS Staff Paper "provide an adequate scientific basis for the EPA to retain or revise primary and secondary standards for ozone."

On October 22, 1991, the American Lung Association and other plaintiffs filed suit under section 304 of the Act to compel the EPA to complete its review of the criteria and standards for O₃ under section 109(d)(1) of the Act [American Lung Association v. Reilly, No. 91-cv-4114 (JRB) (E.D.N.Y.)]. The U.S. District Court for the Eastern District of New York subsequently issued an order requiring the EPA to sign a Federal Register notice announcing its proposed decision on whether to revise the standards for O₃ by August 1, 1992 and to sign a Federal Register notice announcing its final decision by March 1, 1993.

On August 10, 1992 (57 FR 35542), the EPA published its proposed decision under section 109(d)(1) that revisions to existing 1-hour primary and secondary standards were not appropriate at that time. The notice explained in some detail (see 57 FR 35546) that the proposed decision would complete the EPA's review of information on health and welfare effects of O₃ assembled over a 7-year period and contained in the 1986 Air Quality Criteria

Document and its Supplement. The review included an evaluation of key studies published through early 1989, the 1989 OAQPS Staff Paper assessment of the most relevant information in these documents, and the advice and recommendations of the CASAC as presented both in the discussion of these documents at public meetings and in the CASAC's 1986 and 1989 "closure letters." In the same notice, the EPA also announced its plans, in view of the large number of recent scientific papers and ongoing research on the health and welfare effects of O₃, to proceed as rapidly as possible with the next review of the air quality criteria and standards for O₃. On March 9, 1993 (58 FR 13008) EPA published its final decision not to revise the current primary and secondary NAAQS for O₃ and emphasized the Administrator's intention to proceed as rapidly as possible with a review of the scientific research published since 1989.

II. NAAQS Review Process

Based on a thorough examination of the NAAQS review process, the EPA has adopted a number of measures in an effort to accelerate the criteria and standards review for O₃. EPA's objective is to conduct these reviews as rapidly as possible consistent with assuring a scientifically supportable and legally defensible decision. The measures adopted include:

- * Reducing the volume of information on health and welfare effects included in the "criteria" for the NAAQS review by **focusing on relevant key new studies** and fixing a firm date beyond which new studies will not be included.
- * **Conducting the health/welfare effects review** (the Criteria Document) and associated exposure/risk assessments (summarized in the OAQPS Staff Paper) **in a more concurrent fashion than in previous reviews.**
- * Taking steps to ensure **adequate but significantly reduced time for peer** (i.e., CASAC) **and public reviews** of the Criteria Document and OAQPS Staff Paper, by enlisting the CASAC's cooperation in expediting their review and advice to the Administrator and not granting extensions of public comment periods.
- * Establishing a **highly expedited Agency review, issue resolution, and closure process**, as well as undertaking early discussion of possible options with other federal agencies (e.g., Office of Management and Budget).
- * **Issuing a Federal Register Notice announcing the review schedule and the above measures being taken to meet the schedule** to provide early notice to public groups interested in participating in the review process.

Overview of NAAQS Review Schedule

The scientific assessment phase of the accelerated O₃ NAAQS review schedule is shown in Figure 1. This schedule incorporates the measures described above. Given the scientific and technical complexity of the issues likely to be involved in the O₃ review, the diversity of scientific opinion that has characterized previous reviews of the criteria and standards for O₃, and the need to ensure that its ultimate decision is soundly-based, the EPA cannot, of course, provide any absolute assurance that it will meet all of the interim milestone dates indicated in Figure 1. Completion of the necessary steps in a timely manner is also predicated upon the availability of adequate resources during the review process. However, the Administrator has emphasized that she places a high priority on meeting the accelerated schedule outlined in this notice.

III. Scientific Assessment and Standards Development

A. Background and Key Issues

In order to meet the accelerated schedule shown in Figure 1, it is necessary to work as rapidly as possible on various analyses that will provide information for the Administrator's decision on whether to revise the primary and/or secondary NAAQS for O₃. Based on current scientific information and staff judgments, several options are defined below which will be used in various analytic efforts. It is recognized that additional or different options may have to be analyzed based on review of Criteria Document and OAQPS Staff Paper drafts by the CASAC and the public. However, given the time and resource requirements for certain analyses, if additional options are added, it may not be possible to conduct some analyses and still remain on the accelerated schedule.

The initial options listed below reflect the staff's best judgment, at this point in time, of the options to be used for various regulatory analyses, given the current state of scientific information. These options are not prioritized and are subject to change based on the formal review and revision of the Criteria Document.

Analytic Options for the Primary O₃ NAAQS

The basis for a short-term standard to protect against acute 1-hr exposures has been enhanced by additional research findings since the current standard was promulgated in 1979. Recent controlled human exposure and human field/epidemiology studies have strengthened the case for considering establishment of a longer averaging time primary NAAQS on the order of 8 hours to protect against acute effects and possibly provide some protection against potential chronic effects. Evidence is also growing concerning chronic effects that might require a much longer averaging time standard (e.g., seasonal mean). However, it is unlikely that the science will be sufficiently quantitative to support a separate chronic standard within the next 3-5 years. If the criteria review supports this assumption, such

chronic effects information will need to be considered as one of the factors in the Administrator's judgment about which standard(s) provide an adequate margin of safety. The initial options to be analyzed are:

- * Retain the 1-hour NAAQS of 0.12, ppm, using the current form of the standard (i.e., 1 expected exceedance allowed per year).
- * Establish a new 8-hour NAAQS in the range 0.08-0.10 ppm, with 1 expected exceedance allowed per year.
- * Establish a new 8-hour NAAQS in the range 0.06-0.08 ppm, with 5 expected exceedances allowed per year.
- * Whether or not to retain the current 1-hour NAAQS if a separate 8-hour NAAQS is established.

A key issue is whether a new 8-hour NAAQS will provide sufficient protection against 1-hour peaks of concern if changes in O₃ air quality patterns occur in the future.

Analytic Options for the Secondary O₃ NAAQS

Since early 1989, there have been several analyses of the National Crop Loss Assessment Network (NCLAN) data, as well as continued research into the effects of O₃ on trees. The NCLAN reanalyses led to the conclusion that an index that is protective of annual crops (1) cumulates hourly O₃ values over time, (2) is peak-weighted, and (3) places greatest weight on exposures that occur during certain plant growth stages. The NCLAN reanalyses identified several indices as adequate to represent the relationship between O₃ exposures and crop response. One of these, the SUM06 index, sums all hourly O₃ concentrations of 0.06 ppm and higher over a specified period of time. For protection of crops, analysis of the NCLAN data suggests using the 3 months having the highest O₃ concentrations (i.e., the maximum 3 months). For protection of trees, emerging data suggest that a longer time period (up to 5 months) may be appropriate. However, since the NCLAN data are currently the largest set of data available for considering standard-setting options, the options listed below emphasize a 3-month exposure period. In the future, information on effects of trees may suggest a longer exposure period. Alternative SUM06 levels were identified as options for analysis based on prior analyses of percent crop yield loss in a certain percentage of crop species. Since then, concern about the ability of existing air quality models to accurately assess and predict O₃ concentrations below 0.08 ppm, has led to inclusion of alternative SUM08 standards that provide the same level of crop protection as the alternative SUM06 standards under consideration. The options to be analyzed are:

- * Replace the existing 1-hour NAAQS with a new SUM06 standard where the sum of the concentrations ≥ 0.06 ppm is < 16.5 ppm-hrs for the maximum 3 calendar-month period.

- * Replace the existing 1-hour NAAQS with a new SUM06 standard where the sum of the concentrations ≥ 0.06 ppm is < 26.4 ppm-hrs for the maximum 3 calendar-month period.
- * Replace the existing 1-hour NAAQS with a new SUM08 standard where the sum of the concentrations ≥ 0.08 ppm is $< x$ ppm-hrs over the maximum 3 calendar-month period (where x is to be determined by additional analyses underway by ORD/Corvallis).
- * Replace the existing 1-hour NAAQS with a new 8-hour standard of 0.08 ppm with either 1 or 5 expected exceedances allowed per year.

B. Criteria Document Development

Overview

The previous "Air Quality Criteria for Ozone and Other Photochemical Oxidants" (O₃ Criteria Document) was released by EPA in August 1986 and a supplement, "Summary of Selected New Information on Effects of Ozone on Health and Vegetation," was released in January 1992. Review and revision of the O₃ Criteria Document will be performed by the Environmental Criteria and Assessment Office in Research Triangle Park, NC (ECAO/RTP) in accordance with sections 108 and 109 of the Clean Air Act to provide the scientific basis for reevaluation of the O₃ NAAQS. A separate draft work plan is available that discusses the structure, review process, and major scientific issues to be addressed in the revision of the O₃ Criteria Document (ECAO, 1992).

Structure

The proposed structure of the document includes first, an Executive Summary and Conclusions (Chapter 1), providing a concise presentation of key information and conclusions from all subsequent chapters. This is followed by a brief Introduction (Chapter 2) containing information on the legislative background and purpose of the document, as well as an overview of the organization of the document. Chapter 3 provides information on the chemistry, measurement, and transport of O₃ and related photochemical oxidants, whereas Chapter 4 covers environmental concentrations, patterns, and exposure estimates. This is followed by Chapter 5, dealing with environmental (e.g., ecological, agricultural, materials) effects of O₃ and related photochemical oxidants. Chapters 6, 7, and 8 discuss animal toxicological studies, human health effects, and extrapolation of animal toxicological data to humans, respectively. The last chapter (Chapter 9) will be an integrative, interpretative evaluation of health risks to the exposed population.

Status/Schedule

ECAO/RTP began revision of the O₃ Criteria Document by announcing the commencement of the review in the Federal Register (57 FR 38832). The main focus of the revised O₃ Criteria Document is on evaluation and interpretation of those new (i.e., after the 1986 Criteria Document) air quality, health, and welfare effects data identified as being pertinent to development of criteria supporting a decision on possible revision of the O₃ NAAQS. After careful assessment and evaluation of pertinent new studies by scientific experts within and outside the Agency, preliminary draft chapters have been prepared. A series of expert workshops have been held to review the draft revised O₃ Criteria Document chapters, to identify the potential need for additional information to be added to the chapters, and to evaluate the quality of the summarization and interpretation of the literature. Although the reviewers were invited experts, the workshops were announced in the Federal Register and were open to the public. The respective authors of the draft chapters are revising them on the basis of the workshop recommendations. After resolution of outstanding issues and comments, ECAO/RTP will forward the document as the first external review draft for public comment and review by the CASAC. Any necessary revisions will be made in response to public comments and CASAC recommendations in preparing the final version of the revised O₃ Criteria Document for further review by CASAC (if needed) and publication. The schedule for the revised O₃ Criteria Document preparation process is reflected in Figure 1.

C. Staff Paper Development

1. Overview and Structure

Overview

The OAQPS Staff Paper provides the Administrator, CASAC, and others involved in the standard-setting process with a concisely written assessment of the scientific literature and technical analyses which form the basis for recommendations and decisions on a range of alternative NAAQS. The preparation of the OAQPS Staff Paper and its review by the public and the CASAC is intended to ensure that the staff's interpretation of the scientific evidence in the Criteria Document is sound and is supported by the scientific community.

Structure

The OAQPS Staff Paper will provide an assessment of the key health and welfare effects information evaluated in the revised O₃ Criteria Document. Several factors are important in the staff's assessment and development of recommendations on alternative primary NAAQS. These factors include: (1) biological and statistical significance of effects; (2) adversity of effects; (3) credibility of studies; (4) type of study (e.g., human clinical, animal, or epidemiology); (5) nature and magnitude of human exposure to O₃ levels of concern; (6) nature and magnitude of health risks associated with attainment of alternative

primary NAAQS; and (7) basis for selecting appropriate averaging time(s) and form(s) of the primary NAAQS.

Similar factors are relevant for the staff's assessment and development of recommendations on alternative secondary NAAQS. These include: (1) type of welfare effect; (2) biological and statistical significance of effects; (3) extent of effects (e.g., amount of crop yield loss); (4) adversity of effects; (5) credibility of studies; (6) type of study (e.g., chamber, field); (7) assessments of crop and/or forest damage upon attainment of alternative secondary NAAQS, and (8) basis for selecting appropriate averaging time(s) and form(s) of the secondary NAAQS. The OAQPS Staff Paper will include summary discussion of the various analyses relevant to decision making on the primary and secondary NAAQS (e.g., form of the standard, exposure, health risk, crop loss, and welfare benefits).

Status/Schedule

EPA will begin preparation of the OAQPS Staff Paper in early 1994. An external review draft is scheduled to be released in mid 1994 and the CASAC meeting on the first draft of the OAQPS Staff Paper is scheduled for late 1994. After revisions are made, a second CASAC meeting and, hopefully, closure are scheduled for early 1995.

Issues

Many of the policy and technical issues that will be addressed by various types of analyses and then summarized in the OAQPS Staff Paper are identified in the sections below (e.g., air quality, form of the standards, human exposure, health risk, and welfare effects assessment).

2. Air Quality and Form of Standards

Overview

This section will use ambient O₃ data to document status with respect to the current O₃ NAAQS and to provide a brief summary of U.S. O₃ trends. A brief discussion of background O₃ levels will be included based upon material from the revised O₃ Criteria Document. This background information will provide a frame of reference for the discussion of alternative standards and possible modifications to the attainment test. Because high O₃ levels in the east during the summer of 1988 received considerable attention, presentations of ambient data will be structured to illustrate the impact of 1988.

In addition to the form of the standard, this section also will present a discussion of how the attainment test could be modified, including the use of a more robust surrogate or the introduction of a "too close to call" category. Pros and cons of various options will be presented to generate discussion on the potential merits of such approaches.

Structure

Shaded U.S. maps will be used to identify areas exceeding selected NAAQS options: 1 hour (.12 ppm, 1 expected exceedance); 8 hours (.08 and .10 ppm, 1 expected exceedance); and 8 hours (.06 and .08 ppm, 5 expected exceedances). SUM06 and SUM08 areas also will be illustrated for at least two cut-points. To illustrate the impact of 1988, these results will be presented for three different time periods: 1990-92 (the most current 3-year period available); 1987-89 (the 3-year period most commonly used for the 1990 Clean Air Act Amendments classification process); and 1988-92 (the most recent 5-year period which also includes 1988). All of these maps will be determined using the same data handling procedures used for the current O₃ NAAQS.

Alternatives to the attainment test will be presented with a brief discussion of the potential advantages and disadvantages. The use of a more robust surrogate, such as the 95th percentile, the use of a fitted statistical distribution, such as tail exponential, and the use of design values rather than expected exceedances, will use material from the Ozone Design Value Study. New material will be developed for inclusion in the OAQPS Staff Paper concerning the "too close to call" approach.

Issues

With an 8-hour level as low as 0.06 ppm being considered, there will be discussion of what is background. Levels from remote sites may provide some insight but will not necessarily answer the question, and it may be necessary to develop atmospheric chemistry arguments.

The ambient data used in these analyses is based upon data in AIRS from monitors sited primarily to document 1-hour O₃ values. It is possible, particularly for SUM06, that existing networks are not adequate to fully characterize status with respect to these alternative NAAQS.

3. Human Exposure Analyses

Overview

The impact that attaining alternative O₃ NAAQS may have on human exposure will be evaluated using a new version of the Probabilistic NEM (NAAQS Exposure Model) applied to O₃ (pNEM/O₃). The alternative NAAQS that will be evaluated are listed above in section III.A. Exposure estimates will be obtained directly for nine U.S. urban areas located in each EPA Region except Region X. The nine areas display a wide variety in population, geographic area, demographic makeup, climatology, and O₃ air quality. Results from these areas will be extrapolated to the entire U.S. urban population via a functional relationship fit to the nine-area results. Uncertainty in the estimates will be explicitly addressed using Monte Carlo modeling techniques.

The exposure estimates will assist the Administrator in evaluating which alternative primary NAAQS provide an adequate margin of safety.

Issues

1. Resource priorities dictate that only 10 Monte Carlo simulations be undertaken for any one urban area. It is the staff's judgment that the value of additional information provided by conducting additional runs is not worth the cost. Use of 10 simulations is two orders of magnitude fewer simulations than are normally undertaken. Thus, the issue arises whether or not all uncertainty in input data has been adequately addressed. This issue will be quantitatively addressed in the OAQPS Staff Paper.

2. Urban areas used for NAAQS exposure assessment are generally large in size and have adequate home-to-work transportation data needed to model daily population movement within the area. In addition, a minimum of three ambient monitors are needed to adequately characterize the spatial distribution of O₃ in an area. These requirements preclude including in a PNEM/O₃ analysis small urban areas with a limited data base. Many of the excluded areas, however, have more exceedances of the 8-hr levels of interest than the 1-hr levels; in fact, many of these areas do not exceed the current 1-hr NAAQS but have scores of days with 8-hr averages >0.06, 0.08, and 0.10 ppm, which are concentration levels of interest for the longer averaging time. Thus, we are not analyzing all possible types of O₃ air quality problems that currently exist in the U.S.

This issue can only be addressed qualitatively at the current time. The OAQPS Staff Paper will include some discussion of this important issue.

3. The human activity data base used for PNEM/O₃ modeling is limited. In fact, only the mid-1980's Cincinnati data base is used for O₃ analyses. This data base is not representative of true outdoor worker activities (in any climate), and may not be representative of general population or summer camp population activities in warmer climates. Thus, the question arises of how representative are the PNEM/O₃ modeling results? This question will be addressed both quantitatively and qualitatively in the Staff Paper to the extent possible. Special analyses of "summer camper" and "outdoor worker" exposures will be used in part to address this question.

Status/Schedule

The nine-urban-area modeling work is complete. A draft report describing the PNEM model and its inputs was submitted to EPA on September 30, 1993. A draft report describing the methodology and a memo describing results for Los Angeles is being provided to a CASAC Exposure/Risk Subcommittee in November 1993 and will be reviewed by this Subcommittee at a December 16, 1993 meeting. Separate reports will be prepared in early 1994 detailing the "summer camper" and "outdoor worker" analyses mentioned above.

These reports and results for the remaining 8 urban areas will be sent to the Subcommittee and reviewed at a public Subcommittee meeting in early 1994.

The extrapolation work from the nine urban areas will be done in-house starting in early 1994 and will take about one month to complete.

4. Health Risk Assessment

Overview

The primary purpose of the O₃ health risk assessment project is to provide quantitative (probabilistic) estimates of the risk to public health associated with attainment of alternative O₃ NAAQS and qualitative information characterizing the nature and significance of various health effects. A major goal of the risk assessment work is to provide a more explicit and quantitative characterization of the uncertainties in the scientific data base. This information is designed to assist the Administrator in selecting which primary standards will protect the public health with an adequate margin of safety. The probabilistic risk assessment will not cover all of the various health effect categories for which there is some scientific evidence of effects. However, the OAQPS Staff Paper will contain a summary and evaluation of all major health effects categories for which there is scientific evidence that O₃ plays a role.

The last O₃ review included a 1-hr health risk assessment for lung function (FEV₁) and respiratory symptoms (cough, chest discomfort, any) based on 3 human clinical studies of heavily exercising individuals for "as-is" scenario and just attaining 0.08, 0.10, and 0.12 ppm, 1-hr, 1 expected exceedance NAAQS. This information was summarized in the Staff Paper, was favorably reviewed by CASAC at its 1988 meeting, and has been presented and published.

A chronic lung injury risk assessment for O₃ was conducted by Argonne National Laboratory (ANL) for OAQPS in the 1989-1990 period. This project involved elicitation of probabilistic exposure-response relationships for formation of lesions in a critical region of the lung from 6 expert health scientists. This information was not part of the O₃ NAAQS review process, but was used to inform EPA decision makers about the potential significance and magnitude of chronic effects associated with O₃ exposures. The exposure period used was the average of the 8-hr daily maximum over the O₃ season (April-October) and judgments were elicited for 1 and 10 seasons of exposure.

Structure

The three major types of inputs to the health risk assessment for O₃ are: (1) exposure-response relationships used to characterize specific health effects; (2) distributions of 1- and 8-hr O₃ concentrations upon attainment of alternative NAAQS and under the "as is" situation; and (3) distributions of population exposure, both in terms of people exposed

and occurrences of exposure, upon attainment of alternative O₃ NAAQS and under the "as is" situation obtained from the PNEM/O₃ analysis described in Section III.C.3 of this plan.

Current plans are for risk estimates to be generated for the following health endpoints:

- lung function decrements (> 10 , > 15 , $> 20\%$ FEV₁) and respiratory symptoms (e.g., cough, chest discomfort) associated with: 1- to 2.5-hr exposures of heavily exercising subjects, 2.5-hr exposures of moderately exercising subjects, and 6.7- to 8-hr exposures of moderately exercising subjects. (Probabilistic exposure-response relationships developed from data from published controlled human exposure studies of healthy adult subjects.)

- airway reactivity associated with 6.7-hr exposures for moderately exercising subjects. (Probabilistic exposure-response relationships developed from data from published controlled human exposure studies of healthy adult subjects.)

- development of mild and moderate lesions in the centriacinar region of the lung after 1 and 10 seasons of exposure (using mean of O₃ season daily max. 8-hr averages) for NY and LA children and outdoor workers. Plan to use probabilistic exposure-response judgments obtained during chronic risk project in 1989. The purpose is to provide additional information for judgment on adequate margin of safety associated with alternative 1- and 8-hr O₃ NAAQS, not to be used to set a separate chronic standard.

Risk estimates may be generated for inflammatory responses associated with 8-hr exposures for moderately exercising population depending on feasibility and value of information. Discussions between OAQPS, HERL, and ECAO are ongoing to develop consensus on whether there is adequate information to conduct a quantitative risk assessment and how such an assessment should be structured that utilizes both the available animal and human data on this effect category.

Based on meetings with OAQPS staff and HERL and ECAO scientists, it was concluded that there was insufficient "quantitative information" to pursue development of probabilistic risk estimates for the following health endpoints: increased asthma attacks, emergency room visits, or hospital admissions for asthmatics on high O₃ days, increased acute mortality, and increased incidence of infection. The primary limitation for quantitative risk assessment purposes of the data reporting these effects is the lack of adequate characterization of exposure to O₃ and other pollutants and the difficulty of associating any given exposure period to the reported effects. The scientific evidence for each of these effects will be discussed and evaluated in the OAQPS Staff Paper.

Two distinct types of risk measures will be developed. The first measure, "benchmark risk," focuses on the probability of risk of unhealthful air. More specifically, benchmark risk is the probability that pollutant levels will be sufficient to trigger a defined health endpoint in at least a fraction of the sensitive population if they were exposed. The second measure, "headcount risk," focuses on the number of people affected and the number of incidences of a given health effect considering individuals' personal exposures as they go about their daily activities. (Since the exposure analysis will only generate exposure occurrences, headcount risk estimates will be in terms of incidences of effects.) Together, these two types of risk measures capture important perspectives that should be considered in selecting primary O₃ NAAQS that provide an adequate margin of safety.

In an effort to improve the characterization of the health consequences and adversity of the various health endpoints associated with O₃ exposures, OAQPS and ANL will work with ECAO, HERL, and non-Agency scientists to develop a protocol to elicit expert judgments on severity and consequence of effects associated with single and repeated occurrences of 1 to 8-hr exposures (i.e., lung function, respiratory symptoms, airway reactivity, and inflammation). Experts from within and outside of the Agency will be selected and interviewed to obtain their judgments.

Status/Schedule

Development of probabilistic concentration-response relationships is underway. The computer algorithms for generating both benchmark and headcount risk estimates are being setup and tested. Risk estimates and a draft report describing the methodology for the health endpoints indicated above, with the exception of inflammation, will be available for review by the CASAC Exposure/Risk Subcommittee in early 1994. For the significance of effects project a draft report with judgments of experts is scheduled for completion by mid 1994.

Issues

(1) Given the relatively weaker state of information, it is the staff's recommendation that risk estimates not be developed for some of the health effect endpoints (e.g., increased hospital admissions for asthmatics, increased acute mortality) reported in epidemiology studies. The evidence of these effects will be addressed qualitatively in the OAQPS Staff Paper.

(2) Since there will not be exposure estimates for the adolescent population attending summer camps, with the exception of a small (< 100 person) special PNEM/O₃ analysis, it is the staff's recommendation that risk estimates for this important sensitive population group not be produced. There is inadequate information on activity patterns to conduct a more extensive "summer camp" exposure analysis.

(3) The significance of effects project is a new type of product for the risk team and the approach to tackling this problem has not been worked out. It may be difficult to keep

on the tight time schedule indicated above given the interactive nature of this project with feedback from ORD, CASAC, and other external scientists, as well as EPA policy makers, guiding development of this project.

5. Welfare Effects Assessment

Overview

In response to the CASAC closure letter (May 1989) during the last O₃ NAAQS review, EPA's Environmental Research Laboratory in Corvallis, Oregon (ERL/Corvallis): (1) continued to reanalyze the NCLAN database in search of a more appropriate exposure index to relate plant response to acute O₃ exposures and 2) developed a long term research plan titled "Effects of Tropospheric Ozone on Forest Trees" to investigate chronic O₃ exposures on tree species. In the expansion from an acute to a chronic timeframe, additional environmental stressors have the potential to impact the equation (e.g., changing soil characteristics and populations, climate, pathogens).

Research initiated under the "Tropospheric Ozone" research plan has currently produced exposure-response functions (Weibull model) for eleven forest tree species, quantifying tree response in growth and biomass to different O₃ concentrations. These response functions are from seedling and sapling studies conducted in open-top exposure chambers. These studies have not incorporated the influence of multiple environmental factors, and in only a few instances contain results from multiple year exposures. As a means of comparing NCLAN's calculated average predicted relative crop yield losses with the relative predicted biomass loss calculated for the 11 tree species, the same SUMO6 levels of 16.5, 26.4, and 39.7 ppm-hr were evaluated. (The SUMO6 of 26.4 ppm-hr corresponds to protecting 50% of the crops from greater than 10% yield loss.)

Structure

The welfare effects chapter of the OAQPS Staff Paper will provide an assessment of the welfare effects information compiled in the Criteria Document. Several factors are important in the analysis. These factors include: (1) remaining uncertainty about the relationship between acute and chronic O₃ exposure regimes on plant growth; (2) the adequacy of existing air quality and exposure indices to take into account biologically and ecologically significant O₃ regimes; (3) ecosystem-level response to O₃; (4) the extent and biological and statistical significance of the effects observed; and (5) the type and credibility of the studies conducted.

The OAQPS Staff Paper will include summary discussions of analyses relevant to decision making on the secondary NAAQS. These analyses are summarized below:

- Reanalyses of the NCLAN data to compare degree of fit for over 600 different exposure indices which were completed in 1991.

-Additional analyses currently underway at ERL/Corvallis comparing the degree of protection offered between a given SUM06 value and 1) a SUM08 and 2) an 8-hour, .08 ppm standard with either 1 or 5 expected exceedances.

-Interim risk assessment of O₃ impact on eastern U.S. forests will use Geographical Information System (GIS) to integrate and combine various data (estimations of O₃ exposure in forests, landscape and environmental factors, species ranges, empirical exposure-response functions, and model simulations of canopy O₃ uptake, growth rates and stand response over time) to provide a risk characterization of O₃ on forest species in the eastern U.S. The SUM06 values listed in Section III.A. of this project plan are evaluated along with the additional SUM06 value of 39.7 ppm-hr.

-Benefits analysis also will assess in a preliminary fashion the economic significance of O₃'s effects on crops and forests. A contract has been initiated to determine the depth of the database available on O₃ sensitive urban plant species with the potential to develop maps of possible adverse effects in O₃ nonattainment areas. These analyses will occur in the context of the existing standard.

Status/Schedule

A preliminary review of the revised O₃ Criteria Document welfare effects chapters occurred at the peer-review workshop September 27-29, 1993. See the overall review schedule for the OAQPS Staff Paper in Figure 1.

Issues

The following key issues will need to be addressed in the development of the OAQPS Staff Paper:

- How reliable are existing extrapolation methods for calculating long term O₃ impacts on trees?
- To what extent should welfare effects risk assessments be used in the secondary standard-setting process?
- How should EPA determine which welfare effects and what degree of response should be considered "adverse" effects?

6. Significant Harm Levels

Overview

Section 303 of the CAA provides authority for the Administrator to identify exposure levels for ambient air pollutants that constitute "an imminent and substantial endangerment to

the health of persons." This language provides the basis for significant harm levels (SHL) which are set forth in subpart H of 40 CFR Part 51. The SHL is to be set at a level never to be reached at any location. The CAA and EPA regulations governing adoption and submittal of SIPs require States to adopt contingency plans for emission control measures that will prevent levels from reaching the SHL. Contingency plans must specify two or more "episode criteria" (typically "Alert" and "Warning" levels) which require increasing abatement actions. EPA policy is to review the basis for SHLs and guidance/examples of episode levels during the NAAQS review. The current SHL for O₃ is 0.6 ppm, 1-hr average.

Structure

The OAQPS Staff Paper will include a section assessing the scientific evidence reviewed in the revised O₃ Criteria Document that is relevant to determining whether there is a need to revise the SHL. Review of the current episode examples contained in Appendix L of Part 51 will be addressed as part of the implementation assessments.

Status/Schedule

See the overall review schedule for the OAQPS Staff Paper in Figure 1.

D. Standards (Part 50)

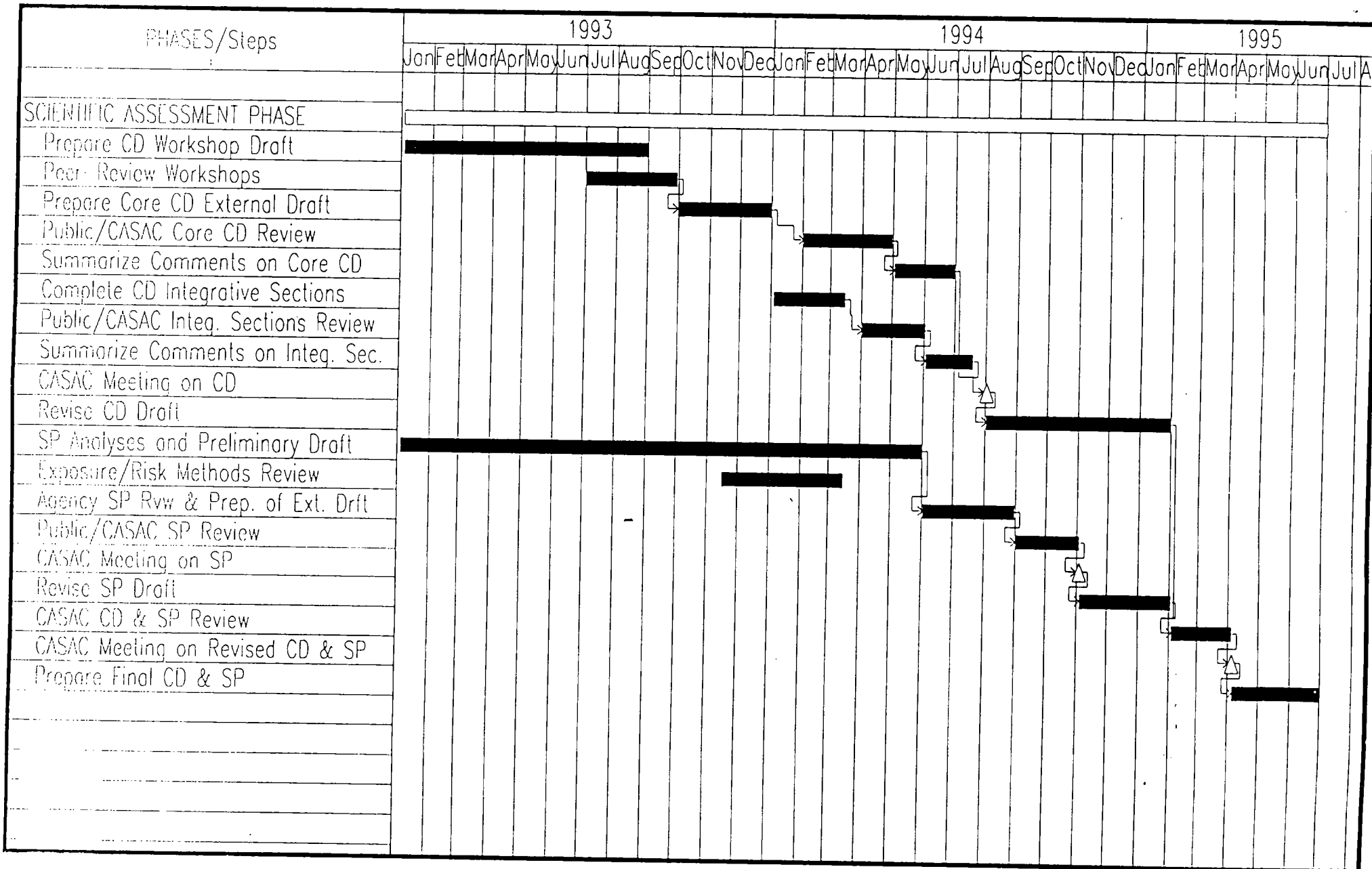
Overview

After CASAC "closure" on the revised O₃ Criteria Document and OAQPS Staff Paper in the Spring 1995, a regulatory options briefing will be prepared for the senior management oversight group and the Administrator. Once guidance has been provided, staff will develop a Federal Register notice which explains in detail the rationale for the proposed decision. Staff probably will draw heavily on the OAQPS Staff Paper and CASAC closure letter in developing the Federal Register proposal preamble.

Status/Schedule

Work on the Federal Register proposal notice will begin in the Spring 1995 when closure is obtained on the revised O₃ Criteria Document and OAQPS Staff Paper.

Projected Ozone NAAQS Review Schedule: Scientific Assessment Phase





Air Quality Criteria for Ozone and Related Photochemical Oxidants

Review

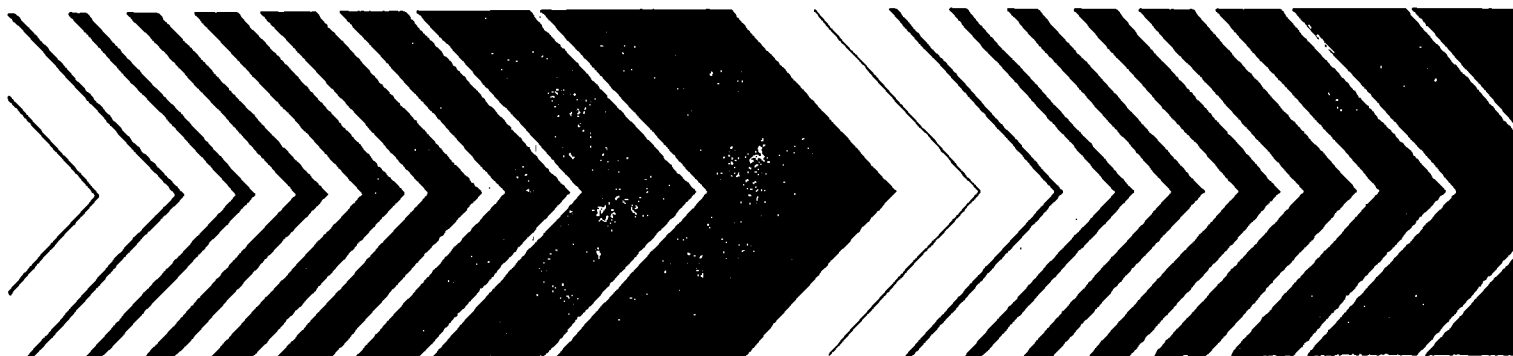
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Chapter 1. Executive Summary

(Do Not
Quote or Cite)

NOTICE

This document is a preliminary draft. It has not been formally released by EPA and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.



Air Quality Criteria for Ozone and Related Photochemical Oxidants

Chapter 1. Executive Summary

and

Chapter 9. Integrative Summary of Ozone Health Effects

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PREFACE

In 1971, the U.S. Environmental Protection Agency (EPA) promulgated National Ambient Air Quality Standards (NAAQS) to protect the public health and welfare from adverse effects of photochemical oxidants. In 1979, the chemical designation of the standards was changed from photochemical oxidants to ozone (O_3). This document, therefore, focuses primarily on the scientific air quality criteria for O_3 and, to a lesser extent, for other photochemical oxidants like hydrogen peroxide and the peroxyacyl nitrates.

The EPA promulgates the NAAQS on the basis of scientific information contained in air quality criteria documents. The previous O_3 criteria document, *Air Quality Criteria for Ozone and Other Photochemical Oxidants*, was released in August 1986 and a supplement, *Summary of Selected New Information on Effects of Ozone on Health and Vegetation*, was released in January 1992. These documents were used as the basis for a March 1993 decision by EPA not to revise the existing 1-h NAAQS for O_3 . That decision, however, did not take into account some of the newer scientific data that became available after the 1986 criteria document. This revised air quality criteria document for O_3 and related photochemical oxidants critically evaluates and assesses the latest scientific data associated with exposure to concentrations of these pollutants found in ambient air. Emphasis is placed on presentation of health and environmental effects data; however, other scientific data are presented and evaluated in order to provide a better understanding of the nature, sources, distribution, measurement, and concentrations of O_3 and related photochemical oxidants and their precursors in the environment. The document is not an exhaustive literature review; rather it assesses the most pertinent literature available through 1993.

The chapters in this volume summarize and interpret key information drawn from the other, more detailed chapters (Chapters 2 through 8) of the present document, which were prepared and peer reviewed by experts from various Federal and State governmental offices, academia, and private industry for use by EPA to support decision making regarding potential risks to public health and welfare. The Environmental Criteria and Assessment Office of EPA's Office of Health and Environmental Assessment acknowledges with appreciation the contributions provided by these authors and reviewers as well as the diligence of its staff and contractors in the preparation of this document at the request of the Office of Air Quality Planning and Standards.

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FOR OZONE AND RELATED PHOTOCHEMICAL OXIDANTS
(cont'd)

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1. EXECUTIVE SUMMARY

1.1 INTRODUCTION

The external review draft document *Air Quality Criteria for Ozone and Related Photochemical Oxidants* evaluates the latest scientific information useful in deriving criteria that form the scientific basis for U.S. Environmental Protection Agency (EPA) decisions regarding the National Ambient Air Quality Standards (NAAQS) for ozone (O₃). This Executive Summary concisely summarizes key conclusions from the document, which comprises nine chapters. Following this Executive Summary is a brief Introduction (Chapter 2) containing information on the legislative and regulatory background for review of the O₃ NAAQS. Chapter 3 provides information on the chemistry, sources, emissions, measurement, and transport of O₃ and related photochemical oxidants and their precursors, whereas Chapter 4 covers environmental concentrations, patterns, and exposure estimates of O₃ and oxidants. This is followed by Chapter 5, dealing with the environmental effects; Chapters 6, 7, and 8 discuss, respectively, animal toxicological studies, human health effects, and the extrapolation of animal toxicological data to humans. The last chapter, Chapter 9, provides an integrative, interpretative evaluation of health effects associated with exposure to O₃. The following subsections follow the chapter organization of the external review draft.

1.2 LEGISLATIVE AND REGULATORY BACKGROUND

The EPA is required under Sections 108 and 109 of the Clean Air Act to periodically evaluate the air quality criteria that reflect the latest scientific information relevant to review of the O₃ NAAQS. These air quality criteria, contained in the criteria document, are useful for indicating the kind and extent of all identifiable effects on public health or welfare that may be expected from the presence of O₃ and related photochemical oxidants in ambient air. The last criteria document was released in 1986, and a supplement was released in 1992. These documents were used as the basis for a March 1993 decision by EPA to not revise the existing 1-h NAAQS for O₃ at that time. That decision, however, did not take into consideration more recent scientific information that has been published since the last literature review in early 1989. The purpose of this revised criteria document, therefore, is to summarize the pertinent information contained in the previous O₃ criteria document and to critically evaluate and assess the more recent scientific data associated with exposure to the concentrations of O₃ and related photochemical oxidants that are found in ambient air.

1.3 TROPOSPHERIC OZONE AND ITS PRECURSORS

Tropospheric Ozone Chemistry

Ozone is found in the stratosphere, the "free" troposphere, and the planetary boundary layer (PBL) of the earth's atmosphere. Ozone occurs in the stratosphere as the result of chemical reactions initiated by short-wavelength radiation from the sun. In the "free"

1 troposphere, O_3 occurs as the result of incursions from the stratosphere; upward venting
2 from the PBL (the layer next to the earth's surface) through certain cloud processes; and
3 photochemical formation from precursors, notably methane (CH_4), carbon monoxide (CO),
4 and nitrogen oxides (NO_x). In the PBL, O_3 occurs as the result of downward mixing from
5 the stratosphere and free troposphere and as the result of photochemical processes occurring
6 within the PBL.

7
8 The photochemical production of O_3 and other oxidants found at the earth's surface
9 (in the PBL, troposphere, or ambient air, used interchangeably in this summary) is the result
10 of atmospheric physical processes and complex, nonlinear chemical processes involving two
11 classes of precursor pollutants, reactive volatile organic compounds (VOCs) and NO_x . The
12 only significant initiator of the photochemical production of O_3 in the polluted troposphere is
13 the photolysis of nitrogen dioxide (NO_2), yielding nitric oxide (NO) and a ground-state
14 oxygen atom that reacts with molecular oxygen to form O_3 . The O_3 thus formed reacts with
15 NO, yielding O_2 and NO_2 . These cyclic reactions attain equilibrium in the absence of
16 VOCs. In the presence, however, of VOCs, which are abundant in polluted ambient air, the
17 equilibrium is upset, resulting in a net increase in O_3 . Methane is the chief VOC found in
18 the free troposphere and in relatively "clean" areas of the PBL. The VOCs found in polluted
19 ambient air are more complex and more reactive than CH_4 , but, as with CH_4 , their
20 atmospheric oxidative degradation is initiated through attack on the VOCs by hydroxyl (OH)
21 radicals. As in the CH_4 oxidation cycle, the conversion of NO to NO_2 during the oxidation
22 of VOCs is accompanied by the production of O_3 and the efficient regeneration of the OH
23 radical. The O_3 and peroxyacyl nitrates (PANs) formed in polluted atmospheres increase
24 with the NO_2/NO concentration ratio.

25
26 At night, in the absence of photolysis of reactants, the simultaneous presence of O_3 and
27 NO_2 results in the formation of the nitrate radical, NO_3 . Reactions with NO_3 radicals appear
28 to constitute major sinks for alkenes, cresols, and some other compounds, although alkyl
29 nitrate chemistry is not well characterized.

30
31 Most inorganic gas-phase processes, that is, the nitrogen cycle and its interrelationships
32 with O_3 production, are well understood. The chemistry of the VOCs in ambient air is not
33 as well understood. It is well-known, however, that the chemical loss processes of gas-phase
34 VOCs, with concomitant production of O_3 , include reaction with OH and NO_3 radicals and
35 O_3 , and photolysis. Reaction with the OH radical is the only important atmospheric reaction
36 (loss process) for alkanes, aromatic hydrocarbons, and the higher aldehydes and ketones that
37 lack $>C=C<$ bonds; and the only atmospheric reaction of alcohols and ethers. Photolysis
38 is the major loss process for formaldehyde and acetone. Reactions with OH and NO_3
39 radicals and with O_3 are all important loss processes for alkenes and for carbonyls containing
40 $>C=C<$ bonds.

41
42 Uncertainties in the atmospheric chemistry of the VOCs can affect quantification of the
43 NO-to- NO_2 conversion and of O_3 yields; and can present difficulties in representation of
44 mechanisms, products, and product yields in O_3 air quality models. Major uncertainties in
45 current understanding of the atmospheric chemistry of the VOCs include (1) chemistry of
46 alkyl nitrate formation, (2) products and reaction rates for $>C_4$ alkanes and for branched

1 alkanes, (3) mechanisms and products of alkene-O₃ reactions, and (4) products of aromatic
2 hydrocarbons in both urban and rural atmospheres.

3
4 It should be noted that the atmospheric chemical processes involved in the
5 photooxidation of VOCs and the formation of O₃ and other photochemical oxidants can lead
6 also to the formation of OH radicals and of particulate-phase organic compounds. The OH
7 radicals produced can not only oxidize VOCs but can also react with NO₂ and sulfur dioxide
8 (SO₂) to form nitric and sulfuric acids, respectively, which become incorporated into aerosols
9 as particulate nitrate and sulfate.

10 11 **Meteorological Influences on Ozone Formation and Transport**

12
13 The surface energy (radiation) budget of the earth strongly influences the dynamics of
14 the PBL. The redistribution of energy through the PBL creates thermodynamic conditions
15 that influence vertical mixing. Growing evidence indicates that the strict use of mixing
16 heights in modeling is an oversimplification of the complex processes by which pollutants are
17 redistributed within urban areas; and that it is necessary to treat the turbulent structure of the
18 atmosphere directly and acknowledge the vertical variations in mixing. Energy balances
19 therefore require study so that more realistic simulations can be made of the structure of the
20 PBL.

21
22 Day-to-day variability in O₃ concentrations depends heavily on day-to-day variations in
23 meteorological conditions, such as the degree of mixing that occurs between release of a
24 pollutant or its precursors and their arrival at a receptor; the occurrence of inversion layers
25 (layers in which temperature increases with height above ground level); and the transport of
26 O₃ left overnight in layers aloft and subsequent downward mixing of that O₃ to the surface.

27
28 The transport of O₃ and its precursors beyond the urban scale (≤ 50 km) to neighboring
29 rural and urban areas has been well documented and was described in the 1986 EPA criteria
30 document for O₃. Episodes of high O₃ concentrations in urban areas are often associated
31 with high concentrations of O₃ in the surroundings. Areas of O₃ accumulation are
32 characterized by (1) synoptic-scale subsidence of air in the free troposphere, resulting in
33 development of an elevated inversion layer; (2) relatively low wind speeds associated with
34 the weak horizontal pressure gradient around a surface high pressure system; (3) a lack of
35 cloudiness; and (4) high temperatures.

36
37 Ultraviolet (UV) radiation from the sun plays a key role in initiating the photochemical
38 processes leading to O₃ formation and affects individual photolytic reaction steps. Still, there
39 is little empirical evidence in the literature linking day-to-day variations in observed UV
40 radiation levels with variations in O₃ levels. An association, however, between tropospheric
41 O₃ concentrations and tropospheric temperature has been demonstrated. Empirical data from
42 four urban areas, for example, show an apparent upper bound on O₃ concentrations that
43 increases with temperature. A similar qualitative relationship exists at a number of rural
44 locations.

1 The relationship between wind speed and O₃ buildup varies from one part of the
2 country to another.

3
4 Statistical techniques (e.g., regression techniques) can be used to help identify real
5 trends in O₃ concentrations, both intra- and interannual, by normalizing meteorological
6 variability. In the Southern Oxidant Study, for example, regression techniques were
7 successfully used to forecast O₃ levels to ensure that specialized measurements were made on
8 appropriate days.

9 10 **Precursors**

11 12 *Nitrogen Oxides Emissions*

13
14 Anthropogenic NO_x is associated with combustion processes. The primary pollutant
15 emitted is NO formed at high combustion temperatures from the nitrogen and oxygen in air
16 and from nitrogen in the combustion fuel. Emissions of NO_x in 1991 in the United States
17 totaled 21.39 Tg. The two largest single NO_x emission sources are electric power generation
18 and highway vehicles. Because a large proportion of anthropogenic NO_x emissions come
19 from distinct point sources, published annual estimates are thought to be very reliable.

20
21 Natural NO_x sources include stratospheric intrusion, oceans, lightning, soils, and
22 wildfires. Lightning and soil emissions are the only two significant natural sources of NO_x
23 in the United States. Combined natural sources contribute about 2.2 Tg of NO_x to the
24 troposphere over the continental United States. Uncertainties in natural NO_x inventories are
25 much larger, however, than for anthropogenic NO_x emissions.

26 27 *Volatile Organic Compound Emissions*

28
29 Hundreds of VOCs, commonly containing from 2 to about 12 carbon atoms, are
30 emitted by evaporative and combustion processes from a large number of source types.
31 Total U.S. VOC emissions in 1991 were estimated at 21.0 Tg. The two largest source
32 categories were industrial processes (10.0 Tg) and transportation (7.9 Tg). Emissions of
33 VOCs from highway vehicles accounted for almost 75% of the transportation-related
34 emissions; studies have shown that the majority of these VOC emissions come from about
35 20% of the automobiles in service, many, perhaps most, of which are older cars that are
36 poorly maintained. The accuracy of VOC emission estimates is difficult to determine, both
37 for stationary and mobile sources.

38
39 Vegetation emits significant quantities of VOCs into the atmosphere, chiefly
40 monoterpenes and isoprene, but also oxygenated VOCs, according to recent studies. The
41 most recent biogenic VOC emissions estimate for the United States showed annual emissions
42 of 29.1 Tg/year.

43
44 Uncertainties in both biogenic and anthropogenic VOC emission inventories prevent
45 establishing the relative contributions of these two categories.

Concentrations of Volatile Organic Compounds in Ambient Air

The VOCs most frequently analyzed in ambient air are the nonmethane hydrocarbons (NMHCs). Morning concentrations (6:00 a.m. to 9:00 a.m.) have been measured most often because of the use of morning data in the Empirical Kinetics Modeling Approach (EKMA) and in air quality simulation models. Measurements made in 22 cities in 1984 and 19 cities in 1985 showed median NMHC concentrations ranging from 0.39 ppm C to 1.27 ppm C for 1984; and from 0.38 ppm C to 1.63 ppm C in 1985. Overall median values from all urban sites were about 0.72 ppm C in 1984 and 0.60 ppm C in 1985.

Concurrent measurements of anthropogenic and biogenic NMHCs have shown that biogenic NMHCs usually constituted much less than 10% of the total NMHCs. For example, average isoprene concentrations ranged from 0.001 to 0.020 ppm C and terpenes from 0.001 to 0.030 ppm C.

Concentrations of Nitrogen Oxides in Ambient Air

Measurements of NO_x made in 22 and 19 U.S. cities in 1984 and 1985, respectively, showed median 6:00-to-9:00 a.m. NO_x concentrations ranging from 0.02 to 0.08 ppm in most of these cities. Nonurban NO_x concentrations, reported as average seasonal or annual NO_x , range from <0.005 to 0.015 ppm.

Ratios of 6:00-to-9:00 a.m. nonmethane organic compounds (NMOC) to NO_x are higher in southeastern and southwestern U.S. cities than in northeastern and midwestern U.S. cities, according to data from EPA's multicity studies conducted in 1984 and 1985. Median ratios ranged from 9.1 to 37.7 in 1984; in 1985, median ratios ranged from 6.5 to 53.2 in the cities studied. Rural NMOC/ NO_x ratios tend to be higher than urban ratios. Morning (6:00-to-9:00 a.m.) NMOC/ NO_x ratios are used in the EKMA type of trajectory model. The correlation of NMOC/ NO_x ratios with maximum 1-h O_3 concentrations, however, was weak in a recent analysis.

Source Apportionment and Reconciliation

Source apportionment (now regarded as synonymous with receptor modeling) refers to determining the quantitative contributions of various sources of VOCs to ambient air pollutant concentrations. Source reconciliation refers to the comparison of measured ambient VOC concentrations with emissions inventory estimates of VOC source emission rates for the purpose of validating the inventories.

Recent findings showed that vehicle exhaust was the dominant contributor to ambient VOCs in seven of eight U.S. cities studied. Whole gasoline contributions have been estimated to be equal to vehicle exhaust in one study and 20% of vehicle exhaust in a second study.

Estimates of biogenic VOCs at a downtown site in Atlanta in 1990 indicated a lower limit of 2% (24-h average) for the biogenic percentage of total ambient VOCs at that location (isoprene was used as the biogenic indicator species). The percentage varies during the 24-h

1 period because of the diurnal (e.g., temperature, light intensity) dependence of isoprene
2 concentrations.

3
4 Source reconciliation data have shown disparities between emission inventory estimates
5 and receptor-estimated contributions. For biogenics, emission estimates are greater than
6 receptor-estimated contributions. The reverse has been true for natural gas contributions
7 estimated for Los Angeles, Columbus, and Atlanta; and for refinery emissions in Chicago.

9 **Analytical Methods for Oxidants and Their Precursors**

11 *Oxidants*

12
13 Current methods used to measure O₃ are chemiluminescence (CL); UV absorption
14 spectrometry; and newly developed spectroscopic and chemical approaches, including
15 chemical approaches applied to passive sampling devices (PSDs) for O₃.

16
17 The CL method has been designated as the reference method by EPA. Detection limits
18 of 0.005 ppm and a response time of <30 s are typical of currently available commercial
19 instruments. A positive interference from atmospheric water vapor was reported in the
20 1970s and has recently been confirmed. Proper calibration can minimize this source of
21 error.

22
23 Commercial UV photometers for measuring O₃ have detection limits of about
24 0.005 ppm and a response time of <1 min. Because the measurement is absolute, UV
25 photometry is also used to calibrate O₃ methods. A potential disadvantage of UV photometry
26 is that atmospheric constituents that absorb 254 nm radiation, the wavelength at which O₃ is
27 measured, will cause a positive interference in O₃ measurements. Interferences have been
28 reported in two recent studies, but assessment of the potential importance of such
29 interferences (e.g., toluene, styrene, cresols, nitrocresols) is hindered by lack of absorption
30 spectra data in the 250 nm range and by lack of aerometric data for the potentially interfering
31 species.

32
33 Calibration of O₃ measurement methods (other than PSDs) is done by UV spectrometry
34 or by gas-phase titration (GPT) of O₃ with NO. Ultraviolet photometry is the reference
35 calibration method approved by EPA. Ozone is unstable and must be generated in situ at
36 time of use to produce calibration mixtures.

37
38 Peroxyacetyl nitrate and the higher PANs are normally measured by gas
39 chromatography using an electron capture detector (GC-ECD). Detection limits have now
40 been extended to 1 to 5 ppt. The preparation of reliable calibration standards is difficult
41 because PAN is unstable (explosive and subject to surface-related decomposition), but several
42 methods are available.

1 *Volatile Organic Compounds*

2
3 Traditionally, NMHCs and other NMOCs have been measured by methods that employ
4 a flame ionization detector (FID) as the sensing element that measures a change in ion
5 intensity resulting from the combustion of air containing organic compounds. The method
6 recommended by EPA for total NMOC measurement involves the cryogenic preconcentration
7 of NMOCs and the measurement of the revolatilized NMOCs using FID. The main
8 technique for speciated NMOC/NMHC measurements is cryogenic preconcentration followed
9 by GC-FID. Systems for sampling and analysis of VOCs have now been developed that
10 require no liquid cryogen for operation, yet provide sufficient resolution of species.

11
12 Stainless steel canisters have become the containers of choice for collection of whole-air
13 samples for NMHC/NMOC data. Calibration procedures for NMOC instrumentation require
14 the generation, by static or dynamic systems, of dilute mixtures at concentrations expected to
15 occur in ambient air.

16
17 Preferred methods for measuring carbonyl species (aldehydes and ketones) in ambient
18 air are spectroscopic methods; on-line colorimetric methods; and the most common method
19 in current use for measuring gas-phase carbonyl compounds in ambient air, which is the
20 high-performance liquid chromatography (HPLC) method employing
21 2,4-dinitrophenylhydrazine (DNPH) derivatization in a silica gel cartridge. Use of an
22 O₃ scrubber has been recommended to prevent interference in this method by O₃ in ambient
23 air. Several methods are available for preparing stable calibration mixtures.

24 25 *Oxides of Nitrogen*

26
27 Nitric oxide and NO₂ comprise the NO_x compounds involved as precursors to O₃ and
28 other photochemical oxidants.

29
30 The most common method of NO measurement is the gas-phase CL reaction with O₃,
31 which is essentially specific for NO. Commercial NO monitors have detection limits of a
32 few parts per billion by volume (ppbv) in ambient air but may not have sensitivity sufficient
33 for surface measurements in rural or remote areas, or for airborne measurements. Direct
34 spectroscopic methods for NO exist that have very high sensitivity and selectivity for NO,
35 but their complexity, size, and cost restrict these methods to research applications. No PSDs
36 presently exist for measurement of NO.

37
38 Chemiluminescence analyzers are the method of choice for NO₂ measurement, even
39 though they do not measure NO₂ directly. Minimum detection levels for NO₂ have been
40 reported to be 5 to 13 ppb, but more recent evaluations have indicated detection limits of
41 0.5 to 1 ppbv. Reduction of NO₂ to NO is required for measurement. In practice, selective
42 measurement of NO_x by this approach has proved difficult, and the NO₂ value inferred from
43 such measurements may be significantly in error.

44
45 Several spectroscopic approaches to NO₂ detection have been developed but share the
46 drawbacks of spectroscopic NO methods. Passive samplers for NO₂ exist, but are still in the
47 developmental stage for ambient air monitoring.

1 Calibration of methods for NO measurement is done using standard cylinders of NO in
2 nitrogen. Calibration of methods for NO₂ measurement include use of cylinders of NO₂ in
3 nitrogen or air, use of permeation tubes, and GPT.

4 5 **Ozone Air Quality Models**

6 7 *Models and Their Components*

8
9 Photochemical air quality models are used to predict how O₃ concentrations change in
10 response to prescribed changes in source emissions of NO_x and VOCs. They operate on sets
11 of input data that characterize the emissions, topography, and meteorology of a region and
12 produce outputs that describe air quality in that region.

13
14 Two kinds of photochemical models are recommended in guidelines issued by EPA:
15 (1) the use of EKMA is acceptable under certain circumstances, and (2) the grid-based Urban
16 Airshed Model (UAM) is recommended for modeling O₃ over urban areas. The 1990 Clean
17 Air Act Amendments mandate the use of three-dimensional (grid-based) air quality models
18 such as UAM in developing State Implementation Plans for areas designated as extreme,
19 severe, serious, or multistate moderate. General descriptions of EKMA and of grid-based
20 models were given in the 1986 EPA criteria document for O₃.

21
22 The EKMA-based method for determining O₃ control strategies has some limitations,
23 the most serious of which is that predicted emissions reductions are critically dependent on
24 the initial NMHC/NO_x ratio used in the calculations. This ratio cannot be determined with
25 any certainty and is expected to be quite variable in an urban area.

26
27 Grid-based, photochemical air quality models have their limitations as well. These are
28 pointed out subsequently.

29
30 Spatial and temporal characteristics of VOC and NO_x emissions are major inputs to a
31 grid-based photochemical air quality model. Greater accuracy in emissions inventories is
32 needed for biogenics and for both mobile and stationary source components. Grid-based air
33 quality models also require as input the three-dimensional wind field for the photochemical
34 episode being simulated.

35
36 A chemical kinetic mechanism (a set of chemical reactions), representing the important
37 reactions that occur in the atmosphere, is used in an air quality model to estimate the net rate
38 of formation of each pollutant simulated as a function of time.

39
40 Dry deposition is an important removal process for O₃ on both urban and regional
41 scales and is included in all urban- and regional-scale models. Wet deposition is generally
42 not included in urban-scale photochemical models, since O₃ episodes do not occur during
43 periods of significant clouds or rain.

44
45 Concentration fields of all species computed by the model must be specified at the
46 beginning of the simulation ("initial conditions"). These initial conditions are determined

mainly with ambient measurements, either from routinely collected data or from special studies; but interpolation can be used to distribute the surface ambient measurements.

Use of Ozone Air Quality Models

Photochemical air quality models are used for control strategy evaluation by first demonstrating that a past episode, or episodes, can be adequately simulated and then reducing hydrocarbon or NO_x emissions or both in the model inputs and assessing the effects of these reductions on O₃ in the region. The adequacy of control strategies based on grid-based models depends in part on the nature of input data for simulations and model validation, on input emissions inventory data, and on the mismatch between model output and the current form of the NAAQS for O₃. Uncertainties in models can obviously affect their outputs. Uncertainties exist in all components of grid-based O₃ air quality models: emissions, meteorological modules, chemical mechanisms, deposition rates, and determination of initial conditions.

Grid-based models that have been widely used to evaluate control strategies for O₃ or acid deposition, or both, are (1) the Urban Airshed Model (UAM), (2) the California Institute of Technology/Carnegie Institute of Technology (CIT) model, (3) the Regional Oxidant Model (ROM), (4) the Acid Deposition and Oxidant Model (ADOM), and (5) the Regional Acid Deposition Model (RADM).

Conclusions

Urban air quality models are becoming readily available for application and have been applied in recent years in several urban areas. Significant progress has also been made in the development of regional models and the integration of state-of-the-art prognostic meteorological models as drivers.

Although there are still many uncertainties in photochemical air quality modeling, prime among which are emission inventories, models are nevertheless essential for regulatory analysis and constitute one of the major tools for attacking the O₃ problem. Grid-based O₃ air quality modeling is superior to the available alternatives for O₃ control planning, but the chances of its incorrect use must be minimized.

1.4 ENVIRONMENTAL CONCENTRATIONS, PATTERNS, AND EXPOSURE ESTIMATES

Ozone is measured at concentrations above the minimum detectable level at all monitoring locations in the world. In this section of the document, hourly average concentration and exposure information was summarized for urban, rural forested, and rural agricultural areas in the United States.

Because O₃ produced from urban area emissions is transported to more rural downwind locations, elevated O₃ concentrations can occur at considerable distances from urban centers.

Urban O₃ concentration values are often depressed because of titration by NO. Because of the absence of chemical scavenging, O₃ tends to persist longer in nonurban than in urban areas and exposures may be higher than in urban locations.

Trends

Ozone hourly average concentrations have been recorded for many years by the state and local air pollution agencies who report their data to the EPA. The 10-year (1983 to 1992) composite average trend for the second highest daily maximum hourly average concentration during the O₃ season shows that the 1992 composite average for the trend sites is 21% lower than the 1983 average. The 1992 value is the lowest composite average of the past 10 years. The 1992 composite average is significantly less than all the previous nine years, 1983 to 1991. The relatively high O₃ concentrations in 1983 and 1988 were likely attributable in part to hot, dry stagnant conditions in some areas of the country that were especially conducive to O₃ formation.

Between 1991 and 1992, the composite mean of the second highest daily maximum 1-h O₃ concentrations decreased 7% and the composite average of the number of estimated exceedances of the O₃ standard decreased by 23%. Nationwide VOC emissions decreased 3% between 1991 and 1992. The composite average of the second daily maximum concentrations decreased in 8 of the 10 EPA Regions between 1991 and 1992, and remained unchanged in Region VII. Except for Region VII, the 1992 regional composite means are lower than the corresponding 1990 levels.

Surface Concentrations

Published data provides evidence showing the occurrence, at some sites, of multihour periods within a day of O₃ at levels of potential health effects. Although most of these analyses were made using monitoring data collected from sites in or near nonattainment areas, in one analysis of five sites (two in New York state, two in rural California, and one in rural Oklahoma), none of which was in or near a nonattainment area, O₃ concentrations showed only moderate peaks but showed multihour levels above 0.10 ppm.

On the basis of O₃ data from isolated monitoring sites, the EPA has indicated that a reasonable estimate of natural O₃ background concentration near sea level in the United States today, for an annual average, is from 0.020 to 0.035 ppm. This estimate included a 0.010- to 0.015-ppm contribution from the stratosphere and a 0.01-ppm contribution from photochemically affected biogenic NMHCs. An additional 0.010 ppm is possible from the photochemical reaction of biogenic methane. The EPA concluded that a reasonable estimate of natural O₃ background concentration for a 1-h daily maximum at sea level in the United States during the summer is on the order of 0.03 to 0.05 ppm. This estimate may be low, however, because available data from sites appearing to be isolated from anthropogenic sources in the western United States indicate that maximum hourly concentrations can reach 0.06 and 0.075 ppm with infrequent occurrences below 0.02 ppm (i.e., lack of scavenging).

Diurnal Variations

Diurnal patterns of O_3 may be expected to vary with location, depending on the balance among the many factors affecting O_3 formation, transport, and destruction. Although they vary with locality, diurnal patterns for O_3 typically show a rise in concentration from low or levels near minimum detectable amounts to an early afternoon peak. The diurnal pattern of concentrations can be ascribed to three simultaneous processes: (1) downward transport of O_3 from layers aloft, (2) destruction of O_3 through contact with surfaces and through reaction with NO at ground level, and (3) in situ photochemical production of O_3 .

Seasonal Patterns

Seasonal variations in O_3 concentrations in urban areas usually show the pattern of high O_3 in late spring or in summer and low levels in the winter; however, weather conditions in a given year may be more favorable for the formation of O_3 and other oxidants than during the prior or following year.

Average O_3 concentrations tend to be higher in the second versus the third quarter of the year for many isolated rural sites. This observation has been attributed to either stratospheric intrusions or an increasing frequency of slow-moving, high-pressure systems that promote the formation of O_3 . However, for several clean rural sites, the highest exposures have occurred in the third quarter rather than in the second. For rural O_3 sites in the southeastern United States, the daily maximum 1-h average concentration was found to peak during the summer months.

Spatial Variations

Concentrations of O_3 vary with altitude and with latitude. There appears to be no consistent conclusion concerning the relationship between O_3 exposure and elevation.

Indoor Ozone

Until the early 1970s, very little was known about the O_3 concentrations experienced inside buildings, and to date, the database on this subject is not large and a wide range of indoor/outdoor O_3 concentration relationships can be found in the literature; reported indoor/outdoor values for O_3 are highly variable. Indoor/outdoor O_3 concentration ratios generally fall in the range from 0.1 to 0.7 and indoor concentrations of O_3 will almost invariably be less than outdoors.

Estimating Exposure

Both fixed-site monitoring information and human exposure models are used to estimate risks associated with O_3 exposure. Because, for most cases, it is not possible to estimate population exposure solely from fixed-station data, several human exposure models have been developed. Some of these models include information on human activity patterns (i.e., the microenvironments people visit and the times they spend there). These models also

1 contain submodels depicting the sources and concentrations likely to be found in each
2 microenvironment, including indoor, outdoor, and in-transit settings.

3
4 Few data are available for individuals using personal exposure monitors. Results from
5 a pilot study demonstrated that fixed-site ambient measurements may not adequately represent
6 individual exposures. Models based on time-weighted indoor and outdoor concentrations
7 explained only 40% of the variability in personal exposures.

8
9 Two distinct types of O₃ exposure models exist: those that focus narrowly on predicting
10 indoor O₃ levels and those that focus on predicting O₃ exposures on a community-wide basis.

11 Peroxyacyl Nitrates

12
13 Peroxyacetyl nitrate and peroxypropionyl nitrate (PPN) are the most abundant of the
14 non-O₃ oxidants in ambient air in the United States, other than the inorganic nitrogenous
15 oxidants such as NO₂, and possibly nitric acid (HNO₃). The concentrations of PAN that are
16 of most concern are those to which vegetation could potentially be exposed, especially during
17 daylight hours in agricultural areas. Most of the available data on concentrations of PAN
18 and PPN in ambient air are from urban areas. The levels to be found in nonurban areas will
19 be highly dependent upon the transport of PAN and PPN or their precursors from urban
20 areas because the concentrations of the NO_x precursors to these compounds are considerably
21 lower in nonurban than in urban areas.

22 Co-occurrence

23
24 Studies of the joint occurrence of gaseous NO₂/O₃ and SO₂/O₃ at rural sites have
25 concluded that the periods of co-occurrence represent a small portion of the potential plant
26 growing period. For human ambient exposure considerations, in most cases, the
27 simultaneous co-occurrence of NO₂/O₃ and SO₂/O₃ was infrequent. Some researchers have
28 reported the joint occurrence of O₃, nitrogen, and sulfur in forested areas, combining
29 cumulative exposures of O₃ with data on dry deposition of sulfur and nitrogen. One study
30 reported that several forest landscapes with the highest dry deposition loadings of sulfur and
31 nitrogen tended to experience the highest average O₃ concentrations and largest cumulative
32 exposure. Although the authors concluded that the joint concentrations of multiple pollutants
33 in forest landscapes were important, nothing was mentioned about the hourly co-occurrences
34 of O₃ and SO₂ or O₃ and NO₂. Acid sulfates, which are usually composed of sulfuric acid,
35 ammonium bisulfate, and ammonium sulfate, have been measured at a number of locations in
36 North America. The potential for O₃ and acidic sulfate aerosols to co-occur at some
37 locations in some form (i.e., simultaneously, sequentially, or complex-sequentially) is real
38 and requires further characterization. For human ambient exposures, the simultaneous
39 co-occurrence of NO₂ and O₃ was infrequent.

40
41 In one study, the relationship between O₃ and hydrogen ions in precipitation was
42 explored using data from sites that monitored both O₃ and wet deposition simultaneously and
43 within one minute latitude and longitude of each other. It was reported that individual sites
44 experienced years in which both hydrogen ion deposition and total O₃ exposure were at least
45
46

moderately high. With data compiled from all sites, it was found that relatively acidic precipitation occurred together with relatively high O₃ levels approximately 20% of the time, and highly acidic precipitation occurred together with a high O₃ level approximately 6% of the time. Sites most subject to relatively high levels of both hydrogen ions and O₃ were located in the eastern portion of the United States, often in mountainous areas.

The co-occurrence of O₃ and acidic cloudwater in high-elevation forests has been characterized. The frequent O₃-only and pH-only single-pollutant episodes, as well as the simultaneous and sequential co-occurrences of O₃ and acidic cloudwater, have been reported. Both simultaneous and sequential co-occurrences were observed a few times each month above cloud base.

1.5 ENVIRONMENTAL EFFECTS OF OZONE AND RELATED PHOTOCHEMICAL OXIDANTS

Ozone is the gaseous pollutant most injurious to agricultural crops, trees, and native vegetation. Exposure of vegetation to O₃ can inhibit photosynthesis, alter carbon (carbohydrate) allocation, and interfere with mycorrhizal formation in tree roots. Disruption of these important physiological processes can suppress the growth of crops, trees, shrubs, and herbaceous vegetation by decreasing their capacity to form the carbon (energy) compounds needed for growth and maintenance and their ability to absorb the water and mineral nutrients they require from the soil. In addition, loss of vigor increases susceptibility of trees and crops to insects and pathogens and impairs their ability to reproduce. The following section summarizes key environmental effects associated with O₃ exposure.

Effects on Agroecosystems

Methodologies Used in Vegetation Research

Most of the knowledge concerning the effects of O₃ on vegetation comes from the exposure-response studies of important agricultural crop plants and some selected forest and urban tree species, mostly as seedlings. A variety of methodologies have been used, ranging from field exposures without chambers to open-top chambers and to exposures conducted in chambers under highly controlled climates. In general, the more controlled conditions are most appropriate for investigating specific responses and for providing the scientific basis for interpreting and extrapolating results.

Mode of Action

Photosynthesis provides plants with the energy and structural building blocks necessary for their existence. The photosynthetic capacity of a plant (i.e., carbohydrate production) is an important aspect of plant response to stresses in natural environments and is strongly associated with leaf nitrogen content and with water movement. Continued acquisition of nitrogen and water uptake are necessary, if photosynthesis is to occur, and involves the

1 allocation of carbohydrates from the leaves to the roots. Leaf photosynthetic capacity is age
2 dependent. As the plant grows, the canopy structure changes, altering the amount and angle
3 of light hitting a leaf. Allocation of carbohydrates and nutrients to new leaves is especially
4 important in stimulating growth production.

5
6 Ozone exposure results in a leaf-mediated plant response. Leaves are important
7 regulators of plant stress response and function. As the major regulators of anatomical and
8 morphological development of the shoot, they control the allocation of carbohydrates to the
9 whole plant. The many regulatory systems contained in leaves change both as a function of
10 leaf development and in response to different environmental stresses.

11
12 Only O₃ that enters the plant through stomata (openings in the leaves) can impair plant
13 processes. In addition, an effect will occur only if sufficient O₃ reaches sensitive sites within
14 leaf cells. Ozone injury will not be detected if (1) the rate of uptake is small enough for the
15 plant to detoxify or metabolize O₃ or its derivatives, or (2) the plant is able to repair or
16 compensate for its impacts at a rate equal to or greater than the rate of uptake. (If the rate
17 of repair is very slow, there may be an effect.)

18
19 The uptake and movement of O₃ to sensitive cellular sites are subject to various
20 biochemical and physiological controls. The magnitude of O₃-induced effects depends upon
21 the physical environment of the plant, including both macro-and microclimatic factors, and
22 the chemical environment of the plant, including other gaseous pollutants and biological
23 factors. Visible foliar injury is usually the first indication of cellular plant response. Once
24 sufficient O₃ enters the leaf, the plant can experience reduced photosynthesis, altered
25 carbohydrate production and allocation, reduced plant vigor, reduced growth or yield or
26 both, and sometimes death. The alterations in the biochemical and physiological processes
27 mentioned above may occur with or without visible injury to the plant.

28
29 Reductions in photosynthesis caused by O₃ are likely to be accompanied by a shift in
30 growth pattern that favors shoots. Plants compensate for differences in resource imbalances
31 by allocating energy, water, and minerals to maintain optimal growth. Allocation of these
32 resources to leaf repair or to new leaf formation and an overall reduction in carbohydrate
33 formation decrease the availability of carbohydrates for both stem and root growth.
34 Alteration of the normal allocation pattern affects all aspects of plant growth and
35 reproduction.

36 37 ***Factors That Modify Plant Response***

38
39 Plant response to O₃ may be modified by a variety of biological, chemical, and physical
40 factors. Both the impact of environmental factors on plant response to O₃ and the effects of
41 O₃ on the responses of plants to environmental factors have to be considered when
42 determining the impact of oxidants on vegetation in the field.

43
44 Biological factors include those both within and external to the plant. Within the plant,
45 its genetic composition and stage of development play critical roles in plant response to O₃ as
46 well as other stresses. Different varieties or cultivars, as well as different individuals of a

species, due to differences in their genetic composition, are known to differ greatly in their responses to a given O₃ exposure.

The magnitude of the response of a particular species or variety depends on such environmental factors as temperature and humidity, soil moisture and nutrition, exposure to other pollutants or agricultural spray chemicals, and interaction with plant pests and pathogens. In other words, the plant's present and past environmental milieu, which includes the temporal exposure pattern and stage of development, dictates the plant response. The corollary is also true: exposure to O₃ can modify plant response to other environmental variables. For example, exposure to O₃ reduces the ability of trees to withstand winter injury caused by freezing temperatures and influences the success of pest and fungal infections by decreasing tree vigor.

Effects Based Air Quality Exposure Indices

Environmental scientists for many years have attempted to characterize and mathematically represent plant exposures to O₃. A variety of averaging times have been used to characterize exposure-response in plants. Though most studies have characterized exposure by using mean concentrations such as seasonal, monthly, weekly, daily, or peak hourly means, other studies have used cumulative measures (e.g., the number of hours above selected concentrations). None of these statistics completely characterizes the relationships among O₃ concentration, exposure duration, interval between exposures, and plant response.

The use of a mean concentration with long averaging times (1) implies that all concentrations of O₃ are equally effective in causing plant responses, and (2) minimizes the contributions of the peak concentrations to the response. Present evidence suggests that higher concentrations, episodic peak occurrences, and duration of exposure have a relatively greater role in producing plant effects than mean concentrations; therefore, an index that cumulates hourly concentrations during the season and gives greater weight to higher concentrations appears to be a more appropriate index for relating ambient exposures to growth or yield effects. From the toxicological perspective, it is the peak occurrences or concentrations above an unidentified effect level that are most likely to have an impact. Effects on vegetation appear when the amount of pollutant that has entered a plant exceeds its ability to repair or compensate for the impact.

An index of ambient exposure that relates well to plant response should directly or indirectly incorporate both environmental influences, (e.g., temperature, humidity, and soil-moisture status) and exposure dynamics.

No experimental studies have been designed specifically to evaluate the adequacy of the various peak-weighted indices that have been proposed. In retrospective analyses when O₃ is the primary source of variation in response, year-to-year variations in plant response are minimized by peak-weighted, cumulative exposure indices. However, a number of different forms of peak-weighted, cumulative indices have been examined for their ability to properly order yield responses from the large number of studies of the National Crop Loss Assessment Network (NCLAN) program. These exposure indices (i.e., SUM00, SUM06, SIGMOID,

1 and W126) all performed equally well, and it is not possible to distinguish between them on
2 the basis of statistical fits of the data.

3 4 *Exposure-Response of Plant Species*

5
6 The number of crop species/cultivars for which information regarding O₃ exposure
7 responses are available encompasses a mere fraction of the total of cultivated crops and even
8 a smaller fraction of native plants. The emphasis of experimental studies has usually been on
9 the more economically important crop plants and tree species, as seedlings.

10
11 Crop species usually are monocultures that are fertilized and in many cases watered.
12 Therefore, because crop plants are usually grown under optimal conditions, their sensitivity
13 to O₃ exposures undoubtedly varies from that of native trees, shrubs, and herbaceous
14 vegetation.

15
16 The concept of limiting values was used in both the 1978 and 1986 criteria documents
17 to summarize visible foliar injury. Limiting values are defined as concentrations and
18 durations of exposure below which visible injury does not occur. The limit for visible injury
19 indicating reduced plant performance was an O₃ exposure of 0.05 ppm for several hours per
20 day for greater than 16 days. When the exposure period was decreased to 10 days, the
21 O₃ concentration required to cause injury was increased to 0.1 ppm. A short, 6-day
22 exposure further increased the concentration to 0.30 ppm. The exposure and concentration
23 periods apply today for those crops where appearance or aesthetic value (e.g., spinach,
24 cabbage, lettuce) is considered important. Limiting values for foliar injury to trees and
25 shrubs range from 0.06 to 0.1 ppm for 4 h.

26
27 Several conclusions were drawn in the 1986 criteria document from the various
28 experimental approaches used to estimate crop yield loss.

- 29
30 1. Ambient O₃ concentrations are sufficiently elevated in several regions of the country to
31 impair growth and yield of plants. This is clearly indicated by comparison of data
32 obtained from crop yield in charcoal-filtered and unfiltered (ambient) exposures. These
33 elevated levels are further supported by data from studies using chemical protectants.
34 These response data make possible extrapolation to plants not studied experimentally.
35 Both approaches mentioned above indicate that effects occur with only a few exposures
36 above 0.08 ppm.
37
38 2. Several plant species exhibited growth and yield effects when the mean O₃ concentration
39 exceeded 0.05 ppm for 4 to 6 h/day for at least 2 weeks.
40
41 3. Data from regression studies conducted to develop an exposure-response function for
42 estimating yield loss indicated that at least 50% of the species/cultivars tested could be
43 predicted to exhibit a 10% yield loss at 7-h seasonal mean O₃ concentrations of 0.05 ppm
44 or less.

45
46 Based on research published since the 1986 criteria document, the following
47 conclusions can be drawn.

1. Monitoring data from 80 to 200 nonurban sites for a period of 10 years were analyzed to determine the ambient 7-h growing-season average O₃ concentrations. For periods of 3 and 5 mo, concentrations ranged from 0.05 to 0.06 ppm and 0.047 to 0.054 ppm, respectively.
2. Open-top chamber studies comparing yields at ambient O₃ exposures with those in filtered air, and retrospective analyses of crop data, indicate that current ambient O₃ concentrations at some sites in the United States are sufficient to reduce the yield of major crops. These results also indicate that visible injury that reduces the market value of certain crops and ornamentals (spinach, petunia, geranium, for example) occurs at O₃ concentrations ranging from 0.04 to 0.10 ppm for 4 h.
3. A growing season SUMO6 exposure of 26.4 ppm · h, corresponding to a 7-h growing season mean of 0.049 ppm, is estimated to prevent a 10% yield loss from O₃ in 50% of the 54 experimental cases analyzed within this document. It is estimated that a 12-h growing season mean of 0.045 ppm would restrict yield losses to 10% in major crop species.

Effects on Natural Ecosystems

Most of the information dealing with the possible responses of ecosystems to O₃ stress is based on the studies in the San Bernardino Forest ecosystem. This mixed conifer forest ecosystem in southern California has been studied more than any other ecosystem in the United States, over 20 years. Chronic O₃ exposures for a period of 50 or more years have been associated with major changes in the ecosystem.

Data from an inventory conducted from 1968 through 1972 indicated that for 5 mo of the year, trees were exposed to O₃ concentrations greater than 0.08 ppm for more than 1,300 h. Concentrations rarely decreased below 0.05 ppm at night near the crest of the mountain slope, approximately 5,500 ft. In addition, during the years 1973 to 1978, average 24-h O₃ concentrations ranged from a background of 0.03 to 0.04 ppm in the eastern part of the San Bernardino Mountains to a maximum of 0.10 to 0.12 ppm in the western part during May through September. Although PAN and NO₂ were present in these studies, symptoms of PAN injury on forest herb-layer plant species could not be distinguished from those caused by O₃, and NO₂ concentrations were too low to cause injury.

Ecosystem responses to stress are hierachial. They begin with the response of the most sensitive individuals of a population. Stresses, whose primary effects occur at the molecular level (within the leaves), must be propagated progressively up through more integrated levels of organ physiology (e.g., leaf, branch, root) to whole plant physiology, to populations within the stand (community), and then to the landscape level to produce ecosystem effects.

Therefore, to understand the effects of a stress, one must utilize a framework of hierarchical scales. This is particularly true of low-level stresses because only a small fraction of stresses at the molecular level become disturbances at the tree, stand, or landscape

1 level. Insect defoliation, for example, may severely reduce the growth of one or several
2 branches, whereas growth of the tree appears not to be affected. The time required for a
3 stress to be propagated from one level to the next determines how soon the effects of the
4 stress can be observed or measured.

5
6 Foliar injury is usually the first visible indication of O₃ exposure in plants. In the San
7 Bernardino forest, injury was first observed on ponderosa pine, with Jeffrey pine, white fir,
8 black oak, incense cedar, and sugar pine following in decreasing order of sensitivity. Foliar
9 injury on sensitive ponderosa and Jeffrey pine was observed when 24-h-average
10 O₃ concentrations were 0.05 to 0.06 ppm.

11
12 The biochemical changes within the leaves were expressed as (1) visible foliar injury;
13 (2) premature needle senescence; (3) a reduction in photosynthesis; (4) a reduction in
14 carbohydrate production; (5) altered carbohydrate allocation, reduced plant vigor; and (6) a
15 reduction in growth and reproduction.

16
17 Tree growth is the culmination of biochemical and physiological processes, during
18 which plants use, accumulate, and store carbon compounds (energy) to build and maintain
19 their structure. Within the leaves during the process of photosynthesis, carbon dioxide
20 absorbed from the atmosphere is converted to carbohydrates. The water and minerals
21 necessary for growth are absorbed from the soil through the roots. Growth and seed
22 formation depend not only on photosynthesis and the uptake of water and mineral nutrients,
23 but also on subsequent metabolic processes and the allocation of carbohydrates to the rest of
24 the plant. Impairment of any of these processes can decrease plant vigor and affect plant
25 growth and reproduction.

26
27 Trees each year require energy to grow new leaves and needles, to produce new fine
28 roots, and to increase radial growth. Factors that inhibit photosynthesis and limit
29 carbohydrate formation shift carbohydrate allocation to new leaves, whereas factors that limit
30 nitrogen or water availability will shift allocation to the roots. Increased carbohydrate
31 allocation to new needles and to repair foliage injured by O₃ can place a drain on
32 carbohydrate reserves. Reduced tree vigor, the result of altered carbohydrate allocation,
33 increases susceptibility of trees to insect pests and fungal pathogens and reduces the
34 formation of mycorrhizae required for water and nutrient uptake.

35
36 Premature needle senescence, as observed in ponderosa and Jeffrey pine, not only
37 decreases the amount of foliage available to carry on photosynthesis, but alters
38 microorganismal succession on conifer needles, thus altering the detritus-forming process and
39 subsequent nutrient cycling.

40
41 The primary effect on the more susceptible members of the San Bernardino forest
42 community (e.g., ponderosa and Jeffrey pine) was that they were no longer able to compete
43 effectively for essential nutrients, water, light, and space. As a consequence of altered
44 competitive conditions in the community, there was a decline in the sensitive species,
45 permitting the enhanced growth of more tolerant species. In addition, changes in the
46 dominant individuals in the ecosystem altered the processes of energy flow and nutrient
47 cycling. These changes that began with the biochemical changes within the leaves of the

1 sensitive conifers were ultimately transferred upward to the whole ecosystem, from the
2 individual, to the population, to the community, and finally, to the ecosystem.

3
4 Functional ecosystem changes associated with the deaths in the conifer populations
5 altered the processes of carbohydrate (energy) flow, mineral nutrient cycling, and water
6 movement. The altered processes also changed, either directly or indirectly, the functioning
7 of other living ecosystem components and ultimately changed the vegetational community
8 patterns. The continuum of changes beginning with injury to the individual trees resulted in
9 ecosystem breakdown and a shift in dominance from ponderosa and Jeffrey pine to
10 O₃-tolerant shrub and oak species.

11
12 The effects that a stress at one level of organization will have on a higher level are
13 determined by variability and compensation. Variability in response to stress can mean that
14 not all trees are equally susceptible to O₃, as was observed, in the San Bernardino Forest, in
15 the Appalachian Mountains, and the Cumberland Plateau of eastern Tennessee. Individuals
16 of Ponderosa, Jeffrey, and eastern white pine were designated as being sensitive,
17 intermediate or tolerant, based on their responses to O₃ exposure. Compensation means that
18 plants tolerant to the stress are able either to detoxify or metabolize O₃ entering the leaves or
19 to repair the injury.

20
21 Variability and compensation can also occur at the population level and, all populations
22 do not respond equally. Plant populations can respond in four different ways: (1) no
23 response, the individuals are tolerant to the stress; (2) mortality of all individuals and local
24 extinction of the extremely sensitive population, the most severe response; (3) physiological
25 accommodation, resulting in growth and reproductive success of tolerant individuals; and
26 (4) differential response, some individuals of the population exhibit better growth and
27 reproductive success due to genetically determined traits.

28
29 The properties of variability and compensation at the individual level determine (1) the
30 severity of the response, (2) whether the effect will be propagated to the next level, and
31 (3) the length of time required for the effect to be expressed functionally and structurally. In
32 most instances, the time required for response at the individual level is a period of at least
33 3 to 5 years. Variability and compensation at the population level determine whether there
34 will be an ecosystem response. These properties help to explain the differences in responses
35 between the San Bernardino Forest and the forest ecosystems in the eastern United States.

36
37 Forest stands differ greatly in age, species composition, stability, and capacity to
38 recover from disturbance. In addition, the position in the stand or community of the most
39 sensitive species is extremely important. Ponderosa and Jeffrey pine are controller species.
40 Their removal altered energy flow, nutrient cycling, and water movement in the San
41 Bernardino forest ecosystem and changed the ecosystem. The removal of the eastern white
42 pine, on the other hand, did not alter the functional ecosystem processes sufficiently to bring
43 about a recognizable change within the ecosystems. For this reason, data dealing with the
44 responses of one forest type (e.g., San Bernardino) may not be applicable to other forest
45 types such as those found in the Appalachian Mountains.

1 Individual eastern white pine trees varied in sensitivity to O₃, and, because of
2 physiological accommodation and compensation, effects at the population level were not
3 reported in the forest stands in the Appalachian Mountains. Plantation plantings of eastern
4 white pine (a monoculture) on the Cumberland Plateau, however, did exhibit overall growth
5 reductions.

6
7 Mycorrhizae (fungus roots) function in the uptake of water and minerals (e.g., nitrogen,
8 phosphorus) and are required for optimal growth by most plants. Nitrogen is a critical
9 element in the process of photosynthesis and is usually the element in shortest supply in both
10 agricultural and natural ecosystems. Increased carbohydrate allocation to new needles and to
11 foliage repair limits allocation to the roots and reduces formation of the mycorrhizae needed
12 to take up water, nitrogen, and other nutrients. Mycorrhizae can also protect plants from
13 attack by root pathogens.

14 15 Effects on Materials

16
17 Over four decades of research show that O₃ damages certain materials such as
18 elastomers, textile fibers, and dyes. The amount of damage to actual in-use materials and
19 the economic consequences of that damage are poorly characterized.

20
21 Natural rubber and synthetic polymers of butadiene, isoprene, and styrene, used in
22 products like automobile tires and protective outdoor electrical coverings, account for most
23 of the elastomer production in the United States. The action of O₃ on these compounds is
24 well known, and concentration-response relationships have been established and corroborated
25 by several studies. These relationships, however, must be correlated with adequate exposure
26 information based on product use. For these and other economically important materials,
27 protective measures have been formulated to reduce the rate of oxidative damage. When
28 antioxidants and other protective measures are incorporated in elastomer production, the
29 O₃-induced damage is reduced considerably, although the extent of reduction differs widely
30 according to the material and the type and amount of protective measures used.

31
32 Both the type of dye and the material in which it is incorporated are important factors
33 in the resistance of a fabric to O₃. Some dyed fabrics, such as royal blue rayon-acetate, red
34 rayon-acetate, and plum cotton, are resistant to O₃. On the other hand, anthraquinone dyes
35 on nylon fibers are sensitive to fading from O₃. Field studies and laboratory work show a
36 positive association between O₃ levels and dye fading of nylon materials. At present, the
37 available research is insufficient to quantify the amount of damaged materials attributable to
38 O₃ alone.

39
40 The degradation of fibers from exposure to O₃ is poorly characterized. In general,
41 most synthetic fibers like modacrylic and polyester are relatively resistant, whereas cotton,
42 nylon, and acrylic fibers have greater but varying sensitivities to O₃. Ozone reduces the
43 breaking strength of these fibers, and the degree of reduction depends on the amount of
44 moisture present. The limited research in this area indicates that O₃ in ambient air may have
45 a minimal effect on textile fibers, but additional research is needed to verify this conclusion.

1 A number of artists' pigments and dyes are sensitive to O₃ and other oxidants. Many
2 organic pigments in particular are subject to fading or other color changes when exposed to
3 O₃. Although most, but not all, modern fine arts paints are more O₃ resistant, many older
4 works of art are at risk of permanent damage due to O₃-induced fading.
5

6 A great deal of work remains to be done to develop quantitative estimates of the
7 economic damage to materials from photochemical oxidants. Most of the available studies
8 are now outdated in terms of the O₃ concentrations, technologies, and supply-demand
9 relationships that prevailed when the studies were conducted. Additionally, little is known
10 about the physical damage functions, so cost estimates have been simplified to the point of
11 not properly recognizing many of the scientific complexities of the impact of O₃.
12
13

14 1.6 TOXICOLOGICAL EFFECTS OF OZONE

15 Respiratory Tract Effects of Ozone

16 *Biochemical Targets of Ozone Interaction*

17
18 Knowledge of molecular targets provides a basis for understanding mechanisms of
19 effects and strengthening animal-to-human extrapolations. Ozone reacts with polyunsaturated
20 fatty acids and sulfhydryl, amino, and some electron-rich compounds. These elements are
21 shared across species. Several types of reactions are involved, and free radicals may be
22 created. Based on this knowledge, it has been hypothesized that the O₃ molecule is unlikely
23 to penetrate the liquid linings of the respiratory tract to reach the tissue, raising the
24 possibility that reaction products exert effects.
25
26

27 *Lung Inflammation and Permeability Changes*

28
29 Ozone disrupts the barrier function of the lung, resulting in (1) the entry of compounds
30 in the airspaces into the blood and (2) the entry of serum components (e.g., protein) and
31 white blood cells (especially polymorphonuclear leukocytes) into the airspaces and lung
32 tissue. This latter impact reflects the initial stage of inflammation. These cells can release
33 biologically active mediators that are capable of a number of actions, including damage to
34 other cells in the lung. In lung tissue, this inflammation can also increase the thickness of
35 the air-blood barrier.
36
37

38 Increases in permeability and inflammation have been observed at levels as low as
39 0.1 ppm (2 h/day, 6 days; rabbits). After acute exposures, the influence of the time of
40 exposure (from 2 h to several hours) increases as the concentration of O₃ increases.
41 Long-term exposure effects are discussed under lung morphology.
42

43 The impacts of these changes are not fully understood. At higher O₃ concentrations
44 (e.g., 0.7 ppm, 28 days), the diffusion of oxygen into the blood decreases, possibly because
45 the air-blood barrier is thicker; cellular death may result from the enzymes released by the
46 inflammatory cells; and host defense functions may be altered by mediators.

Effects on Host Defense Mechanisms

Ozone exposure results in alterations of all defense mechanisms of the respiratory tract, including mucociliary and alveolobronchiolar clearance, functional and biochemical activity of the alveolar macrophage, and immunologic competence. These effects can cause susceptibility to bacterial respiratory infections.

Mucociliary clearance, which removes particles and cellular debris from the conducting airways, is slowed by acute, but not repeated exposures to O₃. Ciliated epithelial cells that move the mucous blanket are altered or destroyed by acute and chronic exposures. Neonatal sheep exposed to O₃ do not have normal development of the mucociliary system. Such effects could prolong the retention of unwanted substances (e.g., inhaled particles) in the lungs, allowing them to exert their toxic potential for a longer period of time.

Alveolar clearance mechanisms, which center on the functioning of alveolar macrophages, are altered by O₃. Short-term exposure to levels as low as 0.1 ppm (2 h/day, 1 to 4 days; rabbits) accelerates clearance, but longer exposures do not. Even so, after a 6-week exposure of rats to an urban pattern of O₃, the retention of asbestos fibers in a region protected by alveolar clearance is prolonged.

Alveolar macrophages engulf and kill microbes, as well as clear the deeper regions of the lungs of nonviable particles. They also participate in immunological responses, but little is known about the effects of O₃ on this function. Acute exposures of rabbits to levels as low as 0.1 ppm decrease the ability of alveolar macrophages to ingest particles. This effect is displayed in decreases in the ability of the lung to kill bacteria after acute exposure of mice to levels as low as 0.4 ppm.

Both the pulmonary and systemic immune system are affected by O₃, but in a poorly understood way. It appears that the part of the immune system dependent on T-cell function is more affected than that part dependent on B-cell function.

Dysfunction of host defense systems results in enhanced susceptibility to bacterial lung infections. For example, exposure as low as 0.08 ppm for 3 h can overcome the ability of mice to resist infection with streptococcal bacteria, resulting in mortality. However, prolonged exposures (weeks, months) do not cause greater effects on infectivity.

Effects on antiviral defenses are more complex and less well understood. Only high concentrations (1.0 ppm, 3 h/day, 5 days; mice) increase viral-induced mortality. Apparently, O₃ does not impact antiviral clearance mechanisms. Although O₃ does not affect acute lung injury from influenza virus infection, it does enhance later phases of the course of an infection (i.e., postinfluenzal alveolitis).

Morphological Effects

Ozone causes similar types of alterations in lung structure in all laboratory animal species studied, from rats to monkeys. In the lungs, the most affected cells are the ciliated

1 epithelial cells of the airways and Type 1 epithelial cells of the gas exchange region. In the
2 nasal cavity, ciliated cells are also affected.

3
4 The centriacinar region (the junction of the conducting airways and gas exchange
5 regions) is the primary target, possibly because this area is predicted to receive the greatest
6 dose of O₃. The ciliated cells can be killed and are replaced by nonciliated cells (i.e., cells
7 not capable of clearance functions that also have increased ability to metabolize some foreign
8 compounds). Mucous-secreting cells are affected, but to a lesser degree. Type 1 cells,
9 across which gas exchange occurs, can be killed. They are replaced by Type 2 cells, which
10 are thicker and produce more lipids. An inflammatory response also occurs in the tissue.
11 The tissue is thickened further in later stages when collagen (a structural protein increased in
12 fibrosis) and other elements accumulate.

13
14 The distal airway is remodeled. More specifically, bronchiolar epithelium replaces the
15 cells present in alveolar ducts. Concurrent inflammation may play a role. This effect has
16 been observed at 0.25 ppm (8 h/day, 18 mo) in monkeys; at a higher concentration, this
17 remodeling persists after exposure stops.

18
19 The progression of effects during and after a chronic exposure is complex. Over the
20 first few days of exposure, inflammation peaks and then drops considerably, plateauing for
21 the remainder of exposure, after which it largely disappears. Epithelial hyperplasia increases
22 rapidly over the first few days and rises slowly or plateaus thereafter; when exposure ends, it
23 begins to return toward normal. In contrast, fibrotic changes in the tissue between the air
24 and blood increase very slowly over months of exposure, and after exposure ceases, the
25 change sometimes persists or increases further.

26
27 The pattern of exposure can make a major difference in effects. Monkeys exposed to
28 0.25 ppm O₃ (8 h/day) every other month of an 18-mo period had equivalent changes in lung
29 structure, more fibrotic changes, and more of certain types of pulmonary function changes
30 than monkeys exposed every day over the 18 mo. From this work and rat studies, it appears
31 that natural seasonal patterns may be of more concern than more continuous exposures.
32 Thus, long-term animal studies with uninterrupted exposures may underestimate some of the
33 effects of O₃.

34
35 There is no evidence that O₃ causes emphysema.

36 37 *Effects on Pulmonary Function*

38
39 Pulmonary function changes in animals resemble those observed in humans after acute
40 exposure.

41
42 During acute exposure, the most commonly observed alteration is an increased
43 frequency of breathing and decreased tidal volume (i.e., rapid, shallow breathing). This has
44 been reported at exposures as low as 0.2 ppm for 3 h (rats). Typically, higher
45 concentrations (around 1 ppm) are required to affect breathing mechanics (compliance and
46 resistance). Extended characterizations of pulmonary function show types of changes

generally seen in humans. For example, there are decreased lung volumes at levels ≥ 0.5 ppm (a few hours; rats).

When rats are exposed to O_3 for 2 h/day for 5 days, the pattern of attenuation of pulmonary function responses is similar to that observed in humans. Other biochemical indicators of lung injury did not return to control values by Day 5, and morphological changes increased in severity over the period of exposure. Thus, attenuation did not result in protection against all the effects of O_3 .

Long-term exposures have provided mixed results on pulmonary function, including no or minimal effects, restrictive effects, or obstructive effects. When changes occurred and postexposure examinations were performed, pulmonary function recovered.

Biochemical Effects

In acute and short-term exposure studies, a variety of lung lipid changes occur, including an increase in arachidonic acid, the further metabolism of which produces a variety of biologically active mediators that can affect host defenses, lung function, the immune system, and other functions.

The level of lung antioxidant metabolism increases after O_3 exposure, probably as a result of the increase in the number of cells (Type 2 cells) rich in antioxidant enzymes.

Collagen (the structural protein involved in fibrosis) increases in O_3 -exposed lungs in a manner that has been correlated to structural changes (e.g., increased thickness of the tissue between the air and blood after prolonged exposure). Some, but not all, studies found that the increased collagen persists after exposure ceases.

Generally, O_3 enhances lung xenobiotic metabolism after both short- and long-term exposure, possibly as a result of morphological changes (increased numbers of nonciliated bronchiolar epithelial cells). The impact of this change is dependent on the xenobiotics involved. For example, the metabolism of benzo[a]pyrene to active metabolites was enhanced by O_3 .

Genotoxicity and Carcinogenicity of Ozone

The chemical reactivity of O_3 give it the potential to be a genotoxic agent.

In vitro studies are difficult to interpret because the culture systems used allowed the potential formation of artifacts, and often high or very high concentrations of O_3 were used. Generally, in these studies, O_3 causes DNA strand breaks, sometimes is weakly mutagenic, and causes cellular transformation and chromosomal breakage. The latter finding has been investigated in vivo with mixed results in animals. A well-designed human clinical study found no such effect.

The few earlier long-term carcinogenic studies, with or without coexposure to known carcinogens, are either negative or ambiguous.

1 The National Toxicology Program (NTP) completed chronic rat and mouse cancer
2 bioassays using commonly accepted experimental approaches and designs. Both males and
3 females were studied. Animals were exposed for 2 years (6 h/day, 5 days/week) to 0.12,
4 0.5, and 1.0 ppm O₃ or for a lifetime to the same levels (except 0.12 ppm). Following their
5 standard procedures for determination of weight-of-evidence for carcinogenicity, the NTP
6 reported "no evidence" in rats, "equivocal evidence" in male mice, and "some evidence" in
7 female mice. The increases in adenomas and carcinomas were observed only in the lungs.
8 There was no concentration response. One of the reasons for the designation of "some
9 evidence" in female mice was that when the 2-year and lifetime exposure studies were
10 combined, there was a statistically significant increase in total tumors at 1.0 ppm. It is not
11 justified to extrapolate these mouse data to humans at the present time because rats were not
12 affected, only a high level of O₃ (1.0 ppm) caused a limited degree of carcinogenic activity
13 in one strain of mice, there was no concentration response, and there is inadequate
14 information to provide a mechanistic support for the finding in mice.

15
16 In a companion NTP study, male rats were treated with a tobacco carcinogen and
17 exposed for 2 years to 0.5 ppm O₃. Ozone did not affect the response and therefore had no
18 tumor promoting activity.

19 20 Systemic Effects of Ozone

21
22 Ozone causes a variety of effects on tissues/organs distant from the lung. Because
23 O₃ itself is not thought to penetrate the lung, these systemic effects are either secondary to
24 lung alterations or result from reaction products of O₃. Effects have been observed on
25 clinical chemistry, white blood cells, red blood cells, the circulatory system, the liver,
26 endocrine organ(s), and the central nervous system. Most of these effects cannot be
27 adequately interpreted at this time and have not been investigated in humans, but it is of
28 interest to note that O₃ exposures causing effects on the respiratory tract of animals cause a
29 wide array of effects on other organs also.

30
31 Several behavior changes occur in response to O₃. For example, 0.12 ppm (6 h, rats)
32 decreases wheel-running activity, and 0.5 ppm (1 min) causes mice to avoid exposure.
33 These effects are not fully understood, but they may be related to lung irritation or decreased
34 ability to exercise.

35
36 Although cardiovascular effects, such as slowed heart rate and decreased blood
37 pressure, occur in O₃-exposed rats, some observed interactions with thermoregulation prevent
38 qualitative extrapolation of these effects to humans at this time.

39
40 Developmental toxicity studies in pregnant rats summarized in the 1986 O₃ criteria
41 document showed that levels up to about 2.0 ppm did not cause birth defects. Rat pups from
42 females exposed to 1.0 ppm O₃ during certain periods of gestation weighed less or had
43 delays in development of behaviors (e.g., righting, eye opening). No "classical"
44 reproductive assays with O₃ were found.

1 Other studies have indicated that O₃ can affect some endocrine organs (i.e., pituitary-
2 thyroid-adrenal axis and parathyroid gland). It appears that the liver has less ability to
3 detoxify drugs after O₃ exposure, but assays of liver enzymes involved in xenobiotic
4 metabolism are not consistent with each other.

5 6 **Interactions of Ozone with Other Co-occurring Pollutants**

7
8 Animals studies of the effects of O₃ in combination with other air pollutants show that
9 antagonism, additivity, and synergism can result, depending upon the animal species,
10 exposure regimen, and health endpoint. Thus, they clearly demonstrate the major
11 complexities and potential importance of interactions, but do not provide a scientific basis for
12 predicting the results of interactions under untested ambient exposure scenarios.

13 14 15 **1.7 HUMAN HEALTH EFFECTS OF OZONE AND RELATED** 16 **PHOTOCHEMICAL OXIDANTS**

17
18 This section summarizes key health effects associated with exposure to O₃, the major
19 component of photochemical oxidant air pollution that is clearly of most health concern to the
20 human population. Another, often co-occurring photochemical oxidant component of "smog"
21 is PAN, but this compound has been demonstrated to be primarily responsible for induction
22 of smog-related eye irritation (stinging of eyes). Limited pulmonary function studies have
23 shown no effects of PAN at concentrations below 0.13 to 0.30 ppm, which are much higher
24 than the generally encountered ambient air levels in most cities.

25 26 **Controlled Human Studies of Acute Ozone Effects**

27 28 *Effects on Lung Function*

29
30 Controlled studies in healthy adult subjects have demonstrated O₃-induced decrements
31 in pulmonary function, characterized by alterations in lung volumes and flow, airway
32 resistance, and airway responsiveness. Respiratory symptoms, such as cough and pain on
33 deep inspiration, are associated with these changes in lung function.

34
35 Ozone-induced decreases in lung volume, specifically forced vital capacity (FVC) and
36 forced expiratory volume in 1 s (FEV₁), can be largely attributed to decreases in inspiratory
37 capacity, or the ability to take a deep breath; although at higher exposure concentrations,
38 there is clearly an additional component that is not volume dependent. They recover to a
39 large extent within 2 to 6 h; normal baseline function is typically reestablished within 24 h,
40 but not fully with more severe exposures.

41
42 Ozone causes increased airway resistance and may cause reductions in expiratory flow
43 and the FEV₁/FVC ratio.
44

Ozone causes an increase in airway responsiveness to nonallergenic stimuli (e.g., histamine or methacholine) in healthy and asthmatic subjects. There is no clear evidence of a relationship between O₃-induced lung volume changes and changes in airway responsiveness.

Inflammation and Host Defense Effects

Controlled studies in healthy adult subjects also indicate that O₃ causes an inflammatory response in the lungs characterized by elevated levels of neutrophils (a type of white blood cell), increased epithelial permeability, and elevated levels of biologically active substances (e.g., prostaglandins, proinflammatory mediators, and cytokines).

Inflammatory responses to O₃ can be detected within 1 h after a single 1-h exposure with exercise to concentrations ≥ 0.30 ppm; the increased levels of some inflammatory cells and mediators persist for at least 18 h. The temporal response profile is not adequately defined, although it is clear that the time course of response varies for different mediators and cells.

Lung function and respiratory symptom responses to O₃ do not seem to be correlated with airway inflammation.

Ozone also causes inflammatory responses in the nose, marked by increased numbers of neutrophils (neutrophilia) and protein levels suggestive of increased permeability.

Alveolar macrophages removed from the lungs of human subjects after 6.6 h exposure to 0.08 and 0.10 ppm O₃ have a decreased ability to ingest microorganisms, indicating some impairment of host defense capability.

Ozone Exposure-Response Relationships

Functional, symptomatic, and inflammatory responses to O₃ increase with increasing exposure dose of O₃. The major determinants of the exposure dose are O₃ concentration (C), exposure duration (T), and the amount of ventilation ($\dot{V}_E$). Of these factors, C has more influence on the response than T or $\dot{V}_E$.

Exercise increases response to O₃ by increasing $\dot{V}_E$ (greater mass delivered), tidal volume, inspiratory flow (greater percentage delivery), and the intrapulmonary O₃ concentration.

Repeated daily exposures to relatively high levels of O₃ doses ($C \times T \times \dot{V}_E$) causing substantial reductions in FEV₁ ($\geq 20\%$ decrement) typically cause exacerbation of the lung function and respiratory symptom responses on the second exposure day. However, attenuation of these responses occurs with continued exposures for a few days. Most inflammatory responses also attenuate; for example, neutrophilia is absent after five consecutive exposures.

Multihour exposures (e.g., for up to 7 h) to O₃ concentrations as low as 0.08 ppm cause small but significant (1) decrements in lung function, (2) increases in respiratory

1 symptoms, and (3) increases in neutrophils and protein levels. Ozone C is a more important
2 factor than exercise $\dot{V}_E$ or T in predicting responses to multihour low-level O₃ exposure.
3 There is now clear evidence of a response plateau in terms of lung volume response to
4 prolonged O₃ exposure. This evidence suggests that for a given combination of exercise and
5 O₃ concentration (i.e., dose rate), there is a response plateau; continued exposure (i.e.,
6 increased T) at that dose rate will not increase response. Therefore, quantitative
7 extrapolation of responses to longer exposure durations is not valid.

8 9 *Mechanisms of Acute Pulmonary Responses*

10
11 The mechanisms leading to the observed pulmonary responses induced by O₃ are
12 beginning to be better understood. The available descriptive data suggest a number of
13 mechanisms leading to the alterations in lung function and respiratory symptoms, including
14 (1) O₃ delivery to the tissue (i.e., the inhaled concentration, breathing pattern, and airway
15 geometry; (2) O₃ reactions with the airway lining fluid and/or epithelial cell membranes;
16 (3) local tissue responses, including injury and inflammation; and (4) stimulation of neural
17 afferents (bronchial C fibers) and the resulting reflex responses and symptoms. The
18 cyclooxygenase inhibitors block production of prostaglandin E₂ and interleukin-6 as well as
19 reduce lung volume responses; however, these drugs do not reduce neutrophilic inflammation
20 and levels of cell damage markers such as lactate dehydrogenase.

21 22 *Effects on Exercise Performance*

23
24 Maximal oxygen uptake, a measure of peak exercise performance capacity, is reduced
25 in healthy young adults if preceded by O₃ exposures sufficient to cause marked changes in
26 lung function (i.e., decreases of at least 20%) and increased subjective symptoms of
27 respiratory discomfort. Limitations in exercise performance may be related to increased
28 symptoms, especially those related to breathing discomfort.

29 30 *Factors Modifying Responsiveness to Ozone*

31
32 Many variables have the potential for influencing responsiveness to O₃; most, however,
33 are inadequately addressed in the available clinical data to make definitive conclusions.

34
35 Active smokers are less responsive to O₃ exposure, which may reverse following
36 smoking cessation, but these results should be interpreted with caution.

37
38 The possibility of age-related differences in response to O₃ has been explored, although
39 young adults historically have provided the subject population for controlled human studies.
40 Children and adolescents have similar lung volume responses to O₃ as young adults, but lack
41 respiratory symptoms at levels to which they have been exposed. Pulmonary function
42 responsiveness in adults appears to decrease with age, whereas symptom rates remain similar
43 to young adults. Group mean lung function responses of adults over 50 years of age are less
44 than those of children, adolescents, and young adults.

45
46 The available data have not conclusively demonstrated that men and women respond
47 differently to O₃. Likewise, pulmonary function responses of women have been compared

1 during different phases of the menstrual cycle, but the results are conflicting. If gender
2 differences exist for lung function responsiveness to O₃, they are not based on hormonal
3 changes, differences in lung volume, or the ratio of FVC to $\dot{V}_E$.

4
5 There is no compelling evidence, to date, suggesting that any ethnic or racial groups
6 have a different distribution of responsiveness to O₃.

7
8 Seasonal and ambient factors may vary responsiveness to O₃, but further research is
9 needed to determine how they affect individual subjects. Individual sensitivity to O₃ may
10 vary throughout the year, related to seasonal variations in ambient O₃ concentrations.

11
12 The specific inhalation route appears to be of minor importance in exercising adults.
13 Exposure to O₃ by oral breathing (i.e., mouthpiece) yields similar results as oronasal
14 breathing (i.e., chamber exposures).

15 16 *Population Groups at Risk from Ozone Exposure*

17
18 Population groups that have demonstrated responsiveness to ambient concentrations of
19 O₃ consist of exercising healthy and asthmatic individuals, including children, adolescents,
20 and adults.

21
22 Available evidence from controlled human studies on subjects with preexisting disease
23 suggests that (1) mild asthmatics have similar lung volume responses, but greater airway
24 resistance responses to O₃ than nonasthmatics; and (2) moderate asthmatics may have, in
25 addition, greater lung volume responses than nonasthmatics.

26
27 Of all the other population groups studied, those with preexisting limitations in
28 pulmonary function and exercise capacity (e.g., chronic obstructive pulmonary disease,
29 chronic bronchitis, ischemic heart disease) would be of primary concern in evaluating the
30 health effects of O₃. Unfortunately, limitations of (1) subject selection, (2) standardized
31 methods of subject characterization, and (3) range of exposure hamper the ability to make
32 definitive conclusions regarding the relative responsiveness of most chronic disease subjects.

33 34 *Effects of Ozone Mixed with Other Pollutants*

35
36 No significant enhancement of respiratory effects has been consistently demonstrated
37 for simultaneous exposures of O₃ mixed with SO₂, NO₂, sulfuric or nitric acid, particulate
38 aerosols, or with multiple combinations of these pollutants. It is fairly well established that
39 simultaneous exposure of healthy adults and asthmatics to mixtures of O₃ and other pollutants
40 for short periods of time (<2 h) induces pulmonary function responses not significantly
41 different from those following O₃ alone when studies are conducted at the same
42 O₃ concentration. Exposure to PAN has been reported to induce greater pulmonary function
43 responses than exposure to O₃ alone, but at PAN concentrations (>0.27 ppm) much higher
44 than ambient levels. Unfortunately, only a limited number of pollutant combinations and
45 exposure protocols have been investigated, and subject groups are small and are
46 representative of only small portions of the general population. Thus, much is unknown
47 about the relationships between O₃ and the complex mix of pollutants found in the ambient air.

1 Prior exposure to O₃ in asthmatics may cause an increase in response to other pollutant
2 gases, especially SO₂. Likewise, prior exposure to other pollutants can enhance responses to
3 O₃ exposure.
4

5 **Controlled Human Studies of Ambient Air Exposures**

6

7 Mobile laboratory studies of lung function and respiratory symptoms in a local subject
8 population exposed to ambient photochemical oxidant pollution provide quantitative
9 information on exposure-response relationships for O₃. A series of these studies from
10 Los Angeles, CA, have demonstrated pulmonary function decrements at O₃ concentrations of
11 0.14 ppm in exercising healthy adolescents, and increased respiratory symptoms and
12 pulmonary function decrements at 0.15 ppm in heavily exercising athletes and at 0.17 ppm in
13 lightly exercising healthy and asthmatic subjects. Comparison of the observed effects in
14 exercising athletes with controlled chamber studies at comparable O₃ concentrations showed
15 no significant differences in lung function and symptoms, suggesting that coexisting ambient
16 pollutants have a minimal contribution to the measured responses under typical summer
17 ambient conditions in Southern California.
18

19 **Field and Epidemiology Studies of Ambient Air Exposures**

20

21 Individual-level field studies and aggregate level time-series studies have addressed the
22 acute effects of O₃ on lung function decrements and increased morbidity and mortality in
23 human populations exposed to real-world conditions of O₃ exposure.
24

25 Camp and exercise studies of lung function provide quantitative information on
26 exposure-response relationships linking lung function declines with O₃ exposure occurring in
27 ambient air. Combined statistical analysis of six recent camp studies in children yields an
28 average relationship between decrements in FEV₁ and previous-hour O₃ concentration of
29 -0.64 mL/ppb. Two key studies of lung function measurements before and after well-
30 defined outdoor exercise events in adults have yielded exposure-response slopes of
31 -0.40 and -1.35 mL/ppb. The magnitude of pulmonary function declines with
32 O₃ exposure is consistent with the results of controlled human studies.
33

34 Daily life studies support a consistent relationship between O₃ exposure and acute
35 respiratory morbidity in the population. Respiratory symptoms (or exacerbation of asthma)
36 and decrements in peak expiratory flow rate are associated with increasing ambient O₃,
37 particularly in asthmatic children; however, concurrent temperature, particles, acidity
38 (hydrogen ions), aeroallergens, and asthma severity or medication status may also contribute
39 as independent or modifying factors. Aggregate results show greater responses in asthmatic
40 individuals than in nonasthmatics, indicating that asthmatics constitute a sensitive group in
41 epidemiologic studies of oxidant air pollution.
42

43 Summertime daily hospital admissions for respiratory causes in various locations of
44 eastern North America have consistently shown a relationship with ambient levels of O₃,
45 accounting for approximately one to three excess respiratory hospital admissions per hundred
46 ppb O₃ per million persons. This association has been shown to remain even after

1 statistically controlling for the possible confounding effects of temperature and copollutants
2 (e.g., hydrogen ions, sulfate, and particles less than 10 μm), as well as when considering
3 only concentrations below 0.12 ppm O_3 .
4

5 Two recent time-series epidemiologic studies indicate a small but statistically significant
6 association between O_3 and total daily mortality in Los Angeles, CA, and New York City,
7 NY, where peak 1-h maximum O_3 reached concentrations greater than 0.2 ppm during the
8 study period. The results were significant even after controlling for the potentially
9 confounding effects of temperature and particles. A third study in regions with lower
10 (≤ 0.15 ppm) maximum 1-h O_3 concentrations (St. Louis, MO, and Kingston-Harriman, TN)
11 did not detect a significant O_3 association with mortality.
12

13 Only suggestive epidemiologic evidence exists for health effects of chronic ambient
14 O_3 exposure in the population. All of the available studies of chronic respiratory system
15 effects in exposed children and adults are limited by a simplistic assignment of exposure or
16 by their inability to isolate potential effects related to O_3 from those of other pollutants,
17 especially particles.
18
19

20 **1.8 EXTRAPOLATION OF ANIMAL TOXICOLOGICAL DATA TO** 21 **HUMANS** 22

23 There have been significant advances in O_3 dosimetry since 1986 that better enable
24 quantitative extrapolation with marked reductions in uncertainty. Experiments and models
25 describing the uptake efficiency and delivered dose of O_3 in the respiratory tract (RT) of
26 animals and humans are beginning to present a clearer picture than has previously existed.
27

28 The total RT uptake efficiency of rats at rest is approximately 50%. Within the RT of
29 the rat, 50% of the O_3 taken up by the RT is removed in the head, 7% in the larynx/trachea,
30 and 43% in the lungs.
31

32 In humans at rest, the total RT uptake efficiency is between 80 and 95%. Total RT
33 uptake efficiency falls as flow increases. As tidal volume increases, uptake efficiency
34 increases and flow dependence lessens. Pulmonary function response data and O_3 uptake
35 efficiency data in humans generally indicate that the mode of breathing (oral versus nasal
36 versus oronasal) has little effect on upper RT or on total RT uptake efficiency, though one
37 study suggests that the nose has a higher uptake efficiency than the mouth.
38

39 When all of the animal and human in vivo O_3 uptake efficiency data are compared,
40 there is a good degree of consistency across data sets. This agreement raises the level of
41 confidence with which these data sets can be used to support dosimetric model formulations.
42

43 Several mathematical dosimetry models have been developed since 1986. Generally,
44 the models predict that net O_3 dose to lung lining fluid plus tissue gradually decreases
45 distally from the trachea toward the end of the tracheobronchial region, and then rapidly
46 decreases in the pulmonary region.

1 When the dose of O₃ to lung tissue is computed theoretically, it is found to be very low
2 in the trachea, to increase to a maximum in the terminal bronchioles of the first generation
3 pulmonary region, and then to decrease rapidly, moving further into the pulmonary region.
4 The increased tidal volume and flow, associated with exercise in humans, shifts O₃ dose
5 further into the periphery of the lung and causes a disproportionate increase in distal lung
6 dose.

7
8 Predictions of delivered dose have been used to investigate O₃ responses in the context
9 of intra- and interspecies comparisons. In the case of intraspecies comparisons, for example,
10 the distribution of predicted O₃ tissue dose to a ventilatory unit in a rat as a function of
11 distance from the bronchoalveolar duct junction is very consistent with the distribution of
12 alveolar wall thickening. In the case of interspecies comparisons (using the delivered
13 O₃ dose to the proximal alveolar regions), although the tachypneic responses (i.e., rapid,
14 shallow breathing) differ markedly between rats and humans, there is similarity of dose-
15 response patterns in inflammation among species, with humans and guinea pigs more
16 responsive than rats and rabbits. In other words, the quantitative relationship between animal
17 and human responses is dependent on the animal species and the endpoint.

18
19 In summary, there is an emerging consistency among a variety of O₃ dosimetry data
20 sets and between the experimental data and theoretical predictions of O₃ dose. The
21 convergence of experimental data with theoretical predictions lends a degree of confidence to
22 the use of theoretical models to predict total and regional O₃ dose. The use of O₃ dosimetry
23 data and models is beginning to bear fruit in attempts to extrapolate effects between animals
24 and humans. The data and models have thus far helped demonstrate that humans may be
25 more responsive to O₃ than rats with respect to inflammatory responses. Thus, chronic
26 effects data in rats may not accurately reflect the degree to which comparably exposed
27 humans would respond.

28 29 30 **1.9 INTEGRATIVE SUMMARY OF OZONE HEALTH EFFECTS**

31
32 This section summarizes the primary conclusions derived from an integration of the
33 known health effects of O₃ provided by animal toxicological, human clinical, and
34 epidemiological studies.

35 36 **1. *What are the health effects of short-term (< 8 h) exposures to ozone?***

37
38 Acute O₃ exposure of laboratory animals and humans causes changes in pulmonary
39 function, including tachypnea (rapid, shallow breathing), decreased lung volumes and flows,
40 and increased airway responsiveness to nonspecific stimuli. Increased airway resistance
41 occurs in both humans and laboratory animals, but typically at higher exposure levels than
42 other functional endpoints. In addition, adult human subjects experience O₃-induced
43 symptoms of airway irritation such as cough or pain on deep inspiration. The changes in
44 pulmonary function and respiratory symptoms occur as a function of exposure concentration,
45 duration, and level of exercise. Recovery of pulmonary function and the absence of

O₃-induced symptoms is usually complete within 24 h of the end of exposure, although other responses may persist somewhat longer.

- Pulmonary function decrements are generally observed in healthy subjects (8 to 45 years of age) after 1 to 3 h of exposure as a function of the level of exercise performed and the O₃ concentration inhaled during the exposure. Group mean data from numerous controlled human exposure and field studies indicate that, in general, statistically significant pulmonary function decrements beyond the range of normal measurement variability (e.g., 3 to 5% for FEV₁) occur

- (1) at >0.5 ppm when at rest,
- (2) at >0.37 ppm with light exercise (slow walking),
- (3) at >0.30 ppm with moderate exercise (brisk walking),
- (4) at >0.18 ppm with heavy exercise (easy jogging), and
- (5) at >0.16 ppm with very heavy exercise (running).

For a number of studies, small group mean changes (e.g., <5%) in FEV₁, the medical significance of which is a matter of controversy, have been observed at lower O₃ concentrations than those listed above. For example, data from one specific study indicate that FEV₁ decrements occur with very heavy exercise in healthy adults at 0.15 to 0.16 ppm O₃, and data from two studies indicate that such effects may occur in healthy adults at levels as low as 0.12 ppm. Also, pulmonary function decrements have been observed in children and adolescents at concentrations of 0.12 and 0.14 ppm O₃ with heavy exercise. Pulmonary function decrements were observed at 0.12 ppm O₃ in healthy young adults undergoing heavy exercise in a recent study. Some individuals within a study may experience FEV₁ decrements in excess of 15% under these exposure conditions, even when the group mean decrement is less than 5%.

- For exposures of healthy subjects performing moderate exercise during longer duration exposures (6 to 8 h), 5% group mean decrements in FEV₁ were observed at

- (1) 0.08 ppm O₃ after 5.6 h,
- (2) 0.10 ppm O₃ after 4.6 h, and
- (3) 0.12 ppm O₃ after 3 h.

For these same subjects, 10% group mean FEV₁ decrements were observed at 0.12 ppm O₃ after 5.6 and 6.6 h. As in the shorter duration studies, some individuals experience changes larger than those represented by the group mean changes.

- An increase in the incidence of cough has been reported at O₃ concentrations as low as 0.12 ppm in healthy adults during 1 to 3 h of exposure with very heavy exercise. Other respiratory symptoms, such as

1 pain on deep inspiration, shortness of breath, and lower respiratory scores
2 (a combination of several symptoms), have been observed at 0.16 to
3 0.18 ppm O₃ with heavy and very heavy exercise. Respiratory symptoms
4 have also been observed following exposure to 0.08, 0.10, and 0.12 ppm
5 O₃ for 6.6 h with moderate levels of exercise.

- 6
7 • Increases in nonspecific airway responsiveness have been observed after
8 1 to 3 h of exposure to 0.40 ppm, but not 0.20 ppm, O₃ at rest, and have
9 been observed at concentrations as low as 0.18 ppm, but not to 0.12 ppm,
10 O₃ during exposure with very heavy exercise. Increases in nonspecific
11 airway responsiveness during 6.6-h exposures with moderate levels of
12 exercise have been observed at 0.08, 0.10, and 0.12 ppm O₃.

13
14 Acute O₃ exposure of laboratory animals and humans disrupts the barrier function of
15 the lung epithelium, permitting materials in the airspaces to enter lung tissue, allowing cells
16 and serum proteins to enter the airspaces (inflammation), and setting off a cascade of
17 responses.

- 18
19 • Increased levels of neutrophils and protein in lung lavage fluid have been
20 observed following exposure of humans to 0.20, 0.30, and 0.40 ppm with
21 very heavy exercise and have not been studied at lower concentrations for
22 1- to 3-h exposures. Increases in protein and/or neutrophils have also been
23 observed at 0.08 and 0.10 ppm O₃ during 6.6-h exposures with moderate
24 exercise; lower concentrations have not been tested.

25
26 Acute O₃ exposure of laboratory animals and humans impairs alveolar macrophage
27 clearance of viable and nonviable particles from the lungs and decreases the effectiveness of
28 host defenses against bacterial lung infections in animals and perhaps humans. The ability of
29 alveolar macrophages to engulf microorganisms is decreased in humans exposed to 0.08 and
30 0.10 ppm for 6.6 h with moderate exercise.

31 32 *2. What are the health effects of repeated, short-term exposures to ozone?*

33
34 During repeated acute exposures, some of the O₃-induced responses are partially or
35 completely attenuated. Over a 5-day exposure, pulmonary function changes are typically
36 greatest on the second day, but return to control levels by the fifth day of exposure. Most of
37 the inflammatory markers (e.g., neutrophil influx) also attenuate by the fifth day of exposure,
38 but markers of cell damage (e.g., lactate dehydrogenase enzyme activity) do not attenuate
39 and continue to increase. Attenuation of lung function decrements is reversed following 7 to
40 10 days without O₃. Some inflammatory markers are also reversed during this time period,
41 but others still show attenuation even after 20 days without O₃. The mechanisms and
42 impacts involved in attenuation are not known, although the underlying cell damage continues
43 throughout the attenuation process. In addition, attenuation may alter the normal distribution
44 of O₃ within the lung, allowing more O₃ to reach sensitive regions, possibly affecting normal
45 lung defenses (e.g., neutrophil influx in response to inhaled microorganisms).

1 **3. *What are the health effects of long-term exposures to ozone***
2

3 Exposure to O₃ for months and years causes structural changes in several regions of the
4 respiratory tract, but effects may be of the greatest importance in the centriacinar regions
5 where the alveoli and conducting airways meet because this region is typically affected in
6 most chronic diseases of the human lung. This information on O₃ effects in the distal lung is
7 derived from animal toxicological studies because, to date, such data are not available in
8 humans. Epidemiological studies attempting to associate chronic health effects in humans
9 with long-term O₃ exposure have yet to provide unequivocal evidence that such a linkage
10 exists.

11
12 Chronic exposure of one strain of female mice to high O₃ levels (1 ppm) caused a
13 small, but statistically significant increase in lung tumors. There was no concentration-
14 response relationship and rats were not affected. Genotoxicity data are either negative or
15 weak. Given the nature of the database, the effects in one strain of mice cannot yet be
16 qualitatively extrapolated to humans. Ozone did not show tumor-promoting activity in a
17 chronic rat study (at 0.5 ppm O₃).

18
19 **4. *What are the health effects of binary pollutant mixtures containing ozone?***
20

21 Combined data from laboratory animal and controlled human exposure studies on
22 O₃ support the hypothesis that coexposure to pollutants, each at low-effect levels, may result
23 in effects of significance. The data from human studies of O₃ in combination with NO₂,
24 SO₂, sulfuric acid, nitric acid, or CO show no more than an additive response on lung
25 spirometry or respiratory symptoms. The larger number of laboratory animal studies with
26 O₃ in mixture with NO₂ and sulfuric acid show that effects can be additive, synergistic, or
27 even antagonistic, depending upon the exposure regimen and the endpoint studied. This issue
28 of exposure to copollutants remains poorly understood, especially with regard to chronic
29 effects.

30
31 **5. *What population groups are at-risk as a result of exposure to ozone?***
32

33 Identification of population groups that may show increased susceptibility to O₃ are
34 based on their (1) biological responses to O₃; (2) physiological status (e.g., preexisting lung
35 disease); (3) activity patterns; (4) personal exposure history; and (5) personal factors (e.g.,
36 age, nutritional status).

37
38 The predominant information on the health effects of O₃ noted above comes from
39 studies on healthy, nonsmoking, exercising subjects, 8 to 45 years of age. These studies
40 demonstrate that among this group, there is a large variation in sensitivity and responsiveness
41 to O₃, with at least a 10-fold difference between the most and least responsive individuals.
42 Individual sensitivity to O₃ may also vary throughout the year, related to seasonal variations
43 in ambient O₃ exposure. The specific factors that contribute to this large intersubject
44 variability, however, remain undefined. Although differences may be due to the dosimetry
45 of O₃ in the respiratory tract, available data show little effect on O₃ deposition after
46 inhalation through the nose or mouth.

1 Controlled studies on mild asthmatics suggest that they have similar lung volume
2 responses but greater airway resistance changes to O₃ than nonasthmatics. Furthermore,
3 limited data from studies of moderate asthmatics suggest that they may have greater lung
4 volume responses than nonasthmatics. Daily life studies reporting an exacerbation of asthma
5 and decrease in peak expiratory flow rates, particularly in asthmatic children, appear to
6 support the controlled studies; however, those studies are confounded by concurrent
7 temperature, particle or aeroallergen exposure, and asthma severity of the subjects or their
8 medication use. In addition, field studies of summertime daily hospital admissions for
9 respiratory causes show a consistent relationship between asthma and ambient levels of O₃ in
10 various locations in the northeastern United States, even after controlling for independent
11 contributing factors.
12

13 Other population groups with preexisting limitations in pulmonary function and exercise
14 capacity (e.g., chronic obstructive pulmonary disease, chronic bronchitis, ischemic heart
15 disease) would be of primary concern in evaluating the health effects of O₃. Unfortunately,
16 not enough is known about the responses of these individuals to make definitive conclusions
17 regarding their relative responsiveness to O₃. Indeed, functional effects in these individuals
18 with reduced lung function may have greater clinical significance than comparable changes in
19 healthy individuals.
20

21 Currently available data on personal factors or personal exposure history known or
22 suspected of influencing responses to O₃ are the following.
23

- 24 • Human studies have identified a decrease in pulmonary function
25 responsiveness to O₃ with increasing age, although symptom rates remain
26 similar. Toxicological studies are not easily interpreted but suggest that
27 young animals are not more responsive than adults.
28
- 29 • Available toxicological and human data have not conclusively demonstrated
30 that males and females respond differently to O₃. If gender differences
31 exist for lung function responsiveness to O₃, they are not based on
32 differences in baseline pulmonary function.
33
- 34 • There is no compelling evidence to date to suggest that any ethnic or racial
35 group has a different distribution of responsiveness to O₃. However, data
36 are not adequate to rule out the possibility of such differences.
37
- 38 • Information derived from O₃ exposure of smokers is limited. The general
39 trend is that smokers are less responsive than nonsmokers. This reduced
40 responsiveness may wane after smoking cessation.
41
- 42 • Although nutritional status (e.g., vitamin E deficiency) makes laboratory
43 rats more susceptible to O₃-induced effects, it is not clear if vitamin E
44 supplementation has an effect in human populations. Such supplementation
45 has no or minimal effects in animals. The role of such antioxidant vitamins
46 in O₃ responsiveness, especially their deficiency, has not been well studied.
47

1 Based on information presented in this document, the population groups that have
2 demonstrated responsiveness to ambient concentrations of O₃ consist of exercising healthy
3 and asthmatic individuals, including children, adolescents, and adults.

Ozone Exposure and Risk Assessment

Briefing for Interagency Ozone NAAQS
Committee - April 6, 1994

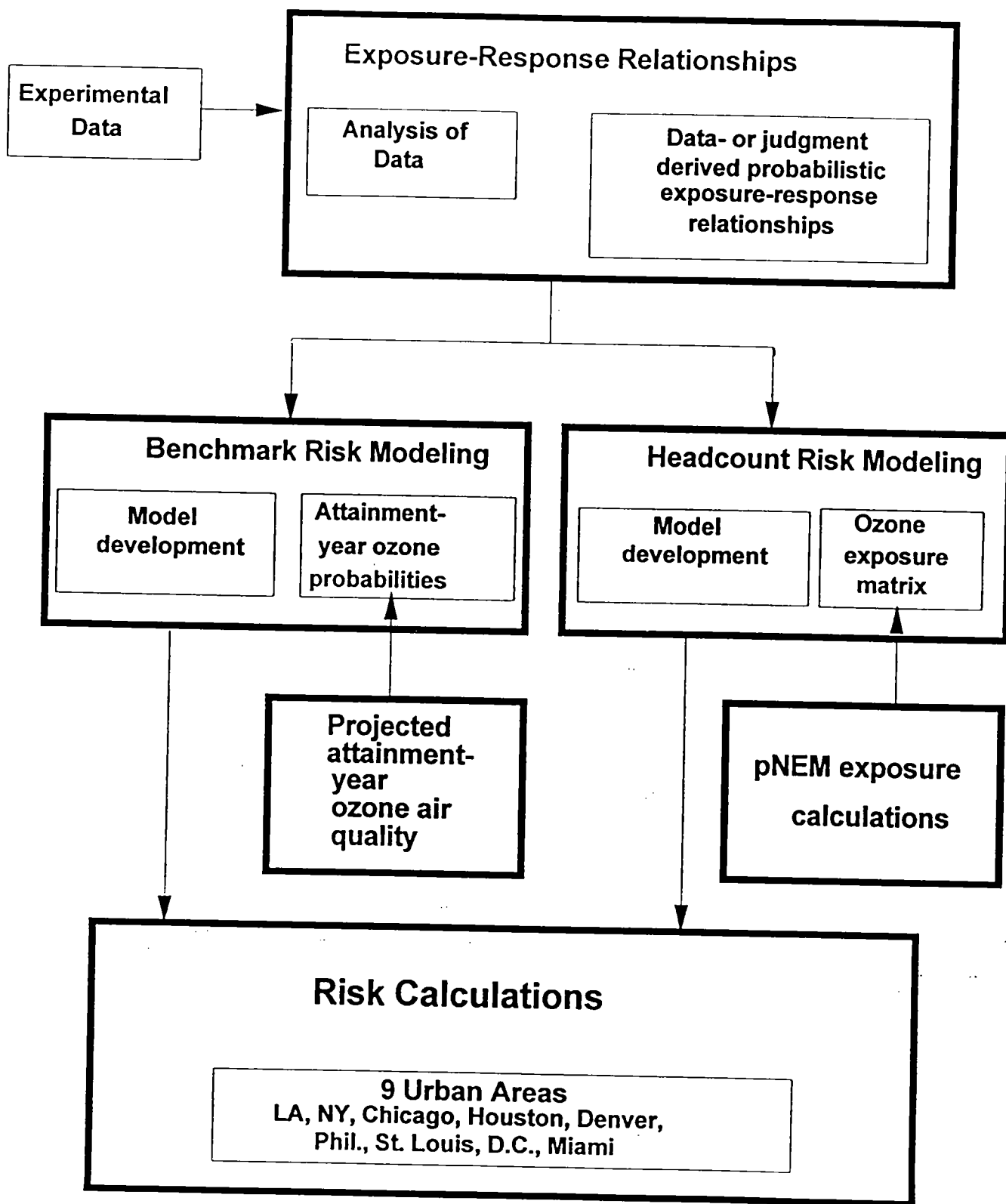


Background

- NAAQS Must Be Set to Protect Most Sensitive Population Group with An Adequate Margin of Safety
- EPA Develops Exposure & Risk Estimates as Additional Tools to Aid Judgment on Which Standard(s) Provide an Adequate Margin of Safety

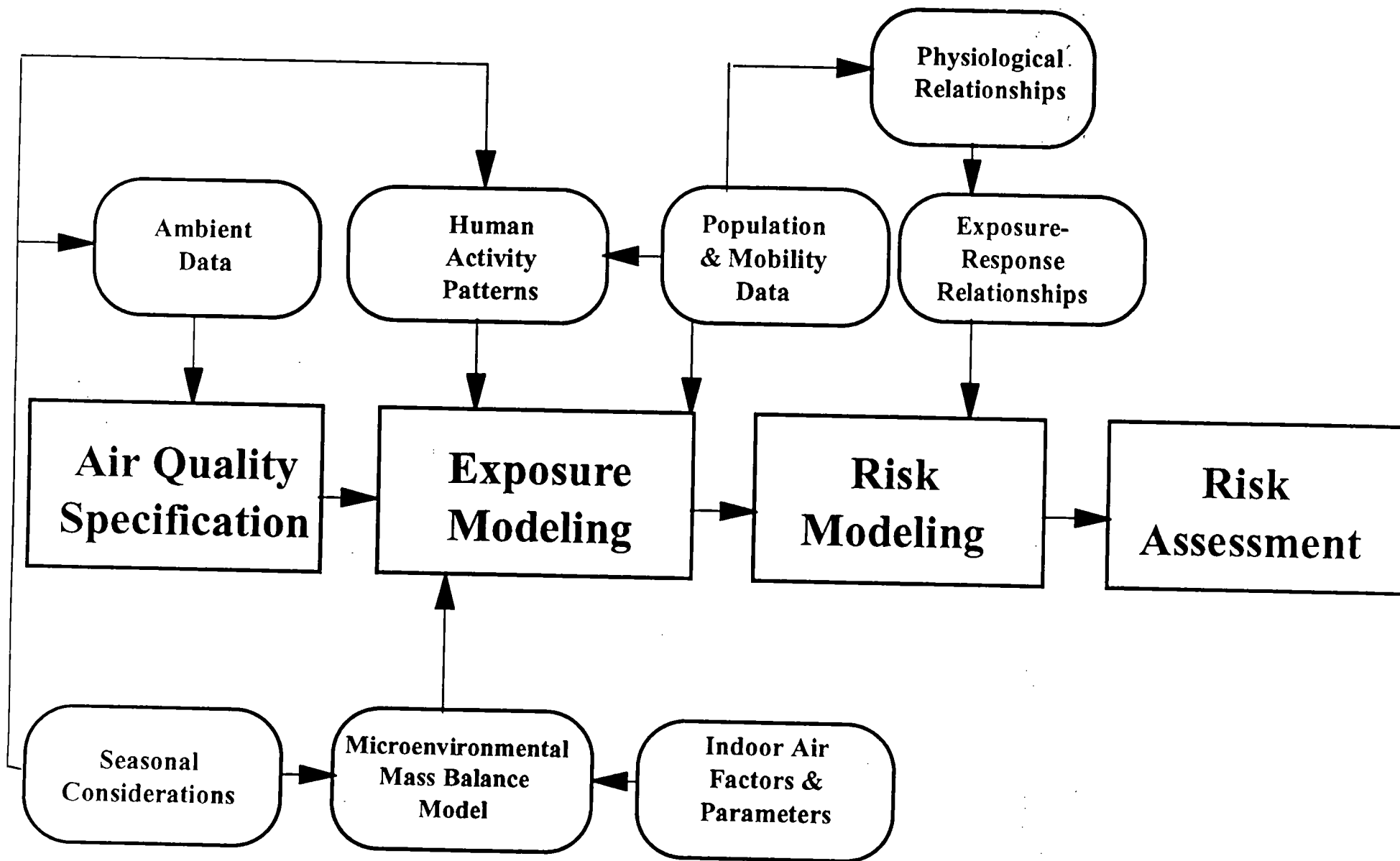
Two Types of Risk Measures

- **Benchmark Risk**
 - **Adverse Event: Probability That Air Quality Would Occur That Would Adversely Affect A Specified Percentage of a Given Subpopulation Under Specified Exposure Conditions If the Whole Group Were Exposed**
 - **Reflects "Right to Clean Air" Regardless of Location of Group**
- **Headcount Risk**
 - **Adverse Event: Probability of Number of Incidents of an Effect or Number of People Suffering an Effect**
 - **If Same Person Suffers an Effect Multiple Times in a Year It Counts as Multiple Incidents**
 - **Reflects Location of Sensitive Population Group**



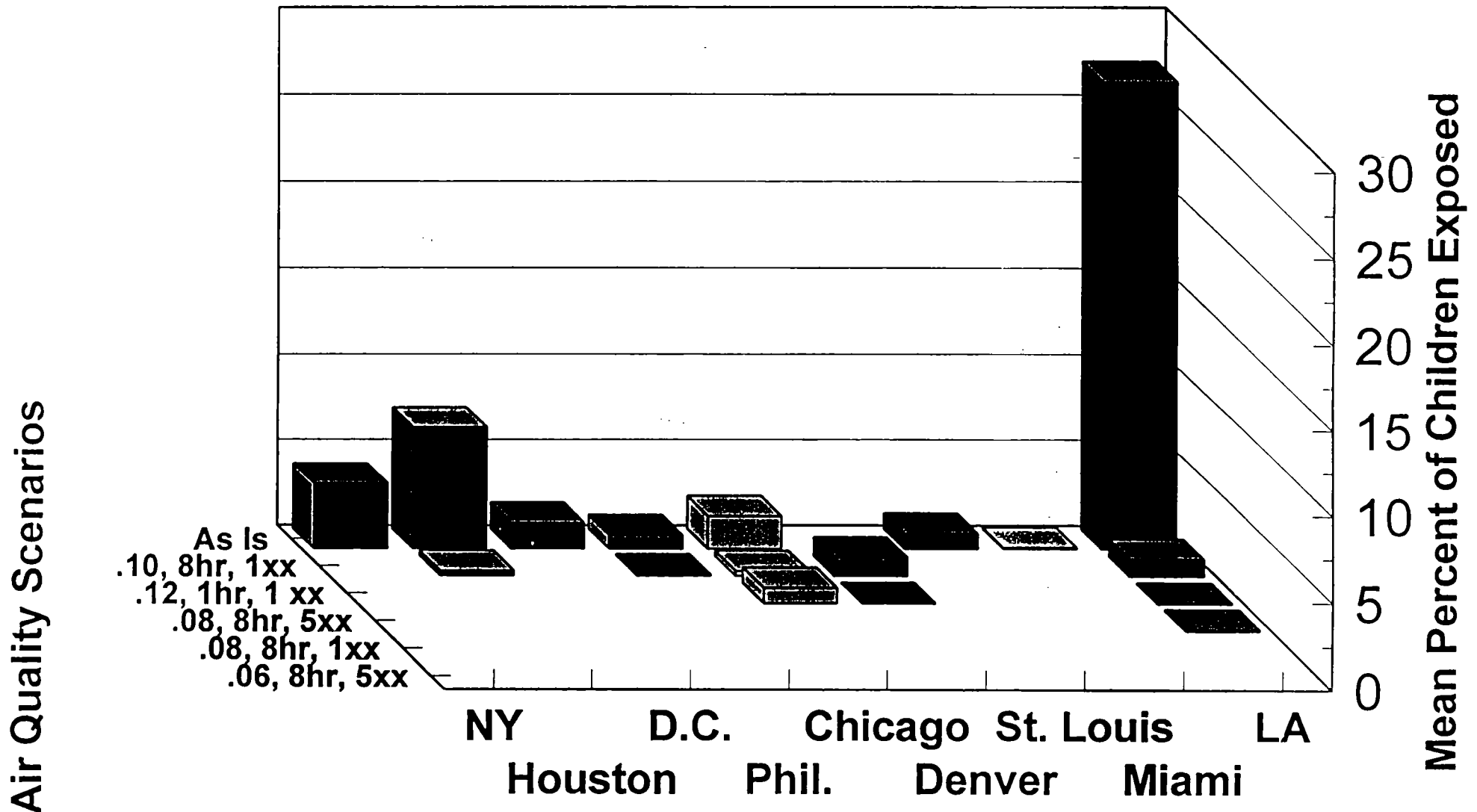
THE GENERAL NEM APPROACH

- **Define the population of interest and subdivide it into an exhaustive set of cohorts based on Census classifications**
- **Define a study area and subdivide it so that fixed-site monitors can be used to characterize ambient air quality for at least some outdoor microenvironments**
- **Develop an exposure event sequence for each cohort for the exposure period of interest**
- **Estimate the pollutant concentration and activity level (breathing rate) associated with each exposure event**
- **Extrapolate cohort exposure estimates to the entire population of interest**



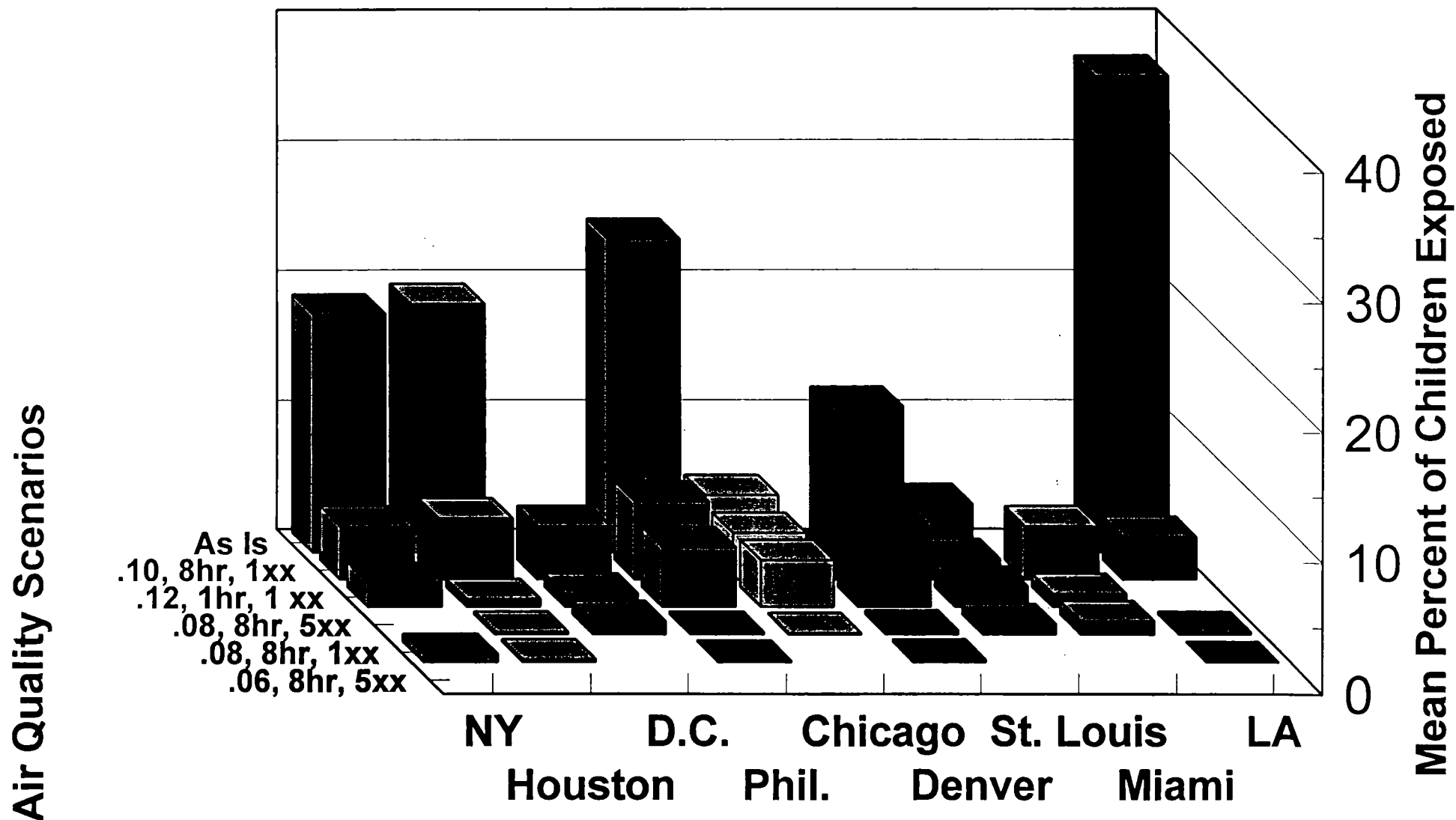
Mean Percent of Children

Exposed on 1 or More Days to ≥ 0.12 ppm, 1-hr Ozone
At Heavy Exercise (EVR >30)



Mean Percent of Children

Exposed on 1 or More Days to ≥ 0.08 ppm, 8-hr Ozone
At Moderate Exercise (EVR >15)



Status of pNEM Work

- **Current Exposure Work**
 - **Have Completed NOW Population for 9 Urban Areas (NY, Chicago, Houston, Denver, Phil., Miami, St. Louis, D.C., LA)**
 - **Have Completed Summer Camp Special Study**
 - **Outdoor Worker Population for 9 Urban Areas Ongoing, Expect by May 1994**

Future Exposure Work

- Initiating Work to include "Active Children" Subpopulation
 - Will Examine Whether or Not Significant Differences in Activity Patterns by Race and Sex for Children
 - Results Should Be Available by Fall
- Will Reexamine Exposure Model to Address Other Technical Issues and Rerun Results for 9 Urban Areas if Significant Changes
 - e.g., Using Distributions of Body Surface Area Rather Than Point Estimates
- Will Examine Impact of Alternative Baseline Years on Air Quality Adjustment Approach Used to Model Just Attaining Alternative Standards

Scope of Ozone NAAQS Risk Assessment

Alternative NAAQS

0.12 ppm, 1-hr, 1 ex.exc.	0.08 ppm, 8-hr, 5 ex.exc.
0.10 ppm, 8-hr, 1 ex.exc.	0.06 ppm, 8-hr, 5 ex.exc.
0.08 ppm, 8-hr, 1 ex.exc.	

**As Is
Scenario**

Health Endpoints

FEV1 Decrement
(>10%, >15%, >20%)

Cough, Chest Discomfort
(Any, Mod./Sev.)

Airway Responsiveness
(100% increase)

**Lower Respir.
Symptoms**
(Any, Mod./Sev.)

**BAL
Endpoints?**

**Lung Lesions
Centriacinar Region**
(Mild, Moderate)

Geographical Scope

9 Urban Areas

LA*, NY*, Chicago, Houston, Phil., Denver, St. Louis, Miami, Wash, D.C.

*Lung Lesion risk estimates only available for LA and NY

Other Health Endpoints

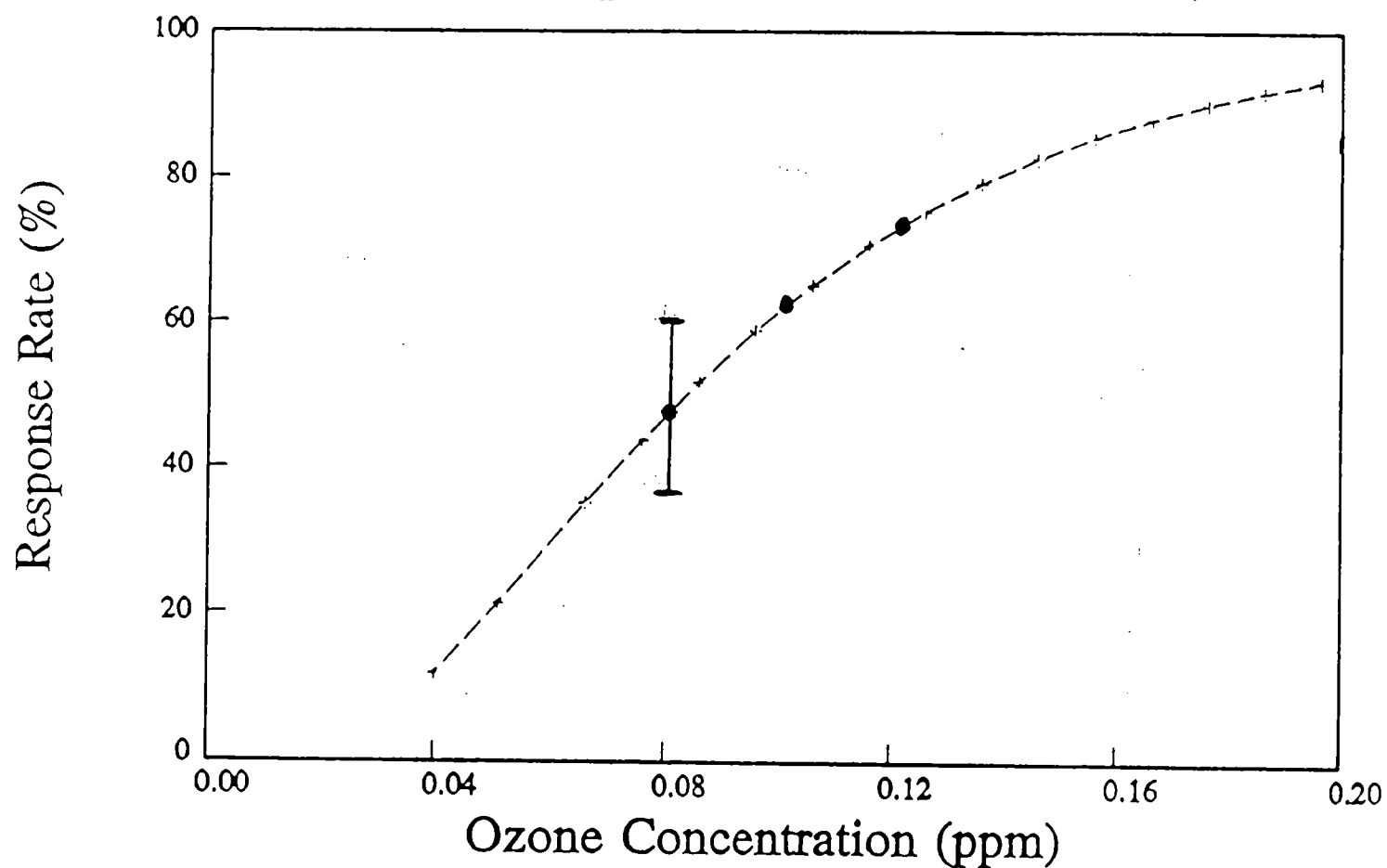
- **Increased Hospital Admissions for Asthmatics**
 - **Multiple Studies Have Consistently Shown That O₃ Is Associated With An Increased Incidence of Admissions Accounting For Roughly 1 to 3 Excess Respiratory Hospital Admissions Per 100 ppb O₃ Per Million Persons (p.7-218, O₃CD Draft)**
 - **Studies Have Related This Effect to the Reported Daily Max Hourly Avg at Fixed Site Monitor**

Past Ozone Risk Assessment Work

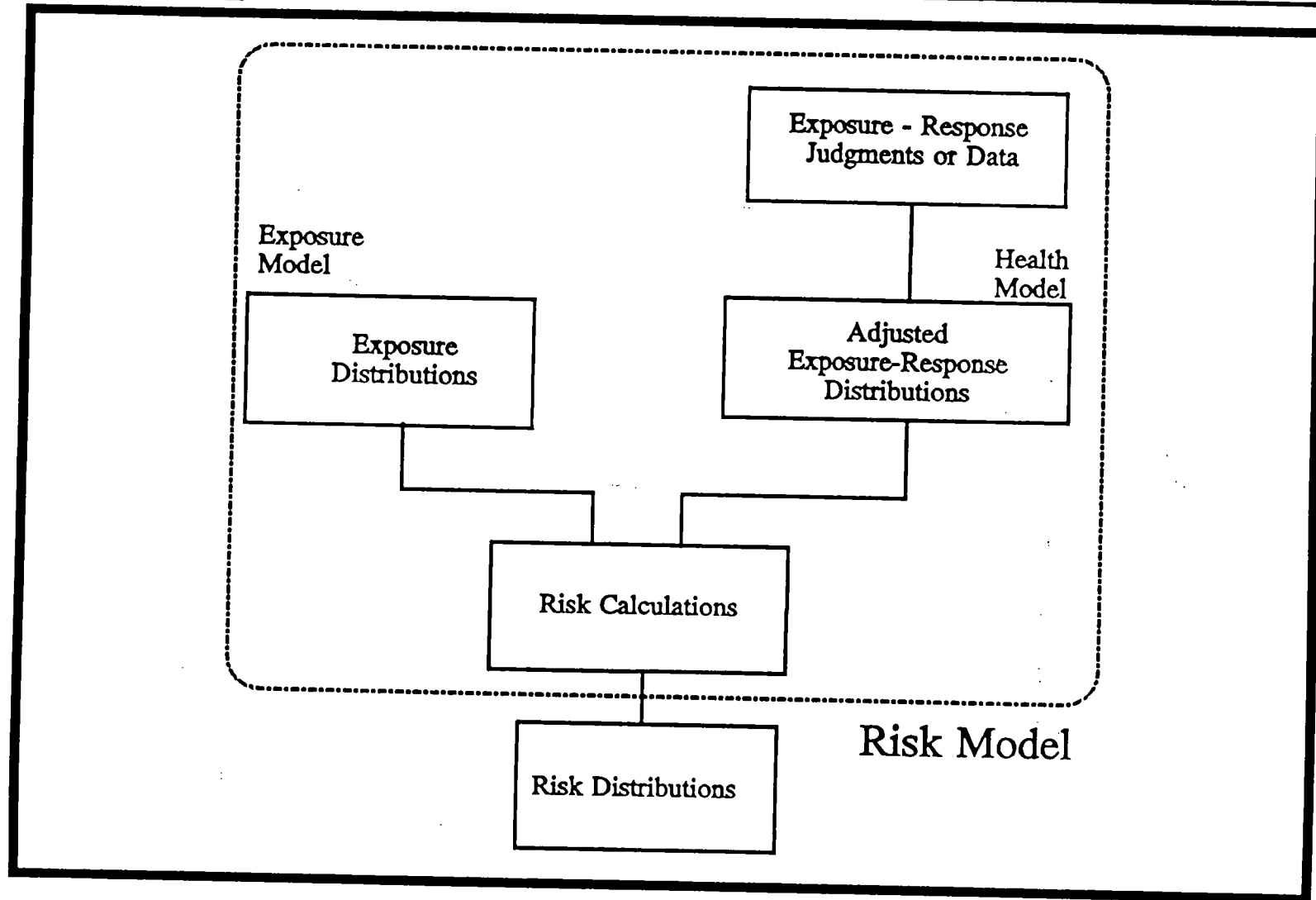
- 1-hr Lung Function and Respiratory Symptoms Risk Assessment
 - Avol et al., 1984; Kulle et al., 1985, McDonnell et al., 1983
 - Summarized in OAQPS Staff Paper
 - Reviewed By CASAC & Public
- Chronic Lung Injury Risk Assessment
 - Encoded Probabilistic Judgments of 6 Health Scientists
 - Occurrence of Mild or Moderate Lesions in CAR of Lung
 - NOT Part of Last NAAQS Review Process

Exposure/Response Relationships

Pain on Deep Inspiration, Moderate Exercise, 8 Hrs

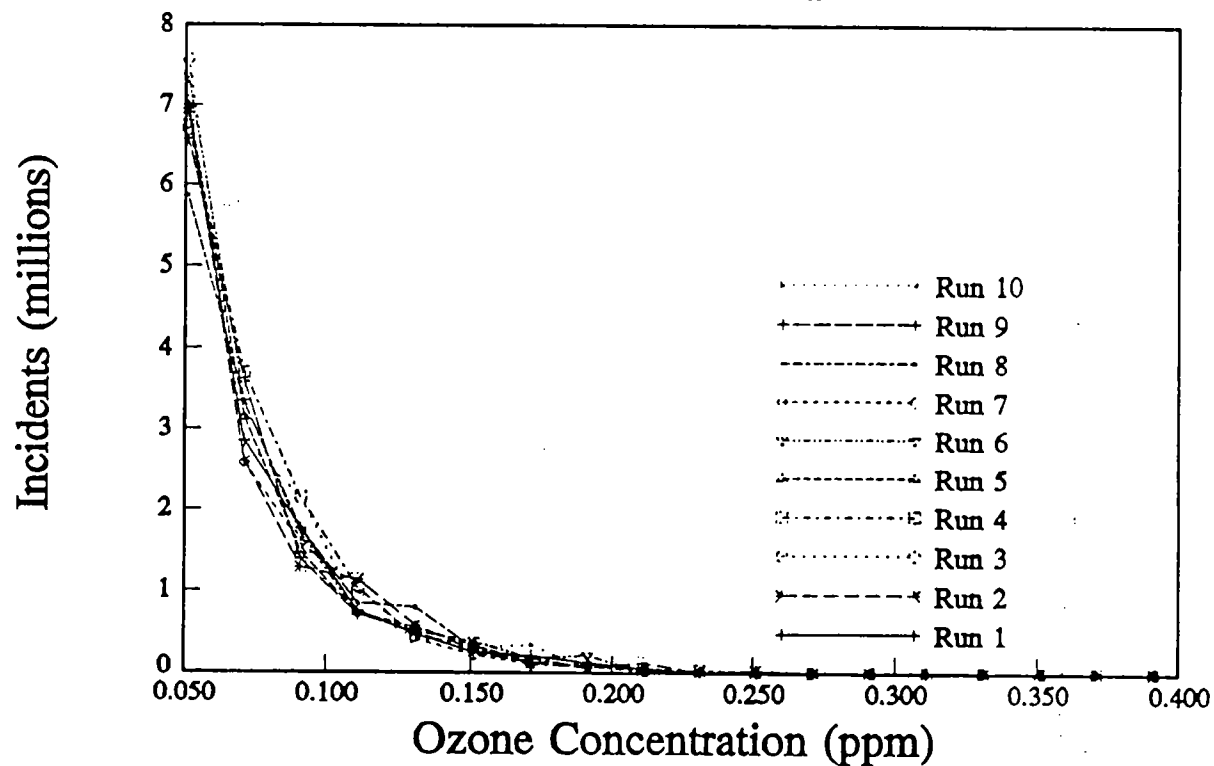


Risk Distributions — the Principal Results — Are Based on Exposure-Response and Exposure Models



Risk Calculations Involve an Exposure Distribution ...

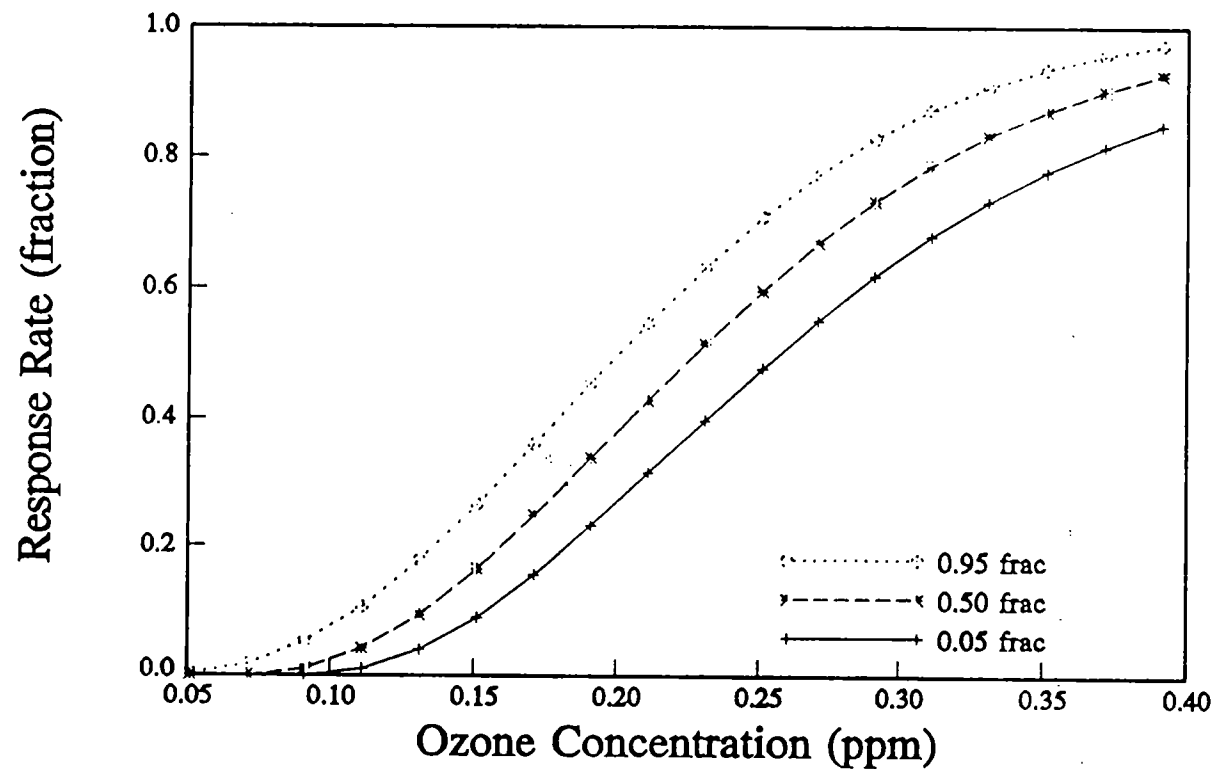
Variability in pNEM runs
Los Angeles, 1 hr, Total Population, As-Is



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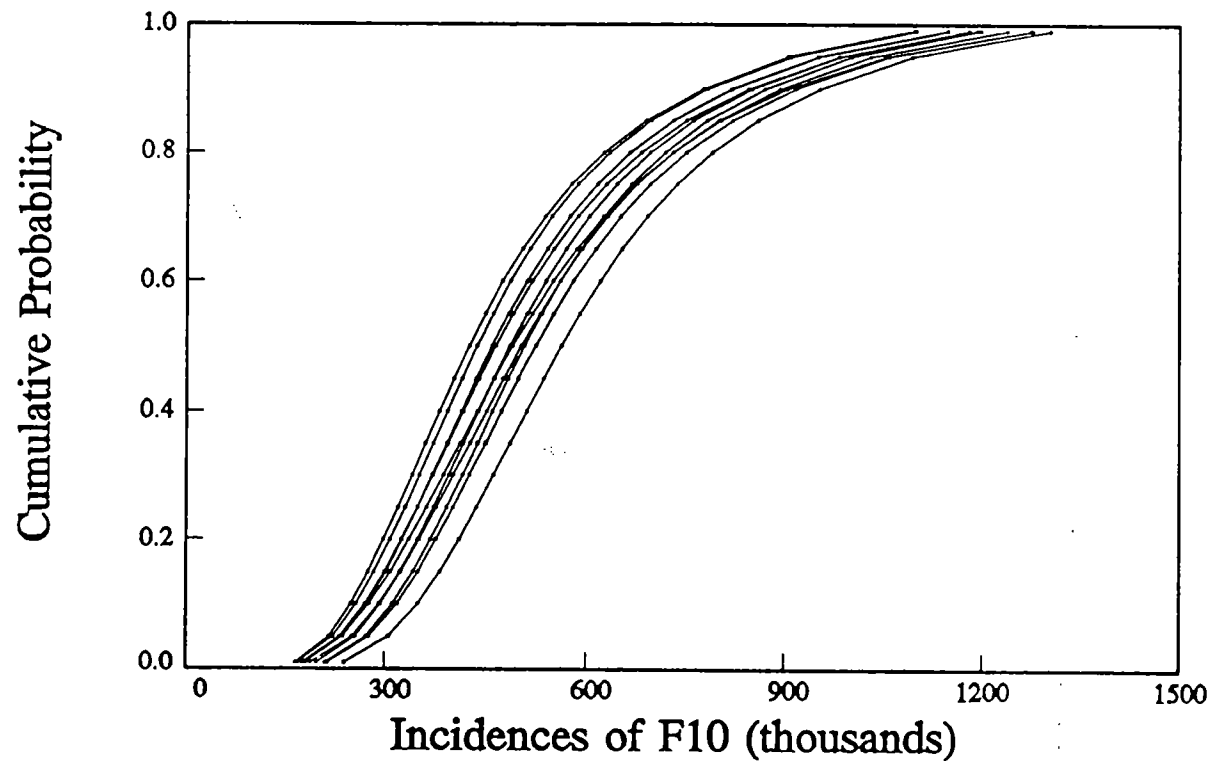
... and a Probabilistic Exposure-Response Relationship

Variability in Response
A_{vol}, FEV₁ ≥ 10%, 1 hr



One Probability Distribution is Determined for Each of the 10 pNEM/O₃ Runs

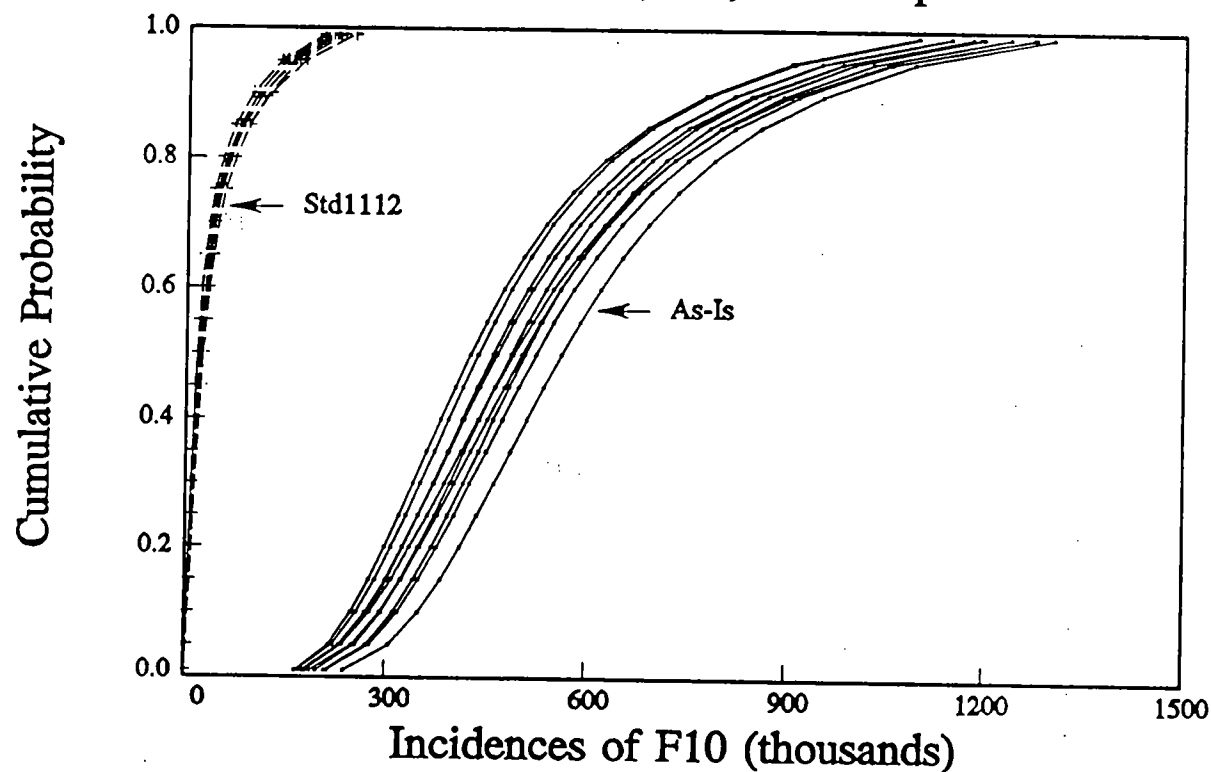
Results for 10 pNEM Runs, As-Is Air Quality
Avol, FEV₁ ≥ 10%, 1hr, Total Population



af10x - 1-27-94 - 15:31

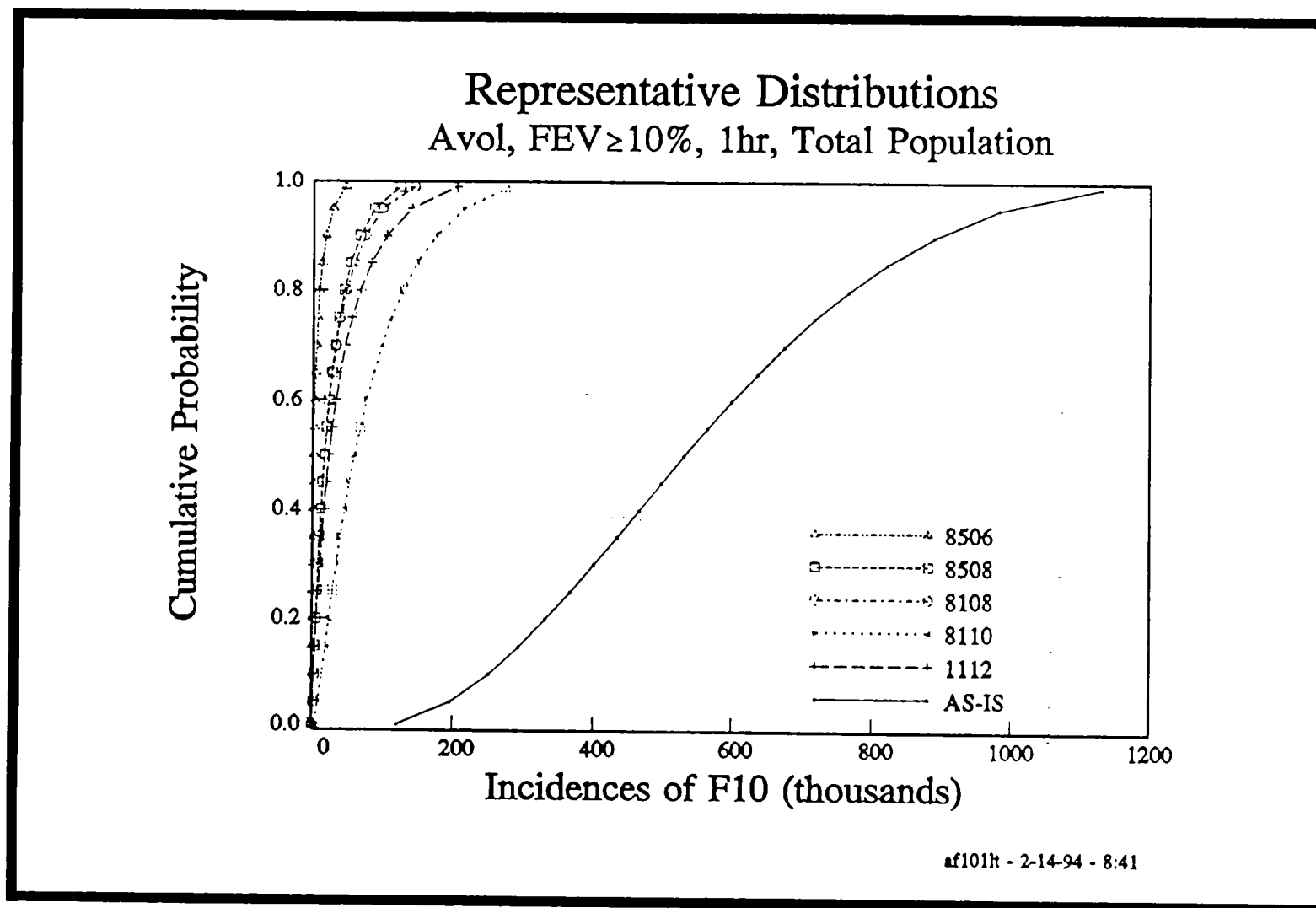
Results for 2 Air Quality Scenarios Can Be Displayed on One Graph

Comparing 1hr, 1 ExEx, 0.12ppm and AS-IS
Avol, FEV $\geq$ 10%, 1hr, Total Population

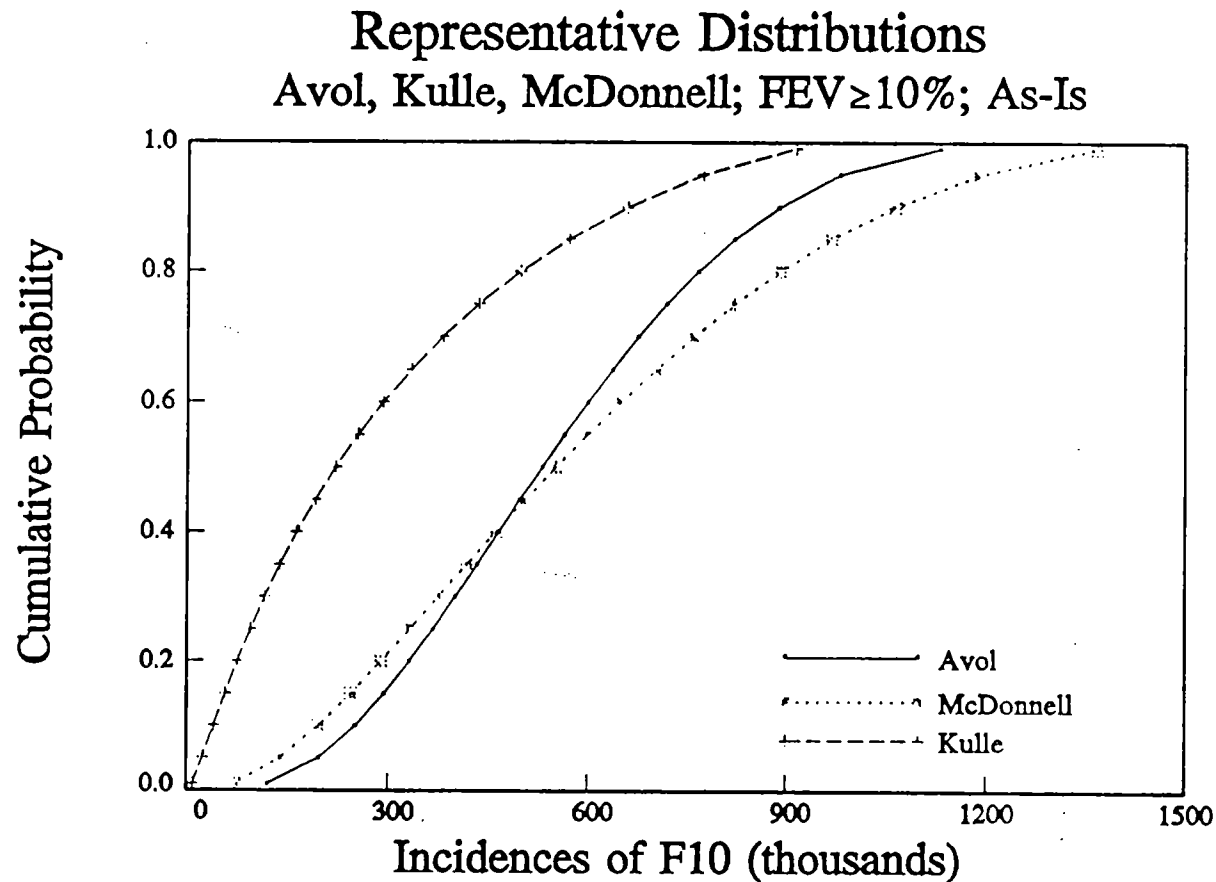


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Using Representative Distributions, It Is Possible to Display Results for All Air Quality Scenarios ...



... Or Compare Results Across Studies for a Specific Air Quality Scenario



Significance of Effects Project

- **EPA Administrator Must Ultimately Make Judgments About Which Effects and Degree of Response Should Be Considered "Adverse Health Effects"**
- **Propose to Develop Protocols for Interviewing Various Health Scientists About the Medical Significance and Public Health Importance of Various Endpoints**

Next Steps & Schedule

- **Summer 1994: Revised Draft Risk Assessment Report**
 - **Will Include Outdoor Worker Results**
- **Fall 1994: CASAC Review of OAQPS Staff Paper Which Includes Summary of Exposure Analysis and Risk Assessment for Non-Outdoor Workers and Outdoor Workers**
- **Spring 1995: CASAC Review of Revised Staff Paper**
 - **Will Summarize Active Children Exposure & Risk Estimates**

Draft — Do Not Cite or Quote

**A PROBABILISTIC ASSESSMENT OF HEALTH RISKS ASSOCIATED WITH
SHORT- AND LONG-TERM EXPOSURE TO TROPOSPHERIC OZONE**

prepared for

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

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work funded through

Interagency Agreement DW89935085-01-3
U.S. Environmental Protection Agency
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February 1994

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ACRONYMS, INITIALISMS, AND ABBREVIATIONS

ACF	any cough
ACH	any chest discomfort
ALR	any lower respiratory symptom
ANL	Argonne National Laboratory
BRT	shortness of breath
CD	criteria document
CI	credible interval
DFEV	decrease in forced expiratory volume
DFEVC	decrease in forced expiratory volume corrected for exercise in clean air
ECAO	Environmental Criteria and Assessment Office
EES	exposure event sequence
ELPM	equivalent ℓ/min (ventilation rate adjusted for [i.e., divided by] body surface area, which is typically assumed to be 1.9 m^2 for adults; the units are $\ell/\text{min-m}^2$)
EPA	U.S. Environmental Protection Agency
FEV	forced expiratory volume - the maximum amount of air that can be expelled from the lungs in 1 second
GCU	geographical census unit
MCF	moderate/severe cough
MCH	moderate/severe chest discomfort
MLR	moderate/severe lower respiratory symptom
NAAQS	national ambient air quality standard
NEM	NAAQS exposure model
O ₃	ozone
OAQPS	Office of Air Quality Planning and Standards
ppm	parts per million
PDI	pain on deep inspiration
pNEM/O ₃	probabilistic NAAQS exposure model for ozone
ScnASIS	as-is air quality scenario
Std1112	current ozone NAAQS: 1-hr averaging time, 1 expected exceedance, 0.12 ppm ozone

ACRONYMS, INITIALISMS, AND ABBREVIATIONS (cont'd)

Std8110	an alternative NAAQS: 8-hr averaging time, 1 expected exceedance, 0.10 ppm ozone
Std8108	an alternative NAAQS: 8-hr averaging time, 1 expected exceedance, 0.08 ppm ozone
Std8508	an alternative NAAQS: 8-hr averaging time, 5 expected exceedances, 0.08 ppm ozone
Std8506	an alternative NAAQS: 8-hr averaging time, 5 expected exceedances, 0.06 ppm ozone

DISCLAIMER

This work was funded through Interagency Agreement DW89935085-01-3 between the U.S. Department of Energy and the U.S. Environmental Protection Agency. Any opinions, finding, conclusions, or recommendations are those of the authors and do not necessarily reflect the views of the U.S. Environmental Protection Agency, U.S. Department of Energy, or Argonne National Laboratory. Comments on the report should be addressed to Harvey Richmond, U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, MD-12, Research Triangle Park, NC 27711.

A PROBABILISTIC ASSESSMENT OF HEALTH RISKS ASSOCIATED WITH SHORT- AND LONG-TERM EXPOSURE TO TROPOSPHERIC OZONE

by

Ronald G. Whitfield and Mariska J.G. Absil

ABSTRACT

The work described here is part of a larger risk assessment project sponsored by the U.S. Environmental Protection Agency. Earlier efforts have: developed exposure-response relationships for acute health effects among heavily-exercising populations; characterized scientific judgment regarding the probability of chronic lung injury to children and outdoor workers due to long-term ozone exposure; developed a probabilistic National Ambient Air Quality Standards Exposure Model; and developed a general methodology for integrating probabilistic dose-response relationships and exposure estimates to calculate overall risk results. In addition, recently published animal and human experimental and observational data make it possible to characterize additional health effects for 1-hr and 8-hr exposures of moderately exercising populations to ozone. Risk results are presented for selected acute and chronic health effects in order to explain the methodology and introduce risk output formats.

1 INTRODUCTION

This report summarizes the risks of acute (short-term) and chronic (long-term) exposure to ozone. The risks are defined by probability distributions (called risk distributions) over the number of person-occurrences of specific health effects. Acute effects include decreased lung function and symptoms. Chronic effects are the formation of lesions in the human lung.

The risk distributions are obtained by combining probabilistic exposure-response relationships with exposure estimates. The exposure-response relationships are derived from a variety of sources, primarily animal and human experimental and observational data for acute effects, and the judgments of health scientists about chronic effects. Exposure estimates, which also are probabilistic, were obtained from the recently-developed probabilistic version of the National Ambient Air Quality Standards (NAAQS) Exposure Model for ozone (pNEM/O₃). pNEM/O₃ output includes results for 10 separate runs of the model to gain insights into the effects of run-to-run variations on risk output.

The motivation for this work is to (1) develop first-time risk results for some acute health endpoints (acute effects for individuals exercising at moderate levels for short and

prolonged periods of time, and chronic effects for children exposed to ozone for 1 year or longer); and (2) update previous risk results using recent exposure estimates from pNEM/O₃ that (3) reflect analysis of possible alternative NAAQS for ozone.

1.1 BACKGROUND

Ozone is a highly reactive irritant gas present in elevated amounts throughout much of the United States. The U.S. Environmental Protection Agency (EPA) estimated that in 1988 about 120 million people lived in urban areas in which the current one-hour ozone NAAQS of 0.12 parts per million (ppm) was exceeded. The current NAAQS requires that the 0.12 ppm ozone concentration not be exceeded on average on more than one day per year. This current standard for ozone is based on concern for acute respiratory effects that have been reported in many controlled human exposure studies, as well as, acute and longer-term effects reported in animal toxicology, human epidemiology, and human field studies.

As stated in the Clean Air Act, the EPA is required to set, review, and revise, as appropriate, the primary NAAQS for criteria pollutants. The primary standards, which are to be set at levels sufficient to protect public health with an adequate margin of safety, are based on scientific evidence reviewed in "criteria documents" (CDs). The CD summarizes and evaluates the human clinical, epidemiological, and animal toxicology evidence regarding physiological and adverse health effects resulting from exposure to ozone and other photochemical oxidants.

To assist in its review of the NAAQS for ozone, the Office of Air Quality Planning and Standards (OAQPS) of the EPA has entered into an interagency agreement with Argonne National Laboratory (ANL) to assess the public health risk associated with the attainment of alternative ozone NAAQS. This risk assessment is intended to characterize, as explicitly as possible, the range and implications of uncertainties in the existing scientific data base while making full use of current scientific knowledge, available animal and human experimental and observational data, and scientific expertise. This risk assessment includes effects of acute (short-term) and chronic (long-term) exposures to ozone. It combines exposure-response relationships and exposure estimates to produce overall risk estimates.

The acute risk assessment addresses effects for individuals engaged in heavy exercise (based on 1-3^{*} hour controlled human exposure studies) and for individuals engaged in moderate exercise (based on results from 2-hour[†] and 6.6-hour[‡] controlled human exposure studies). The chronic risk assessment is based on the judgments of health scientists.[§]

^{*} Avol et al. (1984), Kulle et al. (1985), and McDonnell et al. (1983)

[†] Seal et al. (1993)

[‡] Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991)

[§] Whitfield et al. (1991) and Winkler et al. (1994)

Previous risk assessments have been performed for acute health effects of ozone (Hayes et al. [1987c]). Methods developed in that assessment (Hayes et al. [1987a]), Hayes et al. [1987b]) and an earlier assessment for lead (Wallsten and Whitfield [1986]; Whitfield and Wallsten [1989]) have provided a foundation for the current risk assessment.

1.2 RISK ASSESSMENT APPROACH

The basic risk assessment approach, illustrated in Figure 1, involves developing an exposure model and a health model. The exposure model accounts for human contact with a specific criteria pollutant. Pollutants may enter the human body through one or more pathways: inhalation, ingestion, or absorption. The contact may be described either in terms of intensity or a cumulative exposure over a specified period of time. For this assessment the exposure estimates were generated by pNEM/O₃. Exposure estimates were obtained for nine urban areas, and that portion of the population thought to be potentially most at risk to ozone exposure. The at-risk groups are identified as children and outdoor workers. This determination is based on the discussion of sensitive populations in the ozone CD (EPA [1994]).

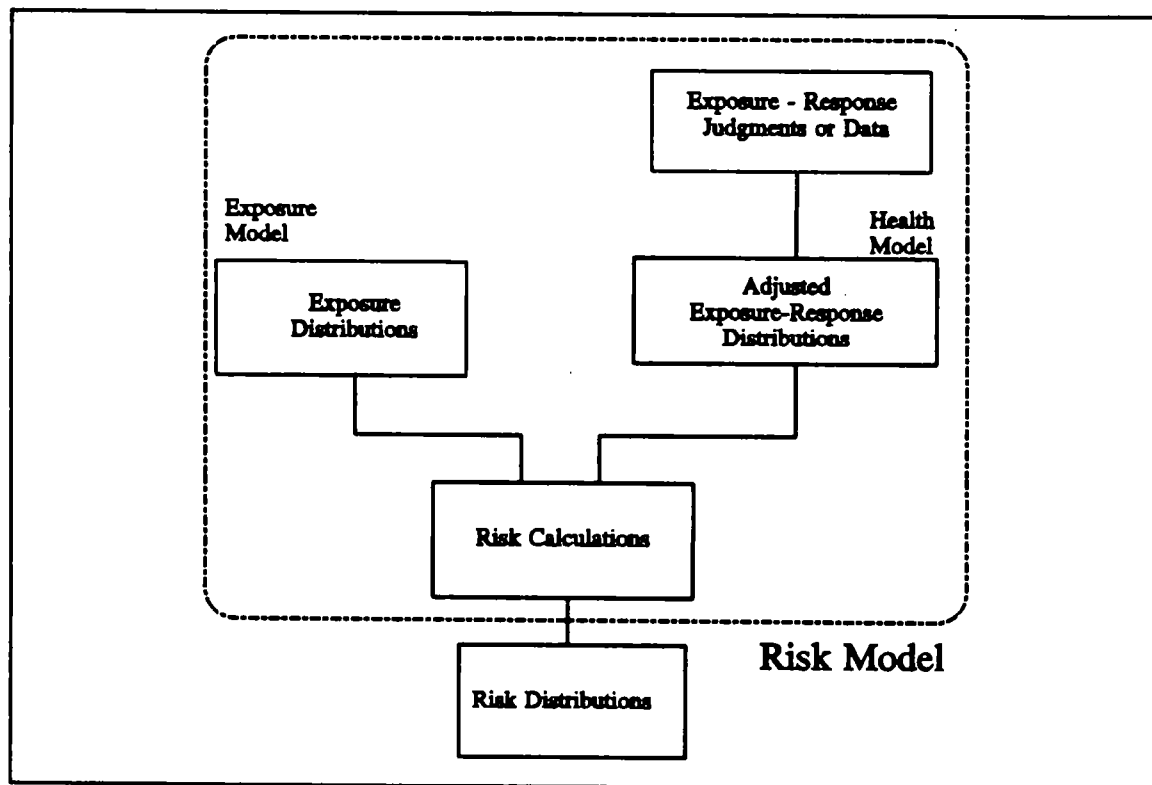


FIGURE 1.1 The Risk Model Includes an Exposure Model and a Health Model

Two types of risk estimates can be made, benchmark and headcount (McKee [1994]). Both of these use the same exposure-response relationships, but different types of air quality data and exposure estimates. Relationships between the two risk models are indicated in Figure 1.2. Benchmark risk estimates measure the risk of potential harm, or hazard, posed by elevated levels

of ozone. Headcount risk estimates measure the risk of actual harm incurred by individuals as they go about their daily lives, moving about from one place to another, and from indoors to outdoors. Only headcount risks are presented in this report. Benchmark risks will be analyzed at a later time.

In addition, there are two types of exposure measures, people and person-occurrences. The people measure counts the number of individuals who are exposed one or more times per ozone season to the exposure-indicator (ozone level and breathing rate) of interest. The person-occurrences measure begins with a count of the number of times per ozone season that a particular individual is exposed to the exposure indicator of interest, and accumulates counts over all individuals. Therefore, the person-occurrences measure confounds people and occurrences: one occurrence for 10 people is counted the same as 10 occurrences for one person. The maximum number of hourly exposure occurrences is equal to the population multiplied by the number of hours in the ozone season. Only person-occurrences measurements are included in this risk assessment.

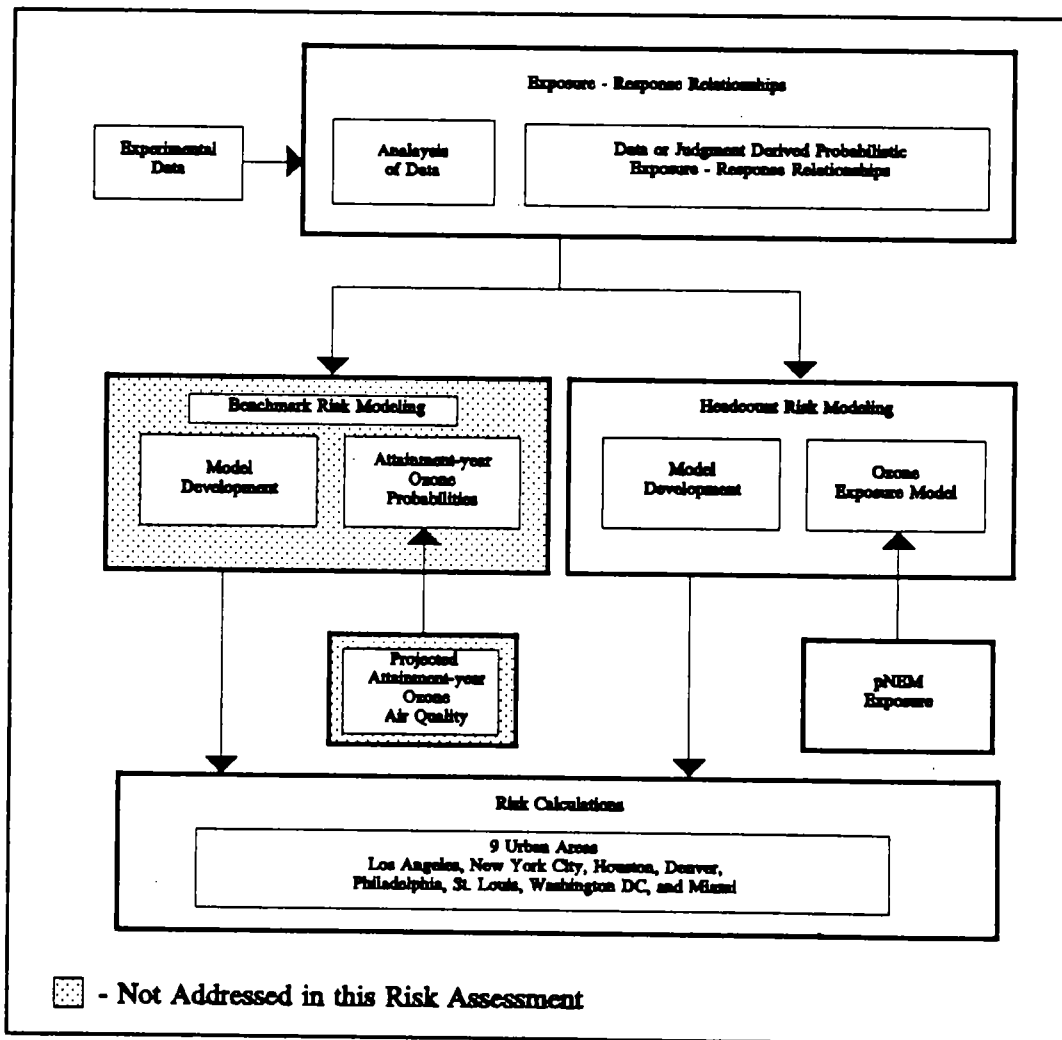


FIGURE 1.2 Relationship Between Benchmark and Headcount Risk Models

A health model accounts for human reaction to contact with a chemical agent. Reactions include symptoms or physiological changes (e.g., reduced pulmonary function, respiratory symptoms, and formation of mild/moderate lesions in the centriacinar region of the lung). A health model can be based either on data, judgment, or a combination of the two. An important aspect of a health model is the "most sensitive population" — people who are most at risk either because they are highly reactive (e.g., children whose lung development may be impaired by exposure to ozone) or more frequently exposed (e.g., commuters and outdoor workers). The Clean Air Act requires that NAAQS be set at a level that will protect the most sensitive populations with an adequate margin of safety.

Exposure-response relationships used to characterize the pulmonary function and respiratory symptom effects of ozone exposure in this study are developed from studies of human exposure data obtained in clinical studies. Controlled human exposure studies, contrasted with epidemiological or field studies, were thought to be most appropriate for specifying the data needed for exposure-response estimation. The 1-hour exposure-response relationships for acute health effects for heavy exercisers are based on the exposure studies performed by Avol et al. (1984), Kulle et al. (1985), and McDonnell et al. (1983). The Seal et al. study (1993) are used to develop exposure-response relationships for moderate exercisers. The Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1983) studies are used as the basis for estimating 8-hour exposure-response relationships for non-exercising individuals.

The exposure-response relationships used to characterize the formation of mild/moderate lesions in the centriacinar region of the lung are not based on controlled human exposure studies, but rather on judgments of health scientists (Whitfield et al. [1994] and Folinsbee et al. [1994]). It is frequently necessary to make inferences about a health effect in one population on the basis of epidemiological or clinical data on different populations, or on different exposure conditions, or laboratory data on other species or in-vitro procedures. Statistical techniques cannot quantify this type of uncertainty because it is judgmental. Uncertainty can be quantified by using appropriate procedures to estimate the probabilities.

1.3 REPORT ORGANIZATION

This report is organized into 6 sections. Section 2 discusses the probabilistic model that generates the exposure data. It includes a description of the model methodology and simulated data. Section 3 discusses controlled human exposure data and probabilistic judgments. Section 4 discusses the methodology used to develop the exposure-response relationships. Section 5 summarizes risk calculations and results are presented in Section 6. Risk estimates are shown for selected health endpoints and 6 air quality scenarios in Los Angeles. Risk results are displayed in Appendix A.

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2 EXPOSURE MODEL

Evaluating alternative NAAQS proposed for a particular pollutant involves assessing the risks to human health associated with air quality that results from each of the standards under consideration. Important factors that need to be considered in an ozone exposure assessment are: magnitude of the exposure, duration of the exposure, concentration pattern of exposure, frequency of repeated peak exposures, and ventilation state of the individual at time of exposure. Several researchers have recommended that such estimates be obtained by simulating the movements of people through zones of varying air quality so as to approximate the actual exposure patterns of people living within a defined area.

Until 1986, the NEM series of models made no attempt to model random processes within the exposure simulation. The latest version of the model, pNEM/O₃ (Johnson et al. [1993]), incorporates probabilistic elements into the original NEM methodology and uses a mass balance model to estimate indoor ozone concentrations. How the pNEM/O₃ methodology fits into the risk assessment is shown in Figure 2.1. A brief description of the pNEM/O₃ and its methodology is given in this section.

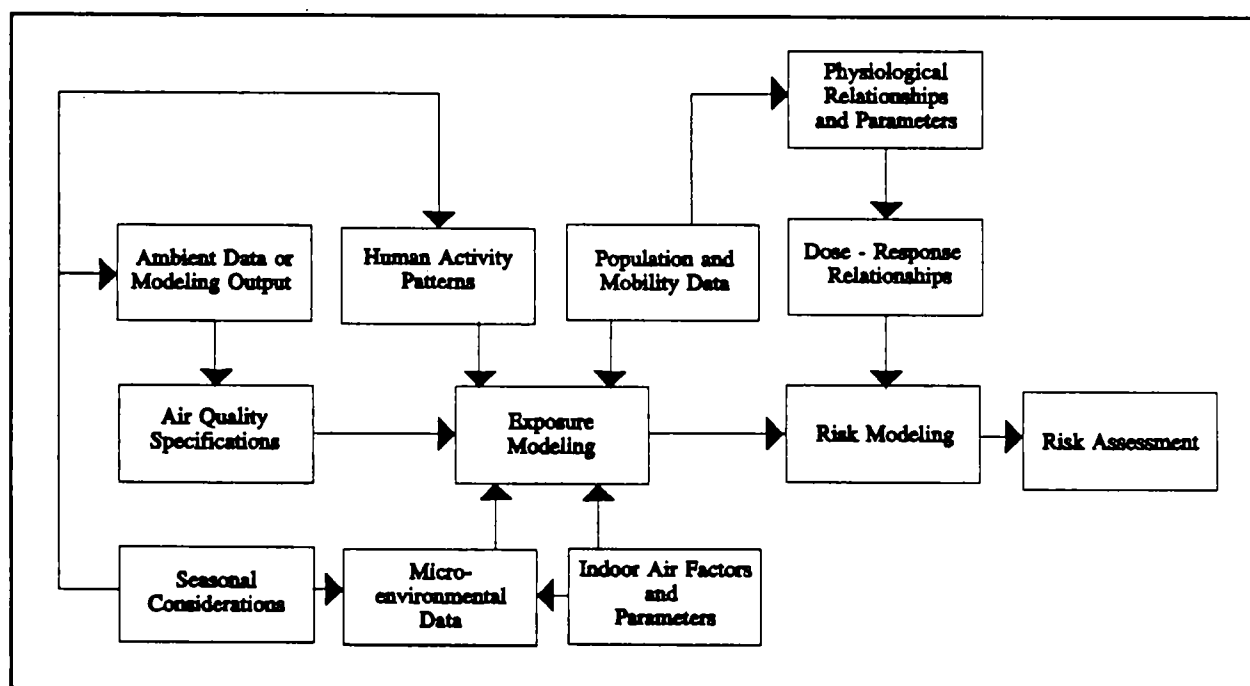


FIGURE 2.1 Major Components of the NEM Series of Exposure Models and Associated Health Risk Assessment Procedures

2.1 EXPOSURE MODELING METHODOLOGY

The pNEM/O₃ model consists of two principal parts, the cohort exposure program and the exposure extrapolation program. The cohort exposure program estimates the sequence of ozone exposures experienced by defined population groups. The exposure extrapolation program estimates the number of persons within a particular study that are represented by each cohort and then combines this information with the cohort exposure sequences to determine the distribution of exposures over a defined population of interest.

The general NEM methodology consists of five steps. The first step is to define a study area, a population of interest, appropriate subdivisions of the study area, and an exposure period. The second step is to divide the population of interest into an exhaustive set of cohorts, while the third step develops an exposure event sequence for each cohort for the exposure period. The fourth step in the procedure is to estimate the pollutant concentration, ventilation rate, and physiological indicator, if applicable, associated with each exposure event. And finally, the cohort exposures are extrapolated to the population of interest and to particular sensitive population groups. Each of these steps will be explained in detail.

2.1.1 Define the Study Area, Subdivisions of the Study Area, the Exposure Period and the Population-of-interest

The study area is defined as an aggregation of exposure districts. Each exposure district is defined as a contiguous set of geographical census units (GCU). Each GCU consists of one or more census tracts as defined by the 1980 census. No census tract is split between two or more GCUs. All GCUs assigned to a particular exposure district are located within a specified radius of a fixed ozone monitor. This radius varies from 2.1 km to 25.0 km.

The exposure period is defined as a series of months within a particular calendar year. The specified months conform to the ozone season specified for the urban area by the EPA. The exposure season is defined as the annual period when high ambient ozone levels are likely to occur. Three ozone seasons are used in the nine urban areas evaluated here: January - December, March - September, and April - October. The ozone periods for the nine cities are listed in Table 2.1.

The population of interest is typically defined as all residents of a defined study area, or the residents of the study area who belong to specific populations at risk.

TABLE 2.1 Ozone Seasons for the Nine Urban Areas

Study Area	Exposure Period
Chicago	April - October
Denver	March - September
Houston	January - December
Los Angeles	January - December
Miami	January - December
New York	April - October
Philadelphia	April - October
St. Louis	April - October
Washington DC	April - October

2.1.2 Divide the Population-of-Interest Into an Exhaustive Set of Cohorts

The population of interest is divided into a set of cohorts such that each person is assigned to only one cohort. Each cohort is assumed to contain persons with identical exposures during the specified exposure period. Cohort exposure is typically assumed to be a function of 1) demographic group, 2) location of residence, and 3) location of work place. Specifying the home and work district of each cohort provides a means of linking cohort exposure to ambient pollutant concentrations. Specifying the demographic group provides a means of linking cohort exposure to activity patterns that vary with age, work status, and other demographic variables.

The exposure of each cohort is determined by an exposure event sequence (EES) specific to the cohort. Each EES consists of a series of events with durations from 1 to 60 minutes. To determine average exposures for specific clock hours, exposure events are defined such that no event falls within more than one clock hour. Each exposure event assigns the cohort to a particular combination of geographic area and microenvironment. Each event also provides an indication of respiration rate. The respiration rates are classified as sleeping, slow, medium, and fast.

2.1.3 Develop an Exposure Event Sequence for Each Cohort for the Exposure Period

EESs are determined by assembling activity diary records relating to individual 24-hour periods into a series of records spanning the ozone season of the associated study area. Because each subject of a typical activity diary study provides data for 1-3 days, the construction of a multi-month EES requires either the repetition of data from one subject or the use of data from multiple subjects. The latter approach is used in pNEM/O₃ analyses to better represent the variability of exposure that is expected to occur among persons included in each cohort. The activity diary data used in pNEM/O₃ were obtained from the Cincinnati Activity Diary Study (Johnson [1987]). During the study, over 900 subjects completed three-day activity diaries and

detailed background questionnaires. A new diary page was completed whenever the location or activity was changed.

A distinct EES is developed for each cohort. The exposure event within an EES is defined by the district, the microenvironment, and the breathing rate associated with the human activity being undertaken by the sampled individual.

The district is defined as being either the home or work district associated with the cohort, and the seven microenvironments are:

- 1) indoors-residence with a central air conditioning system
- 2) indoors-residence with window air conditioning units
- 3) indoors-residence with no air conditioning system
- 4) indoors-nonresidential locations
- 5) outdoors near a road
- 6) outdoors — other locations
- 7) in-vehicle.

2.1.4 Estimate the Pollutant Concentration and Ventilation Rate Associated With Each Exposure Event

The year-long sequence of hourly average ozone values for indoor and in-vehicle microenvironments is generated by a mass balance algorithm. This algorithm estimates the hourly average indoor ozone concentrations during hour h as a function of: indoor ozone concentration at the end of the preceding hour, the outdoor ozone concentration outdoors during hour h , air exchange rate during hour h , and an ozone decay factor. Values for the air exchange rate and the ozone decay factor are sampled from an appropriate distribution on a daily basis. Air exchange rate is permitted to change hourly in the three residential microenvironments depending on whether windows are assigned a status of open or closed. This assignment is determined through the use of a probabilistic model in which the status during each clock hour is assumed to be a function of air conditioning system temperature range and window status during the previous clock hour. In the pNEM/O₃ simulation, the ozone concentration in a particular microenvironment during a particular clock hour is assumed to be constant. For indoor and in-vehicle microenvironments, this value is determined by using a mass balance model to calculate average ozone concentration for the clock hour under the following conditions:

- 1) there are no indoor sources of ozone,
- 2) the indoor ozone concentration at the end of the preceding hour is known,
- 3) the outdoor ozone concentration during the clock hour is constant and known,
- 4) the air exchange rate during the clock hour is constant at a specified value, and
- 5) ozone decays at a rate that is proportional to the indoor ozone concentration.

The pNEM/O₃ mass balance model requires representative ambient air quality data for each exposure district in the form of a time series containing one value for each hour in the

specified ozone season. From 3 to 15 monitoring sites are selected to represent the geographic variation of ozone levels in each of 9 study areas. The number of monitors chosen in an area depends upon a data completeness criterion for each monitor and whether or not home-to-work data exist for a district.

All monitors reporting valid data (i.e., are 75% complete) in an urban area are used to evaluate ozone air quality. In no case is an area with fewer than 3 valid stations included because no ozone concentration surface can be computed from only two monitors. If an area has numerous monitors, the total number used is capped at 16 because of limitations on computational resources. This occurs only in the Los Angeles urban area, where 30 possible monitors are pared down to 16. This paring is accomplished by removing one of nearby pairs of monitors that has similar ozone air quality distributions. Otherwise, all monitors in an area are used.

After the number of monitors is chosen, the districts must be decided upon. Districts must be non-overlapping areas focused on a monitor. In addition, home-to-work trip information must be available for a district to be included in a pNEM study area. This information is not always available and the district is removed from further analysis when this occurs. This restriction results in the exclusion of low density rural areas from pNEM exposure assessments.

2.1.5 Extrapolate the Cohort Exposures to the Population-of Interest and to Individual Sensitive Groups

The fifth and final step is to extrapolate the cohort exposures to the population-of-interest and to individual sensitive groups. The cohort-specific exposure estimates are extrapolated to the general population of each study area by estimating the population size of each cohort.

Cohort populations are estimated by the following three step procedure:

- 1) The number of persons associated with each demographic group is estimated by census tract;
- 2) The fraction of homes falling into each of the three air conditioning categories is estimated by census tract;
- 3) The demographic group populations are multiplied by the air conditioning fractions to provide an estimate of the number of persons in each combination of demographic group and air conditioning category; This results in the cohort population estimates.

2.2 EXPOSURE ESTIMATES USED IN THE RISK ASSESSMENT

pNEM/O₃ estimates were generated for the nine cities listed in Table 2.1 for the total population, children, and outdoor workers. For this risk assessment, the total population and children estimates were used for the acute and chronic effects, respectively.

pNEM/O₃ output for the ozone concentrations given in Table 2.2 included output for ten runs. Although pNEM/O₃ generates exposure distributions for both people and person-occurrences, only person-occurrences results were used in this risk assessment. The particular ozone concentrations of interest for calculating exposure-response relationships are listed in Table 2.3. These concentrations are approximately the midpoints of the intervals listed in Table 2.2. Note that 0.040 ppm for acute endpoints and 0.025 ppm for chronic endpoints are considered to be background ozone levels.

Exposure-response probabilities for each run are computed by dividing the number of person-occurrences at each ozone concentration by the total number of person-occurrences in a run. For example, using the data in Table 2.4 (which is for as-is air quality, Los Angeles, the total population, 1-hour exposures, pNEM/O₃ run number 1), the total number of person-occurrences for this particular run is 94,105,616. At 0.051 ppm there are 6,913,499 person-occurrences. Dividing this value by the total (94,105,616) results in a value of 0.073465. The same computations are performed for the remaining ozone concentrations. Note that the sum of the calculated probabilities does not equal one because the occurrence measurements for background are not included. The probabilities for this example are presented in Table 2.4.

2.3 ALTERNATIVE AIR QUALITY SCENARIOS INCLUDED IN THE ANALYSIS

pNEM/O₃ results are available for 6 alternative air quality scenarios selected by OAQPS for analysis. The first scenario represents as-is air quality. The other 5 scenarios represent ozone air quality when an alternative NAAQS is just attained. They differ with respect to averaging time (1 or 8 hours), the number of expected exceedances that are allowed (1 or 5), and the allowed ozone limit (0.06, 0.08, 0.10, or 0.12 ppm). For easy reference, these scenarios are denoted ScnASIS, Std1112, Std8110, Std8108, Std8508, and Std8506. Explicit definitions of the 6 scenarios are presented in Table 2.5.

TABLE 2.2 Ozone Concentration Intervals (ppm) for which pNEM Data has been Generated

Acute, 1-hour	Acute, 8-hour	Seasonal
0.000	0.000	0.000
0.001 - 0.020	0.001 - 0.020	0.011 - 0.020
0.021 - 0.040	0.021 - 0.040	0.021 - 0.025
0.041 - 0.060	0.041 - 0.060	0.026 - 0.030
0.061 - 0.080	0.061 - 0.070	0.031 - 0.035
0.081 - 0.100	0.071 - 0.080	0.036 - 0.040
0.101 - 0.120	0.081 - 0.090	0.041 - 0.045
0.121 - 0.140	0.091 - 0.100	0.046 - 0.050
0.141 - 0.160	0.101 - 0.110	0.051 - 0.055
0.161 - 0.180	0.111 - 0.120	0.056 - 0.060
0.181 - 0.200	0.121 - 0.130	0.061 - 0.065
0.201 - 0.220	0.131 - 0.140	0.066 - 0.070
0.221 - 0.240	0.141 - 0.150	0.071 +
0.241 - 0.260	0.151 - 0.160	
0.261 - 0.280	0.161 - 0.170	
0.281 - 0.300	0.171 - 0.180	
0.301 - 0.320	0.181 - 0.190	
0.321 - 0.340	0.191 - 0.200	
0.341 - 0.360	0.201 +	
0.361 - 0.380		
0.381 - 0.400		
0.401 +		

TABLE 2.3 Ozone Concentrations (ppm) at which Responses Rates Need to be Estimated^a

Acute, 1-hour	Acute, 8 hours	Seasonal
0.040	0.040	0.025
0.051	0.051	0.029
0.071	0.066	0.034
0.091	0.076	0.038
0.111	0.086	0.043
0.131	0.096	0.049
0.151	0.106	0.054
0.171	0.116	0.058
0.191	0.126	0.064
0.211	0.136	0.068
0.231	0.146	-
0.251	0.156	-
0.271	0.166	-
0.291	0.176	-
0.311	0.186	-
0.331	0.196	-
0.351	-	-
0.371	-	-
0.391	-	-

^aThese concentrations are approximately the midpoints of the intervals listed in Table 2.2

TABLE 2.4 Calculating Exposure Probabilities for pNEM Person-Occurrences Estimates

Ozone Concentrations (ppm) for Acute Data (1-hour)	Person-Occurrences ^a	Probabilities
0.000	7,564,509	(not required) ^b
0.011	59,187,424	(not required) ^b
0.031	13,932,709	(not required) ^b
0.051	6,913,499	0.073465
0.071	2,855,703	0.030346
0.091	1,758,979	0.018692
0.111	754,477	0.008017
0.131	465,824	0.004950
0.151	252,464	0.002683
0.171	207,844	0.002209
0.191	129,184	0.001373
0.211	56,346	0.000599
0.231	3,133	0.000033
0.251	23,523	0.00250
0.271	0	0.00000
0.291	0	0.00000
0.311	0	0.00000
0.331	0	0.00000
0.351	0	0.00000
0.371	0	0.00000
0.391	0	0.00000

^aTotal person-occurrences is 94,105,616

^bCalculations were not made for these concentrations because they are below the background level (0.04 ppm)

TABLE 2.5 Definitions of Six Alternative NAAQS

Designation	Averaging Time (hrs)	Expected Exceedances	Ozone Concentration (ppm)
ASIS	N/A ^a	N/A	N/A
Std1112	1	1	0.12
Std8110	8	1	0.10
Std8108	8	1	0.08
Std8508	8	5	0.08
Std8506	8	5	0.06

^aNot applicable

3 HEALTH EFFECTS DATA AND JUDGMENTS

Exposure to ozone can result in acute and chronic health effects. In this section we describe sources of information (data and judgments) for acute and chronic health effects attributable to ozone exposure. Acute health effects include changes in lung function (e.g., decreases in forced expiratory volume) and the onset of numerous symptoms (e.g., cough, pain on inspiration, chest discomfort). The information from these sources is used to develop a series of models. The models for acute effects are based on controlled human exposure studies. The criteria used to select the laboratory studies and a description of the individual studies used for the acute health effects models are discussed. Chronic health effects include the development of mild or moderate lesions in the centriacinar region of the lung. These chronic health models are based on expert judgments about lung injury attributable to long-term ozone exposure.

3.1 CRITERIA FOR SELECTING LABORATORY DATA

Controlled human exposure studies are thought to be most appropriate for developing exposure-response relationships acute health effects resulting from exposure to ozone. Controlled human exposure studies based on 1-hour, 2-hour, and 6.6-hour exposures are used to develop the health models. Criteria used to select the particular studies included:

- 1) Applicability to the population groups potentially most at risk. Studies with exposures at moderate or heavy exercise are of greatest interest because such subjects are thought to be more at risk than those at rest.
- 2) Comparability of total dose with exercise level and exercise protocol of particular interest.
- 3) Number of subjects. To limit the effects of small sample size, studies with at least 10 subjects per exposure level are desired.
- 4) Exposure concentrations. Studies with multiple concentration levels in the range of ambient levels are desired.
- 5) Individual subject data is needed to develop exposure-response relationships.

3.2 1-HOUR EXPOSURE-RESPONSE RELATIONSHIPS FOR HEAVILY EXERCISING POPULATIONS

Exposure-response relationships for the heavily exercising population are based on controlled human exposure studies performed by Avol et al. (1984), Kulle et al. (1985), and McDonnell et al. (1983). These studies provide enough information so that nine health endpoints can be defined for risk calculations: (1) decreases in forced expiratory volume in one

second (DFEV)* that are greater than or equal to 10% [DFEV $\geq$ 10%], (2) decreases in forced expiratory volume in one second that are greater than or equal to 15% [DFEV $\geq$ 15%], (3) decreases in forced expiratory volume in one second that are greater than or equal to 20% [DFEV $\geq$ 20%], (4) any cough [ACF], (5) any chest discomfort [ACH], (6) any lower respiratory symptoms [ALR], and moderate/severe respiratory symptoms [MCF, MCH, and MLR]. Not all of the studies support all of the endpoints. Table 3.1 indicates the endpoints associated with each study and Table 3.2 summarizes the characteristics of each study.

TABLE 3.1 Health Endpoints Associated with each Study

Endpoint	Avol et al. (1984)	Kulle et al. (1985)	McDonnell et al. (1983)
DFEV $\geq$ 10%	Yes	Yes	Yes
DFEV $\geq$ 15%	Yes	Yes	Yes
DFEV $\geq$ 20%	Yes	Yes	Yes
ACF	No	Yes	Yes
ACH	No	Yes	Yes
ALR	Yes	No	No
MCF	No	Yes	Yes
MCH	No	Yes	Yes
MLR	Yes	No	No

Differences in the three studies exist among the exercise protocols. The Avol study required 60 minutes of continuous exercise with no rest. The McDonnell study had 4 cycles of 15 minutes of rest and 15 minutes of exercise. And finally, the Kulle study consisted of 4 cycles of 14 minutes of treadmill exercise and 16 minutes of rest. These studies are used for 1-hour exposure under heavy exercise (≥ 30 l/min-m²). Even at the same ozone concentration levels, however, 2-hour exposures under intermittent exercise may not be equivalent to 1-hour exposures under continuous exercise. The same individuals were exposed at all concentration levels in the Avol and Kulle studies, while different subjects were exposed at each level in the McDonnell study.

Kulle and McDonnell inquired about cough and chest discomfort symptoms. Avol inquired about lower respiratory, upper respiratory, and nonrespiratory symptoms. Subjects in the Kulle and McDonnell studies ranked individual symptoms separately as either none, mild, moderate, or severe. Avol's subjects rated symptom severity as none, mild but noticeable only upon questioning, mild, moderate, severe, or incapacitating.

*Forced expiratory volume in one second is the maximum volume of air that an individual can expel from the lungs in 1 sec. Although forced expiratory volume can be measured over any length of time, only 1 sec intervals are considered in this report. The studies on which this report is based only provide forced expiratory volume measurements for 1 sec intervals.

TABLE 3.2 Summary of Studies Used in Developing 1-hour Exposure-Response Relationships for Heavily Exercising Individuals

	Avol et al. (1984)	Kulle et al. (1985)	McDonnell et al. (1983)
Number of subjects	50 bicyclists; 42 male and 8 female ^a	20 healthy males; 8 of 20 subjects exposed to 0.30 ppm ^b	135 healthy males
Exposure concentrations (ppm)	0.00, 0.08, 0.16, 0.24, and 0.32 ppm	0.00, 0.10, 0.15, 0.20, 0.25, and 0.30 ppm	0.00, 0.12, 0.18, 0.24, 0.30, and 0.40 ppm
Ventilation Rate	57 l/min	68 l/min	65 l/min
Exercise Pattern	continuous (10 minute warm-up, 60 minutes of continuous exercise, 10 minute cooldown and measurement)	intermittent (4 cycles of 14 minutes exercise alternated with 16 minutes of rest)	intermittent (4 cycles of 15 minutes of exercise and 15 minutes of rest)
Exercise Duration (heavy)	60 minutes	56 minutes	60 minutes
Exposure duration	1.33 hours	2 hours	2.5 hours ^c
Subject exposures	Exposed to all concentrations	Exposed to all concentrations	Divided about equally into 6 groups, each exposed to a single concentration

^aData were available only for 48 of the 50 subjects in the Avol et al. (1984) study.

^bData for 0.30 ppm exposures not reported in Kulle et al. (1985) were taken from Hayes et al. (1987a).

^cIncludes a final 30 minute period during which subjects rested and spirometric and symptoms measurements were made.

Because of the differences, each study is treated separately in this risk assessment. In spite of the differences, all of these studies were matched with 1-hour exposure durations. There are two related reasons for doing this. First, exercise duration for all 3 studies is about 1 hour. Second, it appears that the percentage change in FEV after 2 hours of intermittent heavy exercise is about the same as it is after 1 hour. Therefore, retaining the identity of each study for risk calculations makes it possible to investigate an additional source of uncertainty attributable to differences between the studies.

3.3 1-HOUR EXPOSURE-RESPONSE RELATIONSHIPS FOR MODERATELY EXERCISING POPULATIONS

Exposure-response relationships for moderately exercising populations are based on the laboratory study performed by Seal et al. (1993). The four health endpoints that can be derived from the laboratory data are: (1) DFEV $\geq$ 10%, (2) DFEV $\geq$ 15%, (3) DFEV $\geq$ 20%, and (4) any cough.

Unlike other studies in which only males were exposed, this study exposed white and black males and females. In total, three hundred seventy two subjects, ranging in age from 18 to 35, were exposed once for 2.33 hours to either 0.00, 0.12, 0.18, 0.24, 0.30, or 0.40 ppm ozone. Potential subjects were excluded from the study for any of the following reasons: family histories of cardiovascular disease; personal history of chronic cardiovascular or chronic respiratory disease; an acute respiratory infection within six weeks of the study; deficiency in glucose-6-phosphate dehydrogenase; sickle-cell disease; pregnancy; use of birth control pills within two weeks of the study; use of marijuana one week before exposure; consumption of alcohol 24-hours before exposure; or smoking more than a pack per year within the five years preceding the study.

Before exposure, subjects completed baseline pulmonary function tests and symptom questionnaires. The first 2 hours of exposure included alternating 15 minute periods of rest and exercise on a treadmill. Pulmonary functions tests and questionnaires were administered again after the exposure was completed. The questionnaire included questions concerning the presence of cough, shortness of breath, pain on deep inspiration, headache, eye itching, and sweating. The last three symptoms were classified as shams. The symptoms were rated as: 1 (none), 2 (mild), 3 (moderate), or 4 (severe). The only symptom analyzed in this report is coughing. Additional symptoms (e.g., shortness of breath and pain on deep inspiration) will be analyzed later. The study is summarized in Table 3.3.

3.4 8-HOUR EXPOSURE-RESPONSE RELATIONSHIPS

The Folinsbee et al. (1988), Hortsman et al. (1990), and McDonnell et al. (1991) studies provided the laboratory data for exposure-response relationships for 6.6-hour exposures. All three studies were conducted in EPA's controlled human exposure chambers in Chapel Hill, North Carolina. The data from the three studies are combined and are treated as one study, because there are enough similarities among the studies with respect to exercise protocols, the recruitment of subjects, the ozone concentrations to which subjects were exposed, grouping of symptoms, and the rating of symptom severity. The six health endpoints developed from the combined studies to be used in the risk calculations include: (1) DFEV $\geq$ 10%, (2) DFEV $\geq$ 15%, (3) DFEV $\geq$ 20%, (4) ACF, (5) pain on deep inspiration [PDI], and (6) shortness of breath [BRT]. A summary of the three studies is given in Table 3.4.

TABLE 3.3 Summary of the Study Used to Develop 1-hour Exposure-Response Relationships for Moderately Exercising Populations

Seal (1993)	
Number of subjects	372 black and white males and females;
Exposure concentrations(ppm)	0.00, 0.12, 0.18, 0.24, 0.30, and 0.40 ppm
Ventilation Rate	25 l/min;
Exercise Pattern	intermittent (4 periods of 15 minutes exercise, 15 minutes rest)
Exercise Duration	1 hour
Exposure duration	2.33 hours ^a
Subject exposures	Approximately 60 subjects exposed at each level; each subject exposed to only one concentration level

^aIncludes a final 20 minute period during which subjects rested and spirometric and symptom measurements were made.

The 10 subjects for the Folinsbee et al. (1988) study, who were between the ages of 18 and 33, were exposed once to clean air and once to an ozone concentration of 0.12 ppm. These sessions were separated by a minimum of one week and the exposure sequence was randomized. The exercise protocol included 6 sessions of 50-minutes of exercise on a treadmill or cycle ergometer. Each session was followed by a 10-minute rest and measurement period. Each subject was given an additional 35-minutes to eat lunch after the third period. Physiologic tests were performed prior to exposure, during and after each of the six exercise periods, and at the end of the exposure. The four symptoms that subjects were asked to evaluate were cough, discomfort on deep inspiration, eye irritation, and pain/discomfort in the legs. Symptoms were rated as: 0 (none), 1 (just noticeable), 2 (mild discomfort), 3 (moderate discomfort), or 4 (severe discomfort/pain). The rating scale for evaluating cough was: 0 (none), 1 (cough during spirometry only), 2 (spontaneous single cough), 3 (spontaneous multiple cough), and 4 (repeated spontaneous multiple cough).

Twenty-two males participated in the Horstman et al., (1990) study to evaluate pulmonary responses from exposure to ozone. Candidates were not allowed to participate if they had a condition that could be made worse if exposed to ozone or exercise, or if they had an acute respiratory infection within the previous four weeks. Exposures were separated by a minimum of 1 week and the exposure sequence was randomized. With few exceptions, all subjects were exposed to all four ozone concentrations. Measurements of forced expiratory

TABLE 3.4 Summary of Studies Used to Develop 8-Hour Exposure Response Relationships

	Folinsbee et al. (1988)	Horstman et al. (1990)	McDonnell et al. (1991)
Number of subjects	10 nonsmoking males	22 nonsmoking males	38 males
Exposure concentrations(ppm)	0.00, 0.12 ppm	0.00, 0.08, 0.10, 0.12 ppm	0.00, 0.08, 0.10 ppm
Ventilation Rate	40.0 l/min	42.6 l/min	40.0 l/min
Exercise Pattern	50 minutes exercise, 10 minutes rest for each hour and 35 minute rest period after 3rd hour	50 minutes exercise, 10 minutes rest for each hour and 35 minute rest period after 3rd hour	50 minutes exercise, 10 minutes rest for each hour and 35 minute rest period after 3rd hour
Exercise Duration	5 hours	5 hours	5 hours
Exposure duration	6.6 hours	6.6 hours	6.6 hours
Subject exposures	Exposed to all concentrations;	Exposed to all concentrations; one subject experiences respiratory problems at 0.10 ppm.	28 Subjects exposed only to 0.00 and 0.08; 10 subjects exposed to 0.00, 0.08, and 0.10 ppm.

spirometry and symptoms ratings were obtained during 10 minute rest periods after each session. One of the 22 subjects did not complete all four 6.6 hour exposures; he was not exposed at 0.12 ppm because of severe respiratory symptoms at 0.10 ppm ozone (although his pulmonary function responses at 0.08 and 0.10 ozone were not markedly greater than the means of the group). In addition to the primary spirometric measurements, the subjects also rated the same four symptoms as in the Follinsbee et al. (1988) study.

Of the 38 males who participated in the McDonnell et al. (1991) study, 28 subjects were exposed twice: once to clean air and once to 0.08 ppm of ozone. The remaining 10 subjects were also exposed to 0.10 ppm ozone. Exposures were separated by at least 2 weeks. Candidates were excluded if they had ever smoked regularly, if they had a history of asthma, allergic rhinitis, cardiac disease, or acute respiratory illness within the previous four weeks. Five minutes immediately following the last exercise period, airway resistance, forced expiratory spirometry, and symptoms measurements were performed. Subjects were asked to rate cough, pain in deep inspiration, and shortness of breath. Symptom severity was rated as: 0 (none), 1 (barely noticeable), 2 (mild), 3 (moderate), or 4 (severe).

These 6.6 hour studies have been matched with 8-hour exposure estimates to perform risk calculations. It seems reasonable to do this because response seems to "level off" after several hours of exposure. Thus, it is unlikely that, even if the studies had been conducted for 8 hours, FEV decrements (especially after correction for an exercise effect) would have been appreciably different.

3.5 SEASONAL EXPOSURE-RESPONSE RELATIONSHIPS

During the last review of the ozone standard, which concluded early in 1993, the issue was raised as to whether long-term exposure to ozone at levels observed in areas such as southern California and the Northeast leads to chronic effects in the form of irreversible lung injury or lung disease. The results of animal toxicology studies discussed in Chapter 10 of the then-current ozone CD (EPA [1986]) suggest that ozone exposure at sufficiently high concentrations over a prolonged enough period may result in permanent structural changes to the lung.

To better understand the possible effects of prolonged exposure to ozone, EPA conducted a chronic risk assessment (Whitfield et al. [1991]; Winkler et al. [1994]). For this particular assessment, EPA chose mild and moderate lesions in the centriacinar region of the lung as the health endpoints. This region has been shown to be the location of the maximum ozone dose and maximum lung injury in a number of species exposed to elevated ozone concentrations. The populations of interest are children aged 6 through 18 and all adult outdoor workers in two urban areas — New York City and Los Angeles. These two groups are thought to be at greater risk for chronic effects because their members tend to be outdoors more than most individuals when ozone concentrations are at their highest, and children may be more vulnerable because their lungs are still developing.

While there are a number of newly published animal toxicology studies published since 1989, 5 of the 6 experts involved in the chronic risk assessment project agreed that there would not be any appreciable difference in their judgments about development of mild or moderate lesions in the centriacinar region of the lung if they were to give their judgments today. These same 5 experts also agreed that their judgment could be used by OAQPS to assess potential chronic lung effects associated with recent ozone levels and upon attainment of alternative 1- and 8-hour NAAQS for outdoor workers and children in the Los Angeles and New York urban areas. The sixth expert did not feel comfortable with the use of his/her judgments in the NAAQS review process. EPA does not plan to analyze alternative seasonal or chronic primary NAAQS at this time. Rather, the analysis is intended to provide some preliminary indication of the possible seasonal effects avoided (or remaining) upon attainment of alternative 1- or 8-hour NAAQS. EPA plans to consider this information as one of many factors in judging whether alternative standards provide an adequate margin of safety.

Probability encoding methods were used to develop exposure-response relationships for the formation of mild/moderate lesions in the human lung. It was necessary to perform judgmental probability encoding because adequate direct data regarding exposure-response relationships were not available. Six health scientists actively involved in research of ozone-induced pulmonary health effects provided probability judgments.

The judgments were obtained through a carefully-planned encoding and documentation process that had the following three steps:

1. Develop an encoding protocol.

A carefully developed encoding protocol was crucial to the success of the project. It ensured that the questions for the experts were always phrased identically, that specific assumptions and definitions were always the same, and that the encoding process proceeded similarly for each of the participants. Consequently, the differences in probability judgments could be attributed to true differences of opinion and not to differences in assumptions, understandings, or procedures.

In developing the encoding protocol, background material was assembled and the assessment team consulted extensively with individuals (named in the acknowledgments in Whitfield et al., 1991) having expertise in different aspects of the problem. Of particular concern were the appropriate health endpoints to consider and the best way to represent exposure conditions. However, many other points also required careful attention. Dealing with chronic rather than acute effects greatly increased the number of factors that had to be considered.

On the basis of the literature and discussions with consultants, a draft of the encoding protocol was prepared. At various points, the draft was circulated to some or all of the participating consultants. Written comments were received in some cases; meetings were held in others. In this manner, several drafts of the protocol were generated and revised.

After several revisions, the protocol was pilot-tested on an EPA staff member and an EPA contractor. Some weaknesses not previously recognized became apparent during the pilot testing, and the protocol was revised further to correct them. Consultations and discussions among members of the risk assessment team led to some final fine-tuning to create the protocol that was actually used in the encoding process.

The protocol became the guiding document of the probability encoding sessions that were conducted with the experts. It discussed many issues, including the following:

- Definitions of the health endpoints. The health endpoints of interest were mild and moderate centriacinar lesions.
- Discussion of exposure conditions. To deal with chronic effects, it was decided to consider damage in the centriacinar region of the lung over a single ozone season and also over 10 ozone seasons.
- Populations at risk. The populations considered for the encoding were all children aged 6 through 18 and all adult outdoor workers in Los Angeles and New York City.
- Factors to consider. This discussion reminded the experts of factors that may be relevant to their judgments: results reported in the literature, issues concerning extrapolation from animal studies, stages of response, time scales of effects, levels of repair, effects of varying the exposure concentrations over time (e.g., relative importance of cumulative exposure

versus peak exposure), and possible interactions of ozone with other air pollutants.

- Health significance. This discussion set the stage for an exploration of the experts' opinions about the long- and short-term health consequences of lung damage resulting from long-term ozone exposure. Important questions included how significant the centriacinar lesions are in themselves and what implications they might have for a person's future health.
- Factors to keep in mind when making probability judgments. This discussion was designed to help the experts provide probabilities that accurately represented their judgments. This objective was accomplished primarily through review of some commonly found cognitive biases and simplifying heuristics and through some suggestions on how to try to mitigate their effects. The topics covered include (1) effects related to the order in which evidence is considered or probabilities assessed, (2) the effect of memory on judgment, (3) the tendency to overestimate the reliability of information, (4) the influence of the importance of events on probability judgments, and (5) the difficulty of discriminating between levels of uncertainty.

2. Conduct encoding sessions.

Judgments were obtained during two rounds of encoding sessions. Between the two rounds of encoding sessions, all experts attended a workshop. At the workshop, first-round judgments were presented and discussed. Two or three members of the risk assessment team met privately with each expert to elicit his/her judgments. Judgments were not considered "final" until an expert "signed off" on his/her judgments that were recorded after the second round of encodings. The expert was free to change his/her judgments at any time before "signing off."

3. Review and communicate results.

The entire encoding process and results were carefully documented. Each expert received a written record of his/her judgments after each round of encoding. After the second round of encoding, the experts were asked to "sign off" on their judgments to signify that what was recorded accurately reflected their feelings and beliefs. The experts were free to change any of their judgments until they signed off. The entire process from time of receipt of the encoding protocol to time of sign off covered several months. Thus, there was ample time for the experts to give careful thought to their judgments.

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4 MODELING TECHNIQUES

The ozone risk assessment seeks to quantify the health risks for that portion of the population thought to be most sensitive to ozone exposure. The groups deemed potentially at risk to such exposures are identified by the ozone criteria document as: (1) those individuals with pre-existing respiratory disease, and (2) the general population of normal, healthy individuals, particularly those who are unusually responsive to ozone and those whose outdoor activities result in increased lung ventilation. The studies described in Section 3 are used to develop exposure-response relationships that will assess the impact that short-term exposures to ozone have on the populations identified in the criteria document. In addition, judgments of experts about the effects of long-term exposure to ozone are used to develop exposure-response relationships for chronic endpoints. The methodologies used to develop these exposure-response relationships are discussed in this section.

Three basic modeling techniques are described in this section: (1) correcting FEV decrement calculations for the effects of exercise in clean air; (2) developing probabilistic exposure-response relationships at desired exposure levels for acute health endpoints; and (3) developing exposure-response relationships at desired exposure levels for chronic health endpoints.

4.1 CORRECTING FEV DECREMENT CALCULATIONS FOR THE EFFECTS OF EXERCISE IN CLEAN AIR

Exercise in clean air may result in small increases or decreases in FEV. In principle, only the effect of ozone is of interest and the additional impact exercising in clean air has on FEV should be removed. The exposure-response relationships for changes in lung function are based on FEV measurements from the laboratory studies discussed in Section 3. The data required to compute the correction for exercise in clean air are the pre- and post-exposure FEV measurements in clean air and ozone. This correction is required on an individual subject basis. It was possible to apply this correction only to the 6.6-hr FEV data for moderate exercisers.*†

The first step in correcting the FEV decrement for the effects of exercise in clean air, is to compute the change in FEV, which is the difference between the FEV measurement prior to exposure (pre) and after exposure (post). This change is computed in clean air (i.e., 0 ppm ozone) and after exposure to ozone (i.e., $\Delta\text{FEV}_{\text{air}}$ and $\Delta\text{FEV}_{\text{ozone}}$). The average of the pre-exposure FEV measurements ($\text{AFEV}_{\text{pre, ozone}}$), including the FEV measurement at 0 ppm ozone,

*That is, for the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) studies.

†Thus, only the 8-hr exposure-response relationships for FEV endpoints are corrected for exercise and the risk results do not include any exercise effects. However, the risk distributions for the other endpoints also do not include the effects of exercise in clean air because this effect, if present, is therefore present in "intermediate" results at background, and "intermediate" results at background are subtracted to obtain the "final" risk distributions.

is then computed. The corrected decrement (DFEVC) is computed by dividing the change in FEV in clean air by the average of all pre-exposure FEV measurements and subtracting the result from the percent change in FEV from exercising in ozone. Mathematically, this is represented as:

$$\Delta FEV_{\text{ozone}} = FEV_{\text{pre,ozone}} - FEV_{\text{post,ozone}}$$

$$\Delta FEV_{\text{air}} = FEV_{\text{pre,air}} - FEV_{\text{post,air}}$$

$$AFEV_{\text{pre,ozone}} = \frac{\sum_{j=1}^N FEV_{\text{pre,ozone}}}{N}$$

$$DFEVC = \left[\frac{\Delta FEV_{\text{ozone}}}{FEV_{\text{pre,ozone}}} - \frac{\Delta FEV_{\text{air}}}{AFEV_{\text{pre,ozone}}} \right] \times 100\%$$

where:

N = Number of ozone concentrations.

The laboratory data from the McDonnell et al. (1991) study is used to illustrate the calculations. The FEV measurements for Subject 12 are given in the Table 4.1.

TABLE 4.1 FEV Data from McDonnell et al. (1991) — Subject 12

Obs	Subject	Pre	Post	Concentration (ppm)
67	12	2883	2939	0.00
68	12	2925	2712	0.08
69	12	3004	2535	0.10
70	12	2846	2349	0.12

Therefore, the decrement experienced by Subject 12 at an ozone concentration of 0.10 ppm is:

$$\Delta FEV_{\text{ozone}} = 3004 - 2535 = 469$$

$$\Delta FEV_{\text{air}} = 2883 - 2939 = -56$$

$$FEV_{\text{pre,ozone}} = \frac{(2883 + 2925 + 3004 + 2846)}{4} = 2914.5$$

$$\Delta FEVC = \left[\left[\frac{469}{3004} \right] - \left[-\frac{56}{2914.5} \right] \right] \times 100\% = 17.54\%$$

For simplicity, assume that the same pre FEV measurements occur at all ozone concentrations. As illustrated in Figure 4.1, an increase in DFEVC results when the pre-exposure FEV measurement at 0 ppm ozone is less than the post-exposure FEV measurement at 0 ppm ozone. There is a decrease in DFEVC when there is a decrease in FEV over the hours of exposure at 0 ppm ozone, as illustrated in Figure 4.2.

Some of the protocols did not include FEV measurements at both 0 ppm and non-zero ozone concentrations for individual subjects. For such studies, it is not possible to correct for the effects of exercise in clean air. In those cases, the decrement (DFEV) is simply the change in FEV over the length of exposure divided by the pre-exposure FEV measurement. Mathematically, this is expressed as:

$$DFEV = \frac{FEV_{\text{post,ozone}} - FEV_{\text{pre,ozone}}}{FEV_{\text{pre,ozone}}}$$

The exposure-response relationships for the various symptoms exhibited are based on the surveys administered during and after exposure from the laboratory studies discussed in Section 3. We did not correct symptom data for "exercise in clean air" because the symptoms are coded variables and it is not meaningful to compute the differences between pre-values and post-values. In some instances, the pre-value is greater than the post-value, and subtracting the pre-value from the post-value would result in a negative number. In this analysis we simply use the number of individuals that exhibit a symptom to estimate the fraction of the population experiencing a respiratory symptom.

4.2 DEVELOPING PROBABILITY DISTRIBUTIONS AT DESIRED EXPOSURE LEVELS FOR ACUTE ENDPOINTS

Developing exposure-response relationships for the desired exposure levels is a three step process (illustrated in Figure 4.3). The first step is to calculate the fractions of the individuals that are observed to experience a specific health endpoint at the various ozone concentrations. For example, for the 6.6-hour FEV data, 17 subjects out of 60 exposed at an ozone concentration 0.08 ppm, 13 subjects out of 32 exposed at 0.10 ppm, and 15 subjects out of 30 exposed at 0.12 ppm experienced an FEV decrement $\geq 10\%$. These fractions are

indicated in Figure 4.3. The fractions for FEV decrement are listed in Table 4.2 and the fractions for the symptom endpoints are listed in Table 4.3.

Using the observed data, the second step, as indicated in Figure 4.3, is to estimate the fractions of subjects expected to respond at the desired ozone concentrations that are listed in Table 4.4.* Regressions are performed on the data listed in Table 4.2 and Table 4.3 to estimate the mean response rate at the desired ozone concentrations. Continuing with the illustration in Figure 4.3, a regression equation fit to the points (0.08 ppm, $^{17}/_{60}$), (0.10 ppm, $^{13}/_{32}$), and (0.12 ppm, $^{15}/_{30}$) is used to estimate the fractions of individuals who are expected to experience a $\geq 10\%$ decrement in FEV (DFEVC $\geq 10\%$) at the desired ozone concentrations after 8 hours of exposure.

Various functional forms (normal, normal-on-log-odds, and lognormal) were fit to find the one that has the highest regression r^2 value. The normal-on-log-odds function generally gave the best results. Estimated parameters and regression r^2 values for the exposure-response relationships developed for each of the health endpoints are given in Table 4.5.

We used the expected fraction responding, a representative number of subjects that participated in a particular study, and the beta distribution to estimate uncertainty about the fractions of subjects who may experience a specific health effect at a particular ozone level. This is the third step in the method illustrated in Figure 4.3. For example, the expected numbers and fractions of subjects expected to respond (i.e., experience a DFEVC $\geq 10\%$) for the combined 6.6-hour studies are listed in Table 4.6. The numbers expected to respond and not respond are used as parameters of a beta distribution to calculate uncertainty about response rate at each ozone concentration. The representative number used (40 in this case) is equal or close to the average number of subjects that participated in the study. The values used for each of the acute health endpoints are listed in Table 4.7.

For the 8-hour DFEVC $\geq 10\%$ endpoint illustration, the expected numbers in Table 4.6 were used to calculate the uncertainty (a probability distribution) over the fractions (and percentages) of subjects who may experience DFEVC $\geq 10\%$ at the ozone concentrations of interest. For example, the response rate is $\leq 31.5\%$ with probability 0.95, is $\leq 10.9\%$ with probability 0.05, and is between 10.9% and 31.5% with probability 0.90, given that 8.1 out of 40 hypothetical subjects are expected to respond if exposed at 0.066 ppm of ozone, and that the beta distribution describes the uncertainty. This range is called the 90% credible interval (CI) on response rate and is a result of the third step illustrated in Figure 4.3. In combination with the median estimate, we always develop 10 central CIs. This results in a cumulative probability distribution with 21 points (fractiles) for every probabilistic exposure-response relationship.

* Note that the seasonal (chronic) background level is less than the acute background level. These levels are needed to be consistent with pNEM/O₃ exposure estimates. The first concentration listed is defined to be the background concentration, which will be used later to adjust overall risk results to account for response at background levels of ozone (i.e., to subtract the response at background).

This example corresponds to the results listed for the 0.05 and 0.95 fractiles in the 0.066 ppm column of Table 4.8, which lists all of the probability distributions needed to perform risk calculations for the DFEVC $\geq 10\%$, 8-hour health endpoint. One table like Table 4.8 was developed for every health endpoint, and each table is, in effect, a health model because it represents probabilistic exposure-response relationships for all exposure concentrations of interest.*

Probabilistic exposure-response relationships at moderate exercise developed for acute endpoints at moderate exercise supported by the Seal (1983), Horstman (1990), Folinsbee (1988), and McDonnell (1991) studies are shown in Figures 4.4-4.6. To avoid overly complicated figures, only the median, 0.05 fractile, and 0.95 fractile exposure-response relationships are shown. A total of 10 endpoints are included: 4 for the Seal study and 6 for the combined Folinsbee, Horstman, and McDonnell studies.

A special case arose when the response in clean air was significantly greater than zero. For example, as listed in Table 4.3, 17 subjects in the McDonnell 1-hour study had mild or worse chest discomfort at 0 ppm ozone, while 10 of 21 subjects had mild or worse chest discomfort at 0.12 ppm. In some cases like this, the exposure-response relationship developed without using the data at 0 ppm underestimated the response at background. To offset underestimates like this, we assumed that the results at 0 ppm would also occur at background (i.e., we included an "extra" data point in the regression step). This assumption, when needed, resulted in exposure-response relationships that better represented the data.

*None of the other tables are included in this report.

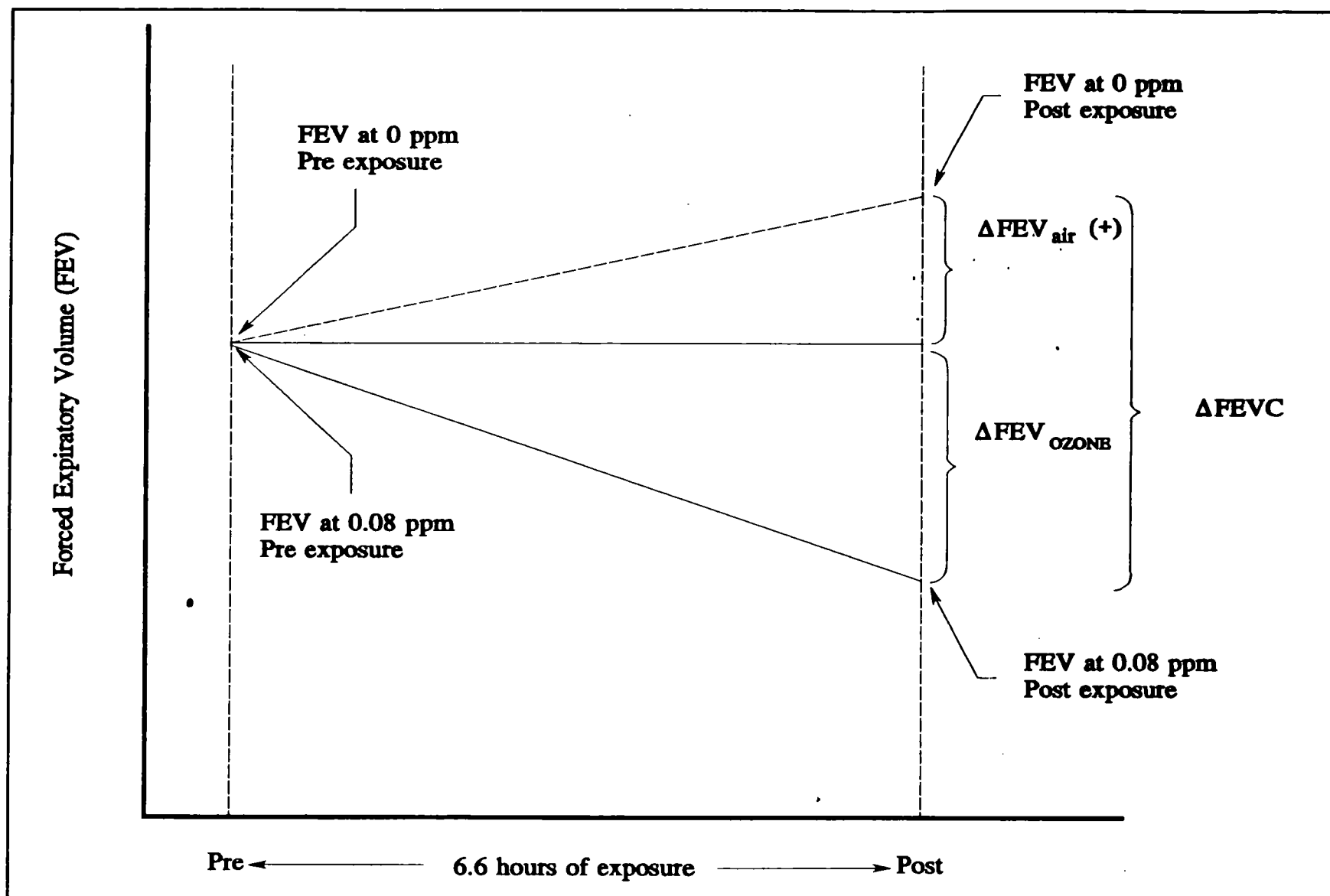
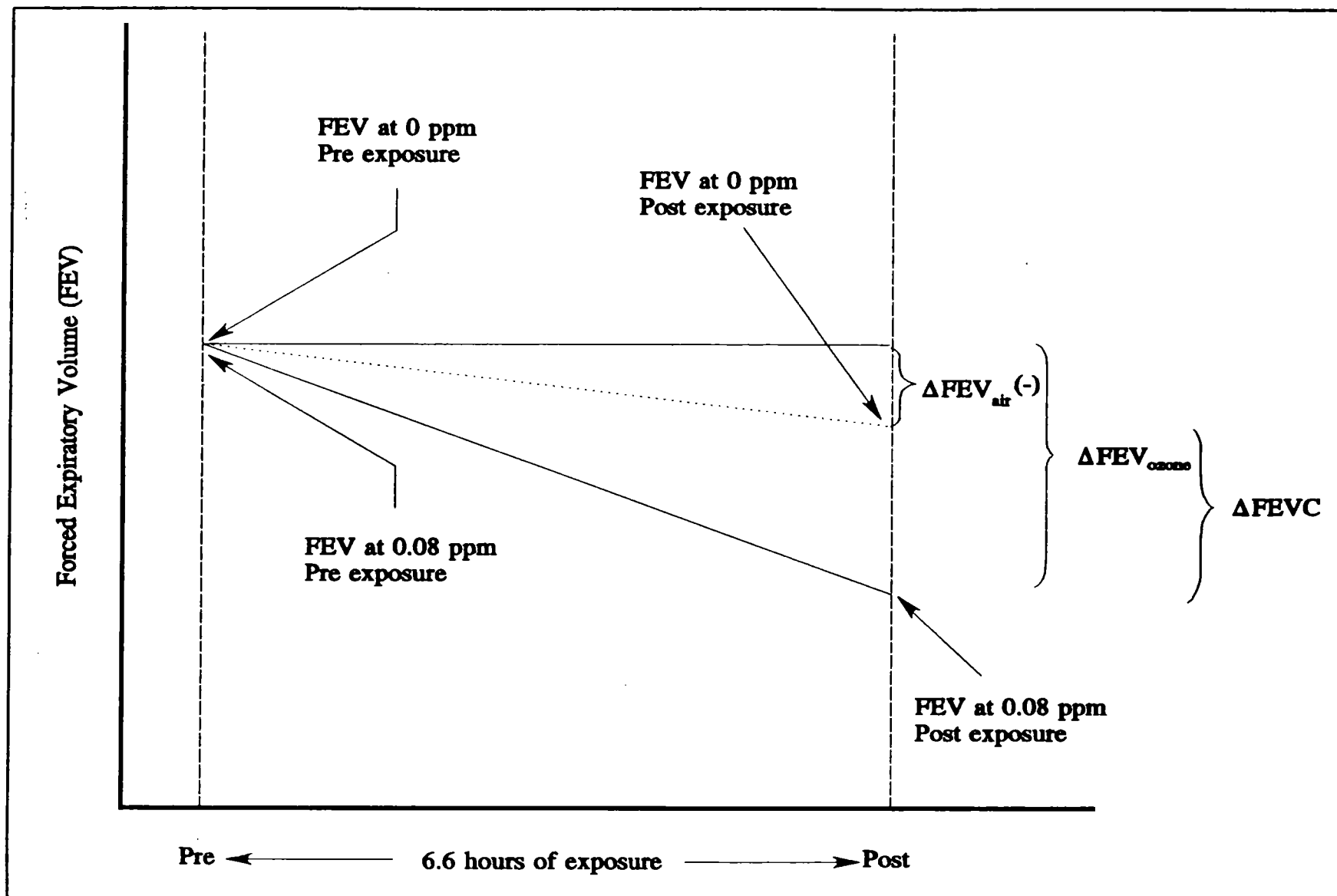
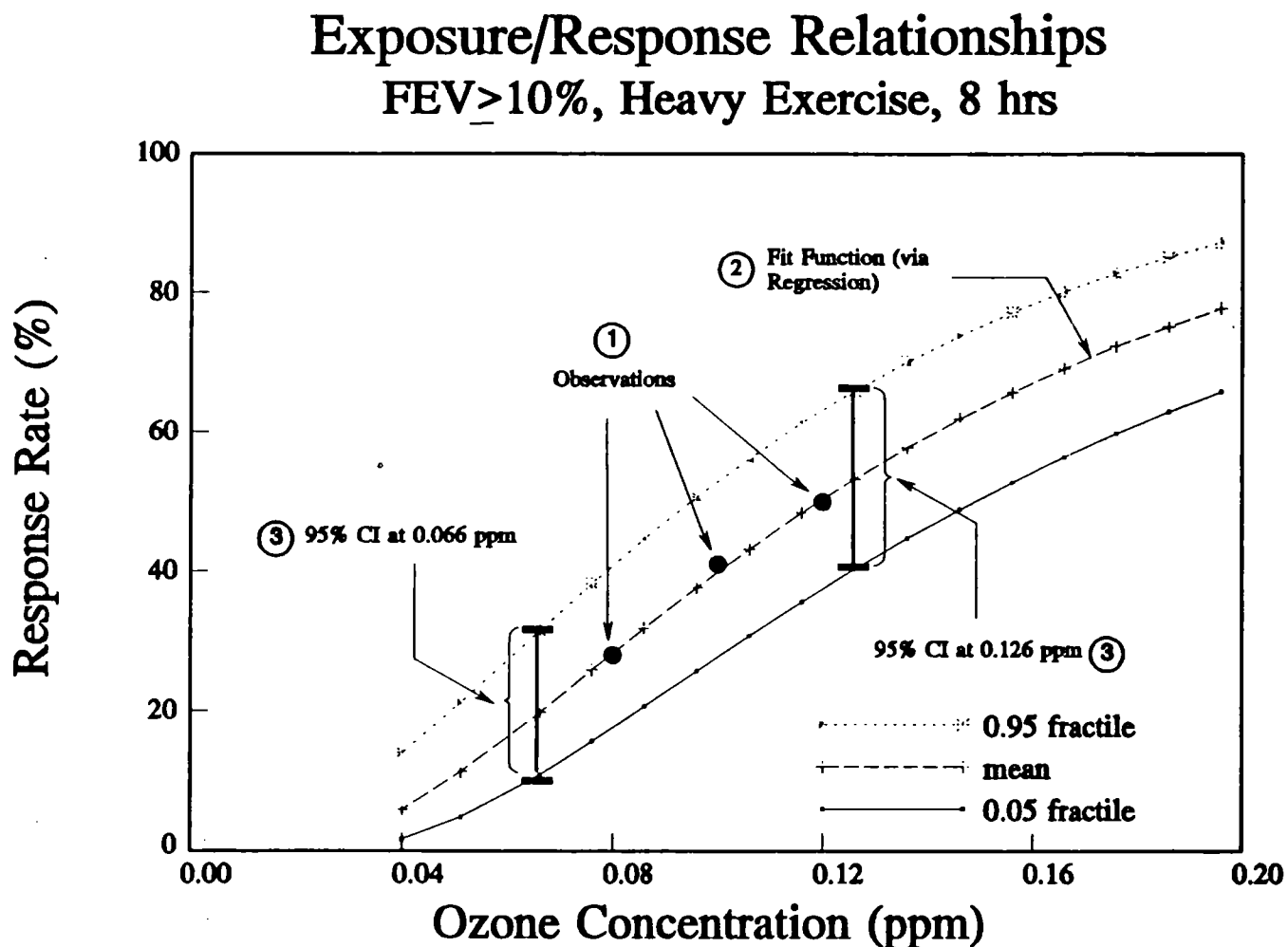


FIGURE 4.1 Effects of an Increase in Forced Expiratory Volume in Clean Air

**FIGURE 4.2** Effects of a Decrease in Forced Expiratory Volume in Clean Air



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FIGURE 4.3 Method to Estimate Response Rates for Acute Effects at Desired Ozone Concentrations.

TABLE 4.4 Exposures at which Responses Need to be Estimated

Acute, 1 hour	Acute, 8 hours	Seasonal
0.040	0.040	0.025
0.051	0.051	0.028
0.071	0.066	0.033
0.091	0.076	0.038
0.111	0.086	0.043
0.131	0.096	0.048
0.151	0.106	0.053
0.171	0.116	0.058
0.191	0.126	0.063
0.211	0.136	0.068
0.231	0.146	-
0.251	0.156	-
0.271	0.166	-
0.291	0.176	-
0.311	0.186	-
0.331	0.196	-
0.351	-	-
0.371	-	-
0.391	-	-

TABLE 4.5 Estimates of Parameters and Associated r^2 Values.

Study	Length of Exposure	Health Endpoint	Normal			LogNormal			NOLO		
			a	b	r^2	a	b	r^2	a	b	r^2
Avol et al. (1984)	1.33 hr	DFEV $\geq$ 10%	0.2232	0.0828	0.97	0.2023	1.6092	0.99	-1.3408	0.5760	0.99
		DFEV $\geq$ 15%	0.2498	0.1099	0.94	0.2405	1.5912	0.97	-1.1339	0.6094	0.96
		DFEV $\geq$ 20%	0.2872	0.1176	0.98	0.2827	1.6581	1.00	-0.9233	0.6600	0.99
"	"	Any Lower Resp	0.2407	0.1191	0.98	0.2216	2.5473	0.94	-1.2310	1.0693	0.96
"	"	Mod/severe Lower Resp	0.4490	0.1025	1.00	-0.6757	0.3687	1.00	-0.1108	0.5113	1.00
Kulle et al. (1985)	2 hrs	DFEV $\geq$ 10%	0.5024	0.2757	0.97	0.7138	3.1913	0.96	0.2834	1.5223	0.96
		DFEV $\geq$ 15%	0.5247	0.2021	0.98	0.7412	2.2472	0.99	0.3569	1.0798	0.99
		DFEV $\geq$ 20%	0.4163	0.1011	1.00	0.4584	1.4456	1.00	-0.2629	0.5080	1.00
"	"	Any cough	0.2563	0.1386	0.98	0.2515	1.8920	0.98	-1.0828	0.8151	0.98
"	"	Any chest discomfort	0.2483	0.0700	0.82	0.2435	1.3989	0.78	-1.1258	0.4240	0.80
"	"	Mod/severe cough	0.2325	-0.0169	1.00	0.2346	0.9403	1.00	-1.1865	-0.0848	1.00
"	"	Mod/severe chest discomfort	0.3167	0.0608	0.89	0.3265	1.2916	0.85	-0.7426	0.3357	0.87
McDonnell et al. (1983)	2.5 hrs	DFEV $\geq$ 10%	0.2944	0.1724	0.88	0.2773	2.0549	0.94	-0.9272	0.9502	0.92
		DFEV $\geq$ 15%	0.3353	0.1444	0.75	0.3266	1.8061	0.87	-0.7085	0.7847	0.83
		DFEV $\geq$ 20%	0.4170	0.2366	0.85	0.4262	2.2241	0.89	-0.3218	1.1376	0.87
"	"	Any cough	0.0857	0.1629	0.97	0.1133	2.0208	0.90	-2.0979	0.9184	0.93
"	"	Any chest discomfort	0.1276	0.2324	0.95	0.0961	4.752	0.85	-2.1871	1.8206	0.88
"	"	Mod/severe cough	0.2652	0.1844	0.36	0.2442	2.0448	0.44	-1.0923	0.9684	0.41
"	"	Mod/severe chest discomfort	0.3456	0.2225	0.96	0.3461	2.5776	0.98	-0.6384	1.2412	0.98

TABLE 4.5 (Cont.)

Study	Length of Exposure	Health Endpoint	Normal			LogNormal			NOLO		
			a	b	r ²	a	b	r ²	a	b	r ²
Seal et al., (1993)	2.33 hrs	DFEV ≥ 10 %	0.2690	0.1244	0.95	0.2493	1.6788	0.98	-1.0677	0.6834	0.98
		DFEV ≥ 15 %	0.3320	0.1437	0.99	0.3291	1.8672	0.97	-0.7077	0.8129	0.99
		DFEV ≥ 20 %	0.3941	0.1616	0.98	0.4364	2.0465	0.90	-0.3453	0.9264	0.93
"	"	Any cough	0.2502	0.1527	0.93	0.2194	2.8162	0.87	-1.2239	1.2068	0.90
Folinsbee et al., 1988; Horstman et al., 1990; McDonnell et al., 1992	6.6 hrs	DFEVC ≥ 10 %	0.1189	0.0699	0.99	0.1194	2.0267	1.00	-1.9991	0.7838	1.00
		DFEVC ≥ 15 %	0.1219	0.0443	0.98	0.1235	1.5761	0.95	-1.9617	0.5040	0.96
		DFEVC ≥ 20 %	0.1796	0.0738	0.95	0.2194	2.0988	0.97	-1.3230	0.8232	0.97
"	"	Shortness of breath	0.1634	0.0659	0.96	0.2762	2.7782	1.00	-1.1142	1.0919	1.00
"	"	Any cough	0.1044	0.0494	0.98	0.1033	1.9974	1.00	-2.1603	0.7443	1.00
"	"	Pain on deep inspiration	0.0909	0.0353	0.96	0.0854	1.6289	0.99	-2.3641	0.5254	0.99

TABLE 4.6 Estimates Regarding DFEVC $\geq 10\%$ for the 8-Hour Exposure-Response Relationships

Ozone Concentration (ppm)	Estimates of FEVC% $\geq 10\%$		
	Number Expected to Respond	Number Expected to Not Respond	Fraction Expected to Respond
0.040	2.652	37.348	0.066
0.051	4.767	35.233	0.119
0.066	8.131	31.869	0.203
0.076	10.491	29.509	0.262
0.086	12.842	27.158	0.321
0.096	15.124	24.876	0.378
0.106	17.303	22.697	0.432
0.116	19.353	20.647	0.484
0.126	21.267	18.733	0.532
0.136	23.039	16.961	0.576
0.146	24.670	15.330	0.617
0.156	26.165	13.835	0.654
0.166	27.530	12.470	0.688
0.176	28.773	11.227	0.719
0.186	29.904	10.096	0.748
0.196	30.931	9.069	0.773

TABLE 4.7 Number of Subjects Used (N) in Developing Probabilistic Exposure-Response Relationships

Study	Length of Exposure	Health Endpoint	N
Avol	1.33 hrs	DFEV $\geq$ 10%	48
		DFEV $\geq$ 15%	48
		DFEV $\geq$ 20%	48
"	"	Any Lower Resp	48
		Mod/Severe Lower Resp	48
Kulle	2 hrs	DFEV $\geq$ 10%	17
		DFEV $\geq$ 15%	17
		DFEV $\geq$ 20%	16
"	"	Any cough	18
		Any Chest Discomfort	18
		Mod/Severe Cough	20
		Mod/Severe Chest discomfort	17
McDonnell	2.5 hrs	DFEV $\geq$ 10%	22
		DFEV $\geq$ 15%	22
		DFEV $\geq$ 20%	22
"	"	Any Cough	22
		Any Chest Discomfort	21
		Mod/Severe Cough	22
		Mod/Severe Chest Discomfort	22
Seal	1.33 hrs	DFEV $\geq$ 10%	62
		DFEV $\geq$ 15%	62
		DFEV $\geq$ 20%	62
"	"	Any cough	61
Folinsbee, Horstman, McDonnell	6.6 hrs	DFEVC $\geq$ 10%	40
		DFEVC $\geq$ 15%	40
		DFEVC $\geq$ 20%	40
"	"	Shortness of Breath	54
		Any cough	48
		Pain on Deep Inspiration	48

TABLE 4.8 Probability Distributions Over the Percentage of the Population Having DFEV $\geq$ 10% (8-hr exposure-response relationships)^a

Frac- tile	Ozone Concentration (ppm)															
	0.040	0.051	0.066	0.067	0.086	0.096	0.106	0.116	0.126	0.136	0.146	0.156	0.166	0.176	0.186	0.196
0.01	0.8	3.1	8.1	12.2	16.7	21.3	26.0	30.6	35.1	39.4	43.4	47.3	50.9	54.3	57.4	60.4
0.05	1.7	4.8	10.9	15.6	20.6	25.7	30.7	35.6	40.2	44.7	48.8	52.7	56.4	59.8	62.9	65.8
0.10	2.3	5.9	12.6	17.7	22.9	28.2	33.3	38.3	43.1	47.5	51.7	55.7	59.3	62.7	65.8	68.6
0.15	2.8	6.8	13.8	19.1	24.5	29.9	35.2	40.2	45.0	49.5	53.7	57.6	61.2	64.6	67.6	70.5
0.20	3.3	7.5	14.9	20.3	25.8	31.3	36.6	41.7	46.5	51.0	55.3	59.2	62.8	66.1	69.1	71.9
0.25	3.7	8.2	15.8	21.3	27.0	32.5	37.9	43.0	47.9	52.4	56.6	60.5	64.1	67.3	70.4	73.1
0.30	4.2	8.8	16.7	22.3	28.0	33.6	39.1	44.2	49.1	53.6	57.8	61.6	65.2	68.5	71.5	74.2
0.35	4.6	9.4	17.5	23.2	29.0	34.7	40.1	45.3	50.2	54.7	58.9	62.7	66.3	69.5	72.5	75.2
0.40	5.0	10.1	18.3	24.1	29.9	35.7	41.2	46.3	51.2	55.7	59.9	63.7	67.3	70.5	73.4	76.1
0.45	5.5	10.7	19.0	25.0	30.9	36.6	42.2	47.4	52.2	56.7	60.9	64.7	68.2	71.4	74.3	76.9
0.50	5.9	11.3	19.8	25.8	31.8	37.6	43.1	48.4	53.2	57.7	61.9	65.7	69.1	72.3	75.2	77.8
0.55	6.4	11.9	20.6	26.7	32.7	38.6	44.1	49.4	54.2	58.7	62.8	66.6	70.1	73.2	76.0	78.6
0.60	6.9	12.6	21.5	27.6	33.7	39.6	45.1	50.4	55.2	59.7	63.8	67.6	71.0	74.1	76.9	79.4
0.65	7.5	13.3	22.3	28.6	34.7	40.6	46.2	51.4	56.3	60.7	64.8	68.5	71.9	75.0	77.8	80.3
0.70	8.1	14.1	23.3	29.6	35.8	41.7	47.3	52.5	57.4	61.8	65.9	69.6	72.9	75.9	78.7	81.1
0.75	8.8	15.0	24.3	30.7	36.9	42.9	48.5	53.7	58.5	63.0	67.0	70.6	73.9	76.9	79.6	82.0
0.80	9.6	16.0	25.5	31.9	38.2	44.2	49.8	55.0	59.8	64.2	68.2	71.8	75.1	78.0	80.6	83.0
0.85	10.6	17.2	26.9	33.4	39.8	45.8	51.4	56.6	61.3	65.7	69.6	73.2	76.4	79.2	81.8	84.1
0.90	11.9	18.7	28.7	35.3	41.7	47.7	53.3	58.5	63.2	67.5	71.3	74.8	77.9	80.7	83.2	85.4
0.95	14.0	21.2	31.5	38.2	44.6	50.6	56.2	61.3	65.9	70.1	73.8	77.2	80.2	82.8	85.2	87.3
0.99	18.5	26.2	36.8	43.7	50.1	56.0	61.5	66.4	70.8	74.7	78.2	81.3	84.0	86.4	88.5	90.3

^aThe first column and any other column together define a cumulative probability distribution. For example, the distribution for 0.04 ppm ozone is specified by the first 2 columns: the response rate is $\leq 0.8\%$ with probability 0.01, $\leq 1.7\%$ with probability 0.25, $\leq 5.9\%$ with probability 0.5, $\leq 14\%$ with probability 0.95, and $\leq 18.5\%$ with probability 0.99.

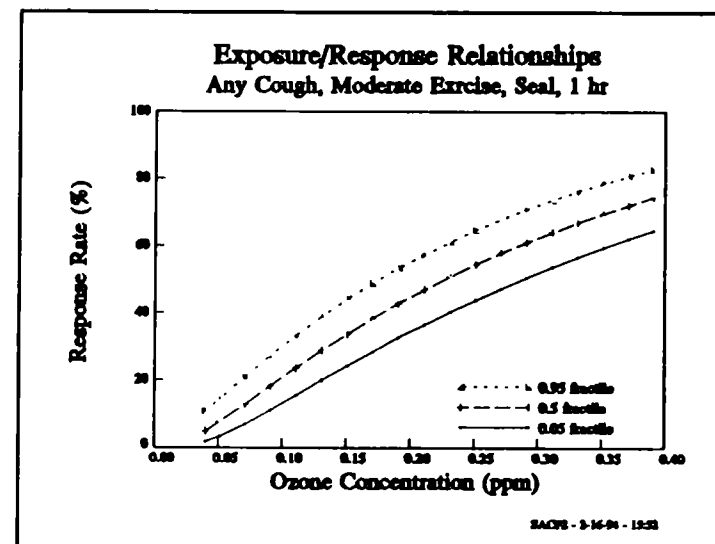
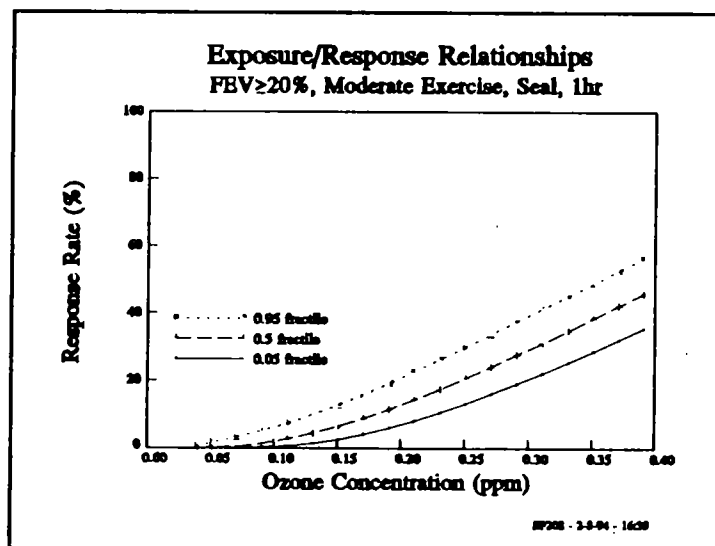
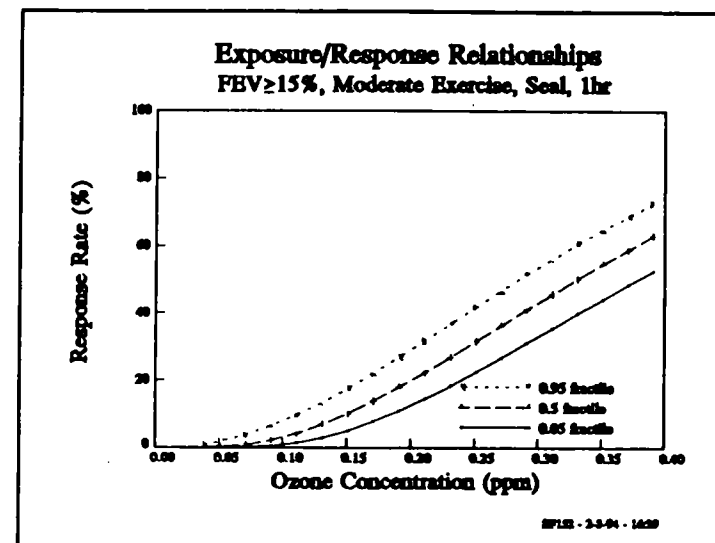
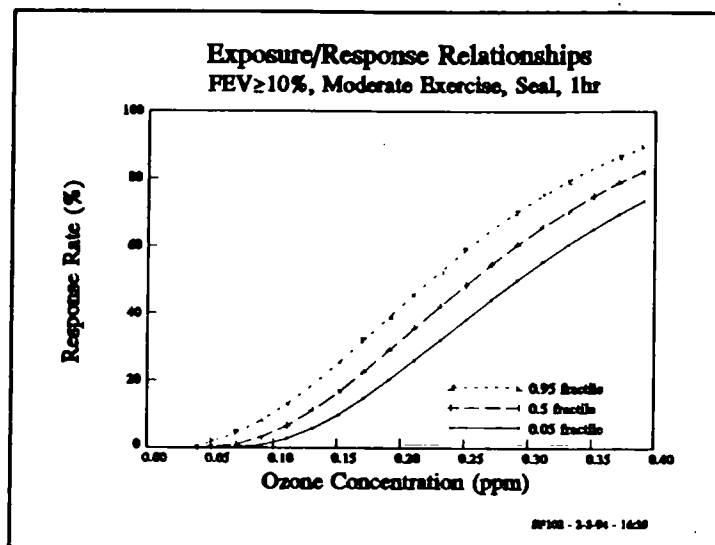


FIGURE 4.4 Medians and 90% CIs for Four 1-Hr Health Endpoints (DFEV ≥ 10%, 15%, 20%, and any cough: moderate exercise, 1 hour exposures; basis: data from Seal et al. [1993])

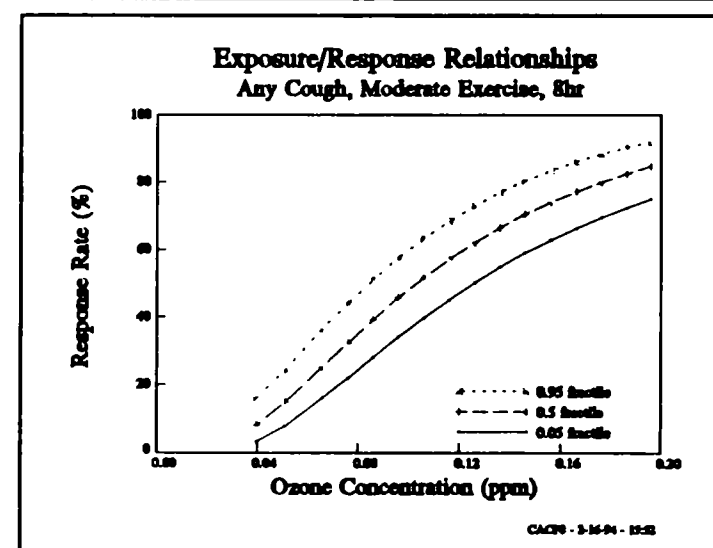
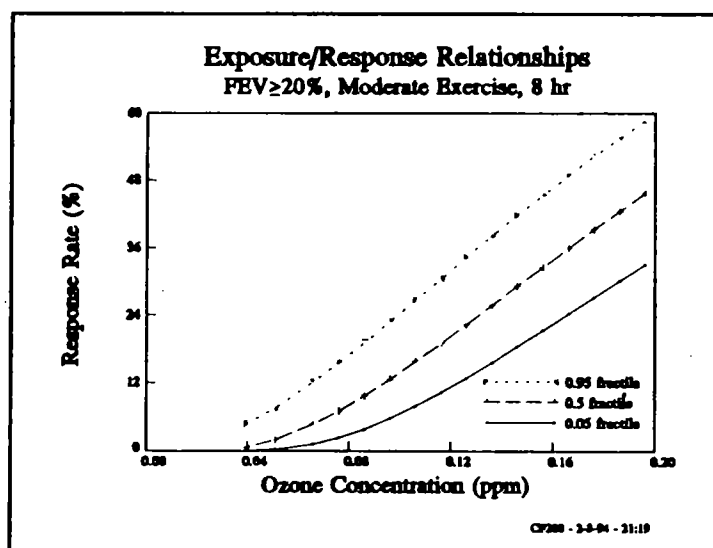
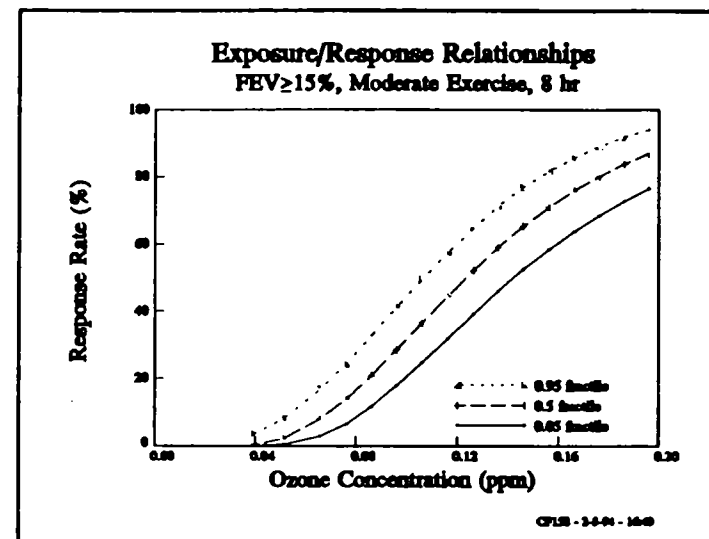
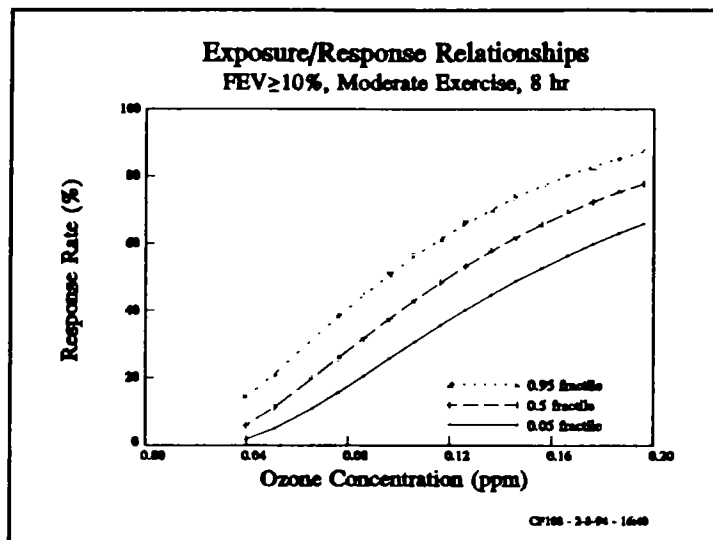


FIGURE 4.5 Medians and 90% CIs for Four 8-Hr Health Endpoints (DFEV₁ ≥ 10%, 15%, 20%, and any cough: prolonged moderate exercise; 8 hr exposures; basis: data from Folinsbee et al. [1988], Horstman et al. [1990], and McDonnell et al. [1991])

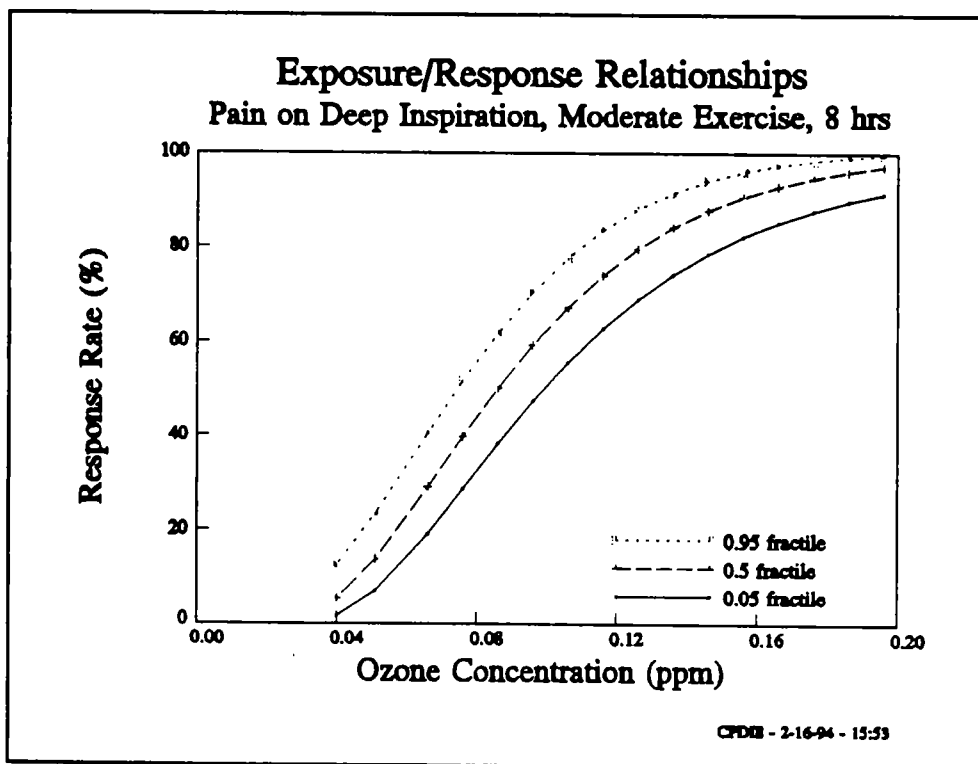
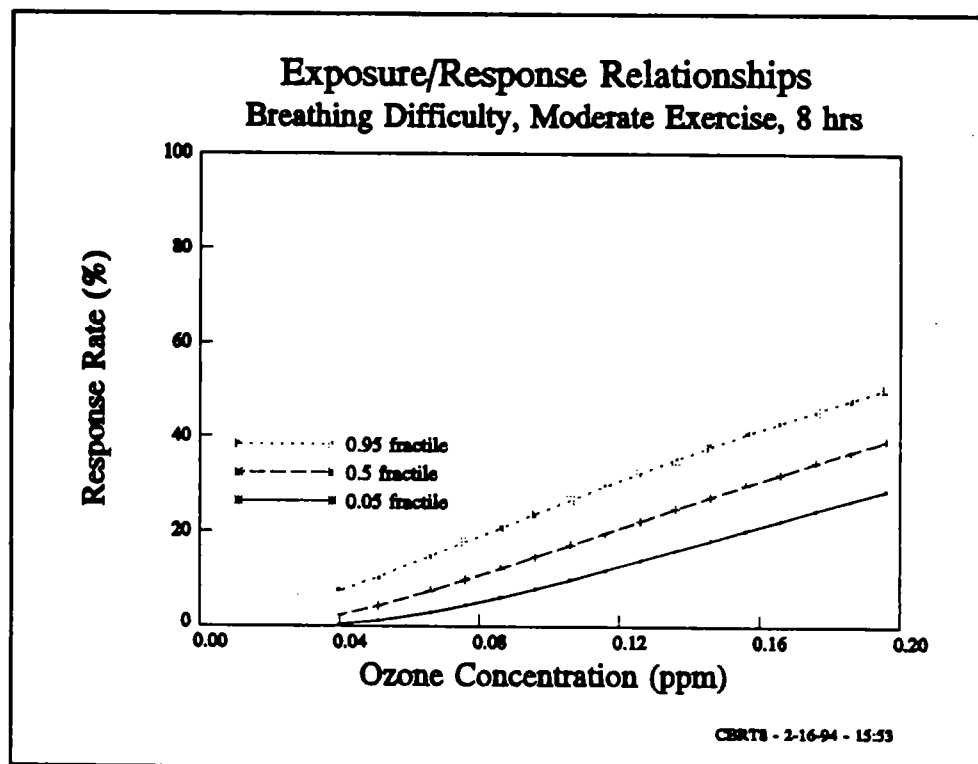


FIGURE 4.6 Medians and 90% CIs for Two 8-Hr Health Endpoints (breathing difficulty and pain on deep inspiration: moderate exercise, 8-hr exposures; basis: data from Folinsbee et al. [1988], Horstman et al. [1990], and McDonnell et al. [1991])

4.3 DEVELOPING EXPOSURE-RESPONSE RELATIONSHIPS FOR CHRONIC HEALTH ENDPOINTS

Six experts provided judgments about the probability of occurrence of ozone-induced lesions in the centriacinar region of the lung after exposure to ozone for 1 and 10 seasons. The judgments were obtained for several seasonal mean daily maximum 8-hour average ozone concentrations of personal exposure prior to any pNEM/O₃ results. At that time, it was decided to obtain judgments at ozone concentrations of 0.025, 0.050, 0.075, and 0.100 ppm. Figure 4.7 depicts the judgments of Expert A regarding the probability of formation of mild lesions among Los Angeles children after exposure to ozone for 1 season. The format reflects the way in which the judgments were obtained: conditional on the 4 ozone concentrations just mentioned.

Because these ozone concentrations do not match those for pNEM/O₃ exposure results, it was necessary to adjust the encoded judgments. The adjustment process is quite simple. The first step is to transform the judgments into a form that is more familiar to health scientists, which is shown in Figure 4.8. It shows exposure-response relationships for three fractiles (the 0.05, 0.50, and 0.95 fractiles). Also shown for completeness is the fact that Expert A (and all other experts) judged that there is no ozone-induced response at 0 ppm. The 0.05- and 0.95-fractile curves were determined by interpolation between assessed points shown in Figure 4.7, and they depict uncertainty in Expert A's judgments. If Expert A had been certain about the relationship between ozone exposure and the occurrence of ozone-induced lesions, only one curve would have been needed to completely characterize this belief. Points on the median (0.5 fractile) curve (which were available directly from the encoded judgments) are median response rates of 35%, 50%, 65%, and 75% for ozone concentrations of 0.025, 0.05, 0.075, and 0.1 ppm, respectively.

Given Figure 4.8, it is straightforward to specify probabilistic exposure-response relationships at any ozone concentration between 0 and 0.10 ppm by linear interpolation. The result of this interpolation is shown in Figure 4.9, which specifies median, 0.05-fractile, and 0.95-fractile exposure-response relationships at the pNEM/O₃ exposure concentrations. For example, the median response rate of 42.8% at 0.038 ppm was obtained by interpolation between the encoded values at 0.025 and 0.05 ppm.

A complete set of probability distributions for all pNEM/O₃ exposure concentrations is shown in Table 4.9. A set of tables like Table 4.9 has been developed for 5 of the 6 experts who provided probability judgments (Whitfield et al. [1989]; Winkler et al. [1994]).* Results only for Los Angeles and children based on one expert's judgments (Expert A) are presented in this report to illustrate the types of information that is available.

*As mentioned in Section 3.5, 5 of the 6 experts involved in the chronic risk assessment project agreed that there would not be any appreciable difference in their judgments about development of mild or moderate lesions in the centriacinar region of the lung if they were to give their judgments today. These same 5 experts also agreed that their judgment could be used by OAQPS in this assessment.

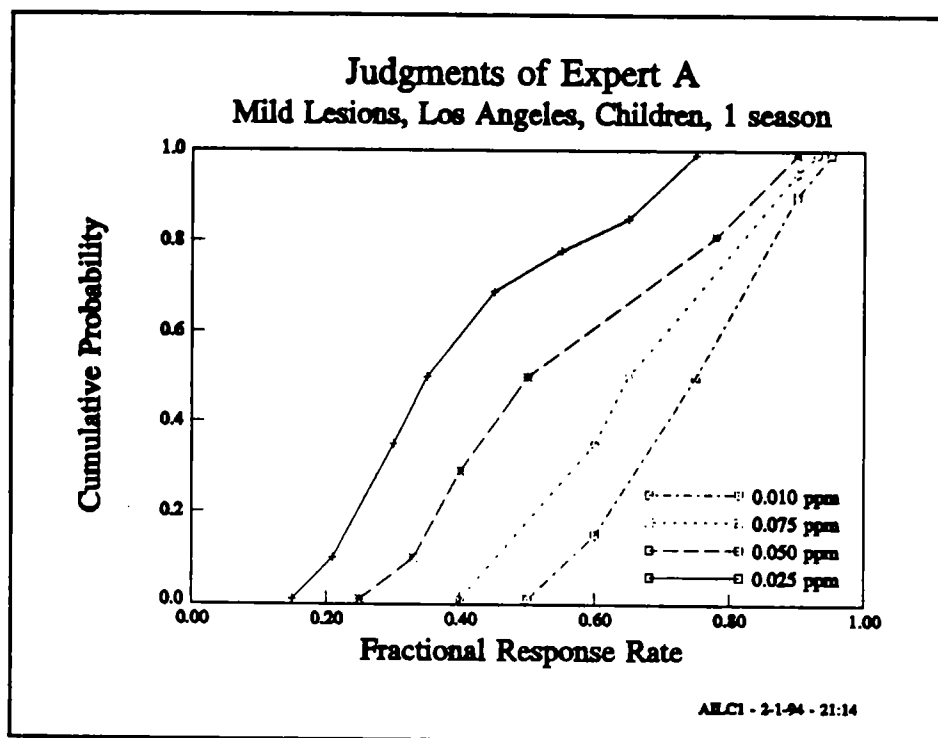


Figure 4.7 Encoded Judgments of Expert A (mild lesions, children, Los Angeles, 1 season)

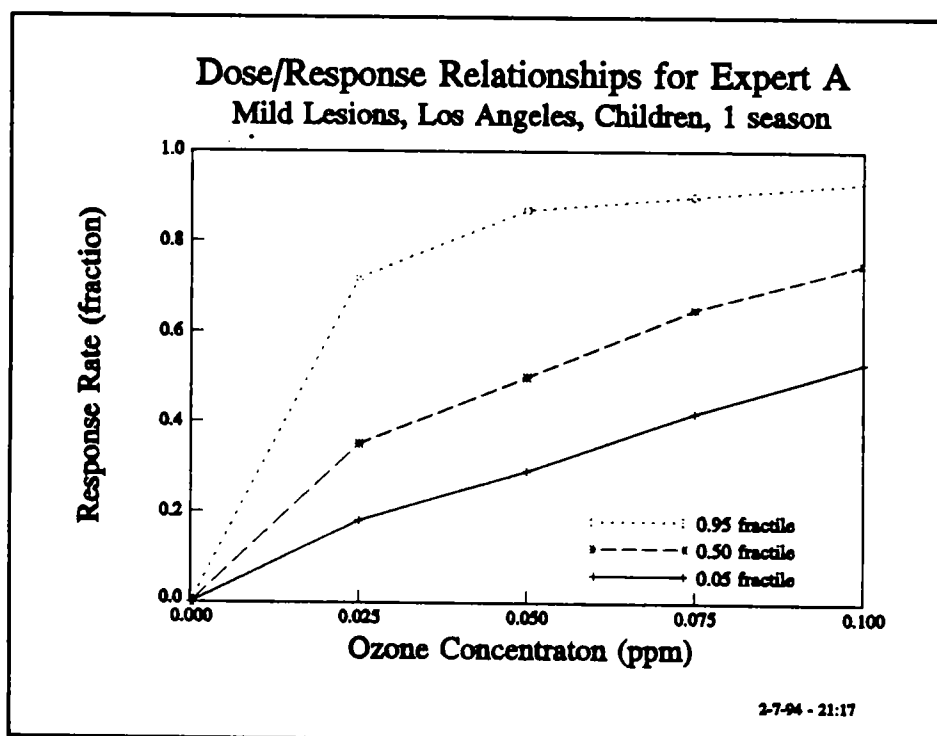


FIGURE 4.8 Judgments of Expert A in Exposure-Response Format

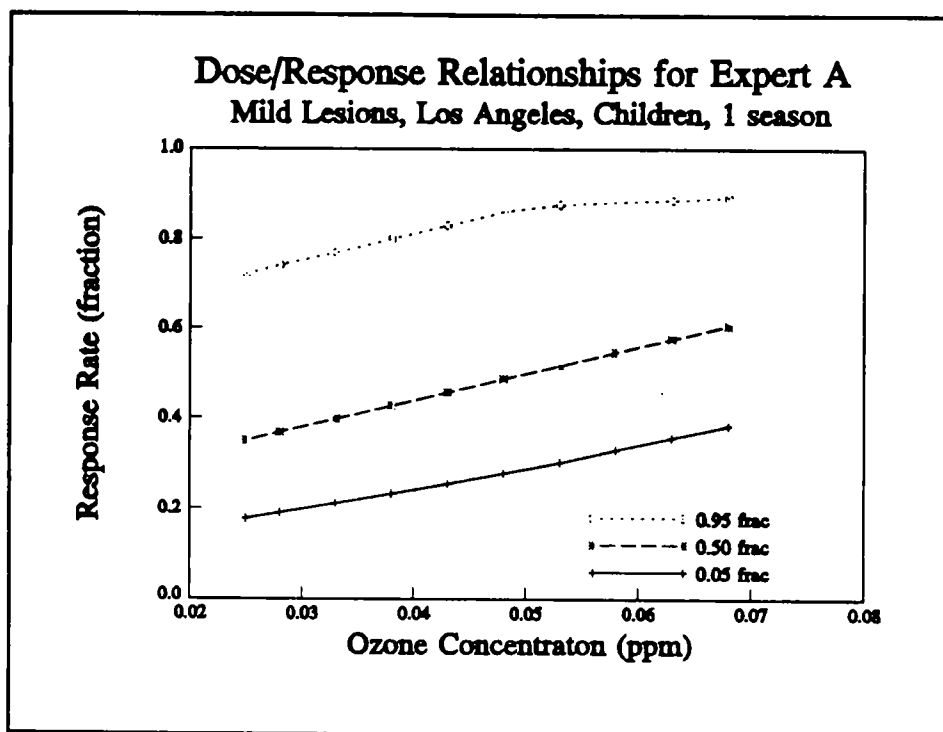


FIGURE 4.9 Judgments of Expert A Adjusted to pNEM/O₃ Exposure Concentrations

TABLE 4.9 Tabular Version of Expert A's Judgments About Percentage Response Rates at Ozone Concentrations Needed for the Risk Calculations (mild lesions, Los Angeles, children, 1 season)

Fractile	Ozone Concentration (ppm)									
	0.025	0.028	0.033	0.038	0.043	0.048	0.053	0.058	0.063	0.068
0.01	15.0	16.2	18.2	20.2	22.2	24.2	26.8	29.8	32.8	35.8
0.05	17.6	18.9	21.1	23.3	25.5	27.6	30.2	32.9	35.7	38.4
0.10	21.0	22.4	24.8	27.2	29.6	32.0	34.4	36.9	39.3	41.8
0.15	22.8	24.2	26.6	29.0	31.4	33.8	36.4	39.1	41.8	44.4
0.20	24.6	26.0	28.4	30.8	33.3	35.7	38.4	41.3	44.2	47.1
0.25	26.4	27.8	30.2	32.7	35.1	37.5	40.3	43.5	46.6	49.7
0.30	28.2	29.6	32.1	34.5	37.0	39.4	42.4	45.7	49.0	52.4
0.35	30.0	31.5	34.1	36.6	39.2	41.8	44.9	48.3	51.7	55.2
0.40	31.6	33.2	36.0	38.7	41.4	44.1	47.2	50.4	53.7	57.0
0.45	33.3	35.0	37.9	40.7	43.6	46.4	49.5	52.6	55.7	58.9
0.50	35.0	36.8	39.8	42.8	45.8	48.8	51.8	54.8	57.8	60.8
0.55	37.6	39.6	43.0	46.4	49.7	53.1	56.1	58.7	61.4	64.0
0.60	40.2	42.5	46.2	50.0	53.7	57.5	60.4	62.7	65.0	67.3
0.65	42.8	45.3	49.5	53.6	57.7	61.8	64.7	66.6	68.6	70.5
0.70	46.1	48.7	53.1	57.5	61.9	66.3	69.0	70.6	72.2	73.8
0.75	51.6	54.1	58.3	62.5	66.7	70.9	73.3	74.5	75.8	77.1
0.80	57.8	60.1	64.0	67.8	71.7	75.5	77.6	78.5	79.4	80.3
0.85	65.0	66.8	70.0	73.1	76.2	79.4	81.1	81.8	82.6	83.3
0.90	68.5	70.4	73.5	76.5	79.6	82.7	84.3	85.0	85.6	86.3
0.95	72.1	73.9	77.0	80.0	83.0	86.1	87.6	88.1	88.7	89.2
0.99	75.0	76.8	79.8	82.8	85.8	88.8	90.3	90.9	91.5	92.1

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5 RISK MODEL

Having discussed the exposure and health models, the risk calculations are conceptually simple. We will illustrate with the calculations for the $FEV \geq 10\%$ health endpoint based on the Avol et al. (1984) data (which corresponds to individuals exercising heavily and continuously for 1 hr). This endpoint applies to the total population in a city, which we will take to be Los Angeles. The calculation requires a set of exposure probabilities for specific ozone concentrations (i.e., personal exposure concentrations) that come from pNEM runs, and a set of response rates that correspond to the exposure concentrations.

To illustrate the calculations, let P_j denote the fraction of the population having personal exposures at an ozone concentration of e_j ppm in a single pNEM/ O_3 run, let $RR_k|e_j$ denote the k -fractile response for $DFEVC \geq 10\%$ at ozone concentration e_j , and let $RR_k|background$ be the k -fractile response at background. In general, the risk (which is an expected fractional response rate) for the k^{th} fractile is:

$$R_k = \sum_{j=1}^N P_j \times [(RR_k|e_j) - (RR_k|background)]$$

or

$$\begin{aligned} R_k &= \sum_{j=1}^N P_j \times RR_k|e_j - \sum_{j=1}^N P_j \times RR_k|background \\ &= R_{k,1} + R_{k,2} \end{aligned}$$

where

N = the number of ozone concentrations.

Recall from Section 4 that it was possible to correct some exposure-response relationships (namely, the 8-hour FEV endpoints) for exercise in clean air. For those cases, the $RR_k|e_j$ values reflect this correction. Therefore, the intermediate result $R_{k,1}$ does not include any exercise effect, nor does $R_{k,2}$ or R_k . Furthermore, even if $R_{k,1}$ and $R_{k,2}$ do include an exercise effect, R_k does not.

Risk calculations for the 0.5-fractile (the median), for pNEM/ O_3 run number 1, and as-is air quality in Los Angeles are shown in Table 5.1. The table indicates that there are 18 ozone concentrations* above background involved in the calculations. Background ozone is considered to be ≤ 0.04 ppm. The entries in column C are the fractions of the heavily exercising population that are exposed to the corresponding ozone concentrations in column B. The entries

*The concentrations indicated in the Table 5-1 are the midpoints of intervals that are 0.02 ppm wide.

in column D are the expected fractional response rates at the corresponding ozone concentrations for the 0.5 fractile (i.e., median). The result is 0.005, or 0.5%. It happens that $RR_{0.5} | \text{background}$ is exactly zero. So, this result is unchanged after correcting for background. The final step is to multiply the fractional response rate by the number of person-occurrences to obtain, in this case, the median estimate of the number of times that individuals experience FEV decrements $\geq 10\%$. Note that an individual can experience an FEV decrement $\geq 10\%$ more than once in an ozone season. For pNEM run 1, the maximum possible number of person-occurrences is 94,105,616, so the median estimate is 485,585 person-occurrences, the measure of risk that we wish to use in this analysis.

TABLE 5.1 Calculating the Median of the Response Rate Distribution

A	B	C	D	E
Index j	e_j (ppm)	P_j	$RR_{0.5} e_j$	$RR_{0.05} = C \times D$
1	0.051	0.073465	0.00010785	0.000008
2	0.071	0.030346	0.01026799	0.000312
3	0.091	0.018692	0.04156534	0.000777
4	0.111	0.008017	0.09403153	0.000754
5	0.131	0.004950	0.16465874	0.000815
6	0.151	0.002683	0.24798385	0.000665
7	0.171	0.002209	0.33767622	0.000746
8	0.191	0.001373	0.42825932	0.000588
9	0.211	0.000599	0.51537905	0.000309
10	0.231	0.000033	0.59607661	0.000020
11	0.251	0.000250	0.66857661	0.000167
12	0.271	0.000000	0.73216012	0.000000
13	0.291	0.000000	0.78667853	0.000000
14	0.311	0.000000	0.83268019	0.000000
15	0.331	0.000000	0.87071312	0.000000
16	0.351	0.000000	0.90174723	0.000000
17	0.371	0.000000	0.92666693	0.000000
18	0.391	0.000000	0.94646038	0.000000
Column E Sum:				0.005160

To develop a probability distribution over person-occurrences that accounts for all of the conditions mentioned earlier, the above calculations are repeated for any number of fractiles. Results will usually appear "smoother" if a large number of fractiles are used. In this analysis, 21 fractiles are used to obtain the results presented in the next section.

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6 A DESCRIPTION OF RISK RESULTS

Risk results are presented in a set of figures in Appendix A. The figures describe all acute results and a sample of chronic results. These results have been "corrected for background," where background is defined as 0.04 ppm for acute exposures and 0.025 ppm for seasonal exposures. This correction, as explained in Sec. 5, involves subtracting the probability distribution over response at the background concentration from the probability distribution over response for ozone concentrations above background. As with many of our computations, this subtraction assumes perfect correlation and allows us to perform the correction by simply subtracting corresponding responses on a fractile-by-fractile basis. If, per chance, there is no response at a particular background concentration, then the "uncorrected" and "corrected" results are identical. This happened quite often in the chronic risk calculations because many of the experts judged that there would no response at concentrations as high as 0.05 ppm.*

One acute (FEV $\geq 10\%$, 1-hr exposure time, total population) and one chronic (mild lesions, children, 1 ozone season of exposure) endpoint are presented. Results are based on the Avol data and the judgments of Expert A for 6 air quality scenarios. We also compare acute results based on the Avol, Kulle, and McDonnell data. Although other results are available (e.g., for other 1-hr endpoints and other experts), the ones discussed in this section and the others presented in Appendix A are meant to be examples of the types of results that are available. Still other results are forthcoming (e.g., airway reactivity and brochoalveolar lavage endpoints for 1-hr exposures; and chronic effects for workers, which will be made available after OAQPS provides exposure estimates for workers).

Table 6.1 is a listing of the risk results for case AF101LT1 (Avol, FEV $\geq 10\%$, 1-hr exposure, Los Angeles, total population, as-is air quality [the first of the 6 scenarios]). Ten distributions are provided — one for each of the 10 pNEM/O₃ runs that are available for 1-hr exposure times in Los Angeles and as-is air quality. The first column lists cumulative probabilities for the distributions. For example, the 0.50 cumulative probability (0.5 fractile) estimates range from 424,896 (run 9) to 562,376 (run 10) person-occurrences. The mean, standard deviation (StdDev), and total number of *possible* person-occurrences (MaxPO) are listed at the bottom of the table. For run 1, the mean is 532,484, the standard deviation is 221,075, and MaxPO is over 94 million. Note that MaxPO is based on the total number of people who reached what we have defined as a heavy level of exercise in each pNEM/O₃ run, and that this number varies from run to run. The significance (if any) of this variation is one of the issues specifically addressed in this risk assessment.

Figure 6.1 is a plot of the data in Table 6.1. It also includes the results for just attaining the current ozone standard (Std1112: 1-hr averaging time, 1 expected exceedance, 0.12 ppm). Note that the risks are much lower if the standard is met (indicated by the fact that the

*For example, the judgments of Expert B about moderate lesions among Los Angeles children after exposure for 1 ozone season (Whitfield et al. [1989]).

TABLE 6.1 Probability Distributions Over Person-Occurrences of FEV $\geq 10\%$.

Code	Cumulative Probability	Incidences of FEV $\geq 10\%$ by pNEM/O ₃ Run									
		1	2	3	4	5	6	7	8	9	10
AF101LT1: Avol (heavy exercisers); forced expiratory volume $\geq 10\%$; 1-hr exposure; Los Angeles; total population; as-is air quality											
	0.01	198452	210669	176784	177397	182577	215202	169396	188993	166300	239602
	0.05	256171	271812	232942	236829	237544	277483	222398	251014	216383	306137
	0.10	294010	311479	270433	276953	273700	318125	257475	292060	249658	349147
	0.15	322986	341616	299410	308210	301474	349203	284440	323644	275437	381822
	0.20	348270	367753	324847	335816	325779	376312	308019	351296	298155	410180
	0.25	371708	391856	348529	361651	348367	401443	329905	376991	319399	436358
	0.30	394235	414916	371370	386680	370129	425603	350960	401737	339979	461431
	0.35	416446	437561	393957	411526	391636	449433	371735	426173	360419	486078
	0.40	438798	460262	416744	436675	413326	473423	392656	450788	381126	510810
	0.45	461704	483446	440154	462576	435602	498021	414110	476024	402482	536085
	0.50	485600	507553	464633	489707	458892	523693	436511	502338	424896	562376
	0.55	510999	533099	490717	518632	483702	550992	460347	530263	448855	590230
	0.60	538555	560735	519090	550075	510682	580623	486246	560476	474990	620342
	0.65	569157	591346	550690	585020	540719	613542	515064	593883	504161	653644
	0.70	604080	626195	586866	624878	575083	651121	548029	631783	537610	691472
	0.75	645253	667192	629658	671787	615702	695436	587003	676134	577217	735836
	0.80	695763	717393	682341	729169	665666	749812	634967	730067	625999	789958
	0.85	760817	781946	750435	802807	730183	819854	696951	798876	689044	859264
	0.90	849689	870025	843760	903038	818518	915546	781896	892045	775408	953451
	0.95	982163	1001236	983207	1052076	950395	1058183	908822	1030116	904348	1093328
	0.99	1180073	1197361	1191756	1275055	1147453	1271235	1098653	1236842	1096871	1302204
	Mean	532484	552747	514965	544334	506316	574307	481762	551155	472570	610654
	StdDev	221075	221685	228831	249084	217326	237771	209134	237445	210236	239341
	MaxPO	94105616	93406960	92967584	96200440	96209240	93398304	92577872	92722712	91940232	90044728

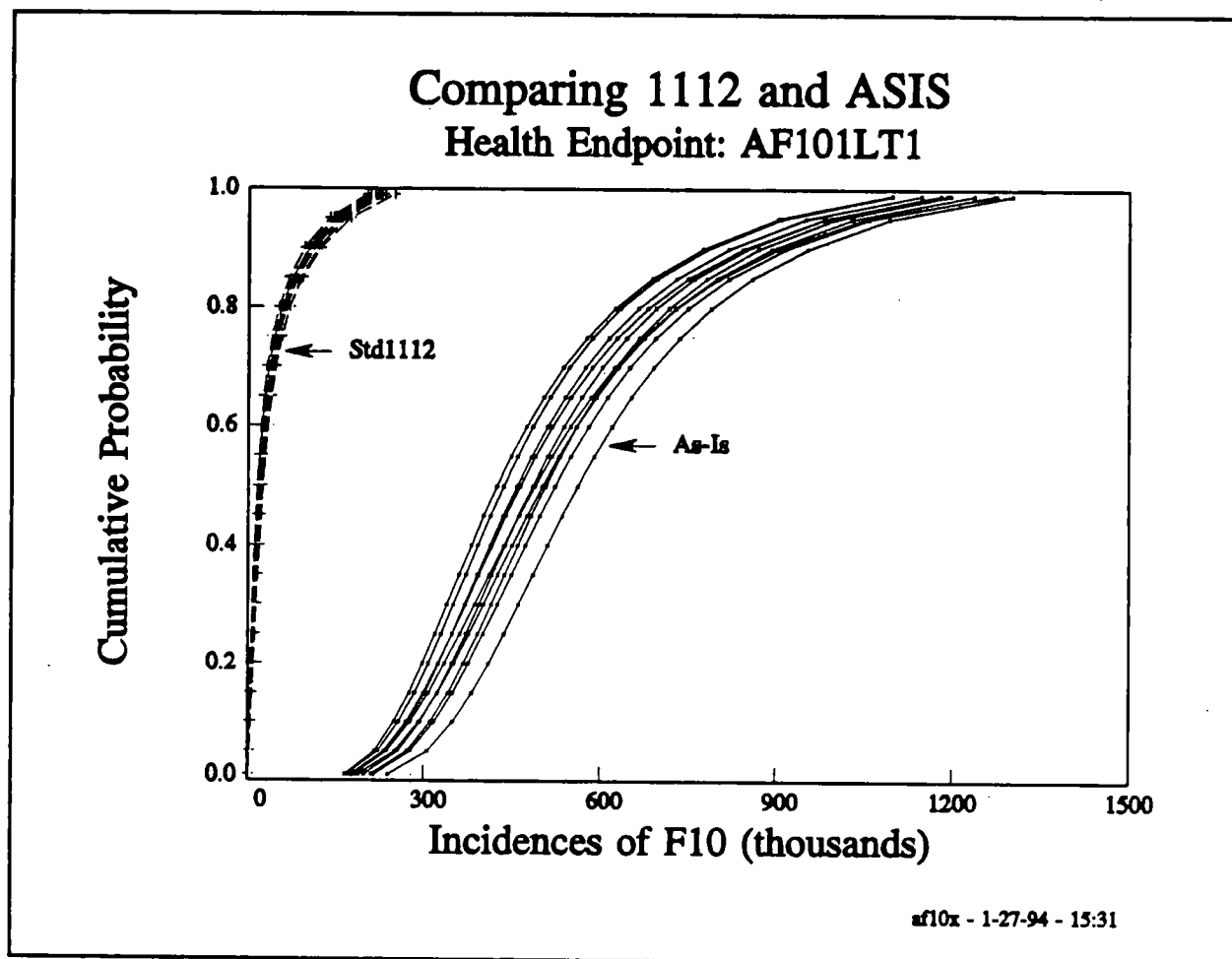


FIGURE 6.1 Risk Results for Two Air Quality Scenarios (as-is air quality and attainment of the current 1-hr standard; DFEV $\geq$ 10%, 1-hr exposures, Los Angeles, total population).

distribution is much closer to the Y-axis than the distribution for as-is air quality). Also note that the variation in results is much smaller for meeting the standard: the distributions are quite close to one another and are nearly indistinguishable, at least on the scale used in the figure. In contrast, the distributions for as-is are generally distinguishable.

On this scale, it is not helpful to plot the distributions for the other scenarios because, except for Std8110, they are even closer to the Y-axis than those for Std1112 and, if they were included, the figure would be quite messy. Figure 6.2 gives some idea of the range of results among each set of 10 distributions. There are 6 plots, one for each air quality scenario. Each plot is "representative" of the 10 distributions for a particular scenario. Since there are only 6 plots instead of 60, it is easier to see patterns. Each of these plots is a valid cumulative

probability distribution.* To gain some insights about the effects of attaining each standard, consider Figure 6.2, which shows that meeting the current standard is “better than” meeting Std8110, and that Std8108 and Std8508 are quite similar. As expected, Std8506 results in the lowest risk.

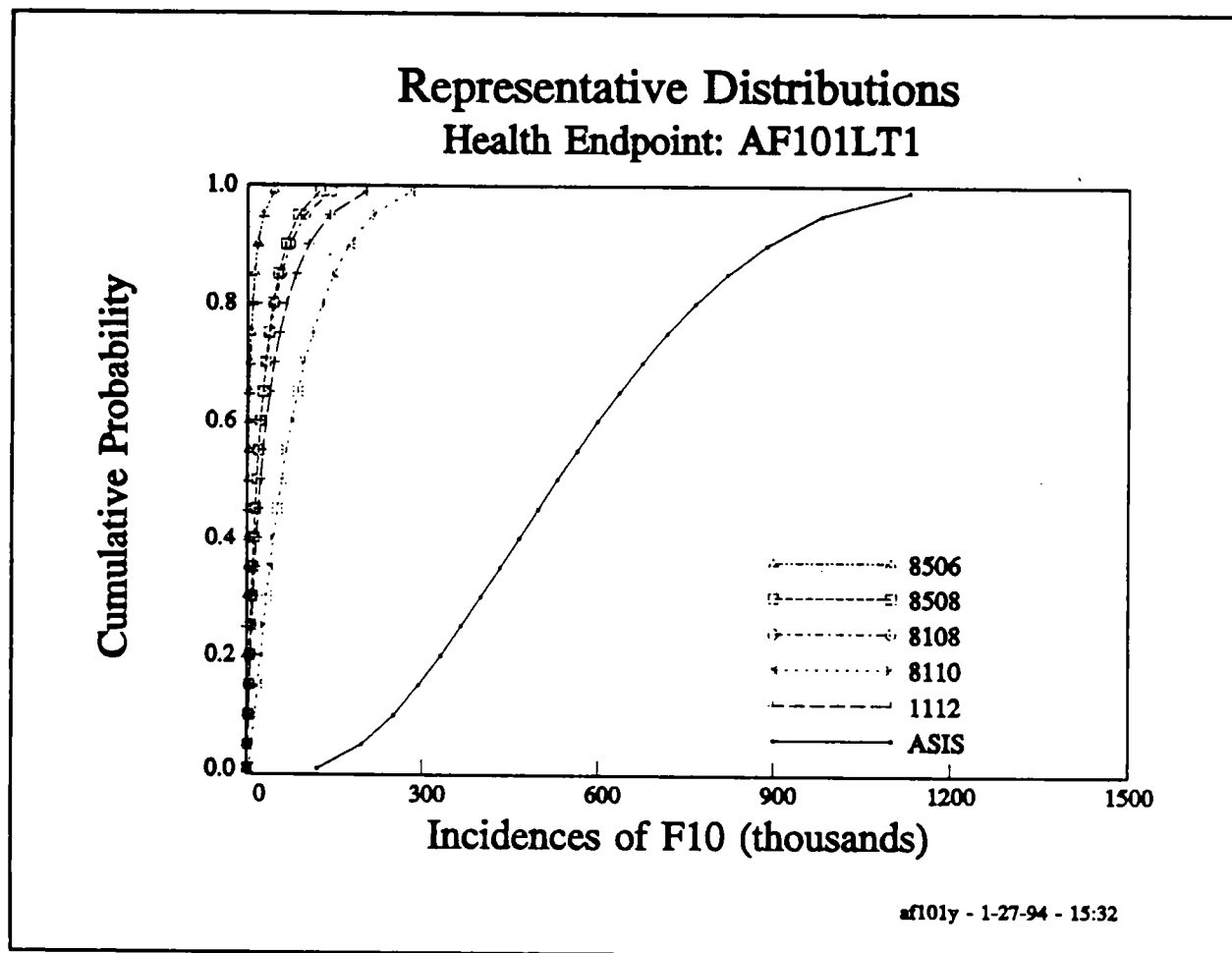


FIGURE 6.2 Representative Distributions for 6 Air Quality Scenarios (Avol, DFEV $\geq$ 10%, 1-hr exposures, Los Angeles, total population)

A final example (for an acute endpoint) of the types of comparisons that can be made is shown in Figure 6.3, which compares the representative risk distributions based on data from the Avol, Kulle, and McDonnell studies for as-is air quality. The highest risk estimates are

*The representative distribution is obtained by effectively integrating across all 10 distributions simultaneously and normalizing the result by dividing by 10. This calculation, like the risk calculations described earlier, implicitly assumes that the distributions are perfectly correlated. It may be argued that perfect correlation, while not correct, is more reasonable than perfect independence, and there is no basis for choosing any other degree of correlation between these 2 extremes.

based on the McDonnell study; but the McDonnell risk distribution intersect with the Avol risk distribution. The risk distribution based on the Kulle results lies strictly to the left of both the McDonnell and the Avol distributions.

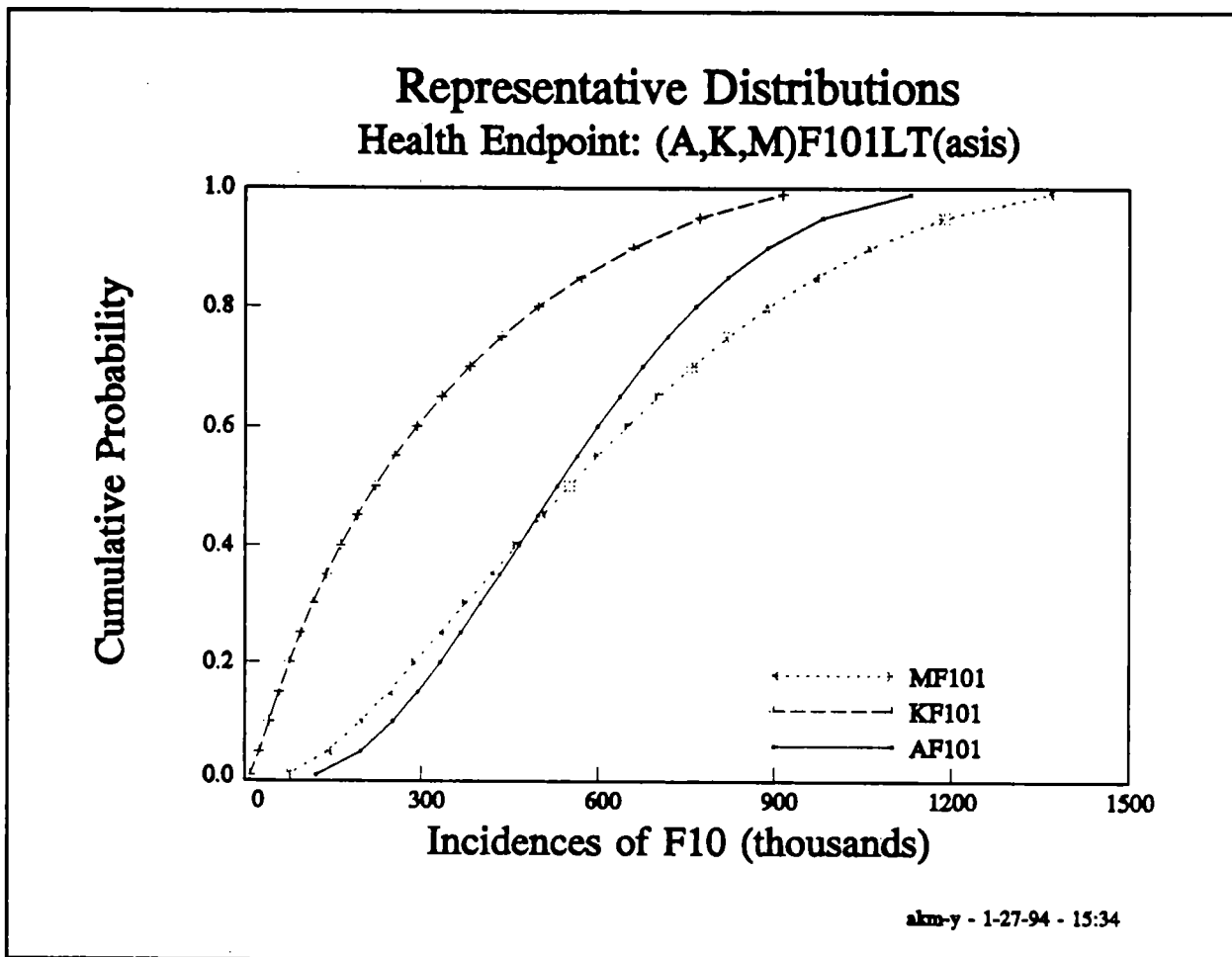


FIGURE 6.3 Comparison of $FEV \geq 10\%$, 1-Hr Exposures, As-Is Results Based on Data from Three Clinical Studies

Appendix A contains figures for all Los Angeles health endpoints associated with 1-hour exposures to ozone. They give an overview of the risk results and serve as a guide to more precise analysis that is made possible by results like those in listed in Table 6.1.

Figure 6.4 contains plots of risk distributions for the chronic endpoint AILC1 (Expert A, mild lesions, Los Angeles, children, 1 ozone season of exposure). There are two sets of 10 distributions, one set for each of two air quality scenarios — ScnASIS and Std8110. This figure is analogous to Figure 6.1 for a 1-hour endpoint. Variability in the risk distributions is partially attributable to run-to-run variations in the pNEM/O₃ exposure results.

Representative distributions for 5 air quality scenarios (results for the most stringent standard — Std8506 — coincide with the Y-axis because there is no risk of formation of mild

lesions when this standard is attained) are shown in Figure 6.5. This figure is analogous to Figure 6.2. Plots like these are shown in Appendix A for Expert A, mild and moderate lesions, Los Angeles, children, and 5 air quality scenarios.

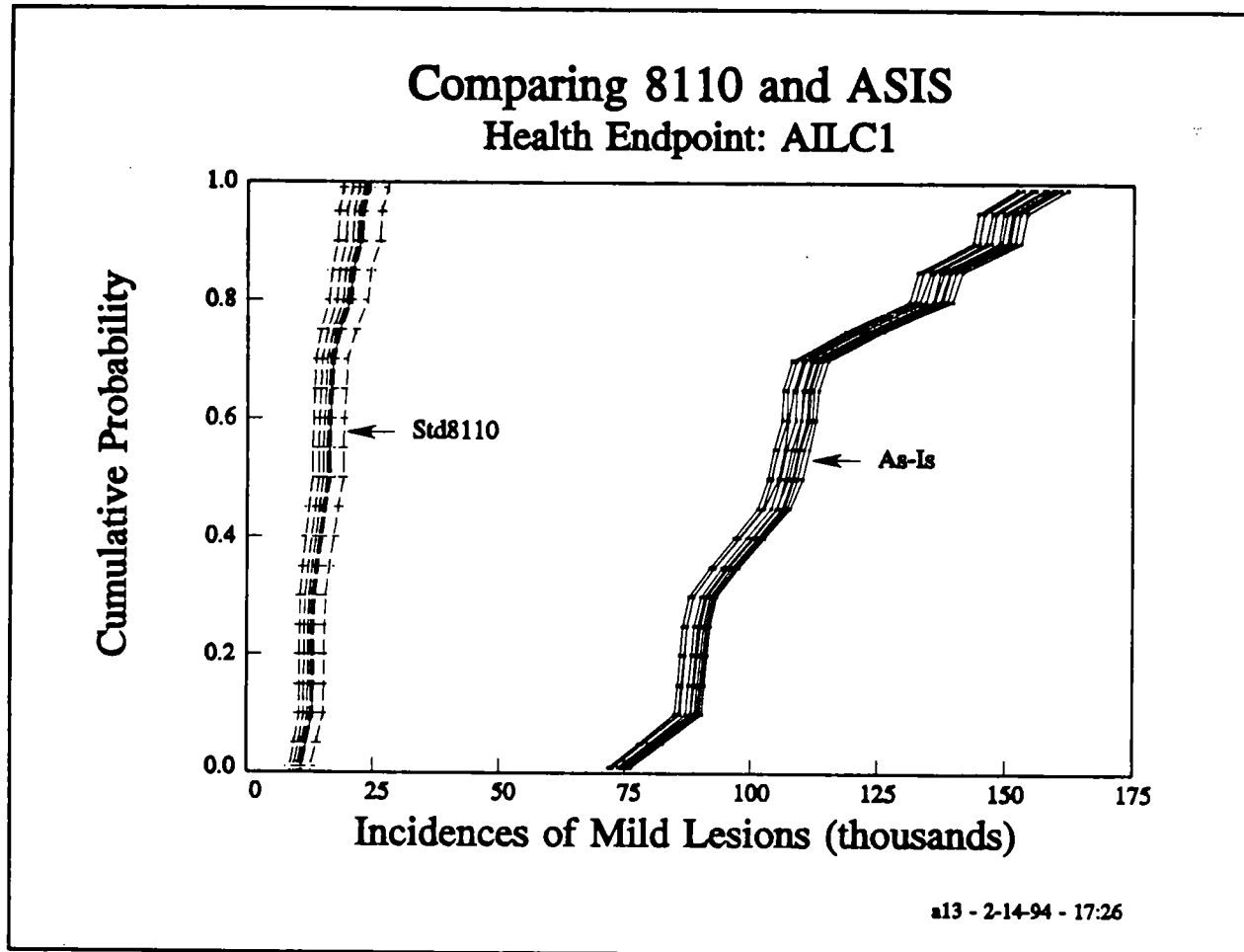


FIGURE 6.4 Risk Distributions for Mild Lesions Based on the Judgments of Expert A

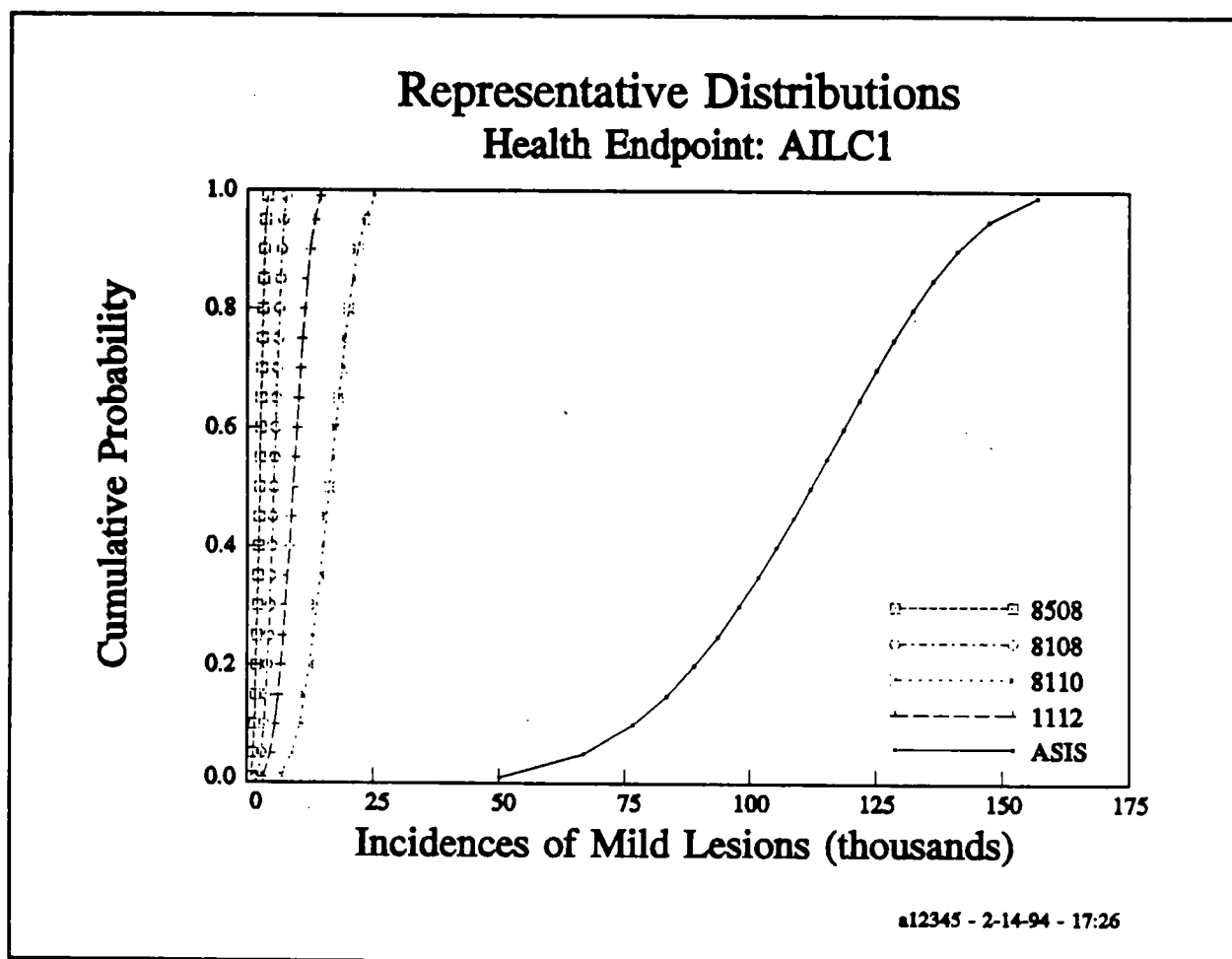


FIGURE 6.5 Representative Risk Distributions for Expert A (Note: Results for the most stringent standard — Std8506 — coincide with the Y-axis because there is no risk of formation of mild lesions when this standard is attained.)

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APPENDIX A

**RISK RESULTS FOR
SELECTED HEALTH ENDPOINTS**

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APPENDIX A

RISK RESULTS FOR SELECTED HEALTH ENDPOINTS

This appendix consists of 33 figures that contain risk distributions for selected health endpoints. Figures A.1-29 address acute endpoints (pulmonary function and symptoms, 1-hr exposures at heavy exercise, Los Angeles, total population) and Figures A.30-33 address chronic endpoints (mild and moderate lesions, Los Angeles, children, 1 and 10 ozone seasons of exposure). The figures are grouped according to health endpoint: 1-hr endpoints are first, 8-hr endpoints are next, and chronic endpoints are last.

In most cases, there is more than one figure for each acute endpoint — one figure for each study that supports an endpoint. For example, four studies* provide data on each 1-hr pulmonary function endpoint ($FEV \geq 10\%$, $\geq 15\%$, and $\geq 20\%$). Figures A.1-4 contain risk distributions for $FEV \geq 10\%$ based on data from the Avol, Kulle, McDonnell, and Seal studies, respectively. The next 4 figures are for $FEV \geq 15\%$, and the next 4 are for $FEV \geq 20\%$.

Each plot in each figure is representative[†] of 10 distributions, which result from available exposure distributions from pNEM/O₃ runs. It was necessary to develop representative distributions because there is generally too much overlap among the individual distributions, which would make it difficult (if not impossible) to distinguish results plotted on the scales that must be used to capture the full range of results for all air quality scenarios. Representative distributions effectively capture the range of variability in the results for a set of 10 runs.

As discussed in Section 6, all results (both acute and chronic) have been corrected for background ozone levels. Only DFEV results for 8-hr endpoints have been corrected for exercise in clean air for reasons discussed in Section 4.1.

Most figures for acute endpoints contain 6 representative distributions, 1 for each of the 6 air quality scenarios used in this analysis.[‡] There are a few exceptions — cases for which only the as-is scenario resulted in measurable risk. (Figure A.10 is an example.)

Figures for chronic endpoints contain 5 representative distributions; in all cases, the distribution for the most stringent standard — Std8506 — results in no risk and is not shown in any of the figures. (If it were shown, it would coincide with the Y-axis.) Only those results

*Avol et al. (1984), Kulle et al. (1985), McDonnell et al. (1983) provide data on heavily exercising individuals, and Seal et al. (1993) provide data on moderately exercising individuals. These data were used to develop 1-hr exposure-response relationships and subsequent risk distributions.

[†]See Section 6 for discussion about developing representative distributions.

[‡]Refer to Table 2.5 for definitions of the 6 air quality scenarios, 5 of which represent attainment of specific air quality standards.

based on the judgments of Expert A are shown. Results for other experts are available but are not included in this report.

The subtitle for each figure contains a code that identifies the health endpoint associated with the figure. The figure caption essentially interprets the code. For acute endpoints, a 7-character code (e.g., AF101LT) indicates the study (A = Avol, K = Kulle, M = McDonnell, S = Seal, and C = combined*), the health endpoint (F10 = FEV $\geq$ 10%), the number of hours of exposure (1), the city (L = Los Angeles, N = New York City), and the population (T = total population). For chronic endpoints, a 5-character code denotes the expert on whose judgments results are based, the lesion type, the city, the population of interest, and the number of ozone seasons of exposure. For example, AILC1 denotes expert A, mIld[†] lesions, Los Angeles, Children, and 1 season[‡] of exposure.

These results could have been presented in tables like Table 6.1 rather than in figures. The drawback of tabular results is that one page is needed per air quality scenario. The figures presented here display results for as many as 6 air quality scenarios, which considerably reduces the number of pages needed to present results.

*That is, the studies conducted by Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991).

[†]The letter "O" in this character position denotes mOderate lesions.

[‡]The letter "T" in this character position denotes Ten ozone seasons.

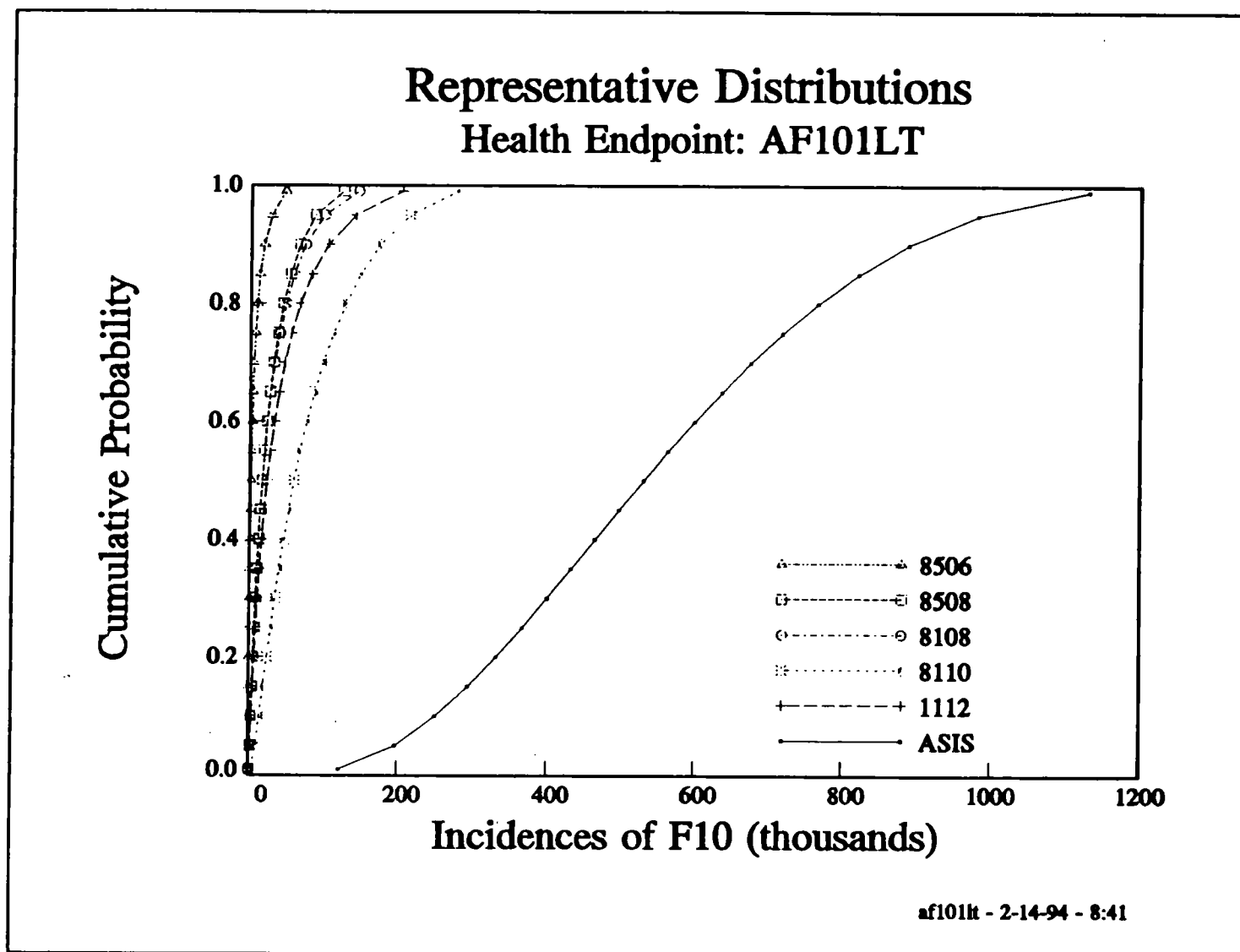


FIGURE A.1 Risk Distributions for FEV Decrements $\geq 10\%$ Based on Data from the Avol et al. (1984) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

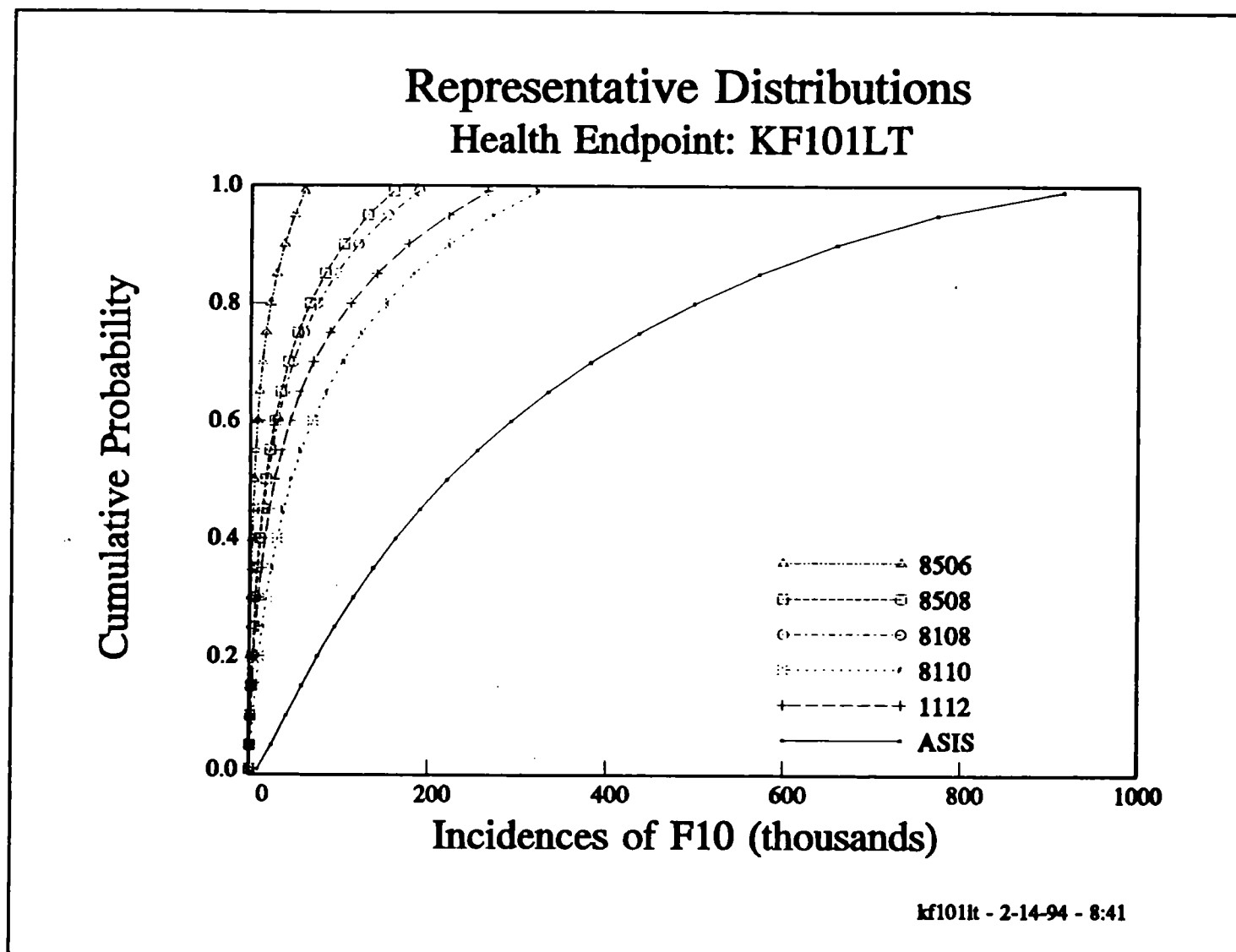


FIGURE A.2 Risk Distributions for FEV Decrements $\geq 10\%$ Based on Data from the Kulle et al. (1985) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

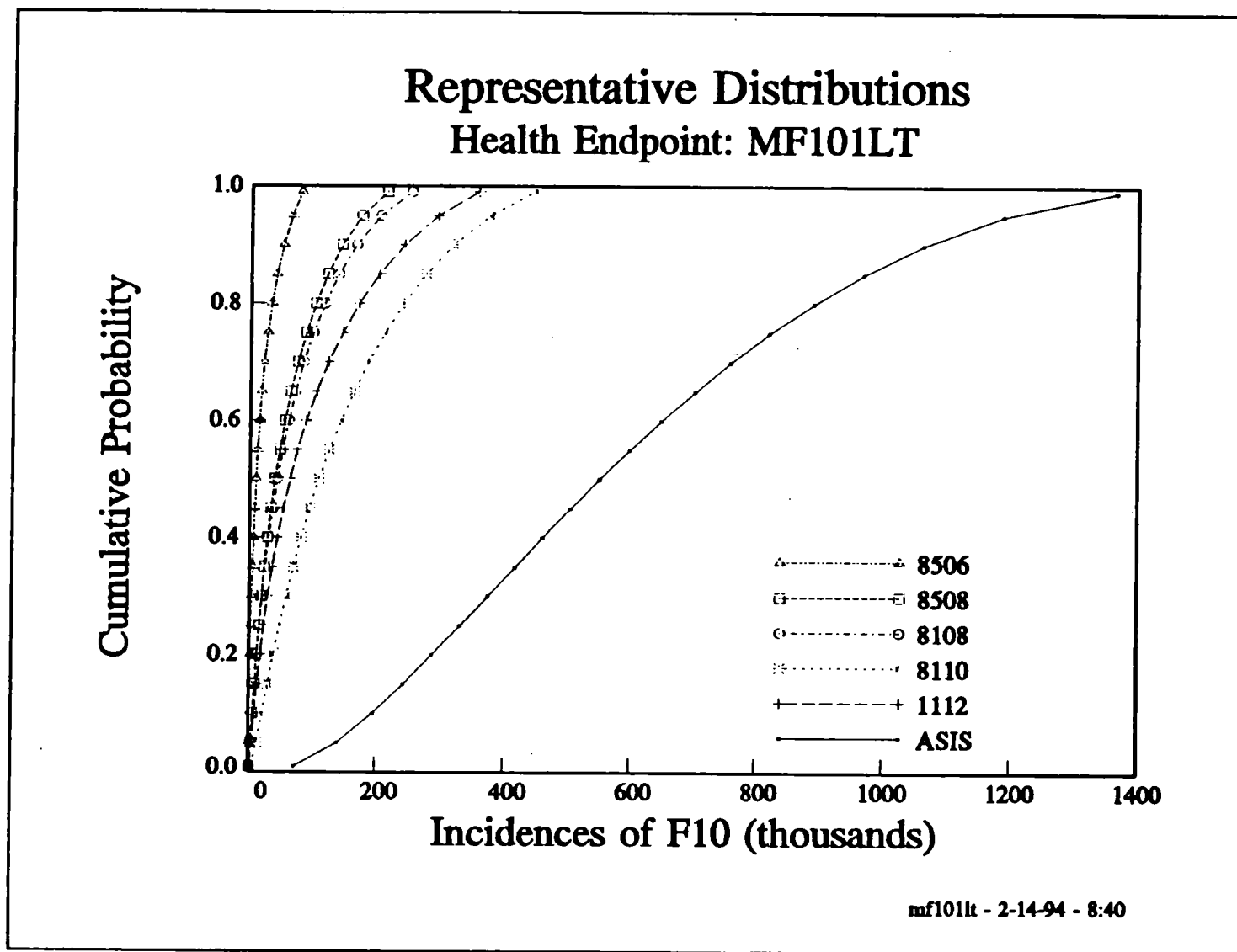


FIGURE A.3 Risk Distributions for FEV Decrement $\geq 10\%$ Based on Data from the McDonnell et al. (1983) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

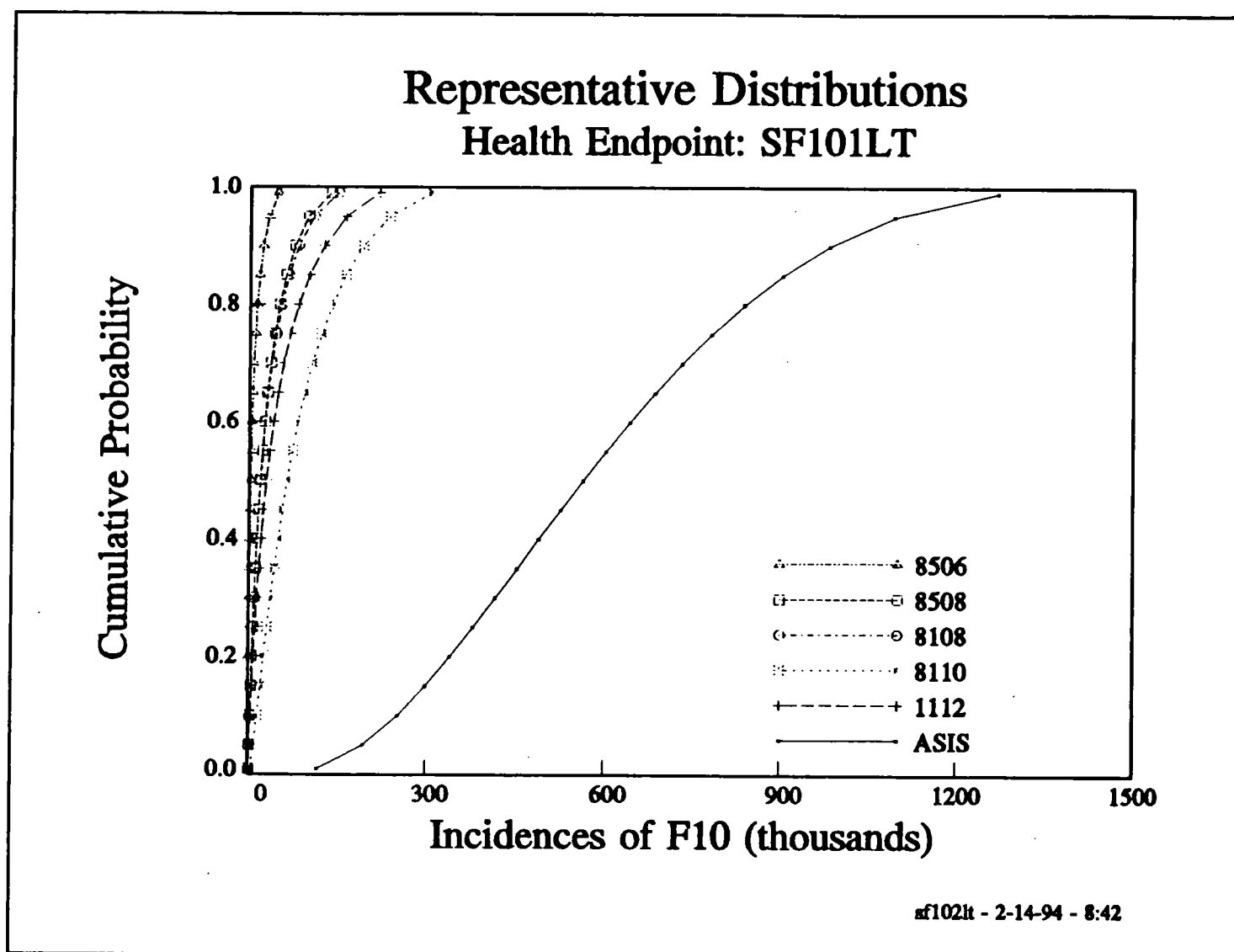


FIGURE A.4 Risk Distributions for FEV Decrement $\geq 10\%$ Based on Data from the Seal et al. (1993) Study (1-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

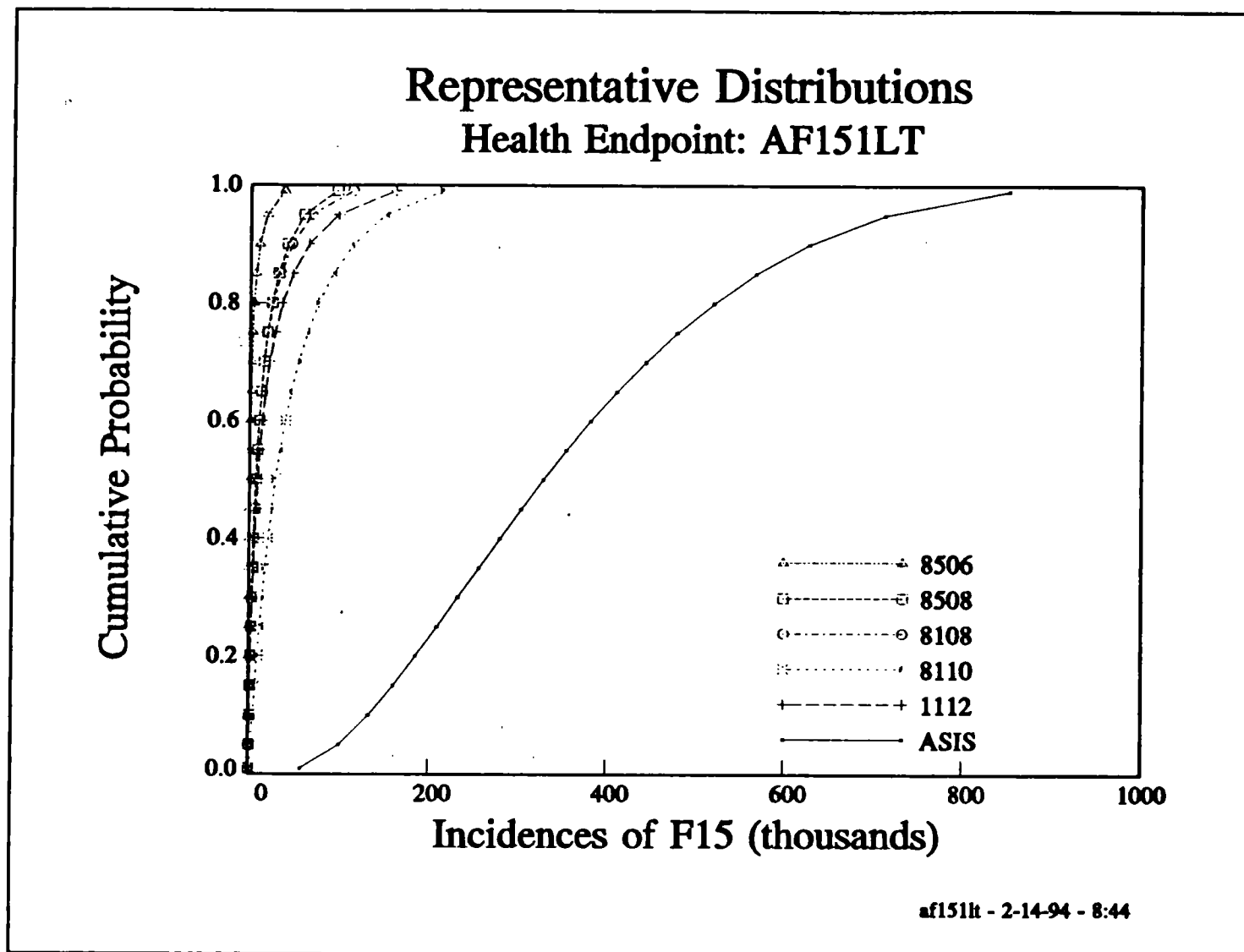


FIGURE A.5 Risk Distributions for FEV Decrement $\geq 15\%$ Based on Data from the Avol et al. (1984) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

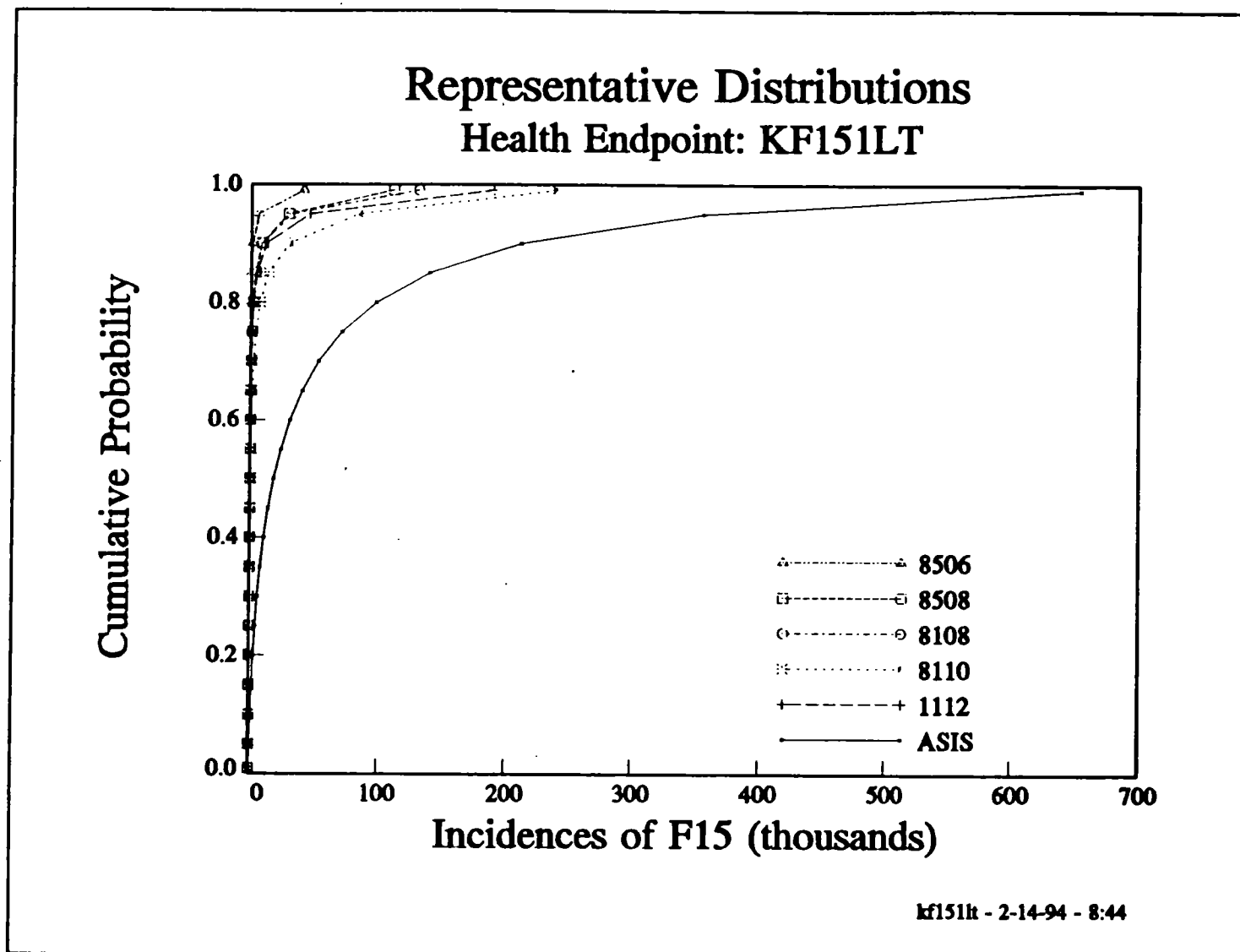


FIGURE A.6 Risk Distributions for FEV Decrement $\geq 15\%$ Based on Data from the Kulle et al. (1985) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

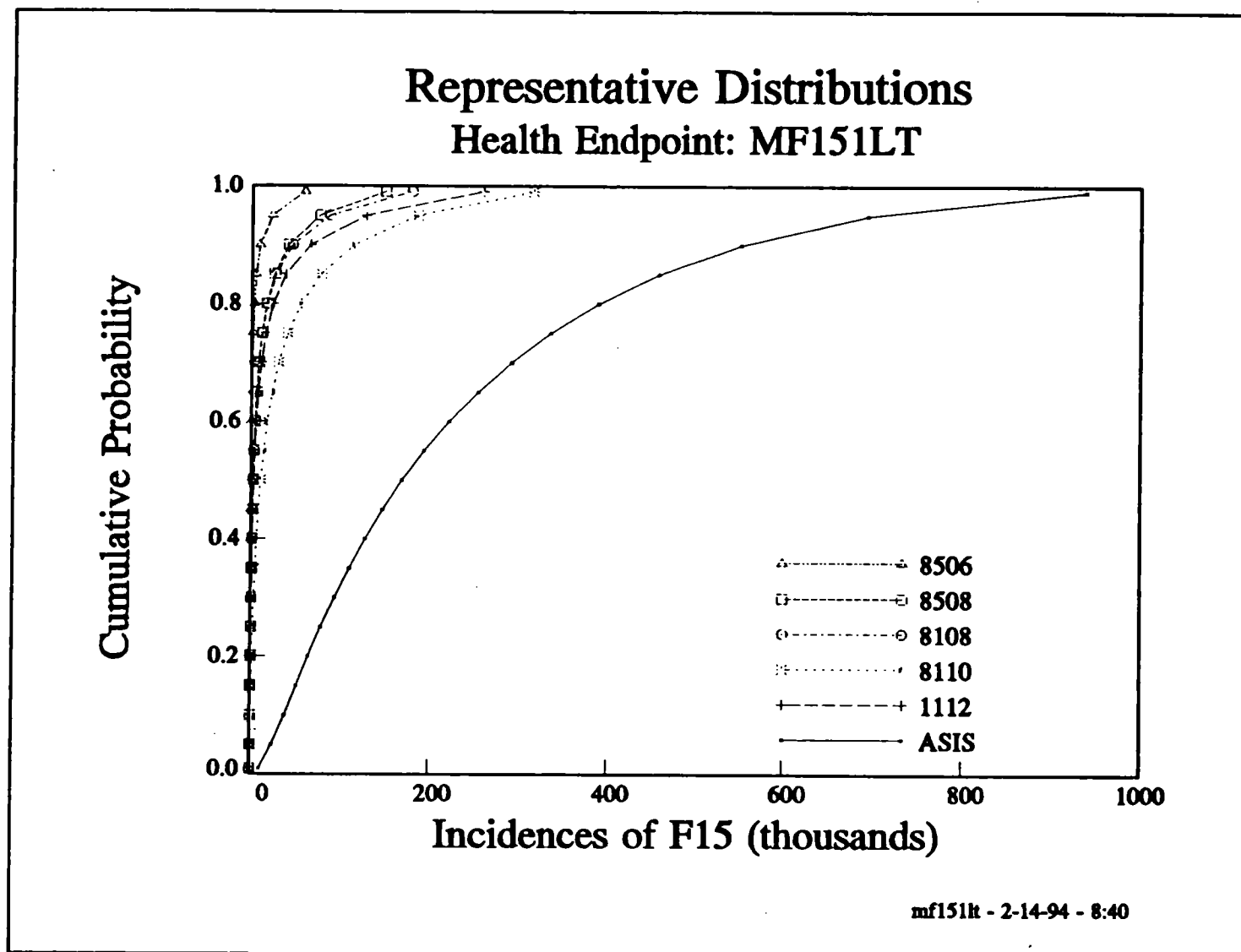


FIGURE A.7 Risk Distributions for FEV Decrement $\geq 15\%$ Based on Data from the McDonnell et al. (1983) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

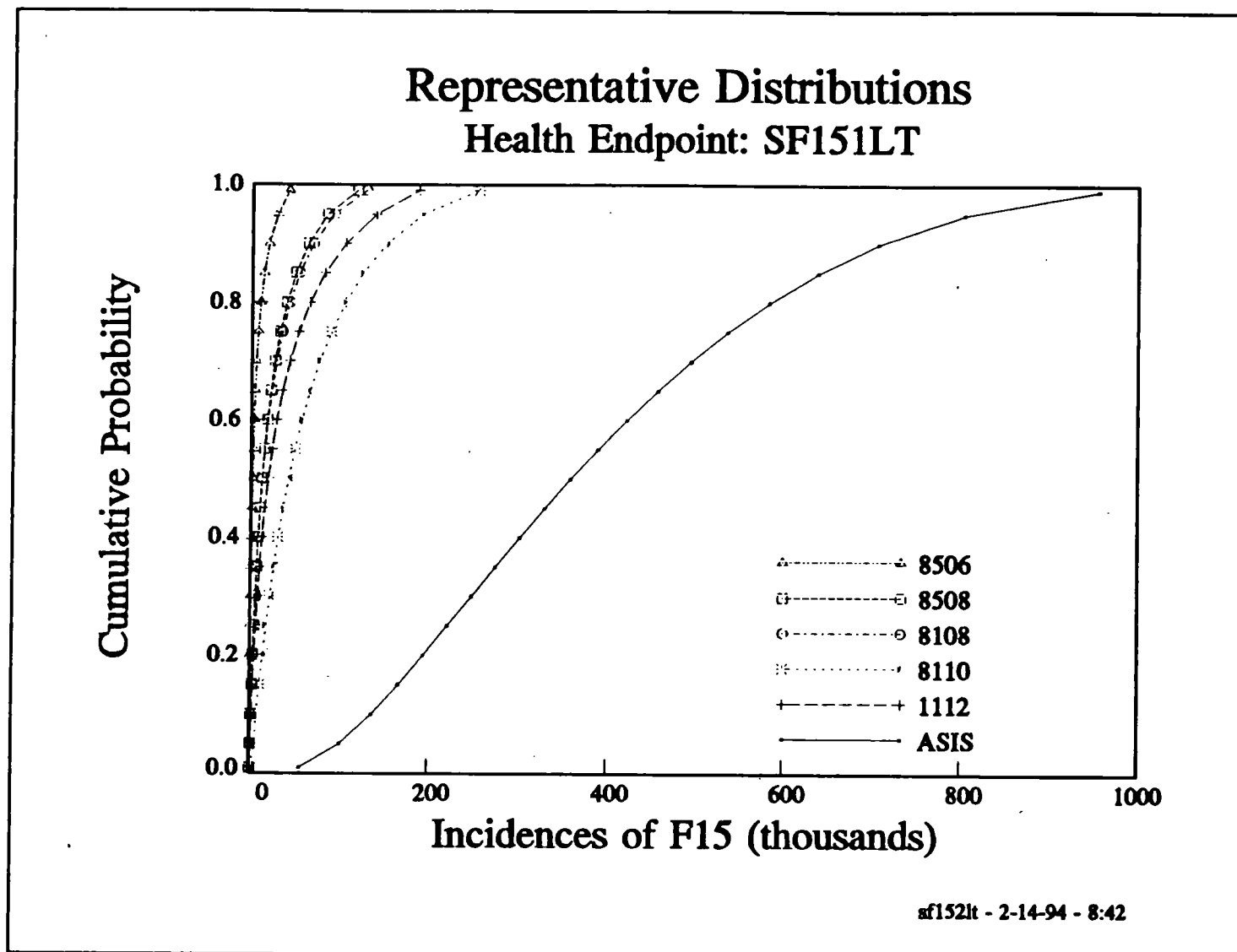


FIGURE A.8 Risk Distributions for FEV Decrement $\geq 15\%$ Based on Data from the Seal et al. (1993) Study (1-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

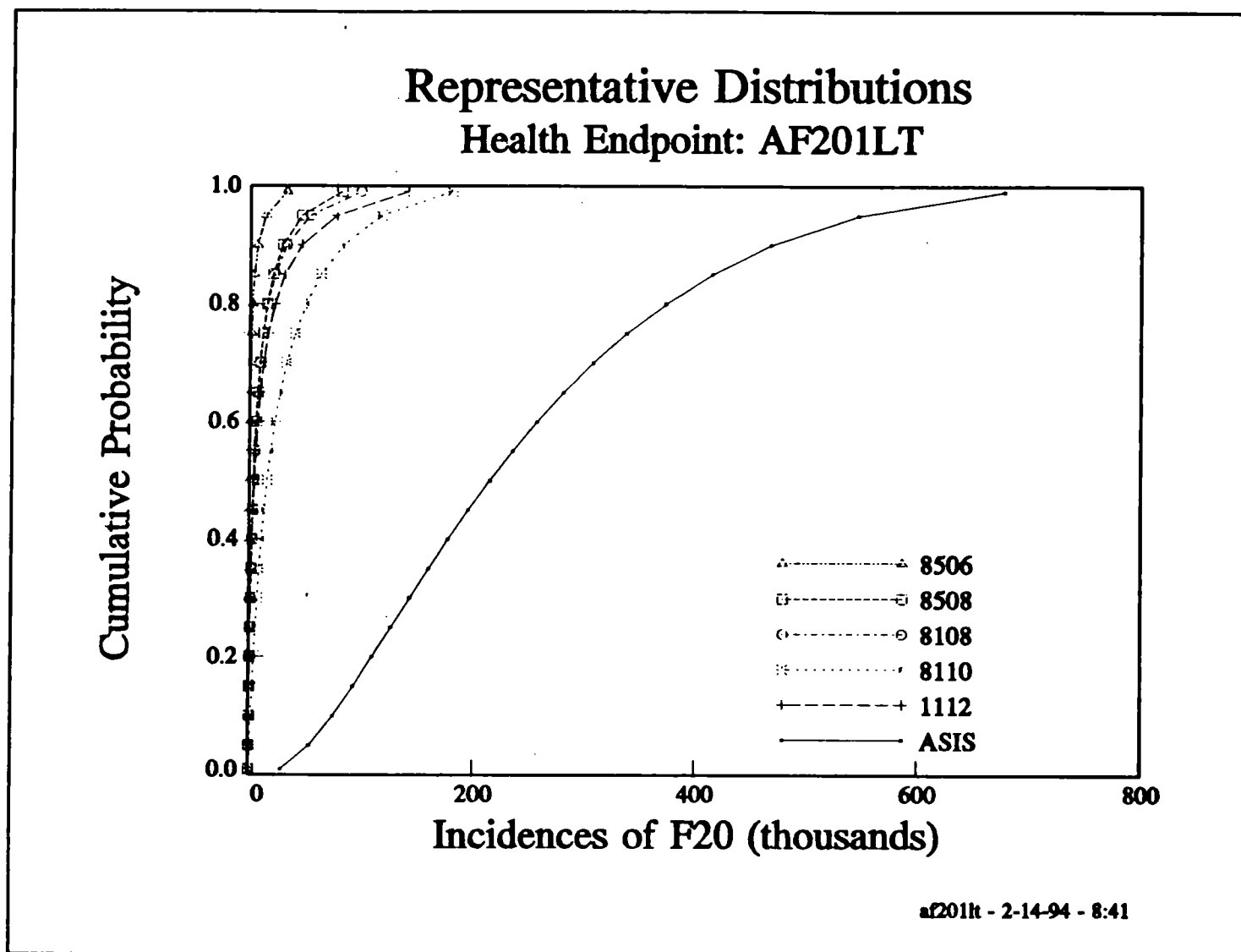


FIGURE A.9 Risk Distributions for FEV Decrement $\geq 20\%$ Based on Data from the Avol et al. (1984) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

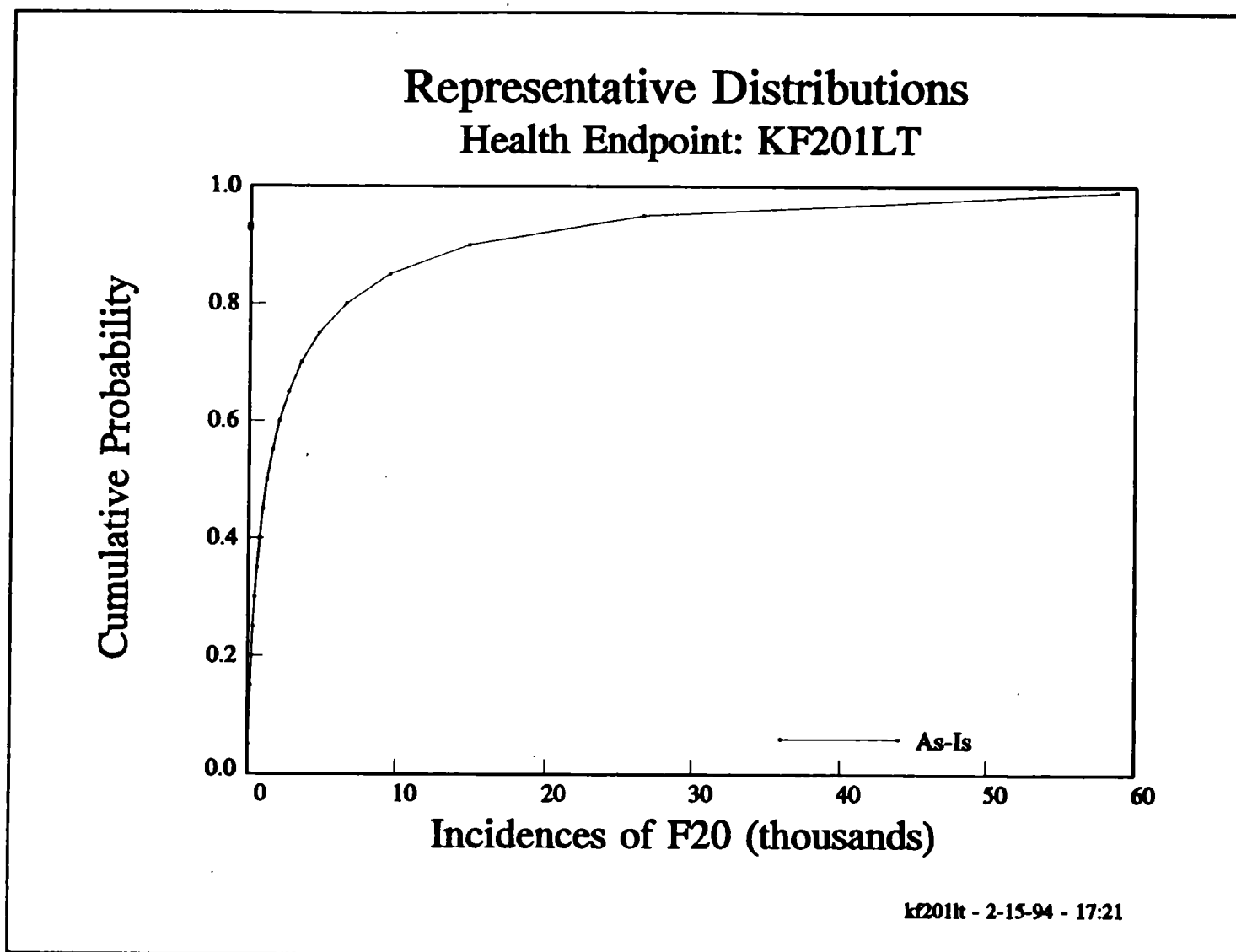


FIGURE A.10 Risk Distributions for FEV Decrement $\geq 20\%$ Based on Data from the Kulle et al. (1985) Study (1-hour exposures at heavy exercise, Los Angeles, total population, as-is air quality [the only non-zero risk distribution])

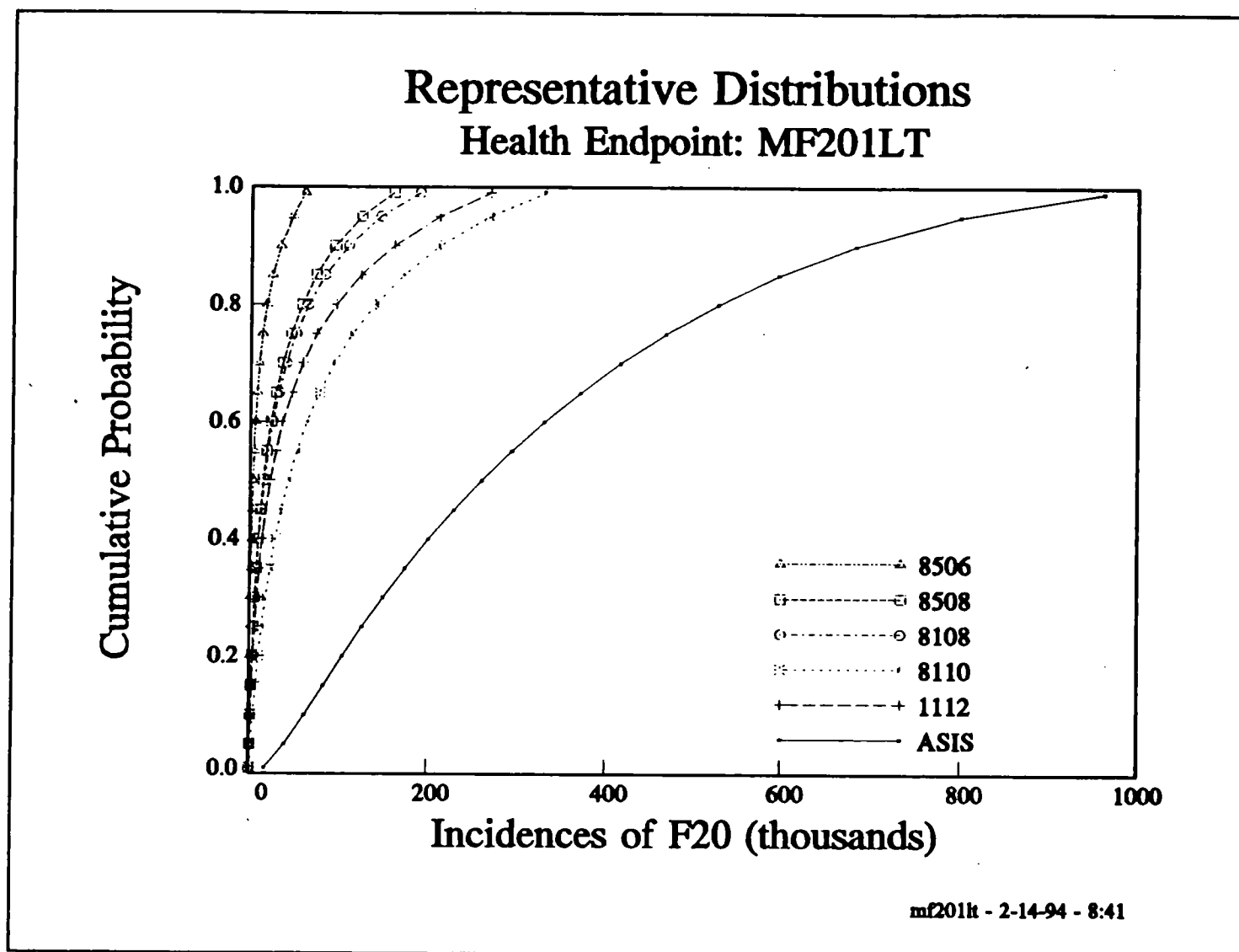


FIGURE A.11 Risk Distributions for FEV Decrement $\geq 20\%$ Based on Data from the McDonnell et al. (1983) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

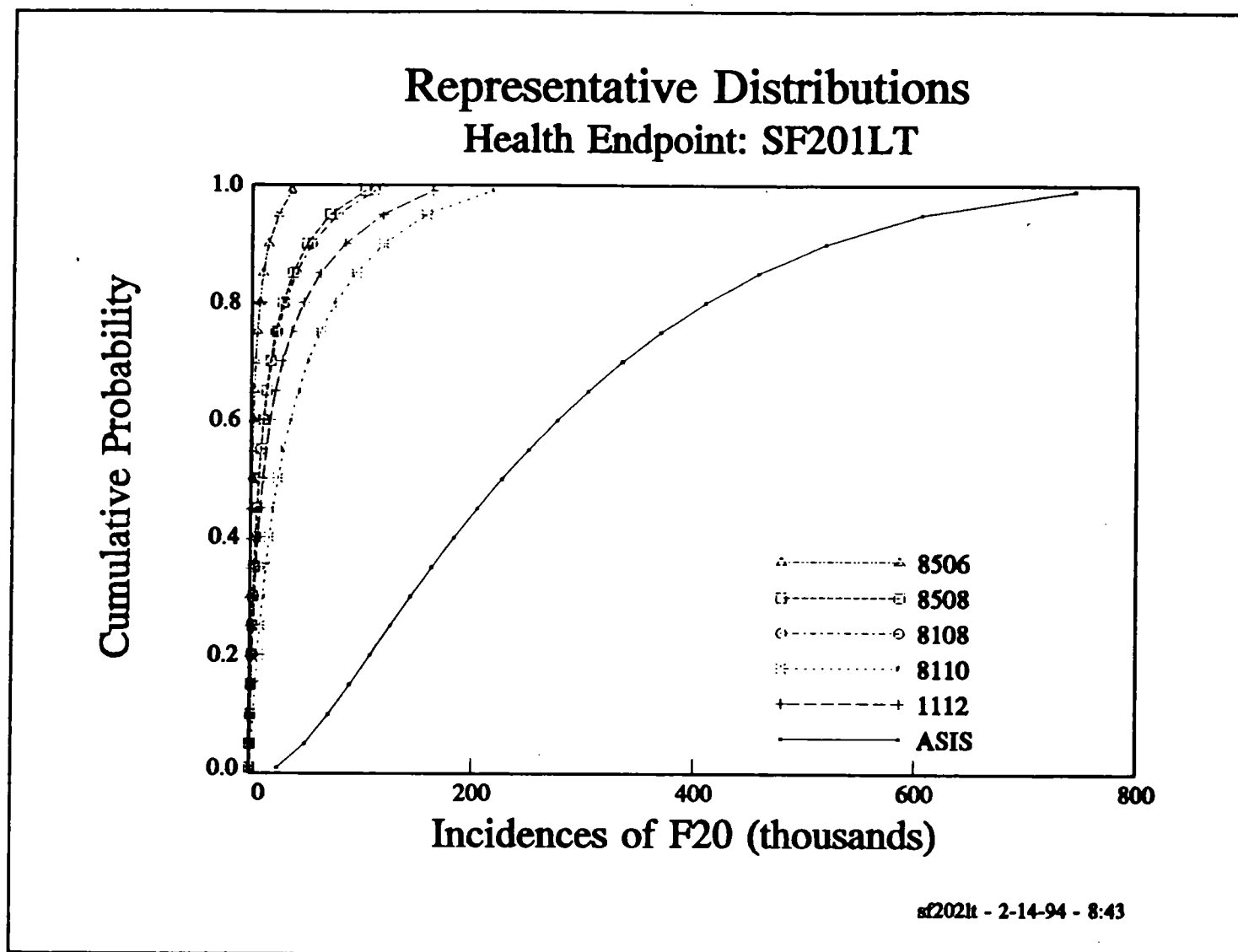


FIGURE A.12 Risk Distributions for FEV Decrement $\geq 20\%$ Based on Data from the Seal et al. (1993) Study (1-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

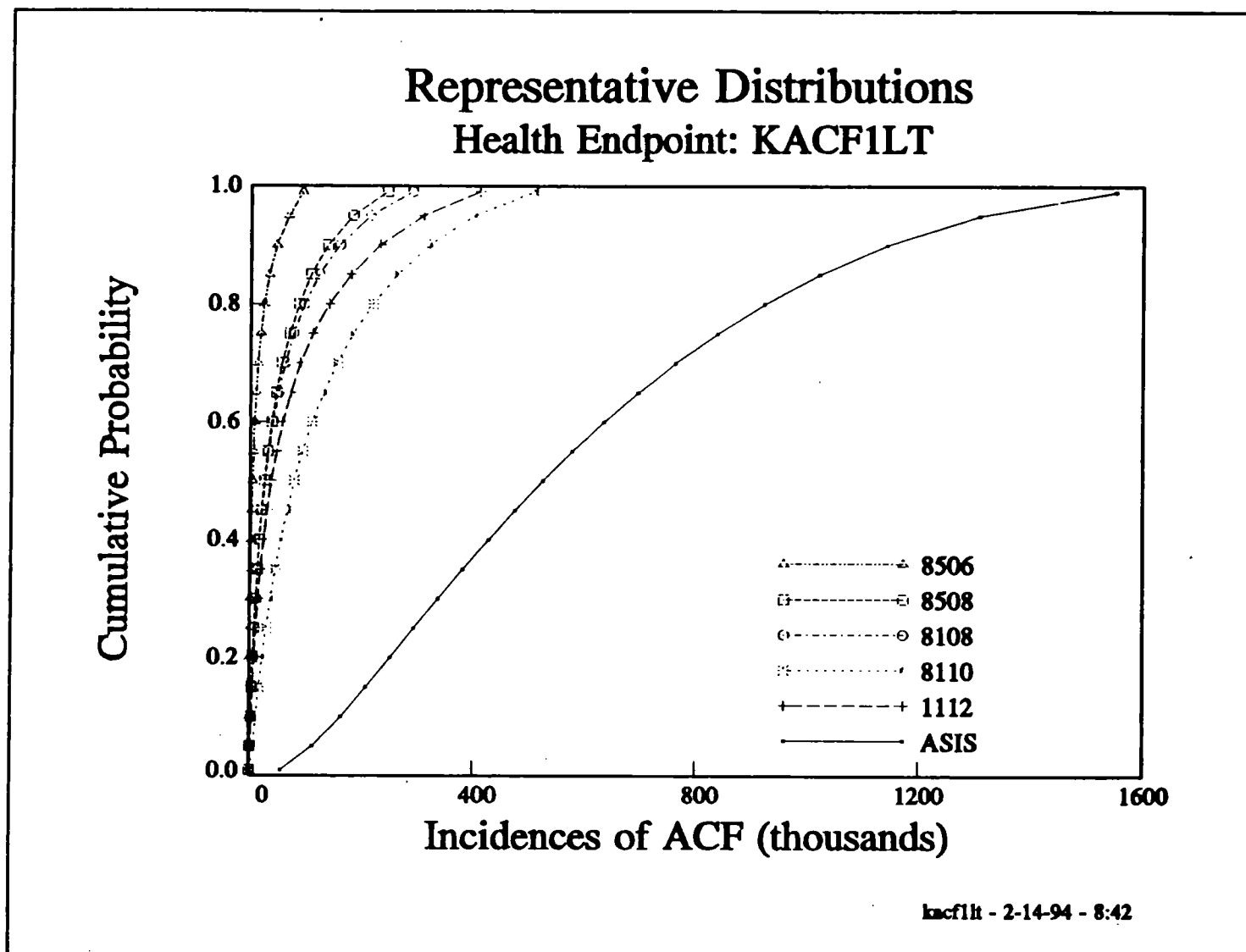


FIGURE A.13 Risk Distributions for Any Cough Based on Data from the Kulle et al. (1985) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

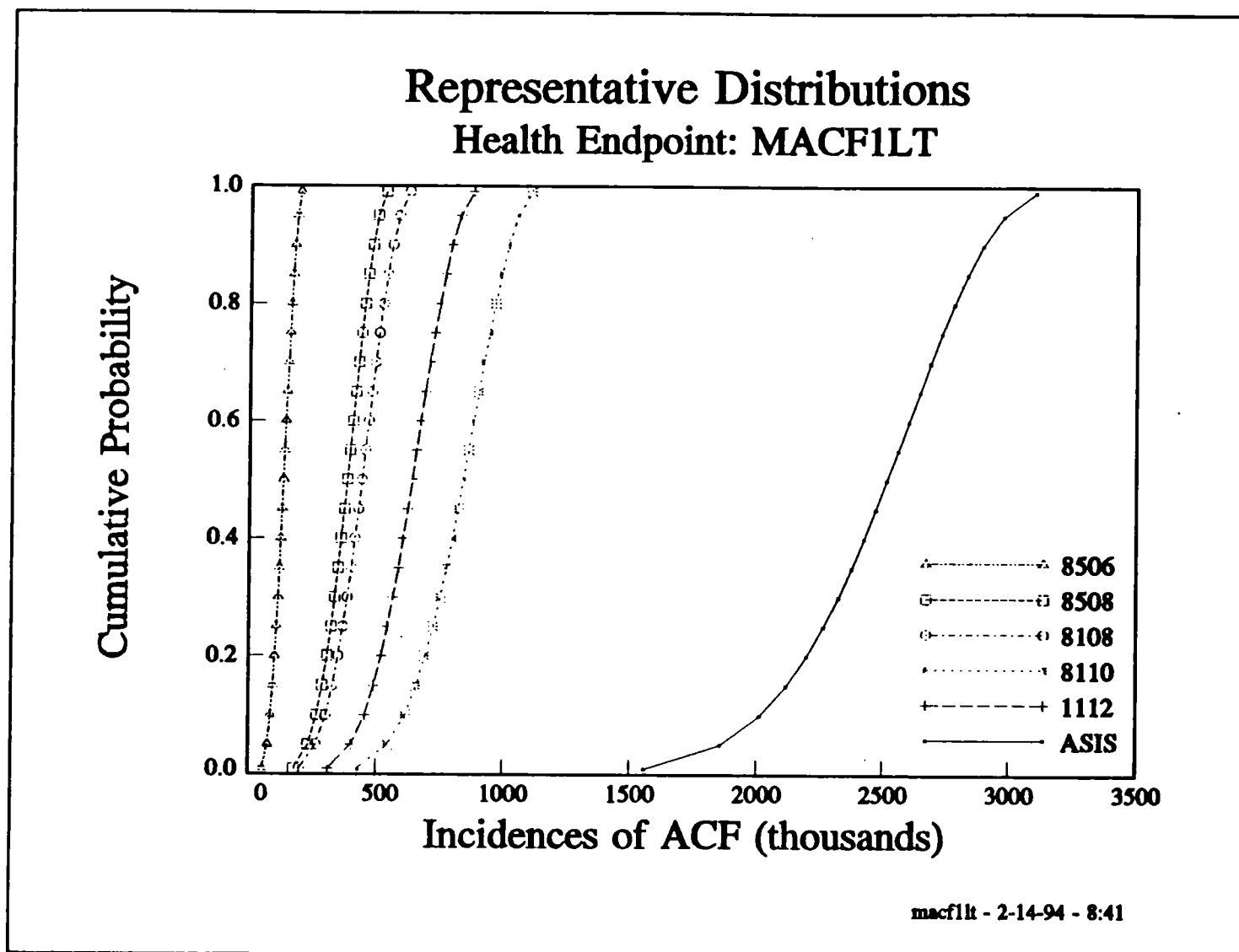


FIGURE A.14 Risk Distributions for Any Cough Based on Data from the McDonnell et al. (1983) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

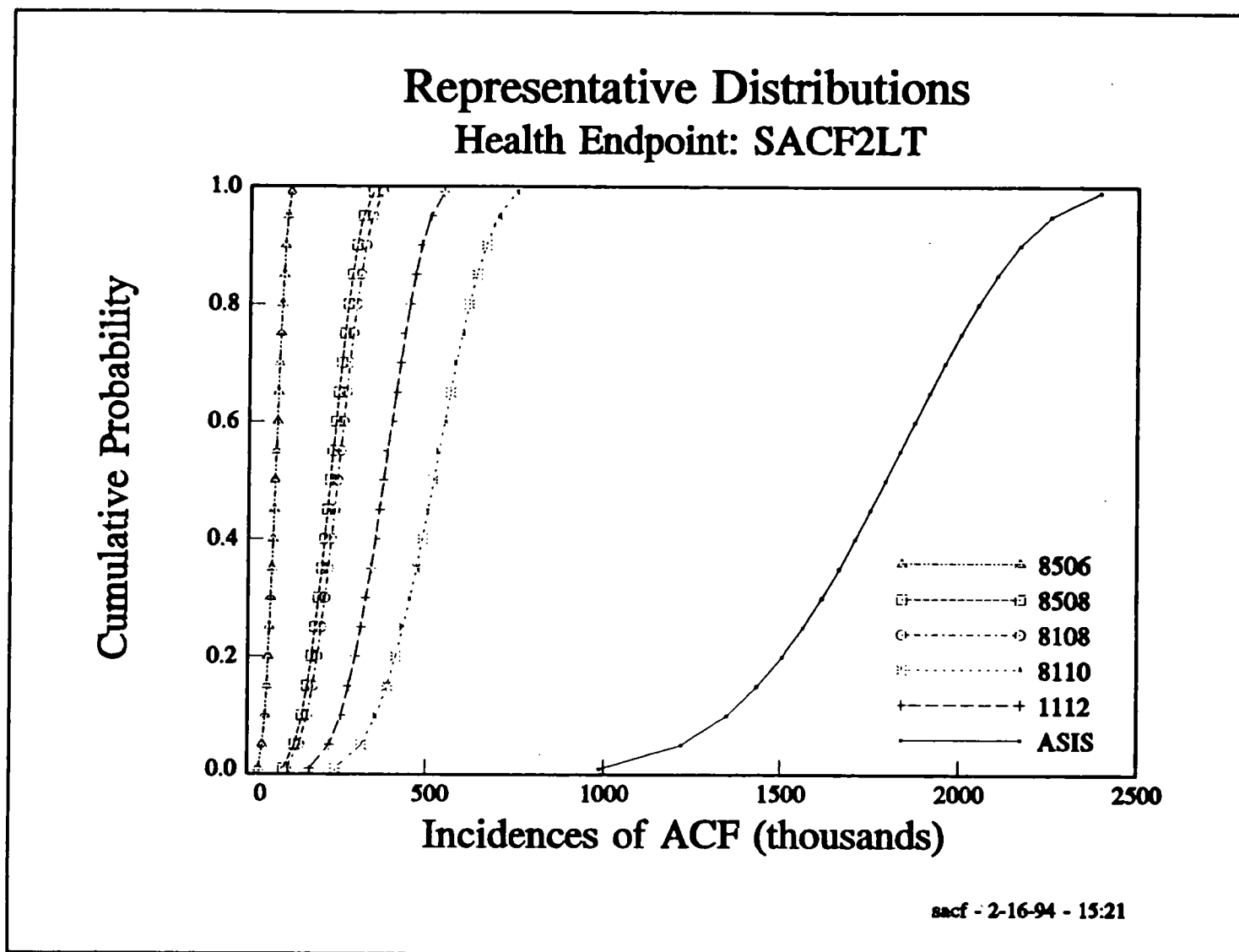


FIGURE A.15 Risk Distributions for Any Cough Based on Data from the Seal et al. (1993) Study (1-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

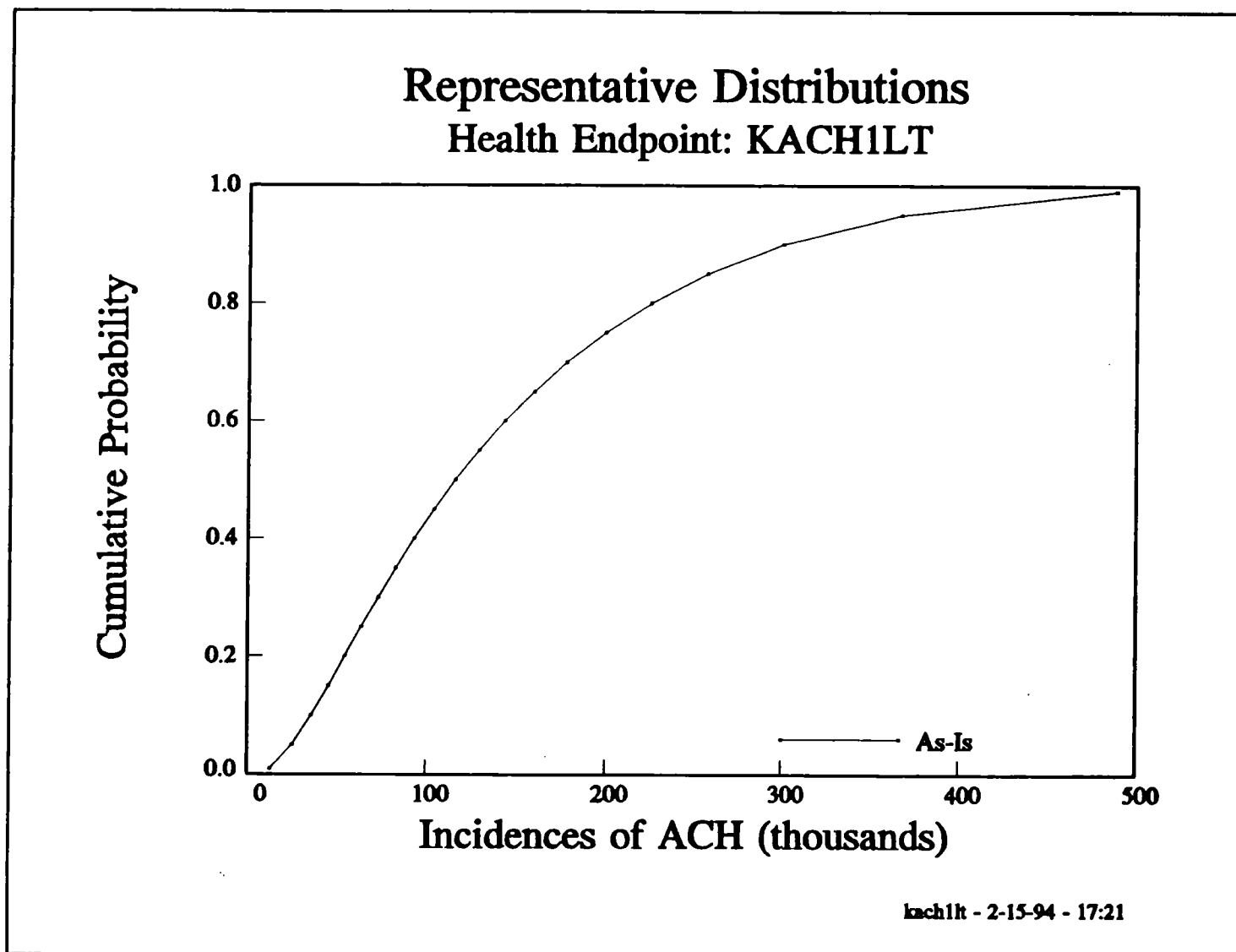


FIGURE A.16 Risk Distributions for Any Chest Discomfort Based on Data from the Kulle et al. (1985) Study (1-hour exposures at moderate exercise, Los Angeles, total population, as-is air quality [the only non-zero risk distribution])

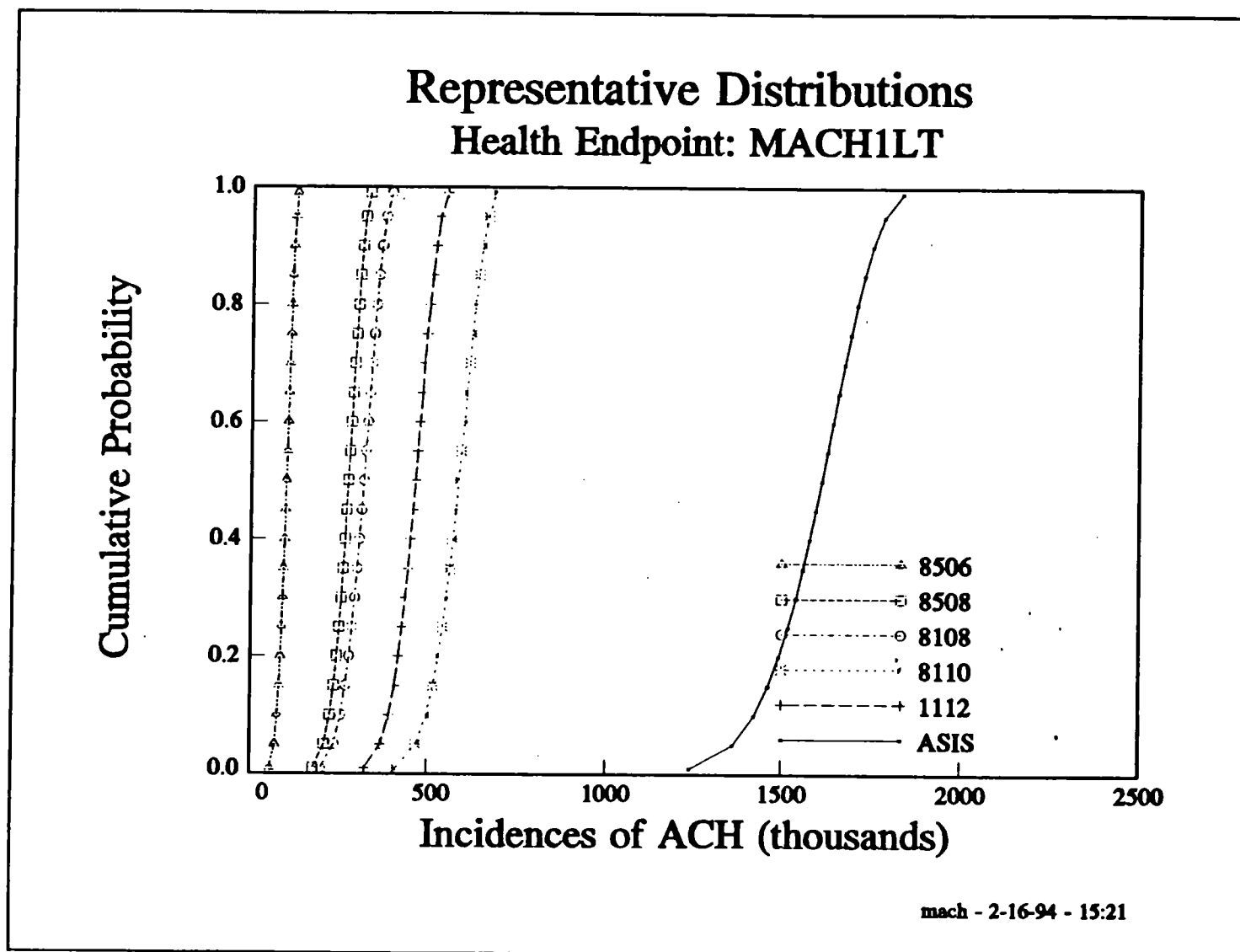


FIGURE A.17 Risk Distributions for Any Chest Discomfort Based on Data from the McDonnell et al. (1983) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

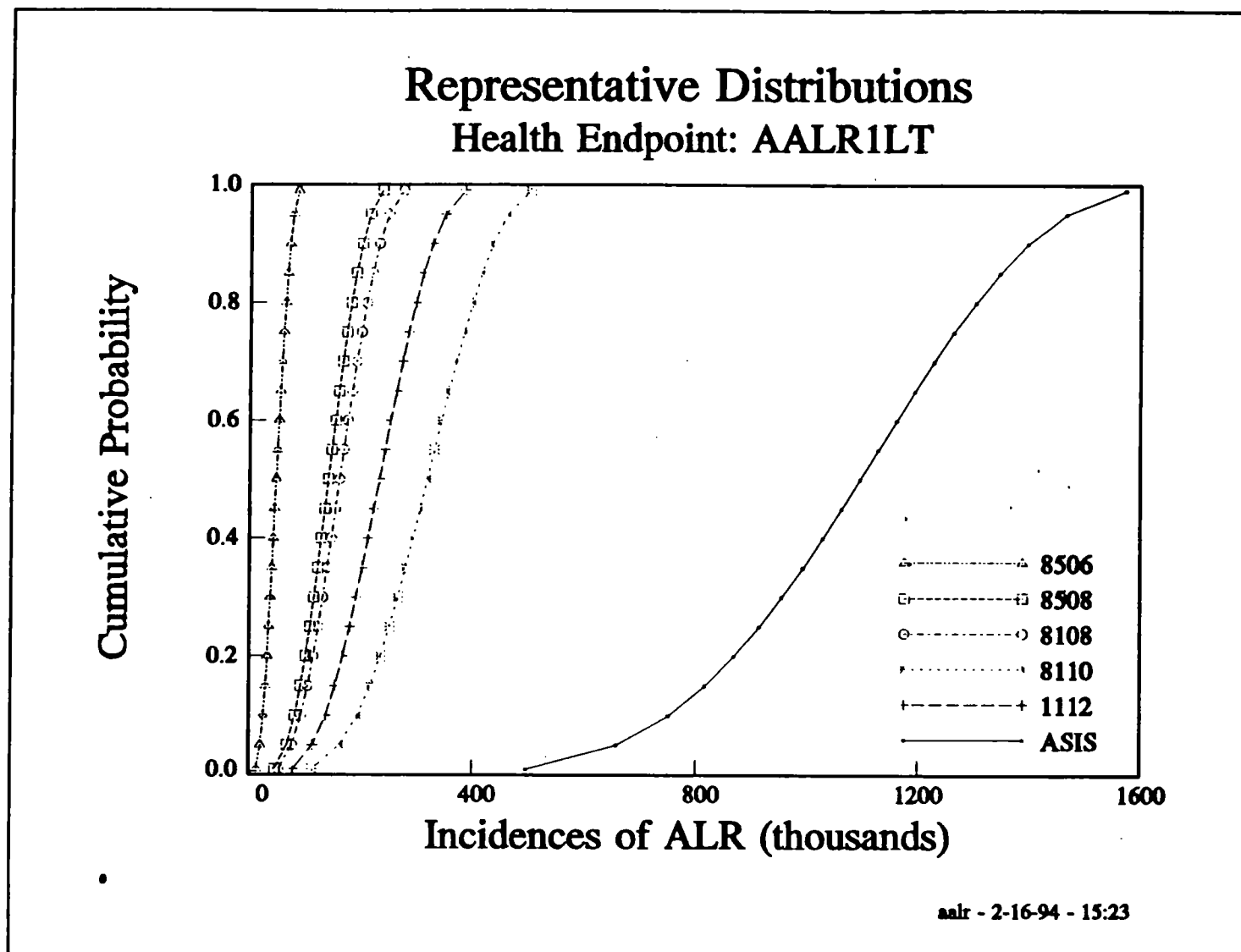


FIGURE A.18 Risk Distributions for Any Lower Respiratory Symptoms Based on Data from the Avol et al. (1984) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

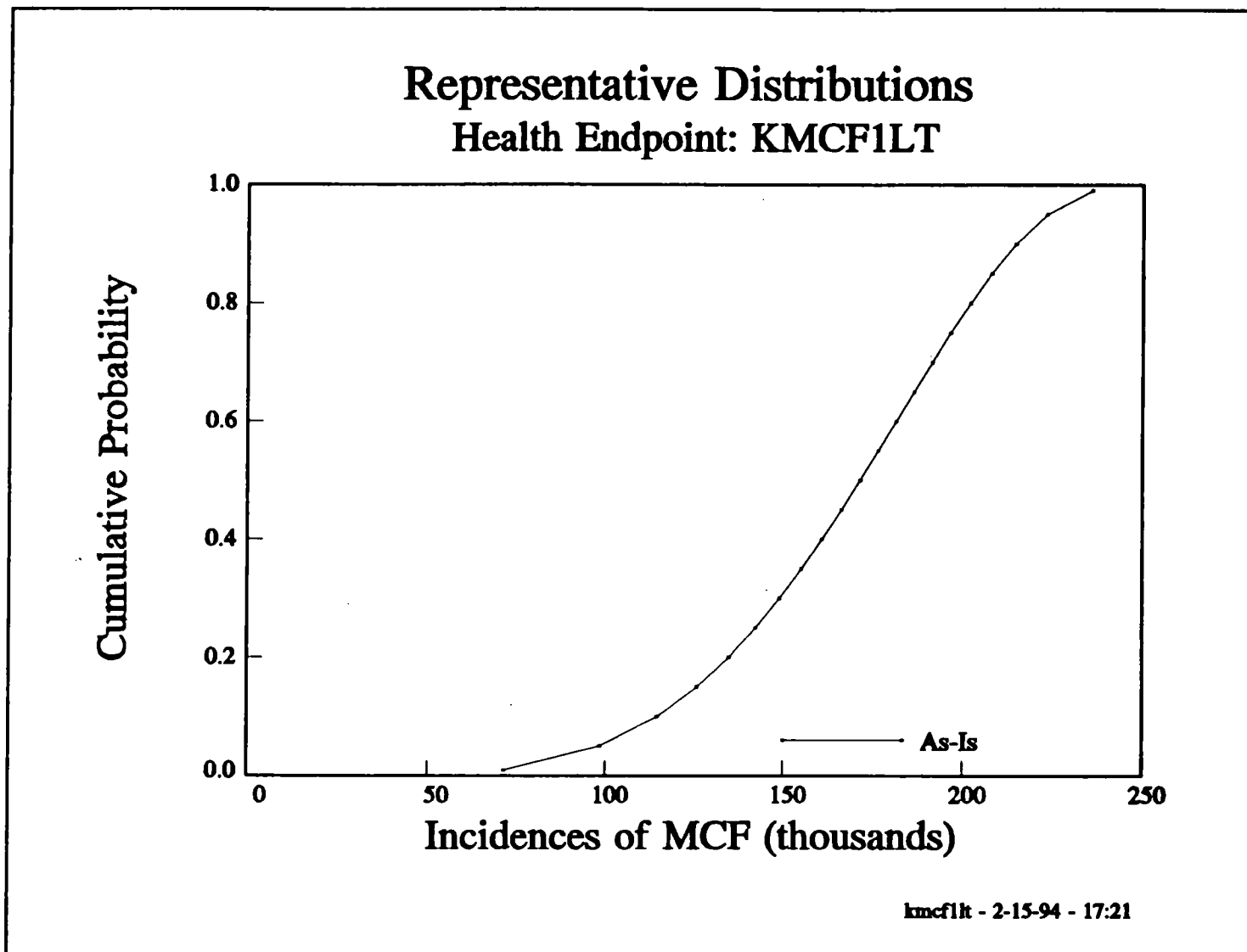


FIGURE A.19 Risk Distributions for Moderate/Severe Cough Based on Data from the Kulle et al. (1985) Study (1-hour exposures at heavy exercise, Los Angeles, total population, as-is air quality [the only non-zero risk distribution])

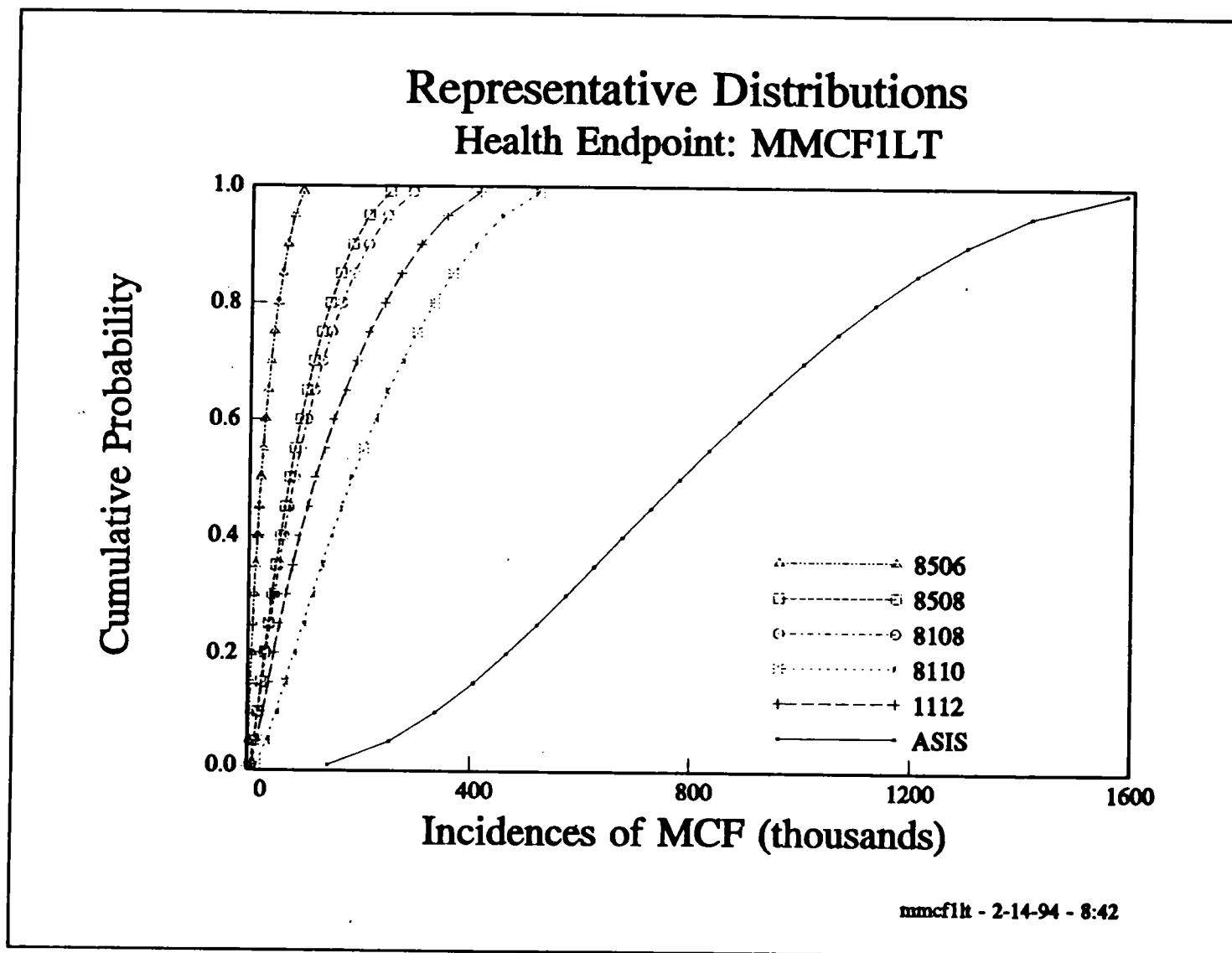


FIGURE A.20 Risk Distributions for Moderate/Severe Cough Based on Data from the McDonnell et al. (1983) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

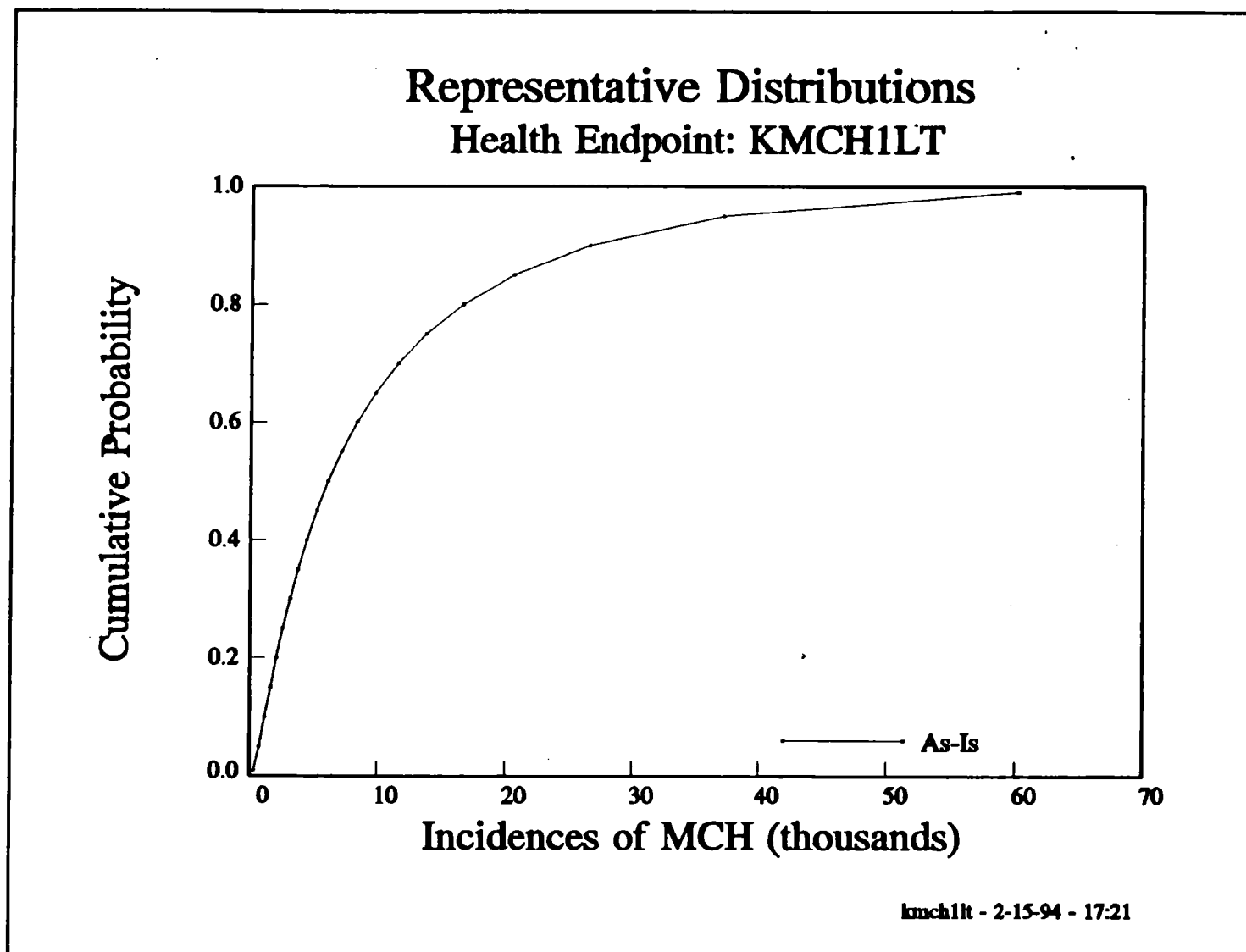


FIGURE A.21 Risk Distributions for Moderate/Severe Chest Discomfort Based on Data from the Kulle et al. (1985) Study (1-hour exposures at heavy exercise, Los Angeles, total population, as-is air quality [the only non-zero risk distribution])

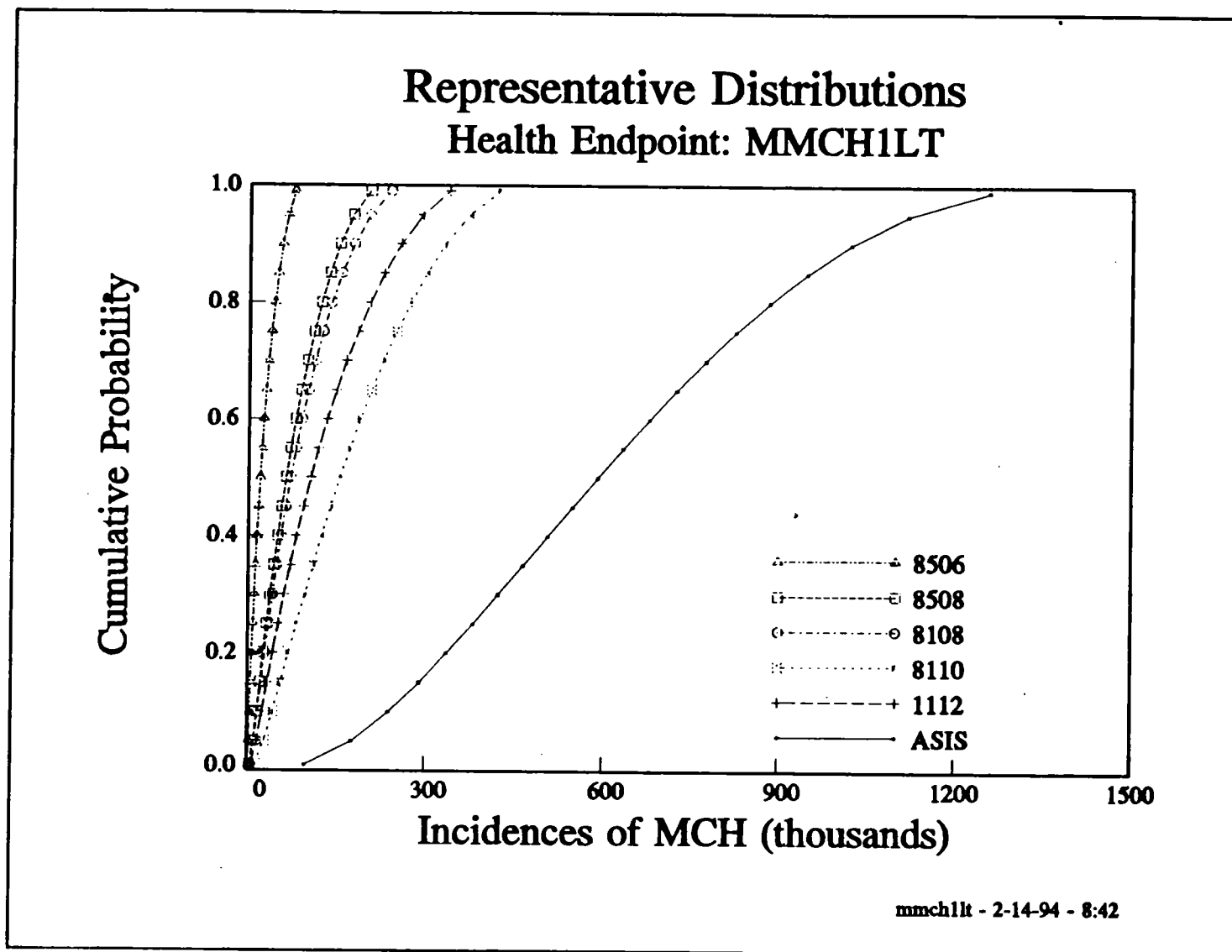


FIGURE A.22 Risk Distributions for Moderate/Severe Chest Discomfort Based on Data from the McDonnell et al. (1983) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

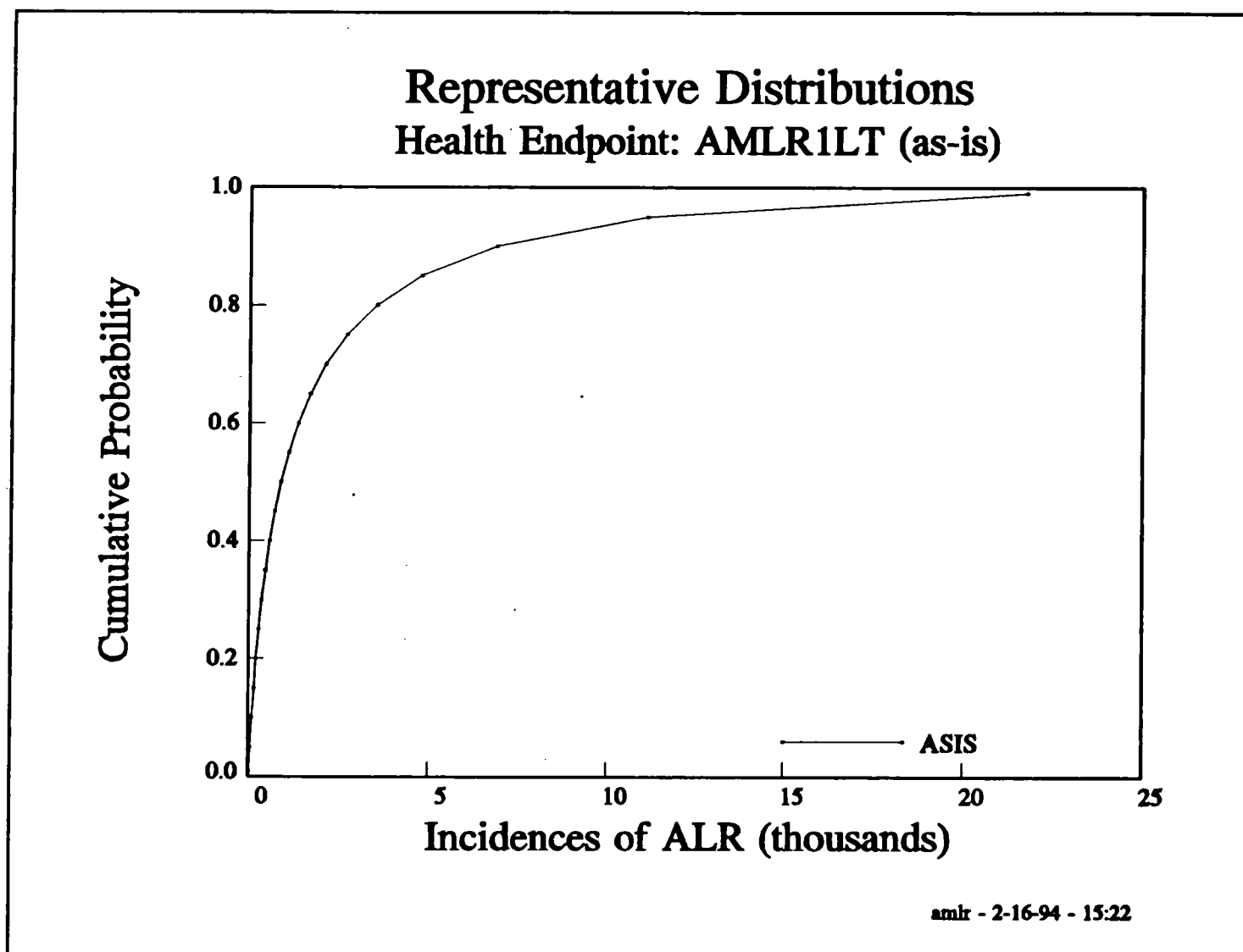


FIGURE A.23 Risk Distributions for Moderate/Severe Lower Respiratory Symptoms Based on Data from the Avol et al. (1984) Study (1-hour exposures at heavy exercise, Los Angeles, total population, all air quality scenarios)

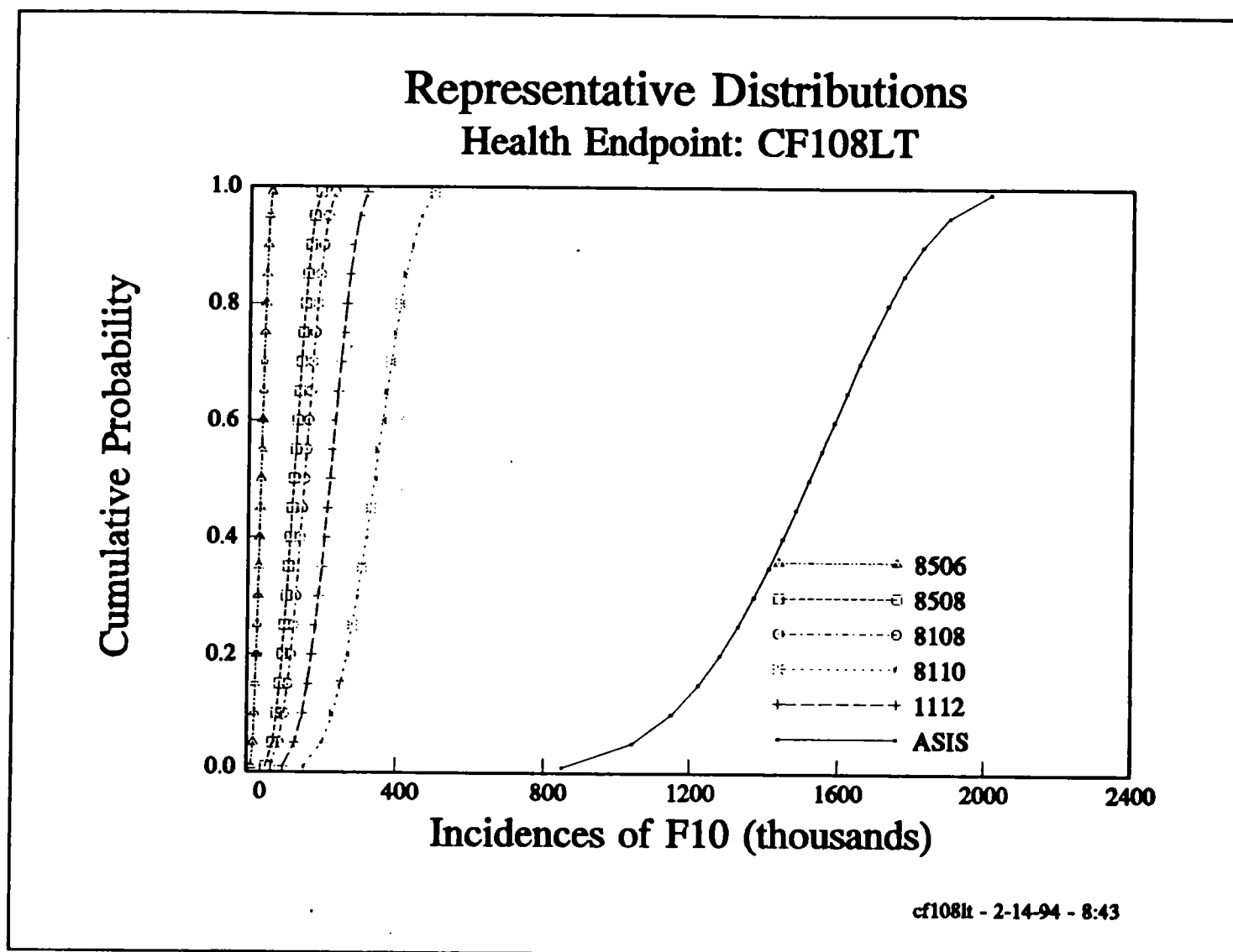


FIGURE A.24 Risk Distributions for FEV Decrement $\geq 10\%$ Based on Data from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) Studies (8-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

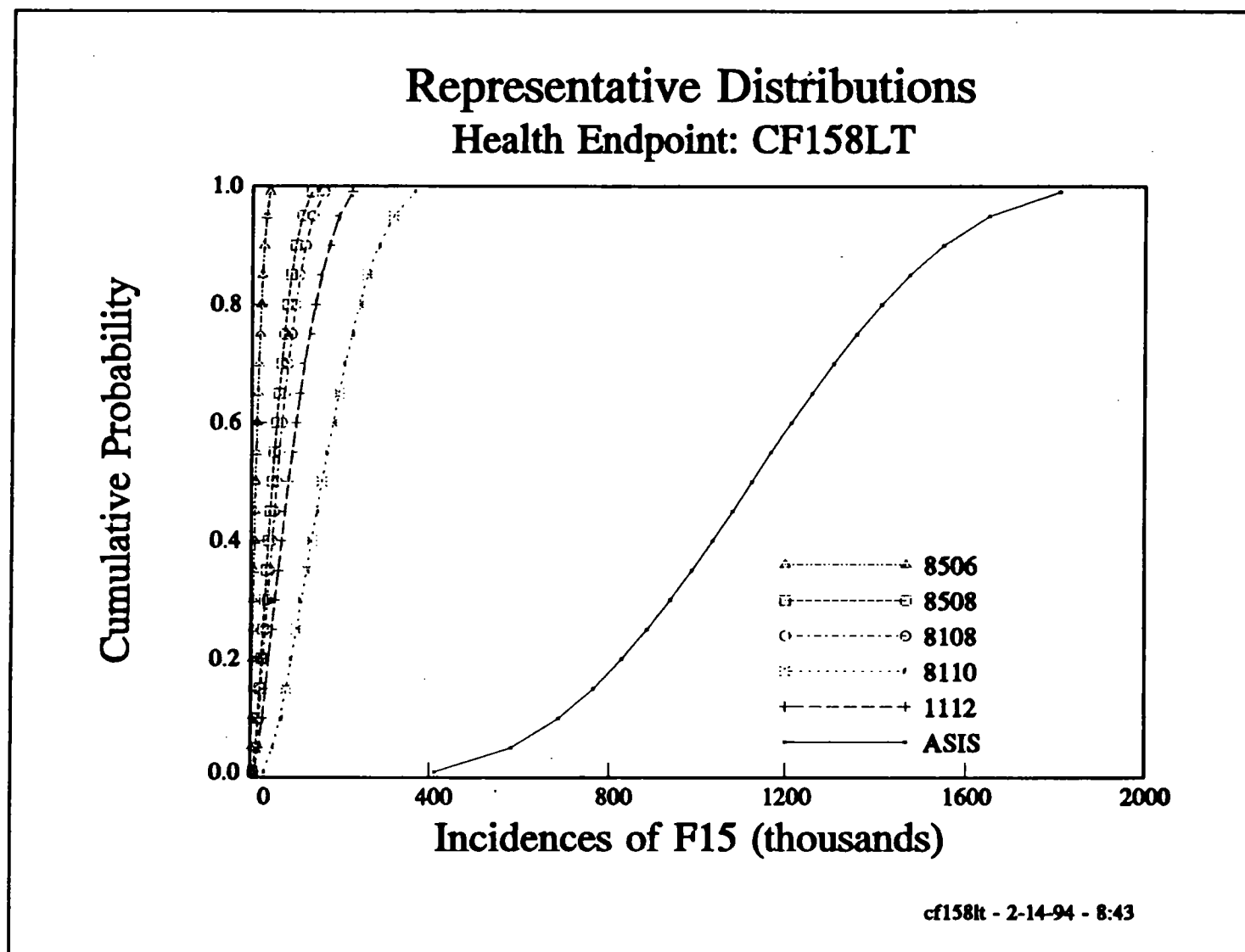


FIGURE A.25 Risk Distributions for FEV Decrement $\geq 15\%$ Based on Data from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) Studies (8-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

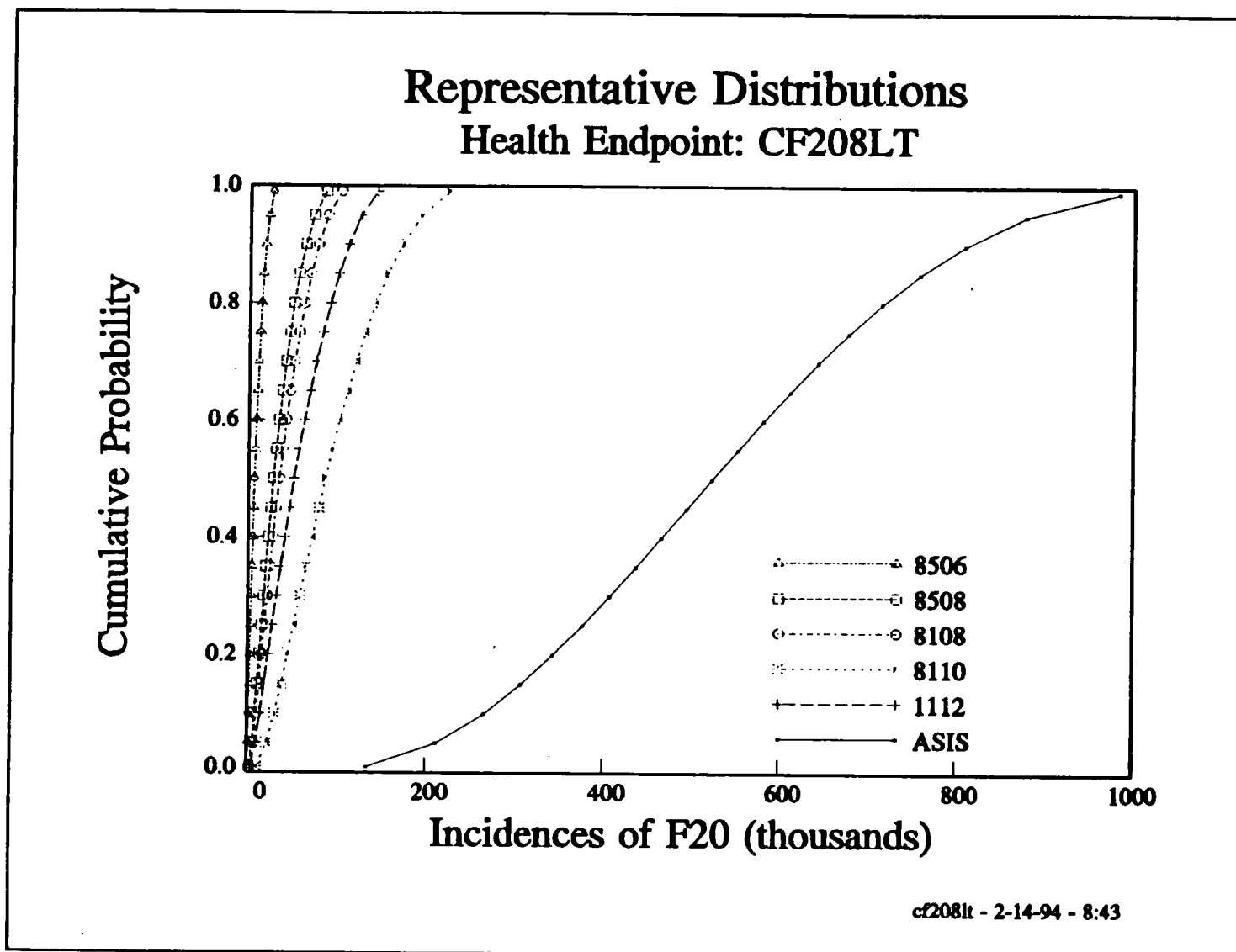


FIGURE A.26 Risk Distributions for FEV Decrement $\geq 20\%$ Based on Data from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) Studies (8-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

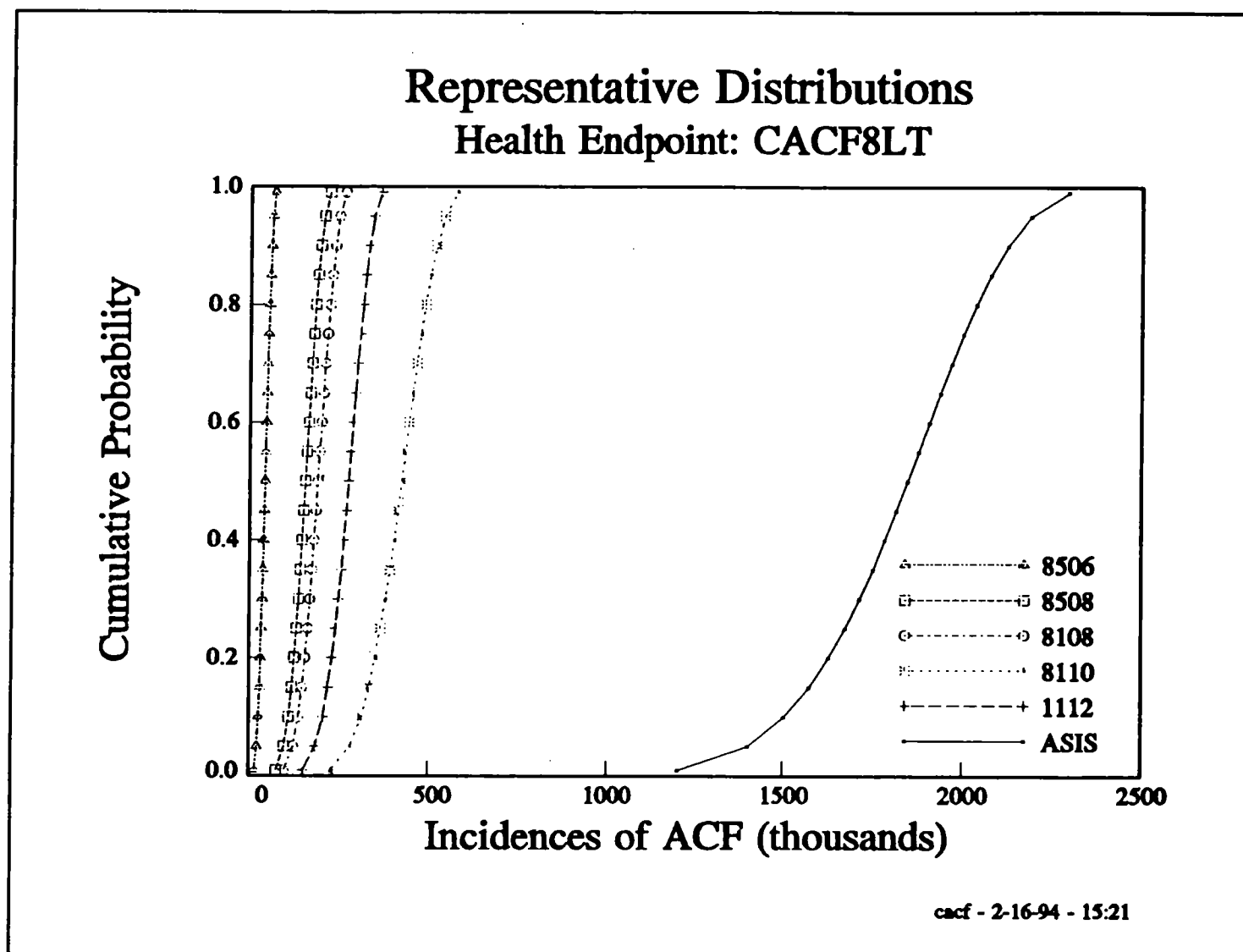


FIGURE A.27 Risk Distributions for Any Cough Based on Data from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) Studies (8-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

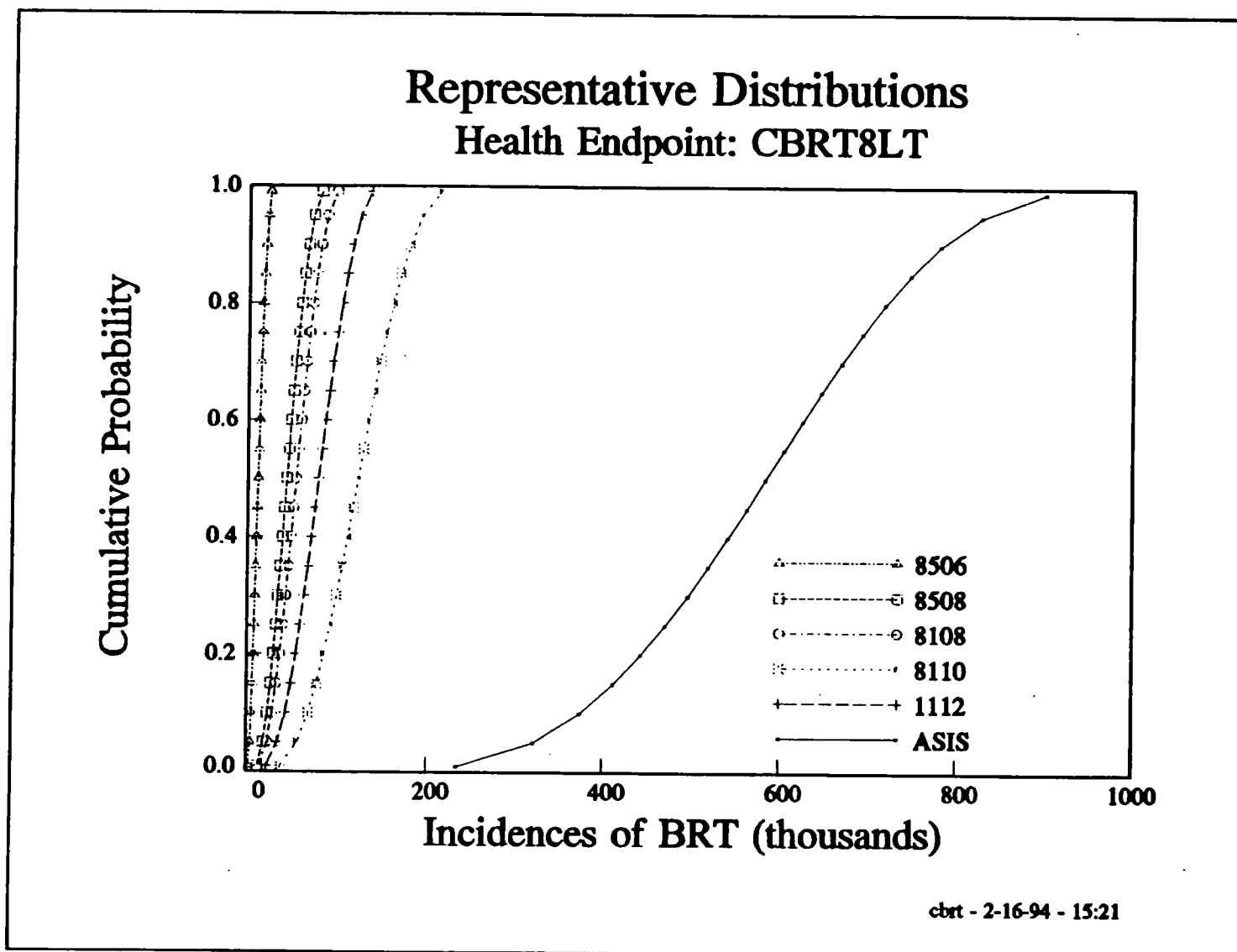


FIGURE A.28 Risk Distributions for Shortness of Breath Based on Data from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) Studies (8-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

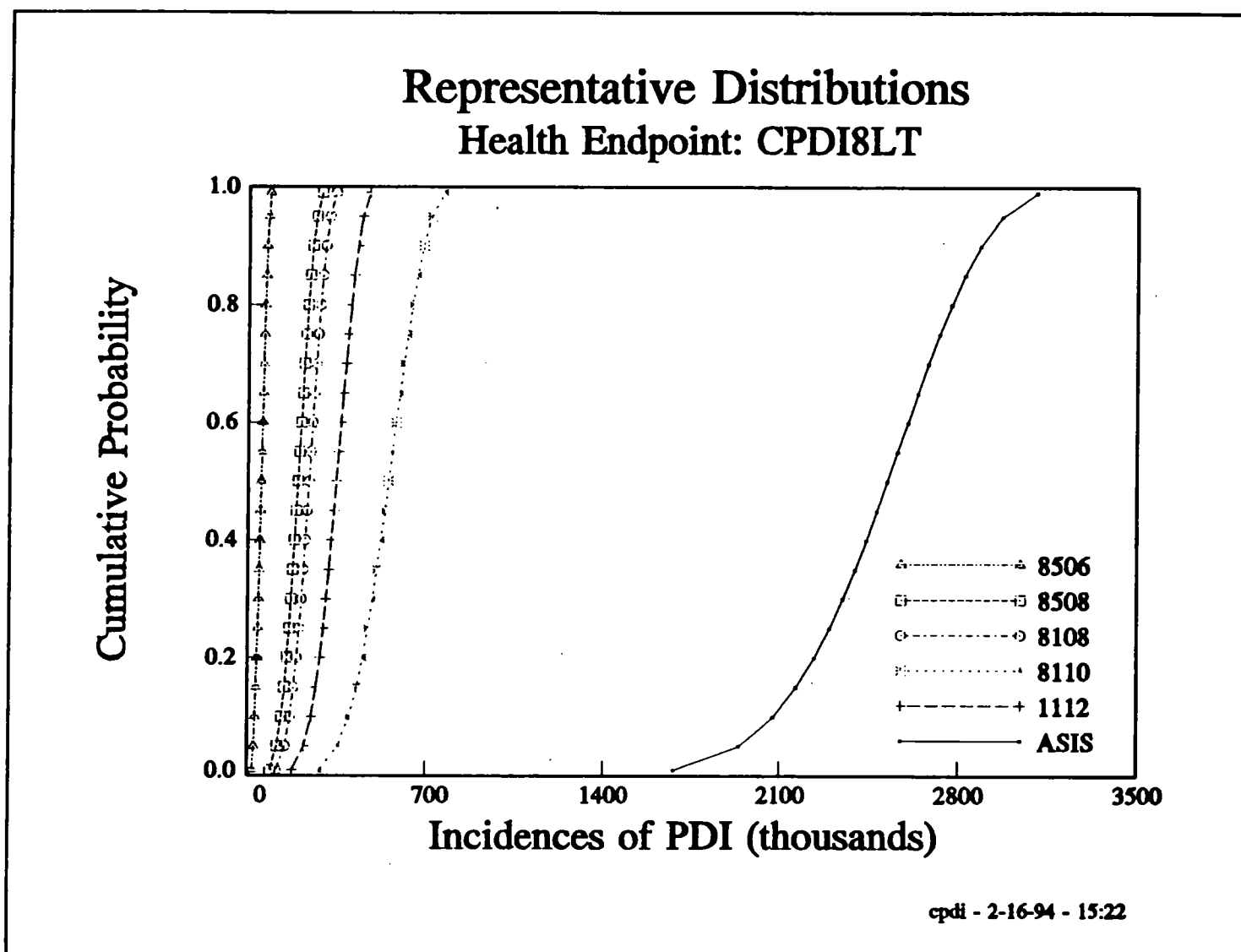


FIGURE A.29 Risk Distributions for Pain on Deep Inspiration Based on Data from the Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991) Studies (8-hour exposures at moderate exercise, Los Angeles, total population, all air quality scenarios)

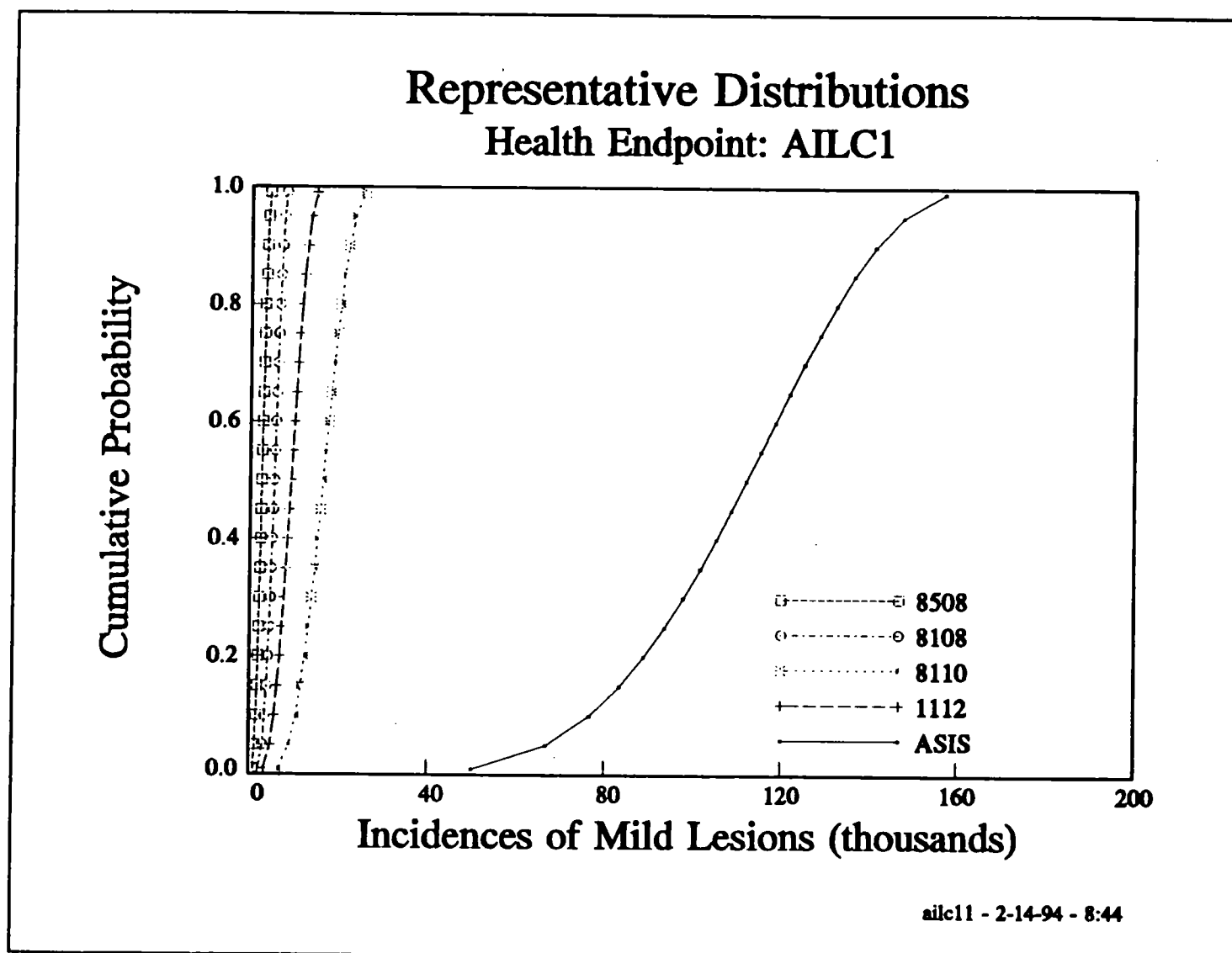


FIGURE A.30 Risk Distributions Expert A, Mild Lesions, Los Angeles, Children, 1 Season, All Air Quality Scenarios

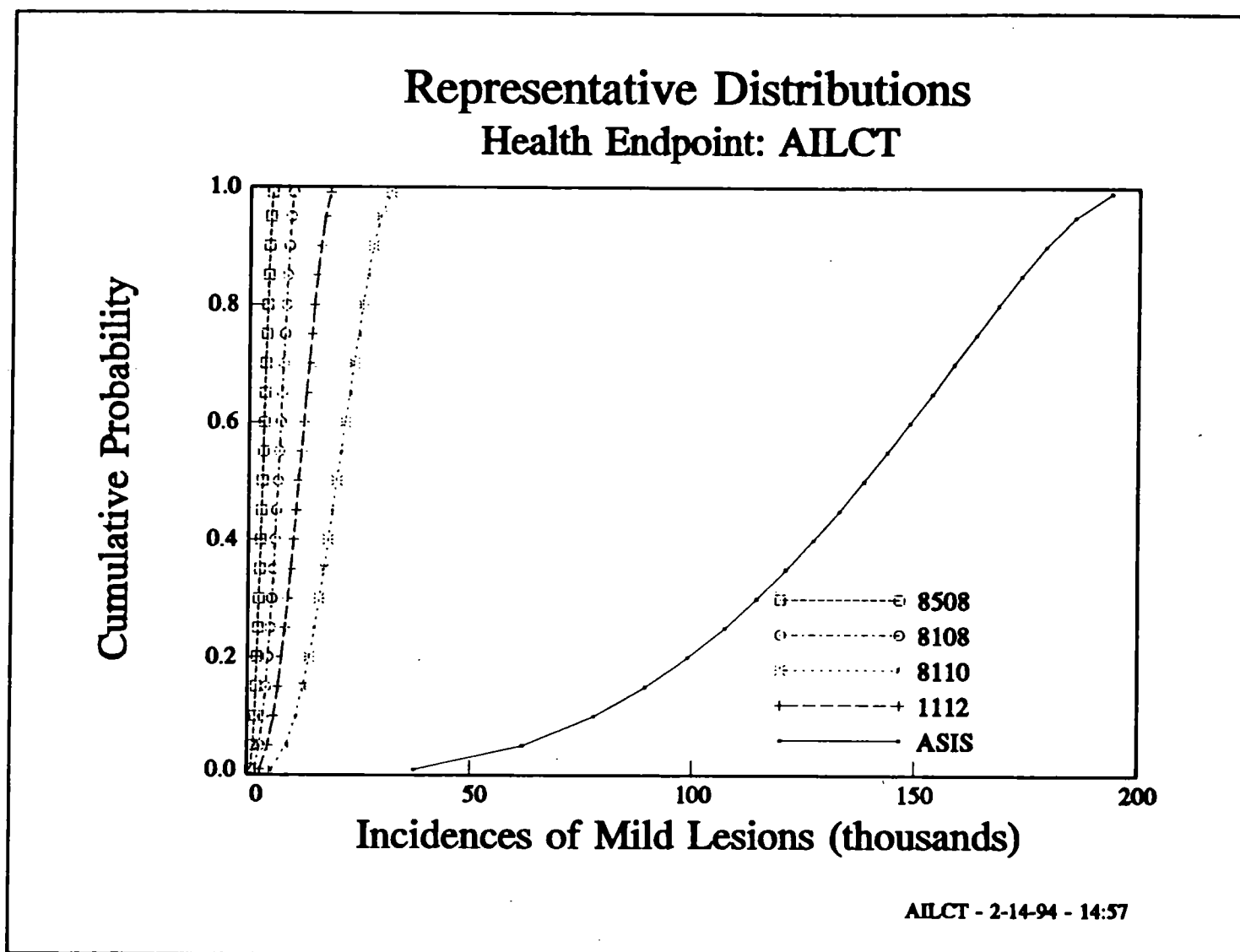


FIGURE A.31 Risk Distributions for Expert A, Mild Lesions, Los Angeles, Children, 10 Seasons, All Air Quality Scenarios

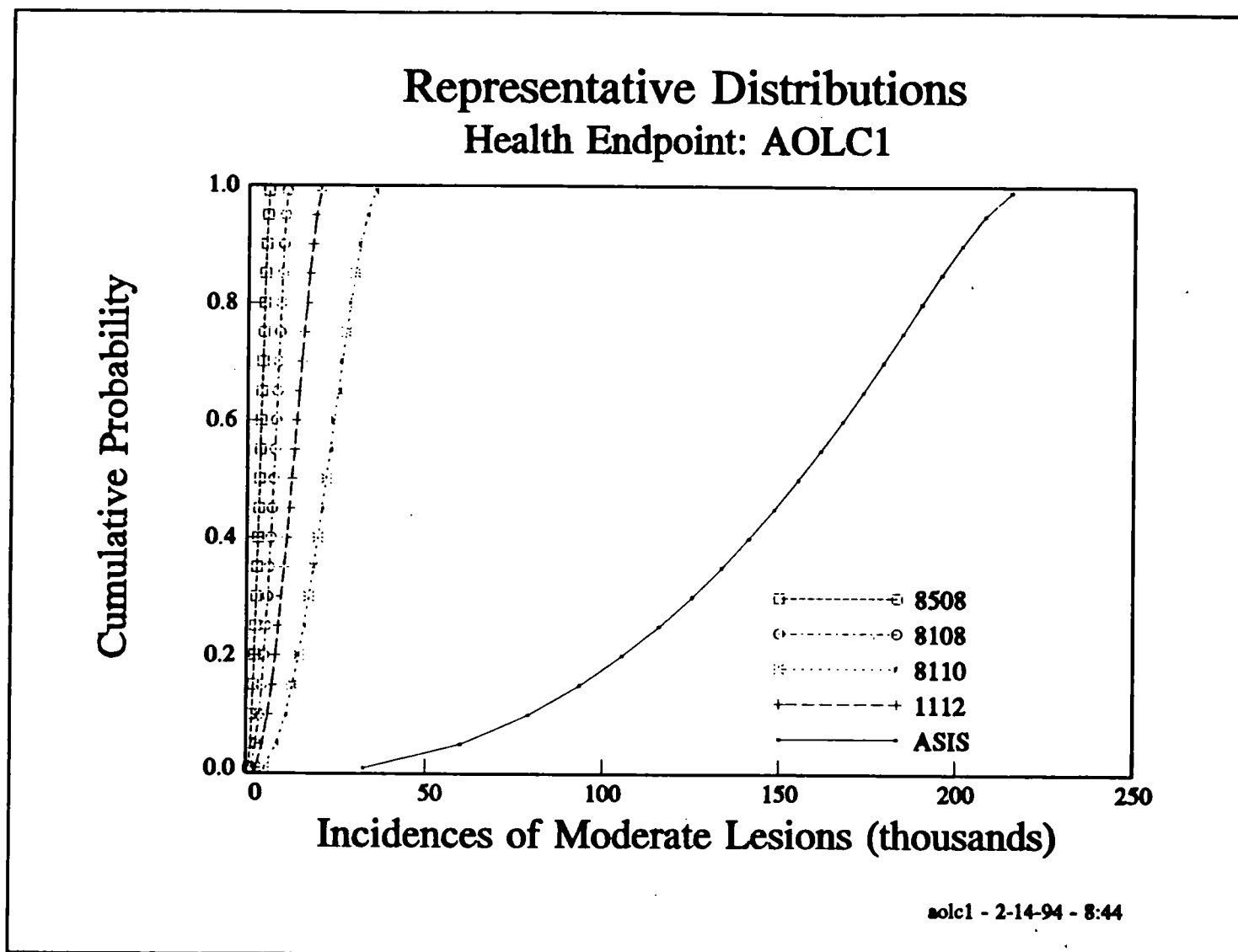


FIGURE A.32 Risk Distributions for Expert A, Moderate Lesions, Los Angeles, Children, 1 Season, All Air Quality Scenarios

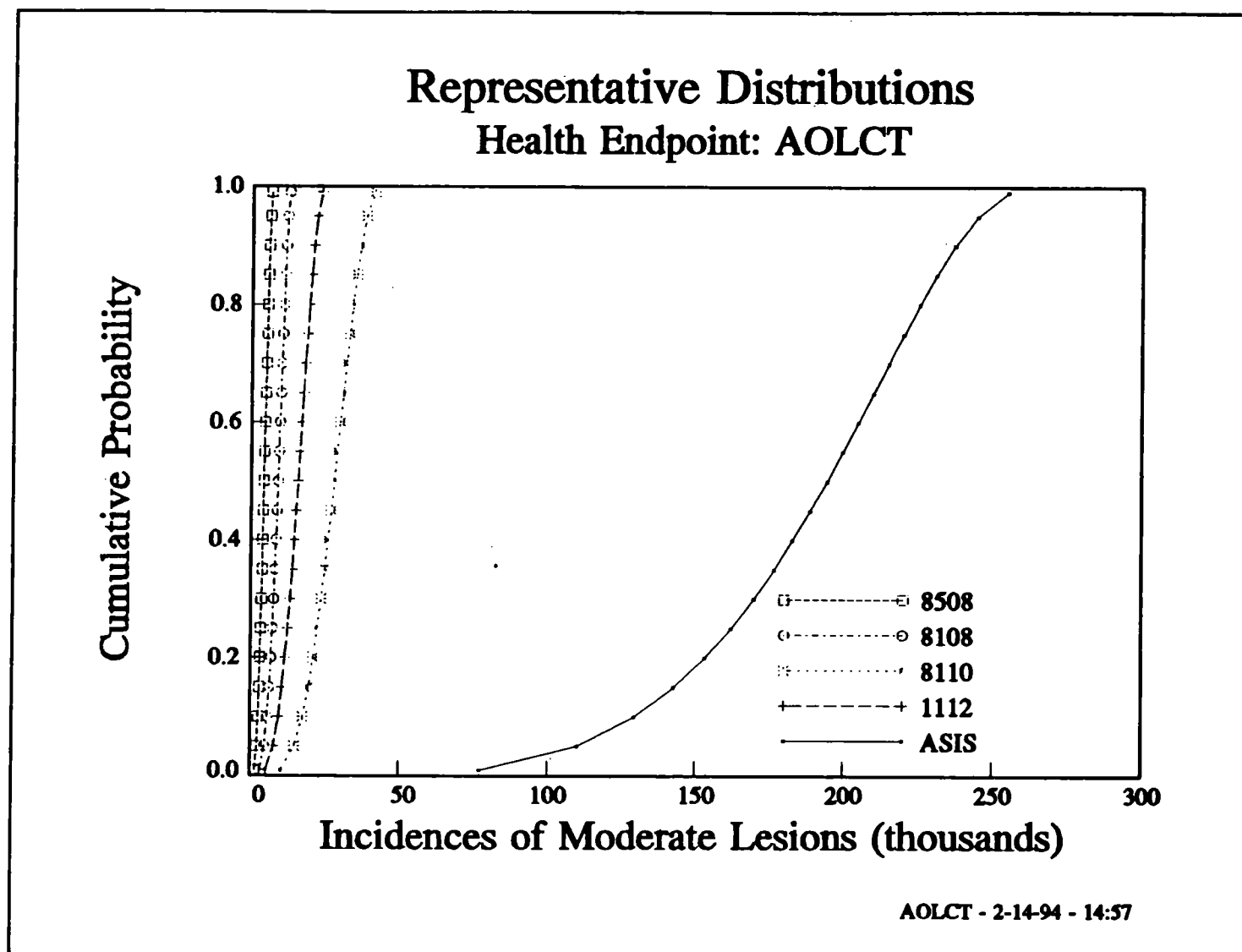


FIGURE A.33 Risk Distributions for Expert A, Moderate Lesions, Los Angeles, Children, 10 Seasons, All Air Quality Scenarios

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