Overview of Ozone Human Exposure and Health Risk Analyses Used in the U.S. EPA's Review of the Ozone Air Quality Standard

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ABSTRACT

This paper presents an overview of the ozone human exposure and health risk analyses developed under sponsorship of the U.S. Environmental Protection Agency (EPA). These analyses are being used in the current review of the national ambient air quality standards (NAAQS) for ozone. The analyses consist of three principal steps: (1) estimating short-term ozone exposure for particular populations (exposure model); (2) estimating population response to exposures or concentrations (exposure-response or concentration-response models); and (3) integrating concentrations or exposure with concentration-response or exposure-response models to produce overall risk estimates (risk model). The exposure model, called the probabilistic NAAQS exposure model for ozone ($pNEM/O_3$), incorporates the following factors: hourly ambient ozone concentrations; spatial distribution of concentrations; ventilation state of individuals at time of exposure; and movement of people through various microenvironments (e.g., outdoors, indoors, inside a vehicle) of varying air quality. Exposure estimates are represented by probability distributions. Exposure-response relationships have been developed for several respiratory symptom and lung function health effects, based on the results of controlled human exposure studies. These relationships also are probabilistic and reflect uncertainties associated with sample size and variability of response among subjects. The analyses also provide estimates of excess hospital admissions in the New York City area based on results from an epidemiology study. Overall risk results for selected health endpoints and recently analyzed air quality scenarios associated with alternative 8-hour NAAQS and the current 1-hour standard for outdoor children are used to illustrate application of the methodology.

INTRODUCTION

As stated in the U.S. Clean Air Act, the U.S. EPA is required to set, review, and revise, as appropriate, the primary NAAQS for criteria pollutants. This review includes a determination on whether the scientific basis for a NAAQS has changed sufficiently to warrant revisions. 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). A CD summarizes and evaluates the scientific literature relevant to setting ambient air quality standards fo a given pollutant or class of pollutants (e.g., particulate matter). With respect to health effects, the ozone CD evaluates the human clinical and field studies and the epidemiological and animal toxicological evidence regarding physiological and adverse health effects that result from exposure to ozone and other photochemical oxidants.

The NAAQS review process consists of three principal components: (1) an assessment

of the scientific and technical basis for deciding on the primary (health effects) and secondary (welfare effects) standards; (2) development of regulatory decision packages for standards and implementation; and (3) development of guidance, technical requirements, and attainment schedules for State implementation of new or revised standards. The Agency obtains comments through an extensive review process involving the public, the Clean Air Scientific Advisory Committee (CASAC), and other federal agencies including the Office of Management and Budget (OMB).

NAAQS are set for ubiquitous pollutants to protect the most sensitive population group(s) such as asthmatics and emphysematics who are exposed to the ambient environment in the course of their normal activities. The standards must protect (1) the sensitive population as a whole, but not necessarily the most sensitive individuals and (2) public health with an adequate margin of safety against effects that have not yet been uncovered by research and effects whose medical significance is a matter of disagreement.

Central to the review process is the definition of adverse health effects. Language of the Washington, D.C. Circuit Court discusses a precautionary mandate to protect against reasonable medical concerns. This does not require a medical consensus that effects are clearly harmful. Adverse effects may include aggravation of preexisting conditions such as asthma and emphysema. While medical experts may differ, the law states that determination of adverse health effects is a matter of judgment by the EPA Administrator.

The concept of providing an adequate margin of safety is a result of EPA's rejection of any attempt to set a risk free standard. Instead, EPA has recognized the importance of assessing the relative acceptability of various degrees of uncertainty about the level of protection against adverse effects afforded by limiting exposures to low levels.

EPA considers many factors in the NAAQS review process, including: the nature and severity of health effects; the degree of human exposure; and health risk estimates for sensitive population groups when a standard is just attained. Exposure and risk analyses are tools used to aid the Administrator's judgments about which standard(s) provide an adequate margin of safety.

EPA has adopted several basic principles for conducting NAAQS exposure and risk analyses. These include: explicit treatment of major uncertainties using (where feasible) probabilistic methods; use of experimental data, models, and expert judgment (as appropriate) to develop probabilistic relationships; deliberate avoidance of conservative assumptions; generation of multiple exposure and risk measures to estimate central tendencies and uncertainties; comprehensive presentation of qualitative information on the nature and severity of effects; and discussion of limitations, caveats, and additional uncertainties that were not characterized quantitatively.

As part of its review of the NAAQS for ozone, EPA's Office of Air Quality Planning and Standards (OAQPS) has for several years led the development of tools and methods for assessing the public health risk associated with attaining alternative ozone NAAQS. The purpose of these developments is to characterize, as explicitly as possible, the range and implications of uncertainties in the existing scientific database, while fully using current scientific knowledge,

available animal and human experimental and observational data, and scientific expertise. This risk assessment addresses the effects of acute exposures to ozone. It combines exposure-response relationships with exposure estimates to produce overall risk estimates. In addition, hourly air quality data in New York City are used to estimate excess respiratory-related hospital admissions of asthmatics during the ozone season. A summary of the results of acute risk assessment and its role in the ozone NAAQS review can be found in the OAQPS Staff Paper (EPA 1996a).

The acute risk assessment addresses the effects of exposure to ozone for populations engaged in either heavy or moderate exertion. The heavy exertion effects are based on 1- to 3-h controlled human exposure studies by McDonnell et al. (1983), Avol et al. (1984), and Kulle et al. (1985). The moderate exertion effects are based on results from 2-h controlled human studies by Seal et al. (1993) and from 6.6-h controlled human studies by Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991). The hospital admissions estimates are based on a multiyear study of air pollution and respiratory hospital admissions in New York City (Thurston et al. 1992).

Previous risk assessments also studied the acute health effects of ozone (Hayes et al. 1987). Methods developed in these assessments (Hayes et al. 1987, 1989) and earlier assessments for lead (Wallsten and Whitfield 1986; Whitfield and Wallsten 1989) provide a foundation for the current risk assessment.

RISK ASSESSMENT APPROACH

The basic risk assessment approach, illustrated in Figure 1, includes developing an exposure model and a health model.* The exposure model accounts for human contact with a specific criteria pollutant. The contact can be described in terms of a cumulative exposure over a specified time. For this assessment, exposure estimates were generated by pNEM/O_3 for nine urban areas and that portion of the population thought to be potentially at greatest risk to ozone exposure. The at-risk groups are outdoor children and outdoor workers. This determination is based on the discussion of at-risk populations in the ozone CD (EPA 1996b).

Two types of exposure measures have been made: persons and person-occurrences. The persons measure counts the number of individuals exposed one or more times per ozone season to the exposure indicator (ozone level and breathing rate) of interest. The person-occurrences measure first counts the times per ozone season that an individual is exposed to the exposure indicator of interest and then accumulates counts over all individuals. Therefore, the person-occurrences measure confounds persons and occurrences: 1 occurrence for 10 persons is counted the same as 10 occurrences for 1 person. The maximum number of daily maximum hourly exposure occurrences is equal to the population multiplied by the number of days in the ozone season. This paper includes both types of measures.

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* Strictly speaking, Figure 1 applies only to headcount risks for acute effects. However, the differences for hospital admissions are subtle. One difference is that hospital admissions estimates are based on a concentration-response relationship involving ambient air quality data observed at a fixed-site monitor rather than on estimates of exposure.

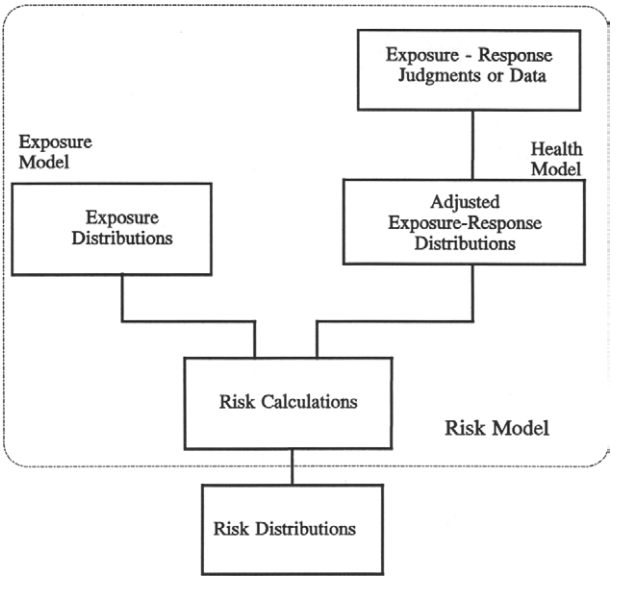

FIGURE 1 Basic Risk Assessment Approach: Risk Model Incorporating Both an Exposure Model and a Health Model

A health model accounts for human reaction to contact with a criteria pollutant. Reactions include symptoms or physiological changes (e.g., reduced pulmonary function or increased respiratory symptoms). A health model can be based on either data, judgment, or a combination of both. One important aspect of a health model is the "most at-risk population" — persons believed to be most at risk because they are either highly reactive (e.g., children whose physiological development may be impaired by exposure to ozone) or more frequently exposed (e.g., outdoor children and outdoor workers). The Clean Air Act requires NAAQS to be set at a level that protects the populations most at risk with an adequate margin of safety.

In this paper, the exposure-response relationships that characterize the effects of ozone exposure on pulmonary function and the respiratory system are based on controlled human exposure data obtained in clinical studies. Controlled human exposure studies, in contrast to epidemiological or field studies, were thought to be most appropriate for specifying the data needed for estimating exposure-response relationships. The concentration-response relationship central to our model for estimating excess hospital admissions is based on epidemiological studies by Thurston et al. (1992).

EXPOSURE MODELING

Evaluating alternative NAAQS proposed for a particular pollutant requires assessing the risks to human health associated with ozone exposures that result while just attaining each of the

standards under consideration. Important factors that need to be considered in an ozone exposure assessment are magnitude of ozone concentrations; duration of ozone concentrations; spatial distribution of concentrations; frequency of repeated peak concentrations; ventilation state of the individual at time of exposure; and movement of people through zones of varying air quality, which affects the actual exposure patterns of people living within a defined area. Figure 2 shows how the pNEM/O_3 methodology fits into the risk assessment.

In evaluating alternative NAAQS proposed for a particular pollutant, OAQPS assesses the risks to human health of air quality meeting each of the standards under consideration (Richmond and McCurdy, 1988). This assessment of risk requires estimates of the number of persons exposed at various pollutant concentrations for specified periods of time. The estimates may be specific to an urbanized area such as Los Angeles or apply to the entire nation. These estimates are 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. OAQPS has implemented this approach through an evolving methodology referred to as the NAAQS Exposure Model (NEM). From 1979 to 1988, IT Air Quality Services (formerly PEI Associates, Inc.) assisted OAQPS in developing and applying pollutant-specific versions of NEM to ozone, particulate matter, and CO. These versions of NEM are referred to as "deterministic" versions in that no attempt was made to model random processes within the exposure simulation.

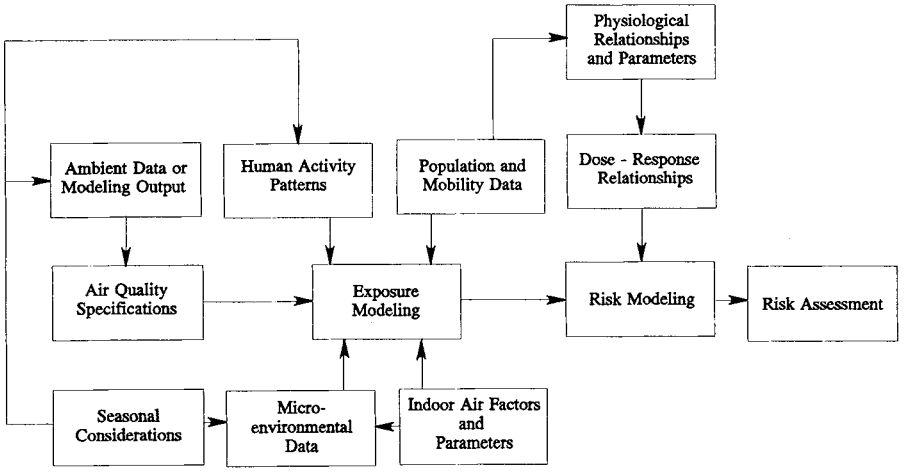

FIGURE 2 Major Components of the NEM Series of Exposure Models and Associated Health Risk Assessment Procedures

In 1988, OAQPS began to incorporate probabilistic elements into the NEM methodology and to apply the resulting model (pNEM) to the criteria pollutants. In 1992, ITAQS developed a special version of pNEM applicable to ozone (pNEM/O_3) that incorporated mass balance techniques. ITAQS subsequently made the following enhancements to this model and its input data bases.

- Use of more recent (1990-91) fixed-site monitoring data for estimating ambient

ozone concentrations. The earlier analysis was based on 1981-84 monitoring data.

- An increase in the number of fixed-site monitors used to represent each urban area.
- Use of more recent (1990) census data for estimating cohort populations. The earlier analysis used 1980 census data.
- A new methodology for adjusting ambient ozone data to simulate attainment of one-hour and eight-hour NAAQS.
- Revision of the algorithm used to determine limiting values for equivalent ventilation rate.
- Development of origin/destination tables through the use of a new commuting algorithm.

A report by Johnson et al. (1996) describes these enhancements and summarizes the results of applying the enhanced model to the general population of each of nine U.S cities.

EPA also directed ITAQS to develop a special version of pNEM/O_3 applicable to outdoor workers and to use it to estimate the ozone exposures of outdoor workers residing in each of the nine cities. A summary of this work can be found in a report by Johnson et al. (1996).

In follow-up work for EPA, ITAQS developed a second special version of pNEM/O_3 applicable to children who tend to be active outdoors (hereafter referred to as "outdoor children"). A report by Johnson et al. (1996) summarizes the results of applying this version of pNEM/O_3 to outdoor children residing in the nine cities.

In each of the recent applications of pNEM/O_3, the ozone levels reported by monitors within each study area were adjusted to simulate the attainment of a specified ozone standard. The standard was defined as a limit to the number of daily maximum one-hour or eight-hour ozone concentrations expected to exceed a specified ozone concentration. The attainment status of each study area was determined by a single year of monitoring data, and the adjustment procedure was applied to this year. EPA is currently evaluating a variety of alternative forms of the ozone NAAQS. Each of these alternative NAAQS limits the average value of the n-th ranked daily maximum 8-hour concentration to a specified concentration, based on three years of data. Five of the alternative NAAQS are formulations of 0.08 ppm and 0.09 ppm ozone standards that permit rounding ov values to the nearest 0.01 ppm:

- 8HA2H-0.084: the second highest daily maximum 8-hr concentration averaged over three years shall not exceed 0.084 ppm (abbreviation: 8284)
- 8HA3H-0.084: the third highest daily maximum 8-hr concentration averaged over three years shall not exceed 0.084 ppm (abbreviation: 8384)

- 8HA5H-0.084: the fifth highest daily maximum 8-hr concentration averaged over three years shall not exceed 0.084 ppm (abbreviation: 8584)

- 8HA2H-0.094: the second highest daily maximum 8-hr concentration averaged over three years shall not exceed 0.094 ppm (abbreviation: 8294)

- 8HA3H-0.094: the third highest daily maximum 8-hr concentration averaged over three years shall not exceed 0.094 ppm (abbreviation: 8394)

In determining attainment status with respect to the 0.084 ppm standards, ozone concentrations between 0.080 ppm and 0.084 ppm are rounded down to 0.08 ppm. Consequently, an ozone concentration of 0.084 ppm is not considered to exceed a standard level of 0.08 ppm. In a similar manner, values between 0.090 ppm and 0.094 ppm are rounded down to 0.09 ppm for the 0.094 ppm standards.

Each of the five standards specifies the maximum ozone concentration permitted for the three-year average of a ranked value. Researchers developed an air quality adjustment procedure (AQAP) for each eight-hour standard that could be used to simulate the ozone levels expected to occur during a single year when a city just attained the standard over the three-year period. They also developed a comparable AQAP that was applicable to the current one-hour standard. This standard is defined as follows:

- 1H1EX-0.124: the daily maximum 1-hr concentration expected to be exceeded once per year shall not exceed 0.124 ppm (abbreviation: 1124)

The new AQAPs used in these exposure assessments differ from the AQAPs used in previous applications of pNEM/O_3 to outdoor children. Each of new AQAPs is applied to a three-year period so as to simulate the attainment of the associated standard over the entire period. The adjustment required for the three-year period is applied to a single year (1990, 1991, 1992, or 1993) within the period and the resulting single-year of ozone data is used in the exposure assessment to represent typical attainment conditions. The selected year is the middle year of the three-year period with respect to relative ozone level. This approach contrasts with the previous AQAPs in which attainment was determined by examining a single year (1990 or 1991) of ozone data. The ozone data for the selected year were adjusted to exactly attain the specified standard and then used in the exposure assessment to represent attainment conditions.

The new AQAPs also use a proportional adjustment procedure for all standards in all cities. In the previous AQAPs, a non-proportional adjustment procedure based on the Weibull distribution was used for all standards in six of the nine cities and for a few standards in the remaining three cities (Chicago, Denver, and Miami). A proportional adjustment procedure was used for the other standards in these three cities.

Exposure estimates are based on a set of 10 runs of pNEM/O_3 for a particular combination of city and standard. To reduce the effects of run-to-run variability caused by the probabilistic elements of pNEM/O_3, each set of 10 runs used the same 10 random number generator "seeds." This approach retained the desired variability within each set of 10 runs but

removed the set-to-set variability. Consequently, the differences in the mean exposure estimates associated with the seven standards were assumed to reflect primarily the differences in ambient ozone concentrations permitted by the standards. In the previous AQAPs, each set of 10 runs used a different set of random number seeds. The resulting variability in random number sequences used in the pNEM/O_3 runs may have produced some of the differences observed among the mean exposure estimates associated with the various standards under evaluation.

Exposure-response probabilities for each run are computed by dividing the number of children at each ozone concentration by the number of children who reached a specific exertion level in a run. For example, the data in Table 1 (which are for just attaining standard 1124, Philadelphia, children, 8-h exposures at moderate exertion, pNEM/O_3 run 2) show that the number of children for this particular run is about 270 thousand. About 40 thousand children were exposed to ozone at concentrations of 0.041-0.06 ppm. Dividing this number by the total number of children at moderate exertion results in a probability of 0.16. The same computations are performed for the remaining ozone concentrations. The sum of the calculated probabilities does not equal 1 because exposures at $\leq$ estimated background are not included. The probabilities for this example are presented in Table 1. Such probabilities are needed to estimate risk distributions. Figure 3 is an example of the variation in exposure estimates among 10 pNEM/0_3 runs for Philadelphia children given that the current standard (1 h, 1 expected exceedance, 0.124 ppm) is just attained.

Table 2 is an example of the summary statistics about air quality scenarios that have been developed for each city. Entries in Table 2 are estimates of the 8-hr maximum dosage exposures experienced by outdoor children during which ozone concentrations exceeded 0.08 ppm and EVR ranged from 13-26 L/min/m^2.

The new exposure and air quality estimates developed by Johnson et al. (1997) were later used in a quantitative risk assessment by Whitfield (1997). Some results of that risk assessment are presented in this paper.

TABLE 1 Calculating Exposure Probabilities for Outdoor Children Exposed for 8 Hours at Moderate Exertion from pNEM/O_3 Estimates for Run 2, Philadelphia, Scenario 1124 Just Attained

Ozone Intervals (ppm)	Number of Children		Probabilities[c]
	In Interval or Higher[a]	In Interval[b]	
0.000	268,923	0	(NR)[d]
0.001 - 0.020	268,923	9,058	(NR)
0.021 - 0.040	259,865	26,012	(NR)
0.041 - 0.060	233,853	43,123	0.1604
0.061 - 0.070	190,730	52,135	0.1939
0.071 - 0.080	138,595	68,048	0.2530
0.081 - 0.090	70,547	44,090	0.1640
0.091 - 0.100	26,457	19,555	0.0727
0.101 - 0.110	6,902	6,902	0.0257
0.111 - 0.120	0	0	0.0000
0.121 - 0.130	0	0	0.0000
0.131 - 0.140	0	0	0.0000
0.141 - 0.150	0	0	0.0000
0.151 - 0.160	0	0	0.0000
0.161 - 0.170	0	0	0.0000
0.171 - 0.180	0	0	0.0000
0.181 - 0.190	0	0	0.0000
0.191 - 0.200	0	0	0.0000
0.201+	0	0	0.0000

[a] A total of 268,923 children reached a moderate exertion level in run 2.

[b] Number in interval i equals number in interval i or higher minus the number in interval $i + 1$ or higher (e.g., 9,058 = 268,923 − 259,865).

[c] Probability of interval i equals the number in interval i divided by 268,923. This probability is also the fraction of children who reached a moderate exertion level while exposed to the ozone concentration for interval i in run 2.

[d] NR means not required. Calculations were not made for these concentrations because they are ≤ the estimated background level (0.04 ppm).

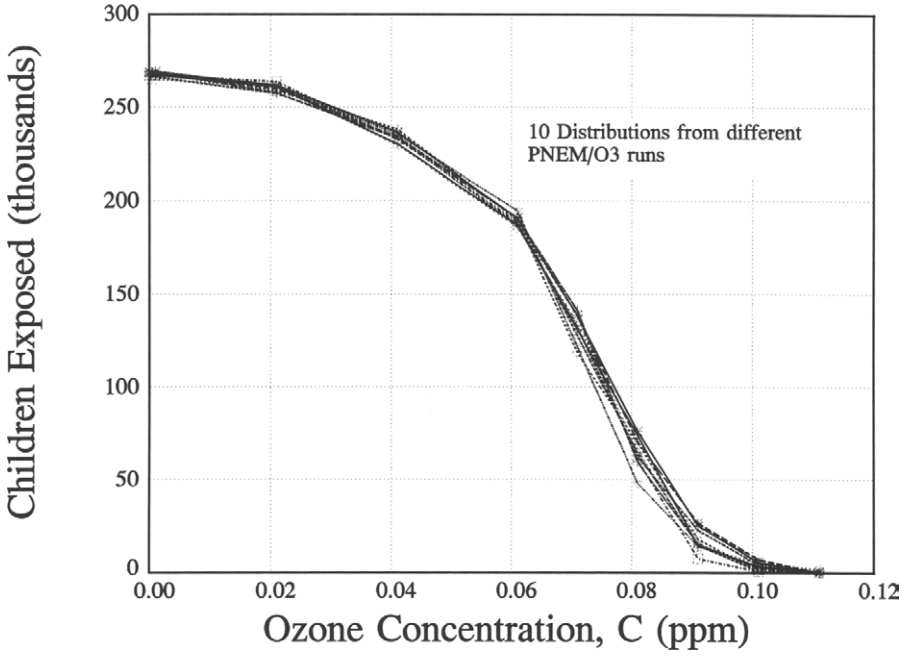

FIGURE 3 Illustration of Variation in Exposure Estimates among 10 pNEM/03 Runs for Philadelphia Children Given that the Current Standard (1 h, 1 expected exceedance, 0.124 ppm) Is Just Attained

TABLE 2 Estimates of 8-H Maximum Dosage Exposures Experienced by Outdoor Children in Philadelphia during which Ozone Concentration Exceeded 0.08 ppm and EVR[a] Ranged from 13-27 L/min/m^2

	Regulatory scenario					
Statistic[b]	1H1EX-0.124[c]	8HA3H-0.094	8HA2H-0.094	8HA5H-0.084	8HA3H-0.084	8HA2H-0.084
Mean Estimate of the Number of Outdoor Children	65,153	40,133	24,752	17,147	10,012	4,243
Percent of Total Outdoor Children Population	23.66	14.58	8.99	6.23	3.64	1.54
Range in this percentage for 10 runs	17.43-27.64	10.22-19.47	6.08-13.02	2.37-9.61	1.64-7.12	0.10-3.05
Mean Estimate of Person-Occurrences	78,918	44,645	26,526	17,899	10,169	4,243
Percent of Total Person-Occurrences	0.13	0.08	0.05	0.03	0.02	0.01
Range in this percentage for 10 runs	0.11-0.17	0.06-0.10	0.03-0.06	0.01-0.05	0.01-0.03	0.00-0.01
Mean Estimate of Occurrences/Person Exposed	1.21	1.11	1.07	1.04	1.02	1.00
Percentage exposed for indicated number of days						
1 Day	82.47	90.22	93.30	94.92	97.52	100.00
2 Days	14.11	8.29	5.89	4.81	2.48	0.00
3 Days	3.05	1.41	0.81	0.27	0.00	0.00
>3 Days	0.38	0.07	0.00	0.00	0.00	0.00

[a]Equivalent ventilation rate = (ventilation rate)/(body surface area).
[b]Mean or range for 10 runs of pNEM/O_3.
[c]Current NAAQS.

HEALTH MODELING

The health models discussed in this section are described more fully in Whitfield et al. (1996). The basis for the development of health models for lung function and symptoms endpoints is a number of controlled human exposure studies:

- 1-h exposures at heavy exertion* studies by McDonnell et al. (1983), Avol et al. (1984), and Kulle et al. (1985),
- 1-h exposures at moderate exertion† studies by Seal et al. ((1993), and
- 6.6-h exposures at moderate exertion‡ by Folinsbee et al. (1988), Horstman et al. (1990), and McDonnell et al. (1991). Results of these studies were used to develop exposure-response relationships for 8-h exposures.

These studies were selected because they best satisfied the following criteria:

- *Applicability to the population groups potentially at greatest risk.* Studies of persons exposed while engaged in moderate or heavy exertion are of greatest interest because such subjects are thought to be at greater risk than those at rest.
- *Comparability.* The total dose must be compared with the level of exertion and the exercise protocol of particular interest.
- *Number of subjects.* To limit the effects of small sample size, studies with at least 10 subjects per exposure level are desired.
- *Exposure concentrations.* Studies with multiple concentration levels in the range of ambient levels are desired.
- *Individual subject data.* These data are needed to develop exposure-response relationships.

It is important to note that, although the controlled human exposure studies used in the ozone risk assessment included adults aged 18-35, exposure-response relationships derived for both "outdoor children" and "outdoor workers" are used. Recent findings support the use of adult-based results to characterize children. These findings include results from other chamber

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* Equivalent ventilation rates (EVRs) >30 L/min/m^2

† EVRs between 16-30 L/min/m^2

‡ EVRs between 13-27 L/min/m^2

studies (McDonnell et al. 1985a) and summer camp field studies in at least six different locations in the northeast United States, Canada, and southern California. These locations reported changes in lung function in healthy children similar to those observed in healthy adults exposed to ozone under controlled chamber conditions. As stated in the CD, "although direct comparisons cannot be made because of incompatible differences in experimental design and analytical approach," the range of response in the summer camp studies "is comparable to the range of response seen in chamber studies at low O_3 concentrations" (EPA 1995, pp. 9-7 and 9-8).

One or more of these studies recorded data that make it possible to construct a probabilistic exposure-response relationship for the following health endpoints:

- decrease in forced expiratory volume in 1 s (FEV_1),
- cough,
- chest pain on deep inspiration, and
- lower respiratory symptoms (any of a number of symptoms that included cough).

We considered three levels of FEV_1 decrements (FEV1 decrements $\geq 10\%$, $\geq 15\%$, and $\geq 20\%$) and two levels for cough, chest pain, and lower respiratory symptoms (any, moderate-to-severe). Although all of the studies did not investigate all of these endpoints, it was possible to develop exposure-response relationships for 33 endpoints (i.e., each exposure-response relationship is associated with a specific endpoint and a specific study). Results for only four of these endpoints are presented in this paper: moderate-to-severe cough (for 1-h exposures at heavy exertion, based on McDonnell et al. 1983), moderate-to-severe chest pain on deep inspiration (for 1-h exposures at moderate exertion, based on Seal et al. 1993), and FEV_1 decrements $\geq 15\%$ and $\geq 20\%$ (for 8-h exposures at moderate exertion, based on Folinsbee et al. 1988, Horstman et al. 1990, and McDonnell et al. 1991).

Developing exposure-response relationships for acute endpoints is a three-step process. (See Appendix A of Whitfield et al. 1996 for details of this process.) The process starts with data from the laboratory experiments described earlier. Before developing the probabilistic exposure-response relationships, we "corrected the data for exercise in clean air," which means that we attempted to remove any systematic bias in the data that might be attributable to an exercise effect. These data become the "observations" shown in Figure 4 (step 1). In step 2, a function is fit to the data via regression techniques. Specifically, the numbers of subjects responding at 0.08, 0.10, and 0.12 ppm are 5 of 60, 5 of 32, and 6 of 30, respectively, which leads to the response rates shown in Figure 4. This step is necessary to estimate response rates at ozone concentrations that differ from those at which laboratory data are available. Step 3 develops, for example, the 90% credible interval (CI) about the fitted (predicted) median response rate at ozone concentrations needed for the risk assessment calculations (i.e., those used in $pNEM/O_3$). This last step is accomplished by applying the inverse beta function with parameters X and $N - X$, where X is the predicted median response rate at a particular ozone concentration, and N is the number of subjects associated with the chosen ozone concentration.

The 90% CI is defined by the 0.05 and 0.95 fractiles. For this risk assessment, response rates are calculated for 21 fractiles (for cumulative probabilities from 0.05 to 0.95 in steps of 0.05, plus probabilities of 0.01 and 0.99) at a number of ozone concentrations that depend on the health endpoint. The functions chosen "best fit" the data according to the following principles and rules:

- *Linear functions were favored, especially when the number of observation points (i.e., ozone concentrations at which laboratory data are available) was small.* As few as two usable observation points and as many as six observation points were available for the 33 endpoints mentioned earlier.

- *Functions with high regression r^2 values were more desirable than functions with low r^2 values.* This principle allowed choosing a nonlinear function over a linear function — even if the number of observation points was small — if the r^2 value of the nonlinear function was considerably larger than that for the linear function.

- *All functions for each of the fractiles must be monotonic increasing (i.e., they must never decrease) as ozone concentration increases.* This factor is a logical *rule*, and it came into play when the number of subjects varied considerably at different ozone concentrations. Such a condition made it necessary to use an average number of subjects at all ozone concentrations.

A linear function with slope 2.925 and intercept -0.1462 best fits the data subject to the above principles for FEV_1 decrement $\geq 20\%$ and 8-h exposures. This function defines the fractional* median exposure-response relationship. Because the linear function intercepts the X-axis at 0.05 ppm and response rates cannot be negative, the response rate is 0 at ozone concentrations ≤ 0.05 ppm. Thus, the median exposure-response relationship used in this risk assessment may be thought of as having a "hockey stick" shape with an "inflection point" at 0.05 ppm and zero response for ozone concentrations ≤ 0.05 ppm. In Figure 4, note that the curves for fractiles other than the median are not linear. This is attributable to the construction of credible intervals at the ozone concentrations needed for the subsequent risk calculations; the credible interval widths depend in part on the number of subjects at each ozone concentration, which, for this case, varies. Since 60 subjects were subjected to exposures at 0.08 ppm, the credible interval is smaller than at, for example, 0.10 ppm, at which 32 subjects were exposed.

* To obtain response rate in percent, multiply the fractional result by 100%.

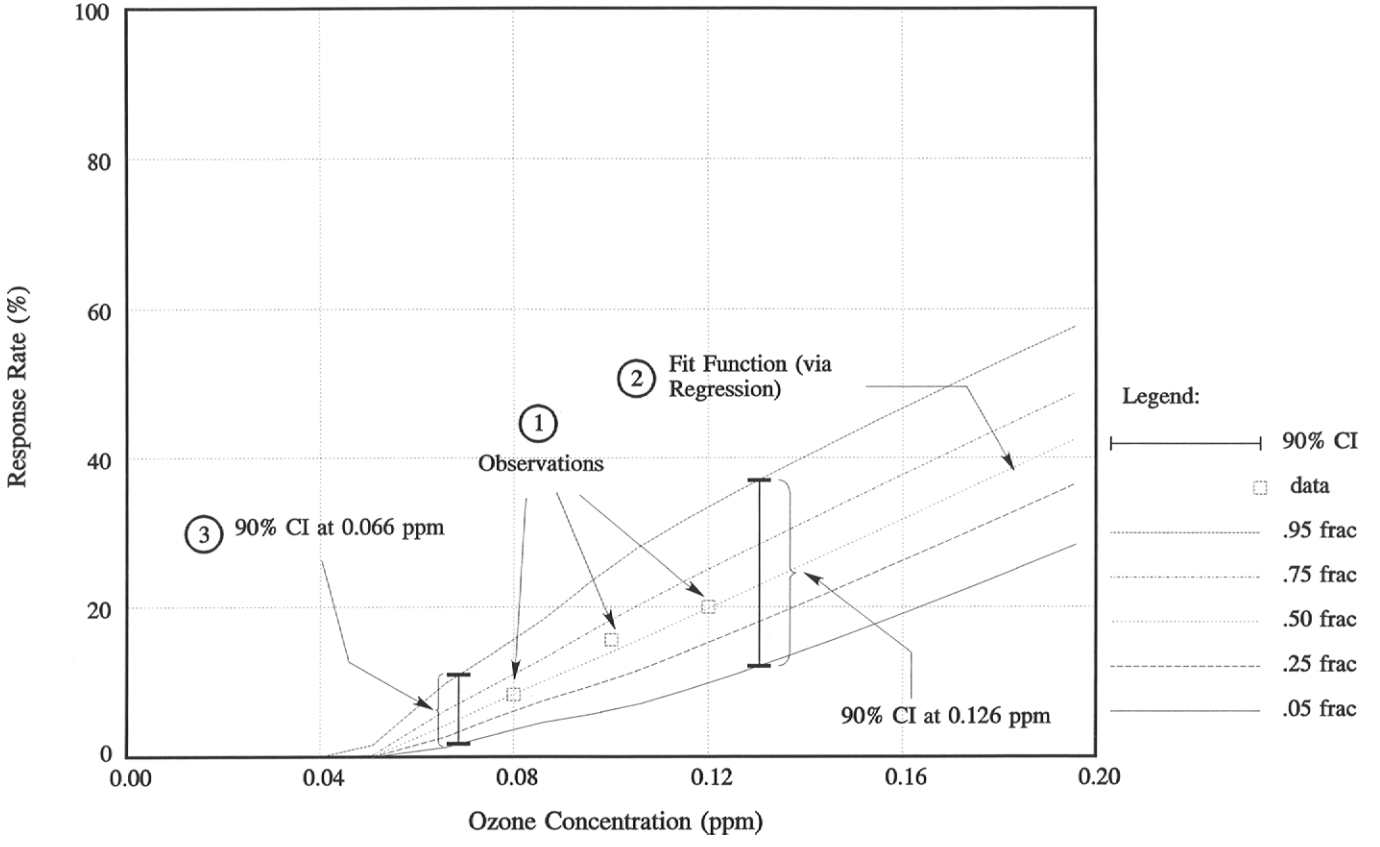

FIGURE 4 Steps Used to Develop Probabilistic Exposure-Response Relationships, FEV_1 Decrement ≥20%, 8-h Exposure, Moderate Exertion (Derived from: Folinsbee et al. 1988; Horstman et al. 1990; and McDonnell et al. 1991)

RISK ESTIMATES FOR 8-HOUR EXPOSURES TO OZONE

The risk computations (which comprise the risk model) are conceptually simple and based on exposure and health models. In general, the risk (which is an expected fractional response rate) for the k'th fractile R_k is

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

or

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

where:

P_j = fraction of the population having personal exposures at an ozone concentration of e_j ppm in a single pNEM/O_3 run;

$RR_k|e_j$ = k-fractile response at ozone concentration e_j;

$RR_k|\text{background}$ = k-fractile response at background; and

N = number of ozone concentrations.

The Pj values used to calculate risk results are based on the assumption that the air quality scenario under study is just attained.

As discussed earlier, it was possible to correct exposure-response relationships for exercise in clean air. The $RR_k|e_j$ values reflect this correction for the FEV_1 decrements $\geq 20\%$ endpoint for 8-h exposures at moderate exertion (based on study results from Folinsbee et al. 1988, Horstman et al. 1990, and McDonnell et al. 1991). Table 3 shows the risk computations for the 0.5-fractile (the median), for pNEM/O_3 run 2, exposures to outdoor children, based on air quality in Philadelphia that just attains the current standard (1124) for the persons measure. Background ozone is ≤ 0.04 ppm. The entries in column C are the fractions of the population engaged in moderate exertion who are exposed to the corresponding ozone concentrations in column B. The entries 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 about 0.06, or 6%. Since $RR_{0.5}$ | background is exactly zero, this result is unchanged after correcting for background. The final step is to multiply the fractional response rate by the number of outdoor children who achieved moderate exertion for 8 h to obtain, in this case, the median estimate of

the number of individuals that experience FEV_1 decrements ≥20%. For $pNEM/O_3$ run 2, nearly 270 thousand outdoor children achieved the heavy exertion level, so the median estimate is about 16 thousand outdoor children.

To develop a probability distribution over outdoor children that accounts for all of the conditions mentioned earlier, the above computations are repeated for any number of fractiles. Results usually appear "smoother" if a large number of fractiles are used. In this analysis, 21 fractiles are used to calculate risk results.

TABLE 3 Calculating the Median of a Risk Distribution

A	B	C	D	E
Index j	e_j (ppm)	P_j	$RR_{0.5} \mid e_j$	$RR_{0.5} = C \times D$
1	0.051	0.1604	0.000233	0.0000
2	0.066	0.1939	0.041839	0.0081
3	0.076	0.2530	0.071412	0.0181
4	0.086	0.1640	0.100205	0.0164
5	0.096	0.0727	0.128108	0.0093
6	0.106	0.0257	0.156623	0.0040
7	0.116	0	0.186317	0.0000
8	0.126	0	0.216072	0.0000
			Column E Sum:	0.0559

Headcount risk results have been "corrected for background," that is, 0.04 ppm for acute exposures. This correction, as explained earlier, "subtracts" the probability distribution over response at the background concentration from the probability distribution over response for ozone concentrations above background. As with many computations in this analysis, this subtraction assumes perfect correlation and allows corrections to be made by simply subtracting corresponding responses on a fractile-by-fractile basis. If no response occurs at a particular background concentration, the "uncorrected" and "corrected" results are identical.

Table 4 lists risk results for this endpoint when the 1124 standard is just attained in Philadelphia. Ten distributions are provided — 1 for each of the 10 available $pNEM/O_3$ runs. The first column lists cumulative probabilities for the distributions. Each row in the table lists the number of children having FEV_1 decrements ≥20% for each of 10 $pNEM/O_3$ runs. For example, the 0.50 cumulative probability (0.5 fractile) estimates range from about 13.5 thousand (run 6) to about 15 thousand (run 10) outdoor children. The mean, standard deviation, and total number of people (TotPop) are listed at the bottom of the table. For run 1, the mean is about 14 thousand, the standard deviation is about 7 thousand, and TotPop is about 270 thousand. Note that TotPop is based on the total number of outdoor children who reached a moderate level of exertion in each $pNEM/O_3$ run. This number varies from run to run.

TABLE 4 Probability Distributions over Number of Outdoor Children Having FEV_1 Decrements ≥20% During One Ozone Season, Philadelphia, 8-Hour Exposures, Moderate Exertion, Just Attaining Standard 1124[a]

Cumulative Probability	Number of Outdoor Children Having FEV_1 Decrements ≥20% by pNEM/O_3 Run									
	1	2	3	4	5	6	7	8	9	10
0.01	3,794	3,988	3,773	3,667	3,645	3,424	3,609	3,747	3,772	4,028
0.05	5,920	6,229	5,889	5,741	5,730	5,443	5,679	5,876	5,910	6,277
0.10	7,355	7,739	7,316	7,144	7,143	6,822	7,085	7,315	7,354	7,792
0.15	8,451	8,892	8,406	8,216	8,226	7,882	8,163	8,416	8,457	8,949
0.20	9,400	9,889	9,348	9,144	9,164	8,803	9,097	9,369	9,412	9,948
0.25	10,269	10,802	10,212	9,995	10,025	9,650	9,955	10,243	10,288	10,863
0.30	11,094	11,669	11,032	10,803	10,844	10,456	10,771	11,073	11,119	11,731
0.35	11,897	12,512	11,829	11,590	11,641	11,243	11,566	11,880	11,928	12,575
0.40	12,693	13,348	12,621	12,371	12,433	12,025	12,356	12,682	12,731	13,413
0.45	13,497	14,191	13,419	13,159	13,232	12,815	13,154	13,491	13,541	14,257
0.50	14,321	15,055	14,237	13,967	14,052	13,626	13,972	14,320	14,371	15,122
0.55	15,177	15,953	15,088	14,808	14,905	14,471	14,825	15,183	15,235	16,021
0.60	16,083	16,901	15,988	15,697	15,808	15,366	15,728	16,095	16,147	16,972
0.65	17,058	17,921	16,955	16,655	16,781	16,330	16,701	17,077	17,130	17,994
0.70	18,129	19,041	18,019	17,707	17,850	17,391	17,771	18,157	18,209	19,116
0.75	19,336	20,303	19,218	18,894	19,056	18,588	18,981	19,375	19,426	20,381
0.80	20,746	21,775	20,618	20,282	20,465	19,988	20,395	20,798	20,846	21,858
0.85	22,478	23,581	22,338	21,987	22,198	21,710	22,137	22,546	22,591	23,671
0.90	24,794	25,993	24,639	24,270	24,518	24,015	24,473	24,887	24,924	26,094
0.95	28,509	29,854	28,329	27,936	28,243	27,719	28,231	28,644	28,664	29,977
0.99	36,354	37,986	36,123	35,695	36,123	35,558	36,206	36,587	36,562	38,166
Mean	15,393	16,161	15,301	15,031	15,139	14,721	15,077	15,409	15,451	16,235
StdDev[b]	7,040	7,358	6,993	6,920	7,022	6,953	7,039	7,098	7,092	7,383
TotPop[c]	267,352	268,923	265,077	267,324	266,275	268,386	268,292	269,471	269,538	268,874

[a] Based on Folinsbee et al. 1988, Horstman et al. 1990, and McDonnell et al. 1991.

[b] StdDev means standard deviation.

[c] TotPop means total population (i.e., children).

Figure 5 is a plot of the data listed in Table 4 for just attaining standard 1124. It also provides results for scenario 8284. Note that the risks are lower when standard 8284 is attained than when the current standard is attained (indicated by the fact that all distributions for the 8284 standard are closer to the Y axis than all distributions for the 1124 standard).

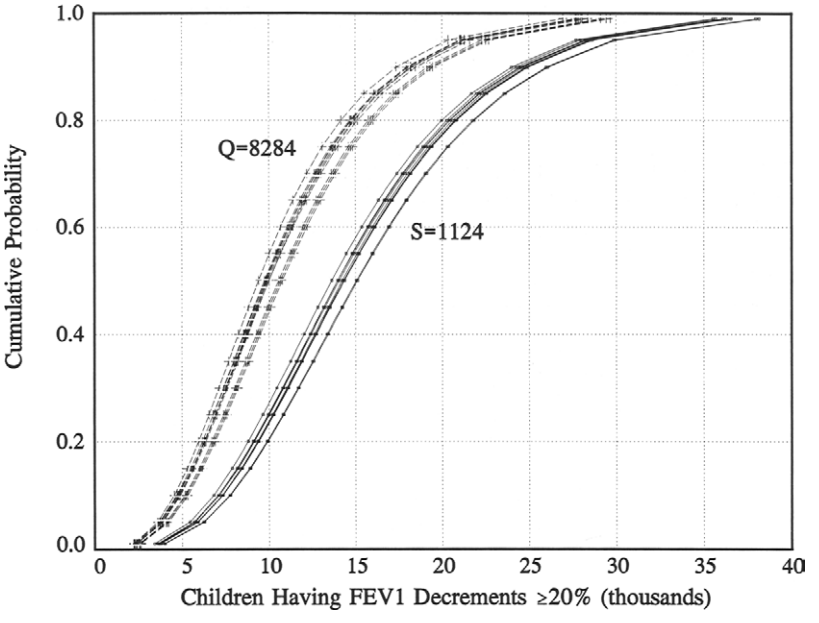

FIGURE 5 Comparison of 2 Sets of 10 Risk Distributions (just attaining scenarios 1124 and 8784, FEV_1 decrements ≥20%, Philadelphia, outdoor children, 8-h exposure, moderate exertion level; based on Folinsbee et al. 1988, Horstman et al. 1990, McDonnell et al. 1991)

On this scale, it is not usually helpful to plot the distributions for the other scenarios because, for many urban areas, many of them are nearly identical and, if they were included, the figure would be quite cluttered. This is especially true for Denver and Miami. Figure 6 provides an indication of the range of results within each set of 10 distributions. Six plots are shown, one for each air quality scenario. Each plot is "representative" of the 10 distributions for a particular scenario. Because only 6 plots are shown rather than 70, it is easier to see patterns. Each of these plots is a valid cumulative probability distribution.* For Philadelphia,

* The representative distribution is obtained by computing the average cumulative probability at selected points along the X-axis. 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 that perfect independence, and no basis exists for choosing any other degree of correlation between these 2 extremes.

the following insights can be gained about the effects of attaining each standard by examining Figure 6:

- Attainment of any alternative standard provides more protection than that afforded by attainment of the current standard (because the representative risk distribution for 1124 lies to the right of the distributions for all other standards).
- Standard 8284 provides the greatest protection (i.e., results in the lowest risk).
- The level of protection associated with standard 8294 is less than that associated with standard 8584 and greater than that associated with standards 8394 and 1124 (the current standard).

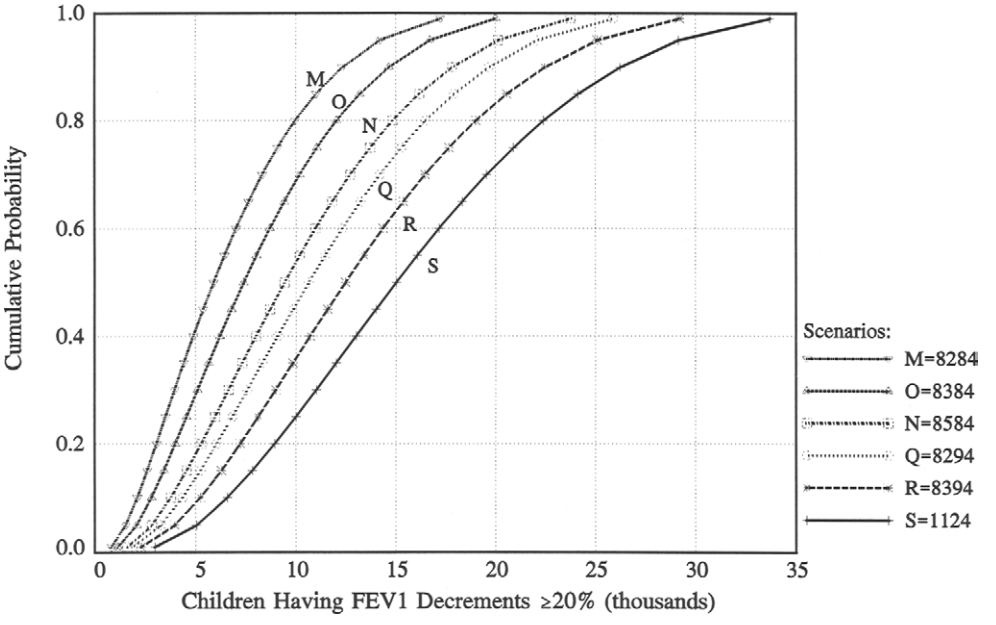

FIGURE 6 Representative Distributions for 6 Sets of 10 Risk Distributions (just attaining 6 standards, FEV_1 decrements ≥20%, Philadelphia, outdoor children, 8-h exposure, moderate exertion; based on Folinsbee et al. 1988, Horstman et al. 1990, and McDonnell et al. 1991)

These observations about standard 8294 are specific to Philadelphia do not apply to all other urban areas. Standard 8294 is less protective than the current standard (1124) for three other urban areas (Chicago, Houston, Los Angeles, and New York City). This finding is illustrated in Figure 7, which shows risk results for 9 urban areas for which exposure estimates have been

developed using pNEM/O_3. The figure consists of 54 sets of connected rectangles, which are variations of the Tukey box plot described in Morgan and Henrion (1990), that indicate uncertainty in the risk distributions. For example, there are three rectangles above letter S (the code letter for standard 1124; letter codes for all standards considered here are listed in Table 5) for each urban area. The top rectangle represents the range of the 0.95 fractiles; the middle rectangle represents the range of the medians; and the bottom rectangle represents the range of the 0.05 fractiles. A line connects the bottom of the 0.95-fractile rectangle and the top of the 0.05-fractile rectangle and passes through the 0.5-fractile rectangle.

When the risk distributions for a particular air quality scenario are quite "similar," the rectangles are small. When the variances of a set of risk distributions are small, the rectangles are close together. When the distributions are spaced far enough apart (indicative of widely varying risk estimates for different pNEM/O_3 runs), the rectangles overlap. There are no overlapping cases in Figure 7.

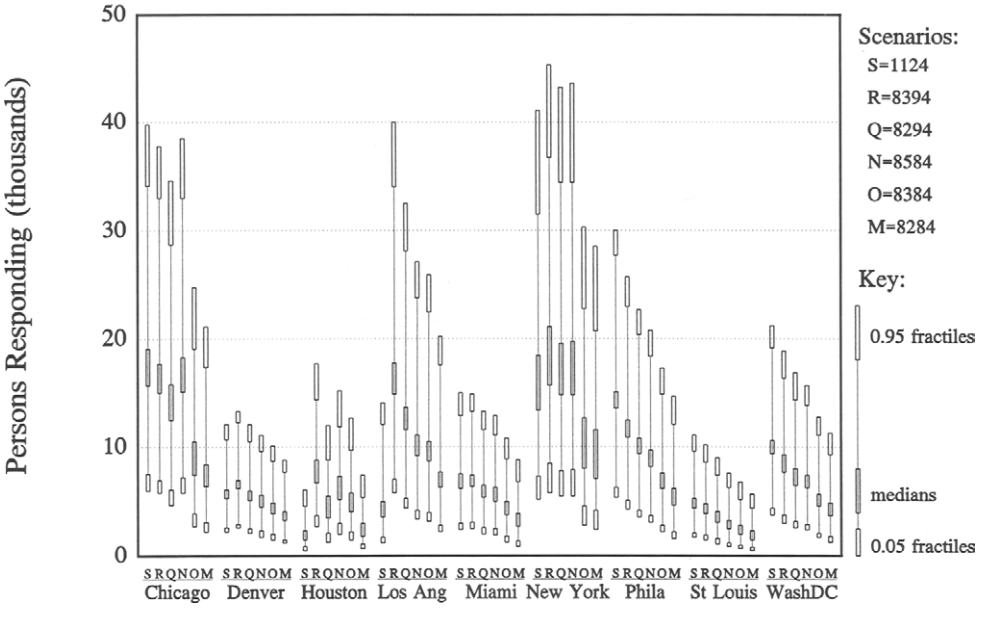

FIGURE 7 Using Box Plots to Represent Variability in 54 Sets of 10 Risk Distributions Attributable to Differences in pNEM/O_3 Exposure Estimates (health endpoint: 8-h exposures at moderate exertion, number of children having FEV_1 decrements ≥20%)

Figure 7 indicates that the current standard (1124) is most protective of children in Houston and Los Angeles; least protective in Philadelphia, St. Louis, and Washington, D.C. Scenario 8284 is most protective in all areas except Houston and Los Angeles. For areas other than Houston and Los Angeles, scenario 8284 results in a reduction of about 50% in the number of children responding compared to the current standard.

Another way to view the same data is shown in Figure 8, in which the measure is percentage of children responding rather than children responding. Under attainment of the current standard, the smallest percentages of children responding result in Houston and Los Angeles, with median response rates less than 1% in both urban areas; for the other areas, the median response rates are about 4-6%. Under scenario 8284, the median response rates are about 1% in Houston and Los Angeles and about 1-4% in the other areas. So, while the current standard is best for Houston and Los Angeles, scenario 8284 results in a level of protection that is more comparable across all nine urban areas. Thus, from a risk equity point of view, it may be argued that scenario 8284 is preferable to the current standard.

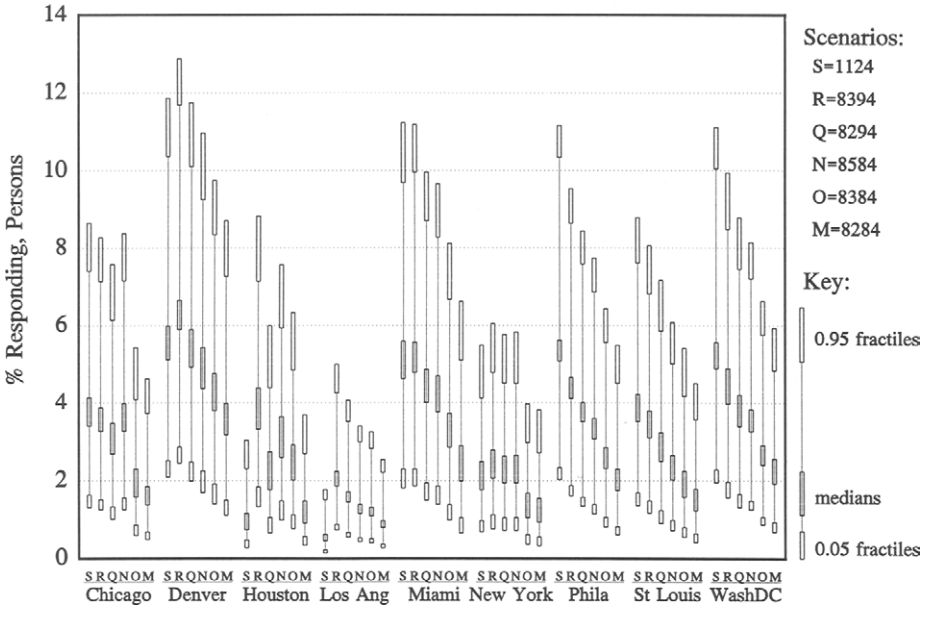

FIGURE 8 Headcount Risk Results for Percentage of Children Responding for FEV_1 Decrement ≥20%, 8-h Exposures, and Moderate Exertion (persons basis; underlying exposure-response relationship based on Folinsbee et al. 1988, Horstman et al. 1990, and McDonnell et al. 1983)

TABLE 5 Summary of Air Quality Scenarios

Letter Code	Abbreviations		Definition of Scenario
	Short	Long	
M	8284	8HA2H-0.084	an alternative NAAQS: 8-hr averaging time, 2nd highest average daily maximum of 0.084 ppm ozone
N	8584	8HA5H-0.084	an alternative NAAQS: 8-hr averaging time, 5th highest average daily maximum of 0.084 ppm ozone
O	8384	8HA3H-0.084	an alternative NAAQS: 8-hr averaging time, 3rd highest average daily maximum of 0.084 ppm ozone
Q	8294	8HA2H-0.094	an alternative NAAQS: 8-hr averaging time, 2nd highest average daily maximum of 0.094 ppm ozone
R	8394	8HA3H-0.094	an alternative NAAQS: 8-hr averaging time, 3rd highest average daily maximum of 0.094 ppm ozone
S	1124	1H1EX-0.124	a variation of the current ozone NAAQS: 1-hr averaging time, 1 expected exceedance, 0.124 ppm ozone

EXCESS ADMISSIONS OF ASTHMATICS IN NEW YORK CITY

The hospital admissions model is based on (1) regression coefficients and corresponding standard errors developed by Thurston et al. (1992) and (2) 1-h daily maximum ozone concentrations developed by Johnson et al. (1997). The model applies only to New York City and includes two types of respiratory admissions: asthmatics and members of the general population (including asthmatics) for any of a number of respiratory ailments (i.e., acute bronchitis or bronchiolitis, pneumonia, chronic obstructive pulmonary disease not related to asthma).

Regression coefficients and corresponding standard errors (for asthmatics, the regression coefficient and standard error are 11.7 and 4.7, respectively) define "concentration-response" relationships that include related uncertainties. Figure 9 is a graph of the relationship (which is a set of 21 "curves," one for each of 21 fractiles) for asthmatics. Only the 0.05, 0.50 (median), and 0.95 fractiles are shown to avoid clutter. Although the concentration-response relationship is defined over the range of 0-0.04 ppm ozone, the risk calculations in this section pertain, unless otherwise stated, to ozone levels greater than the estimated background (0.04 ppm). The fractiles at each ozone concentration are obtained from the normal probability distribution.

The main results are shown in Figure 10 and Tables 6-7. Figure 10 shows cumulative probability distributions over excess annual hospital admissions of New York City asthmatics for seven air quality scenarios (based on air quality data from Queens County monitor with background ozone at 0.04 ppm). For example, the 0.05, 0.5 (median), and 0.95 fractiles of the distribution for scenario R (8-h averaging time, 3rd highest daily maximum value, allowed ozone

level of 0.094 ppm) are 50, 150, and 250, respectively. In the figure, the distributions for scenarios Q and N appear to be identical. In fact, this is the case as can be seen in Table 6, which lists the data for Figure 10. Each distribution is defined in terms of number of admissions at each of 21 fractiles. Similar results (not shown here) are available for background ozone of 0 ppm. As expected, the numbers of admissions are higher for the 0 ppm case compared to the 0.04 ppm case.

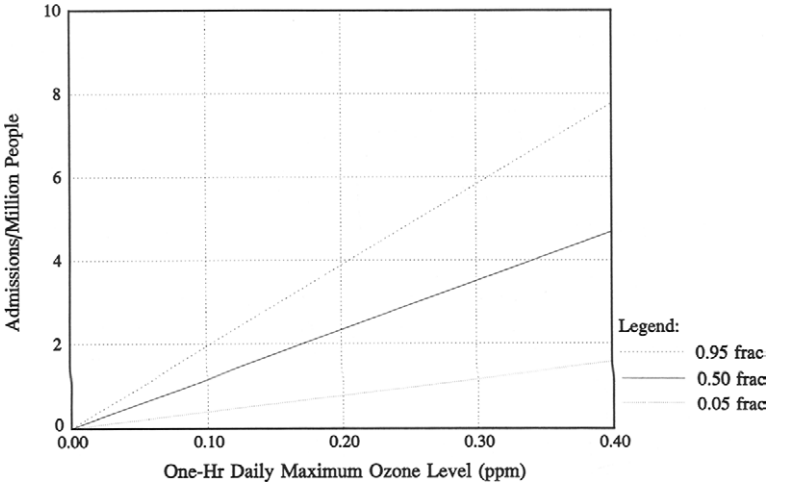

FIGURE 9 Uncertainty about Daily Hospital Admissions of Asthmatics in Relation to Ozone Concentration

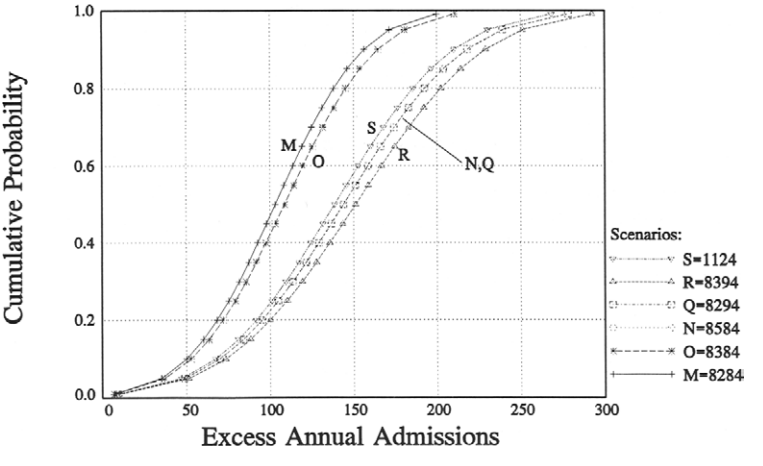

FIGURE 10 Excess Annual Hospitalizations of New York City Asthmatics for Seven Air Quality Scenarios and Monitor 9 Air Quality Data with Background of 0.04 ppm

TABLE 6 Annual Excess Hospital Admissions of Asthmatics Based on the Queens County Monitor Data with a Background Ozone Level of 0.04 ppm (1-h daily maximum ozone levels)

	Air Quality Scenario					
Fractile	S=1124[a]	R=8394[b]	Q=8294	N=8584	O=8384	M=8284
0.01	9	10	9	9	7	7
0.05	47	51	49	49	37	35
0.10	67	73	70	70	53	50
0.15	81	88	84	84	63	60
0.20	92	100	95	95	72	68
0.25	101	110	105	105	79	75
0.30	109	119	114	114	86	82
0.35	117	128	122	122	92	87
0.40	125	136	129	129	98	93
0.45	132	144	137	137	103	98
0.50	139	151	144	144	109	103
0.55	146	159	151	151	114	108
0.60	153	167	159	159	120	114
0.65	160	175	166	166	126	119
0.70	168	183	174	174	132	125
0.75	176	192	183	183	138	131
0.80	186	202	193	193	145	138
0.85	196	214	204	204	154	146
0.90	210	229	218	218	165	156
0.95	230	251	239	239	181	171
0.99	268	293	279	278	210	200
Mean	139	151	144	144	109	103
StdDev	56	61	58	58	44	42

[a] Key to code for scenario S: character 1 specifies averaging time (1 h); character 2 specifies the number of exceedances (1); characters 3 and 4 define the ozone level (0.124 ppm)

[b] Key to code for scenario R and the remaining scenarios: character 1 specifies averaging time; character 2 specifies n of the n^{th} highest 8-h average daily maximum ozone level; and characters 3 and 4 define the allowed ozone level (e.g., 8394 means 8-h averaging time, 3^{rd} highest 8-h average daily maximum ozone level, and 0.094 ppm).

It is important to discuss precision of the estimates listed in Table 6. The estimates are model results that have been rounded to the nearest whole number. This level of precision is presented because further calculations in Table 7 could be distorted if results in Table 6 were rounded to the nearest multiple of 10 or to 2 significant digits. The final calculations in Table 7 involve percentage reductions from the current standard. These estimates have been rounded to either 2 significant whole number digits or 1 significant decimal digit to emphasize the fact that these distributions cannot be known precisely. Besides, a more important indicator of the precision of estimates is the width of the 90% CI associated with each distribution, which in turn relates to variance; without exception, the CIs are large and further emphasize the uncertainty associated with these estimates.

Table 7 compares meeting the current standard (1124) vs. meeting the other standards. The excess admissions estimates come from the hospital admissions model. The estimates for all admissions are based on (1) the 14-16 thousand admissions per ozone season estimates provided by Thurston (1995) and (2) excess admissions attributable to exposures at ozone levels >0.04 ppm. For example, for the current standard (1-h, 1 expected exceedance, 0.124 ppm), the median number of admissions of asthmatics for any respiratory-related reason is 14,800 [which is approximately equal to 15,000 (the median of total admissions in the As-Is scenario) *minus* 388 (the median number of excess admissions in the As-Is scenario attributable to ozone exposure at concentrations greater than the estimated 0.04 ppm background level; from Whitfield et al. 1996) *plus* 139 (the median number of excess admissions associated with attainment of the current standard [scenario 1124] for ozone exposures at concentrations $>$ 0.04 ppm).

As expected, as the base for comparison increases (from excess admissions with background at 0.04 ppm, to excess admissions with background at 0 ppm, to admissions for any respiratory-related reason), the percentage reduction relative to admissions under the 1124 (current standard) scenario decreases substantially. For example, excess admissions of asthmatics attributable to exposures to ozone levels >0.04 ppm decrease from about 140 for scenario 1124 to about 100 for scenario 8384 - a decrease of about 40 admissions or 20%. Considering exposures to any level of ozone, the decrease for the same scenarios is about 50 admissions or 8%. For admissions for any respiratory-related reason, the decrease is about 40 admissions or 0.2%.

One important conclusion that can be drawn from the results in Tables 6-7 is that the scenarios 1124 (the current standard), 8294, and 8584 are quite similar with respect to estimates of excess hospital admissions. In fact, scenarios 8294 and 8584 lead to identical results that are larger than those for the current standard, and estimates for scenario 8394 are slightly higher than those for scenarios 8294 and 8584. Scenarios 8384 and 8284 lead to admissions estimates that are lower than those for the current standard.

TABLE 7 Admissions of New York City Asthmatics — Comparison Relative to Meeting the Current Standard (1-h, 1 expected exceedance, 0.124 ppm)

Case No./Issue	Air Quality Scenario					
	S = 1124 (1 h, 1 ex,[a] 0.124 ppm)	R = 8394 (8 h, A3H, 0.094 ppm)	Q = 8294 (8 h, A2H, 0.094 ppm)	N = 8584 (8 h, A5H, 0.084 ppm)	O = 8384 (8 h, A3H, 0.084 ppm)	M = 8284 (8 h, A2H, 0.084 ppm)
1. Excess admissions[b] (background = 0.04 ppm)	139[c] (47 to 230)[d]	151 (51 to 251)	144 (49 to 239)	144 (49 to 239)	109 (37 to 181)	103 (35 to 171)
Percent reduction from current standard[e]	–	-9	-4	-4	22	26
2. Excess admissions[b] (background = 0 ppm)	697 (236 to 1,157)	720 (236 to 1,157)	707 (236 to 1,157)	707 (236 to 1,157)	643 (236 to 1,157)	631 (236 to 1,157)
Percent reduction from current standard[e]	–	-3	-1	-1	8	9
3. All admissions[f] (thousands)	14.8 (13.9 to 15.6)	14.8 (13.9 to 15.6)	14.8 (13.9 to 15.6)	14.8 (13.9 to 15.6)	14.7 (13.9 to 15.5)	14.7 (13.9 to 15.5)
Percent reduction from current standard[e]	–	-0.08	-0.03	-0.03	0.2	0.2

[a] ex means expected exceedance.

[b] Admissions of asthmatics because of exposure to ozone.

[c] Median estimate.

[d] 90% credible interval (about the median).

[e] Because of the necessary assumption that results across scenarios are highly correlated (i.e., if admissions are high for one scenario, they are high for all scenarios), very little variation occurs in the percentage reduction from the current standard. Decreases are positive and increases are negative numbers.

[f] Admissions of asthmatics for any respiratory-related reason; for scenario *i*, based on estimates of all admissions and excess admissions attributable to ozone levels >0.04 ppm for the As-Is scenario, and estimates of excess admissions attributable to ozone levels >0.04 ppm for scenario *i* (e.g., for scenario 1124: 14,800 ≈ 15,000 − 388 + 139). Fifteen thousand is the number of admissions of New York City asthmatics for any respiratory-related reason during the 1988-1990 ozone seasons (Thurston 1995); 388 is the median number of excess admissions associated with the As-Is scenario (Whitfield et al. 1996); and 139 is the median number of excess admissions for scenario S with a background ozone level of 0.04 ppm. The corresponding 0.05- and 0.95-fractile estimates for excess admissions associated with the As-Is scenario, which are needed to calculate the 0.05- and 0.95-fractile estimates for the third case (all admissions), are 132 and 644, respectively (Whitfield et al. 1996).

LIMITATIONS OF THE ANALYSIS

Reports by Johnson et al. (1996) and Whitfield et al. (1996) present results of earlier exposure and risk assessments, respectively. The earlier ozone risk assessment was similar to the one reported here in that both assessments used results from the pNEM/O_3 exposure model to estimate ozone exposures. Differences between the two risk assessments are primarily due to differences in the exposure assessments: the standards that were evaluated, the procedures used to adjust ozone data, and the treatment of run-to-run variability.

Johnson et al. (1996) provide a comprehensive discussion of the principal limitations of the pNEM/O_3 methodology, which in turn necessarily impact the risk results. These limitations include:

- The availability and level of detail of input data bases (e.g., time and activity diary data);
- The necessarily broad assumptions used in estimating cohort populations; and
- The lack of available data bases integral to the mass balance model used by pNEM (e.g., air exchange rates).

and these limitations also apply to the new pNEM/O_3 exposure estimates used here to obtain risk results.

The new air quality adjustment procedures (AQAPs) for estimating ozone levels and exposures used in these assessments differ from the AQAPs used in the previous application of pNEM/O_3 to outdoor children. Each of the new AQAPs was applied to a three-year period to simulate attainment of the associated standard over the entire period. The adjustment required for the three-year period was applied to a single year (1990, 1991, 1992, or 1993) within the period and the resulting single year of ozone data was used in the exposure assessment to represent typical attainment conditions. The selected year is the middle year of the three-year period with respect to relative ozone level. This approach contrasts with the previous AQAPs in which attainment was determined by examining a single year (1990 or 1991) of ozone data. The ozone data for the selected year were adjusted to exactly attain the specified standard and then used in the exposure assessment to represent attaining conditions.

The new AQAPs use a proportional adjustment procedure for all standards in all cities. In the previous AQAPs, a non-proportional adjustment procedure based on the Weibull distribution was used for all standards in six of the nine urban areas and for a few standards in the remaining urban areas (Chicago, Denver, and Miami). A proportional adjustment procedure was used for the other standards in these three urban areas.

The new AQAPs reduce hourly ozone concentrations in each portion of the distribution by the same proportion. It should be noted that while these "proportional" AQAPs may provide a better representation of the central part of the distribution, they may over-estimate concentration values in the upper tail of the distribution.

Of concern is the effectiveness of any AQAP for estimating ozone concentrations in cities, such as Los Angeles, that have "as-is" ozone levels that are much higher than those in most U.S. cities. Most cities evaluated in this report require "moderate" reductions to attain the various standards under condition. Historical records of high- and low-year ozone level patterns make it possible to reasonably calibrate results. However, because current conditions in Los Angeles must be radically adjusted downward to simulate attainment of all of the standards, and because Los Angeles has never approached any of the specified conditions, there are no empirical data available that could be realistically used to calibrate a proposed AQAP.

Finally, with respect to exposure modeling, is the issue of excessive random influences on exposure estimates. In the current work, Johnson et al. (1997) used a special version of pNEM/O_3 that allows the user to specify the random number generator seed for each model run. Each seed produces a unique, repeatable sequence of random numbers for the probabilistic elements of pNEM/O_3. Thus, Johnson et al. (1997) constrained each set of 10 pNEM/O_3 runs to use the same 10 random number generator seeds. This procedure retained desirable variability within each set of 10 runs and removed undesirable set-to-set variability. As a result, it seems plausible that the differences in the exposure estimates associated with the seven standards are mainly attributable to differences in ambient ozone concentrations permitted by the standards. Consequently, this variability propagates through the risk calculations and leads to a similar conclusion.

With respect to risk results, Whitfield et al. (1996) discussed a number of limitations of exposure-response modeling and risk modeling that remain applicable. These include the following issues:

- *Length of exposure.* Data from controlled human exposure studies were assumed to be appropriate for modeling responses of 1-h exposures at heavy exertion, 1-h exposures at moderate exertion, and 8-h exposures at moderate exertion. Exposure protocols differed among the studies and did not match exactly the conditions of the regulatory standards analyzed here, but it is unlikely that these differences would appreciably affect the results described here.

- *Extrapolation of exposure-response relationships.* The lowest ozone level at which controlled human exposure studies have been conducted is 0.08 ppm. Because large numbers of people are exposed to ozone concentrations between 0.04-0.08 ppm, it was necessary to estimate

exposure-response relationships at ozone concentrations much lower than those for which data are available. The accuracy of these estimates is unknown.

- *Reproducibility of ozone-induced responses.* This study assumed that ozone-induced responses for individuals are reproducible. This assumption is supported by the criteria document, which cites several confirming studies.

- *Age and lung function.* None of the studies used to develop the exposure-response used in this study exposed children. However, a number of studies indicate that children aged 8-11 experience FEV_1 changes similar to those of adults aged 18-35 and exposed to ozone concentrations of 0.12 ppm at equivalent ventilation rates of 35 L/min/m^2.

- *Age and symptoms.* None of the studies involving children (primarily summer camp studies) reported symptoms. Therefore, it was necessary to use the same exposure-response relationships involving symptoms for adults and children.

- *Interaction between ozone and other pollutants.* All of the controlled human exposure studies, which formed the basis for the exposure-response relationships used here, controlled only for ozone. Although there is some evidence that the presence of other pollutants might enhance the respiratory effects of ozone (or even cause the same effects), it is not consistent across studies. Therefore, it was assumed that the estimates of ozone-induced health effects would not be affected by the presence of other pollutants such as sulfur dioxide, nitrogen dioxide, carbon monoxide, sulfuric acid, or other aerosols.

- *Smoking status.* All of the subjects in the controlled human exposure studies used here excluded smokers. There is some evidence that smokers may be less responsive to ozone exposures than nonsmokers. To the extent that is true, the risk estimates in this report are overstated.

- *Exposure history.* It is assumed that ozone-induced response at any particular exposure period (1 or 8 h) is not affected by previous exposures. It is possible that ozone-induced responses can be enhanced or attenuated by previous exposures. The absence of data concerning this issue increases uncertainty about results.

- *Naturally occurring ozone.* Risk results do not include exposure to background ozone levels (i.e., ozone concentrations that would be observed in the U.S. in the absence of anthropogenic precursor emissions of volatile

organic compounds and nitrous oxides in North America). Responses attributable to exposure to naturally occurring ozone levels were removed from the risk estimates. The criteria document estimates that the summer, 1-h average range for background ozone is 0.03-0.05 ppm. The midpoint, 0.04 ppm, is used in this report.

- *Correction for background ozone.* The procedure for removing responses attributable to background ozone assumed that distributions over total response and response at background are perfectly correlated (i.e., correlation is 1).

- *Output graphs.* The box plots render indistinguishable characteristics of results for individual pNEM/O_3 runs. Therefore, the box plots should be used as a guide for identifying possible trends and developing insights that can by verified only by investigating detailed results.

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REFERENCES

Avol, E.L., et al., 1984, "Comparative Respiratory Effects of Ozone and Ambient Oxidant Pollution Exposure during Heavy Exercise," *Journal of the Air Pollution Control Association* 34:804-809.

EPA: see U.S. Environmental Protection Agency.

Folinsbee, L.J., et al., 1988, "Pulmonary Function and Symptom Responses after 6.6-Hour Exposure to 0.12 ppm Ozone with Moderate Exercise," *JAPCA* 38:28-35.

Horstman, D.H., et al., 1990, "Ozone Concentration and Pulmonary Response Relationships for 6.6-Hour Exposures with Five Hours of Moderate Exercise to 0.08, 0.10, and 0.12 ppm," *American Review of Respiratory Disease* 142:1158-1163.

Johnson, T., et al., 1996, *Estimation of Ozone Exposures Experienced by Outdoor Children in Nine Urban Areas Using a Probabilistic Version of NEM*, prepared by IT/Air Quality Services for U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, N.C. (April). (For copies, contact H.M. Richmond, U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, MD-15, Research Triangle Park, N.C. 27711; phone 919-541-5271.)

Johnson, T., J. Mozier, and J. Capel, 1997, "Supplement to 'Estimation of Ozone Exposures Experienced by Outdoor Children in Nine Urban Areas Using a Probabilistic Version of NEM'", prepared by IT/Air Quality Services for U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, N.C. (Jan.). (For copies, contact H.M. Richmond, U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, MD-15, Research Triangle Park, N.C. 27711; phone 919-541-5271.)

Kulle, T.J., et al., 1985, "Ozone Response Relationships in Healthy Nonsmokers," *American Review of Respiratory Disease* 132:36-41.

McDonnell, W.F., et al., 1983, "Pulmonary Effects of Ozone Exposure during Exercise: Dose-Response Characteristics," *Journal of Applied Physiology: Respiratory Environmental Exercise Physiology* 54:1345-1352.

McDonnell, W.F., et al., 1985, "Respiratory Responses of Vigorously Exercising Children to 0.12 ppm Ozone Exposure," *American Review of Respiratory Disease* 132:875-879.

McDonnell, W.F., et al., 1991, "Respiratory Response of Humans Exposed to Low Levels of Ozone for 6.6 Hours," *Archives of Environmental Health* 46:145-150.

Morgan, M.G., and M. Henrion, 1990, *Uncertainty: A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis,* Cambridge University Press, New York, N.Y.

Seal, E., Jr., et al., 1993, "The Pulmonary Response of White and Black Adults to Six Concentrations of Ozone," *American Review of Respiratory Disease* 147:804-810.

Thurston, G.D., et al., 1992, "A Multi-Year Study of Air Pollution and Respiratory Hospital Admissions in Three New York State Metropolitan Areas: Results for 1988 and 1989 Summers," *Journal of Exposure Analysis and Environmental Epidemiology* 2:429-450.

Thurston, G.D., 1995, New York University Medical Center, personal communication (Dec. 5)

U.S. Environmental Protection Agency, 1996a, *Review of National Ambient Air Quality Standards for Ozone: Assessment of Scientific and Technical Information*, draft Office of Air Quality Planning and Standards (OAQPS) Staff Paper, EPA-450/R-96-007, June. (For copies, contact David McKee, U.S. Environmental Protection Agency, OAQPS, MD-15, Research Triangle Park,

N.C. 27711; phone 919-541-5288.)

U.S. Environmental Protection Agency, 1996b, *Air Quality Criteria for Ozone and Related Photochemical Oxidants (Review Draft)*, EPA/600/P-93/004 af, bf, cf, National Center for Environmental Assessment, Office of Research and Development, Research Triangle Park, N.C.

Whitfield, R.G., et al., 1996, "A Probabilistic Assessment of Health Risks Associated with Short-Term Exposure to Tropospheric Ozone," Argonne National Laboratory Report No. ANL/DIS-3 (June).

Whitfield, R.G., 1997, *A Probabilistic Assessment of Health Risks Associated with Short-Term Exposure to Tropospheric Ozone: A Supplement*, Letter report prepared by Argonne National Laboratory for the U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards covering analysis of seven new air quality scenarios (Jan.). (For copies, contact H.M. Richmond, U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, MD-15, Research Triangle Park, N.C. 27711; phone 919-541-5271.)