Responses to Significant Comments on the 2006 Proposed Rule on the National Ambient Air Quality Standards for Particulate Matter

(January 17, 2006; 71 FR 2620)

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List of Acronyms

The following acronyms have been used for the sake of brevity in this document:

Act	Clean Air Act
ACS	American Cancer Society
API	American Petroleum Institute
AQS	Air Quality System
ARIES	Aerosol Research and Inhalation Epidemiological Study
ARMs	Approved Regional Methods
CAA	Clean Air Act
CAPs	Concentrated ambient particles
CARB	California Air Resources Board
CASAC	Clean Air Scientific Advisory Committee
CDC	Centers for Disease Control
COPD	Chronic obstructive pulmonary disease
ECG	Electrocardiogram
EPA	Environmental Protection Agency
FEM	Federal Equivalent Method
FRM	Federal Reference Method
GAMs	Generalized additive models
GLMs	Generalized linear models
HEI	Health Effects Institute
HML	Highest measured level
IMPROVE	Interagency Monitoring of Protected Visual Environment
LML	Lowest measured level
NAAQS	National ambient air quality standards
NESCAUM	Northeast States Coordinated Air Use Management
NCore	National Core Monitoring Network
NMMAPS	National Morbidity, Mortality, and Air Pollution Study
NRC	National Research Council
PM	Particulate matter
$PM_{2.5}$	particles generally less than or equal to 2.5 μm in diameter
PM_{10}	particles generally less than or equal to 10 micrometers (μm) in diameter
$PM_{10-2.5}$	particles generally larger than 2.5 and up to 10 μm in diameter
QA	Quality assurance
ROFA	Residual oil fly ash
RR	Relative risk
SAB	Science Advisory Board
STAPPA/ALAPCO	State and Territorial Air Pollution Program Administrators/ Association of Local Air Pollution Control Officials
TSD	Technical support document
TSP	Total suspended particulate
UARG	Utility Air Regulatory Group
WHO	World Health Organization

Frequently Cited Documents

The following documents are frequently cited throughout EPA's response to comments, often by means of the short names listed below:

Criteria Document:

Environmental Protection Agency (2004a). Air Quality Criteria for Particulate Matter. National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711; report no. EPA/600/P-99/002aF and EPA/600/P-99/002bF. October 2004.

Preamble to the final rule: Preamble to the Final Rule on the Review of the National Ambient Air Quality Standards for Particulate Matter; to be published in the *Federal Register* on October ?, 2006.

Proposal notice: National Ambient Air Quality Standards for Particulate Matter: Proposed Rule. 71 FR 2620, January 17, 2006.

Staff Paper:

Environmental Protection Agency (2005). Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information, OAQPS Staff Paper. Research Triangle Park, NC 27711: Office of Air Quality Planning and Standards; report no. EPA-452/R-05-005a. December 2005.

Risk Assessment Technical Support Document:

Abt Associates Inc. (2005). Particulate Matter Health Risk Assessment for Selected Urban Areas. Final Report. Bethesda, MD. Prepared for the Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Contract No. 68-D-03-002. EPA 452/R-05-007A.

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I. INTRODUCTION

This document, together with the preamble to the final rule on the review of the national ambient air quality standards (NAAQS) for particulate matter (PM), presents the responses of the Environmental Protection Agency (EPA) to the more than 120,000 public comments received on the 2006 PM NAAQS proposal notice (71 FR 2160). All significant issues raised in the public comments have been addressed.

Due to the large number of comments that addressed similar issues, as well as the sheer volume of the comments received, this response-to-comments document does not generally cross-reference each response to the commenter(s) who raised the particular issue involved, although commenters are identified in some cases where they provided particularly detailed comments that were used to frame the overall response on an issue.

The responses presented in this document are intended to augment the responses to comments that appear in the preamble to the final rule or to address comments not discussed in the preamble to the final rule. Although portions of the preamble to the final rule are paraphrased in this document where useful to add clarity to responses, the preamble itself remains the definitive statement of the rationale for the revisions to the standards adopted in the final rule.

In many instances, particular responses presented in this document include cross references to responses on related issues that are located either in the preamble to the PM NAAQS final rule, or in this Response to Comments document. In addition, because EPA proposed rules to amend the PM NAAQS and rules to amend the monitoring requirements in support of these revisions in parallel Federal Register notices issued on the same day, a natural consequence was that many commenters submitted a single set of comments addressing issues from both proposals. In general, EPA is addressing the comments relating exclusively to monitoring in the monitoring rulemaking record, and is addressing comments relating to monitoring which overlap both rulemakings either in the monitoring rulemaking record or in both rulemaking records. In view of the large number of comments received by EPA, and the fact that many comments related to both rulemakings, the cross references contained in this document may not be complete and information relevant to a particular comment may be contained in responses to other comments within this Response to Comments document or within the monitoring rulemaking record. All issues on which the Administrator is taking final action in the PM NAAQS final rule are addressed in the PM NAAQS rulemaking record. Issues on which the Administrator is taking final action in the monitoring final rule are addressed in that rulemaking record.

Accordingly, this Response to Comments document, together with the preamble to the PM NAAQS final rule and the information contained in the Criteria Document (EPA, 2004) and the Staff Paper (EPA, 2005), should be considered collectively as EPA's response to all of the significant comments submitted on EPA's 2006 PM NAAQS proposed rule. This document incorporates directly or by reference the significant public comments addressed in the preamble to the PM NAAQS final rule as well as other significant public comments that were submitted on the proposed rule.

Consistent with the final decisions presented in the notice of final rulemaking, comments on the primary standards for fine particles and for thoracic coarse particles are addressed separately in this document in sections II.A and II.B, respectively. Comments on secondary standards for fine and thoracic coarse particles are addressed below in section II.C. Comments on related federal reference methods (FRMs) for monitoring PM are addressed below in section II.D. Section III includes responses to legal, administrative, procedural, or misplaced (implementation-related) comments.

In the PM NAAQS proposal, EPA recognized that there were a number of new scientific studies on the health effects of PM that had been published recently and, therefore, were not included in the Criteria Document (71 FR at 2625). The EPA committed to conduct a review and assessment of any significant "new" studies, including studies submitted during the public comment period. The purpose of this review was to ensure that the Administrator was fully aware of the new science before making a final decision on whether to revise the current PM NAAQS. The EPA screened and surveyed the recent literature, including studies submitted during the public comment period, and conducted a provisional assessment that places the results of those studies of potentially greatest policy relevance in the context of the findings of the Criteria Document. This provisional assessment, entitled *Provisional Assessment of Recent Studies on Health Effects of Particulate Matter Exposure* (EPA, 2006), is included as Appendix A of this document.

II. RESPONSES TO SIGNIFICANT COMMENTS ON PROPOSED PM STANDARDS

A. Primary $PM_{2.5}$ Standards

1. General Comments on Proposed Primary $PM_{2.5}$ standards

A large number of comments on the proposed primary standards for $PM_{2.5}$ were very general in nature, basically expressing one of two substantively different views: (1) support for revisions to the primary standards to be more health-protective or (2) opposition to any modification of the current $PM_{2.5}$ standards. Many of these commenters simply expressed their views without stating any rationale, while others gave general reasons for their views but without reference to the factual evidence or rationale presented in the proposal notice as a basis for the Agency's proposed decision. The preamble to the final rule in its entirety presents the Agency's response to these very general views.

Specific public comments on a range of issues related to the proposed primary $PM_{2.5}$ standards are addressed in the preamble to the final rule and/or in this document. In particular, significant public comments related to whether or not the current $PM_{2.5}$ standards should be revised are addressed in section II.B of the preamble. Sections II.C, D, E, and F of the preamble discuss significant comments addressing the four basic elements of the standard: indicator, averaging time, form, and level, respectively. Significant comments on the data handling conventions for $PM_{2.5}$ are discussed in section V.A of the preamble. Below, EPA provides more specific responses to the full range of significant issues raised in the public comments on these issues. Specific comments on the interpretation of the scientific evidence and EPA's health risk assessment for $PM_{2.5}$ are also addressed in this document in sections II.A.4 and II.A.5 below, respectively.

2. Specific Comments on Proposed Primary $PM_{2.5}$ Standards

a. Need to Revise Current $PM_{2.5}$ Standards

Comments based on relevant factors that either support or oppose any change to the current $PM_{2.5}$ primary standards are addressed in this section. The responses to these comments are generally discussed in section II.B of the preamble to the final rule and discussed more fully below. Significant comments on specific short- and long-term exposure studies that relate to consideration of the appropriate level of the 24-hour and annual $PM_{2.5}$ standards are addressed in sections II.F.1 and II.F.2 in the preamble to the final rule and discussed more fully below in sections II.A.2.e.i and II.A.2.e.ii, respectively. Incorporating responses contained in sections II.B of the preamble to the final, EPA provides the following responses to specific issues related to the need to revise the fine particle standards.

i. Support for Revising the Current Standards

Many public comments received on the proposal asserted that, based on the available scientific information, the current $PM_{2.5}$ standards are insufficient to protect

public health with an adequate margin of safety and revisions to the standards are appropriate. Among those calling for revisions to the current standards are medical groups, including the American Medical Association, the American Thoracic Society, the American Academy of Pediatrics, and the American College of Cardiology, as well as medical doctors and academic researchers. Similar conclusions were also submitted in comments from many national, state, and local public health organizations, including, for example, the American Lung Association, the American Heart Association, the American Cancer Society, the American Public Health Association, and the National Association of Local Boards of Health, as well as in letters to the Administrator from EPA's advisory panel on children's environmental health (Children's Health Protection Advisory Committee, 2005, 2006). All of these medical and public health commenters stated that the current $PM_{2.5}$ standards need to be revised, and that even more protective standards than those proposed by EPA are needed to protect the health of sensitive population groups. Many individual commenters also expressed such views.

State and local air pollution control authorities who commented on the $PM_{2.5}$ standards supported revision of the suite of current $PM_{2.5}$ standards, as did the National Tribal Air Association. The State and Territorial Air Pollution Program Administrators and the Association of Local Air Pollution Control Officials (STAPPA/ALAPCO) argued that EPA should revise the $PM_{2.5}$ standards in accordance with the recommendations of CASAC. Each of the individual State environmental/public health agencies that commented on the $PM_{2.5}$ standards supported revisions to the current standards, with most supporting standards consistent with CASAC's recommendations. The Northeast States for Coordinated Air Use Management (NESCAUM) argued for even more stringent revisions to the standards.

(1) *Comment:* In general, all of these commenters agreed on the importance of results from the large body of scientific studies reviewed in the Criteria Document and on the need to revise the $PM_{2.5}$ standards as articulated in Section II.A of the preamble to proposal, while generally differing with EPA's proposed judgments about the extent to which the standards should be revised based on this evidence. These commenters generally concluded that the body of evidence assessed in the Criteria Document was stronger and more compelling than in the last review. In addition, these commenters generally placed much weight on CASAC's interpretation of the body of available evidence and the results of EPA's risk assessment, both of which formed the basis for CASAC's recommendation to revise the $PM_{2.5}$ standards to provide increased public health protection was based. In arguing for more health protective standards, these commenters expressed the following specific views:

- Independent reanalysis of the original American Cancer Society (ACS) and Six Cities long-term exposure studies conducted by the Health Effects Institute (HEI) (Krewski et al., 2000) concluded that the original data were of high quality, the original results could be fully replicated, and the results were robust to alternative model specifications.
- Particular studies, such as the ACS extended study (Pope et al., 2002) and the Southern California children's cohort study (Gauderman et al., 2002) provided

evidence of mortality and morbidity effects associated with long-term exposures to $PM_{2.5}$ at lower levels than had previously been studied.

- Specific short-term exposure studies were cited as providing evidence of mortality and morbidity effects at levels well below the level of the current 24-hour $PM_{2.5}$ standard.
- Progress has been made in reducing the many the uncertainties identified in the last review and in better understanding mechanisms by which $PM_{2.5}$ may be causing the observed health effects.
- EPA's health risk assessment showed that the risks estimated to remain when the current standards are met are large and important from a public health perspective and warrant increased protection.
- $PM_{2.5}$-related risks are likely larger than those estimated in EPA's risk assessment, in part because EPA based its risk assessment on the ACS extended study which had greater exposure measurement error than other studies, leading to an underestimate of the relative risk, and because EPA incorporated an assumed "cutpoint" in its assessment that is not supported by studies that find no evidence of a threshold.

Response: The EPA generally agrees with these commenters' conclusion regarding the need to revise the suite of $PM_{2.5}$ primary standards. The scientific evidence noted by these commenters was generally the same as that assessed in the Criteria Document and the Staff Paper, and EPA agrees that this evidence provides a basis for concluding that the current $PM_{2.5}$ standards, taken together, are not adequately protective of public health. For reasons discussed in section II.F of the preamble to the final rule and in section II.A.2.e below, EPA disagrees with aspects of these commenters' views on the level of protection that is appropriate and supported by the available scientific information.

(2) *Comment:* Some of these commenters also identified "new" studies that were not included in the Criteria Document as providing further support for the need to revise the $PM_{2.5}$ standards. A number of long-term exposure studies were cited by these commenters. For example, an ACS cohort study in Los Angeles by Jerrett et al. (2005) was offered as evidence that when exposure is measured with less error, mortality risks associated with $PM_{2.5}$ are higher than previously believed. A follow-up to the Six Cities study (Laden et al., 2006) was cited as an intervention study that provides strong evidence that reducing long-term average $PM_{2.5}$ levels improves public health and that the benefits of reducing $PM_{2.5}$ levels are greater than previously reported.

Some commenters also cited a follow-up to the Southern California children's cohort study (Gauderman et al., 2004) as stronger evidence of an irreversible effect on lung function growth in school age children at lower levels of exposure. Toxicological evidence cited included a study by Sun et al. (2005) that some commenters believe demonstrates a plausible biological mechanism that supports epidemiological evidence of cardiovascular-related mortality. Short-term exposure studies cited by some of these commenters notably included the Johns Hopkins study by Dominici et al. (2006), the largest multi-city study for $PM_{2.5}$ to date, which reports cardiovascular- and respiratory-related hospital admissions at generally lower long-term average $PM_{2.5}$ levels than had

been observed in other studies reporting $PM_{2.5}$-related effects. These commenters generally agreed with CASAC's conclusion and believed that the "new" science appears to support a conclusion that revision of the $PM_{2.5}$ standards is appropriate, but that it is not needed to reach that conclusion.[1]

Response: The EPA notes that, as discussed in section I.C of the preamble to the final rule, EPA conducted a provisional assessment of "new" science. Specifically, EPA screened and surveyed the recent literature, including studies submitted during the public comment period, and conducted a provisional assessment (EPA, 2006) that placed the results of those studies of potentially greatest policy relevance in the context of the findings of the Criteria Document (EPA, 2004). The EPA's provisional assessment found that the "new" studies expand the scientific information and provide important insights on the relationship between PM exposure and health effects of PM. The provisional assessment also found that the "new" studies generally strengthen the evidence that acute and chronic exposure to fine particles are associated with health effects, some of the "new" toxicology and epidemiologic studies report link various health effects with a range of fine particle sources and components, and, taken in context with the findings of the Criteria Document, the new information and findings do not materially change any of the broad scientific conclusions regarding the health effects of $PM_{2.5}$ exposure made in the Criteria Document.

As further noted in section I.C of the preamble, as in past NAAQS reviews, EPA is basing its decision in this review on studies and related information included in the Criteria Document and Staff Paper, which have undergone CASAC and public review and will consider the newly published studies for purposes of decision making in the next PM NAAQS review. The rigor of that review makes these documents including the integrative assessments, the most reliable source of scientific information on which to base decision on the NAAQS, decisions that all parties recognize as of great import.

ii. Support for Retaining the Current Standards

Another group of commenters representing industry associations and businesses opposed revising the current $PM_{2.5}$ standards. These views are most extensively presented in comments from the Utility Air Regulatory Group (UARG), representing a group of electric generating companies and organizations and several national trade associations and from Pillsbury, Winthrop, Shaw and Pittman (Pillsbury et al.) on behalf of 19 industry and business associations (including, for example, the Alliance of Automobile Manufacturers, the American Iron and Steel Institute, the National Association of Manufacturers, the American Petroleum Institute, and the U.S. Chamber of Commerce).

[1] The CASAC noted in its request for reconsideration to the Administrator on the proposed PM NAAQS (Henderson, 2006, p. 6) that scientific literature published since the close of the Criteria Document "appears to support the findings of the PM Panel, but is not needed to support the original conclusions of the PM Panel," which included the recommendation that the $PM_{2.5}$ standards should be modified to provide increased public health protection (Henderson, 2005a).

These and other commenters in this group generally mentioned many of the same studies that were cited by the commenters noted above who supported revising the standards, as well as other studies, but highlighted different aspects of these studies in reaching substantially different conclusions about their strength and the extent to which progress has been made in reducing uncertainties in the evidence since the last review. These commenters generally expressed the view that the current standards provide the requisite degree of public health protection. They then considered whether the evidence that has become available since the last review has established a more certain risk or a risk of effects that are significantly different in character to those that provided a basis for the current standards, or whether the evidence demonstrates that the risk to public health upon attainment of the current standards would be greater than was understood when EPA established the current standards in 1997.

In supporting their view that the present suite of primary $PM_{2.5}$ standards continues to provide the requisite public health protection and should not be revised, UARG and others generally stated that:

- the effects of concern have not changed significantly since 1997
- the uncertainties in the underlying health science are as great or greater than in 1997
- the estimated risk upon attainment of the current $PM_{2.5}$ standards has decreased since 1997
- "new" studies not included in the Criteria Document continue to increase uncertainty about possible health risks associated with exposure to $PM_{2.5}$.

These comments are discussed in turn below.

(1) *Comment:* In asserting that effects of concern have not changed significantly since 1997, some of these commenters stated that more subtle physiological changes in the cardiovascular system is the only type of new PM-related effect identified in this review. They argued that such subtle effects are far less serious than the cardiovascular effects such as aggravation of cardiovascular disease that had been considered in the last review.

Response: The EPA disagrees with the assertion that subtle changes in the cardiovascular system are the only type of new PM-related effect identified in this review. Further, EPA believes that evidence of physiological changes in the cardiovascular system is important in that increased confidence in inferences about the causal nature of the associations between fine particles and cardiovascular-related mortality and hospital admissions.

As discussed in the Criteria Document (EPA, 2004, p. 9-75), epidemiologic studies published since the last review have expanded upon and extended the evidence examining possible links between long-term exposures to fine particles and increased risk of lung cancer incidence and mortality, which was considered to be insufficient to support such a linkage in the last review. In this review, however, the epidemiologic evidence now available "support(s) an association between long-term exposure to fine particles and lung cancer mortality; and the new toxicological studies provide credible evidence for the biological plausibility of these associations" (EPA, 2004, p. 9-76). More

specifically, the Criteria Document highlighted the newer results of the extension of the ACS study analyses (that include more years of participant follow-up and address previous criticisms of the earlier ACS analyses), which indicate that long-term ambient PM exposures are associated with increased risk of lung cancer. That increased risk appears to be in about the same range as that seen for a nonsmoker residing with a smoker, with any consequent life-shortening due to lung cancer" (EPA, 2004, p. 9-94).

In addition, as noted earlier, the Criteria Document identified increased nonhospital medical visits (physician visits) and aggravation of asthma associated with short-term exposure to $PM_{2.5}$ as being newly identified effects since the last review, and concluded that findings of such effects "suggest likely much larger health impacts and costs to society due to ambient PM than just those indexed either by just hospital admissions/visits and/or mortality." *Id.* Further, the Criteria Document (EPA, 2004, p. 9-79) noted that there may be PM-related health effects in infants and children, although only very limited evidence of such effects exists.

In asserting that the uncertainties in the underlying health science are as great or greater than in 1997, some commenters variously discussed a number of issues including: the lack of demonstrated mechanisms by which $PM_{2.5}$ may be causing mortality and morbidity effects; uncertainty in the shape of the concentration-response functions; the potential for co-pollutant confounding; uncertainty in the role of individual constituents of fine particles; and the sensitivity of epidemiological results to statistical model specification. Each of these issues is addressed below. In summary, these commenters concluded that the substantial uncertainties present in the last review have not been resolved, that a previously unrecognized sensitivity to model specification has been newly identified, and/or that the uncertainty about the possible health risks associated with $PM_{2.5}$ exposure has not diminished (e.g., UARG). As discussed below, although EPA agrees that important uncertainties remain, and that future research directed toward addressing these uncertainties is warranted, EPA believes that overall uncertainty about possible health risks associated with both short- and long-term PM2.5 exposures has diminished since the last review.

(2) *Comment:* With regard to the issue of mechanisms, some commenters noted that although EPA recognizes that much new evidence is now available on potential mechanisms and plausible biological pathways, the evidence still does not resolve all questions about how $PM_{2.5}$ at ambient levels could produce the effects in question in this review. They further asserted that even if more recent information has advanced our understanding of such mechanisms, it would not justify revision of the standard.

Response: The EPA notes that in the last review, the Agency considered the lack of demonstrated biologic mechanisms for the varying effects observed in epidemiologic studies to be an important caution in its integrated assessment of the health evidence, upon which the standards were based. Since the last review, there has been a great deal of research directed toward advancing our understanding of biologic mechanisms. While this research has not resolved all questions, and further research is warranted, it has provided important insights as discussed in section II.A.1 of proposal (71 FR at 2626-2627). As noted there, the findings from this new research indicate that different health

responses are linked with different particle characteristics and that both individual components and complex particle mixtures appear to be responsible for many biologic responses relevant to fine particle exposures. The Criteria Document (EPA, 2004, p. 7-206) concluded: "Thus, there appear to be multiple biologic mechanisms that may be responsible for observed morbidity/mortality due to exposure to ambient PM. It also appears that many biological responses are produced by PM whether it is composed of a single component or a complex mixture." Further, EPA believes that progress made in gaining insights into potential mechanisms lends support to the biologic plausibility of results observed in epidemiologic studies (71 FR at 2636). The mechanistic evidence now available, taken together with newly available epidemiologic evidence, increases the Agency's confidence that observed associations are causal in nature, such that the risks of health effects attributed to short- and long-term exposures to $PM_{2.5}$, acting alone and/or in combination with gaseous co-pollutants, are now more certain than was understood in the last review.

(3) *Comment:* Some commenters argued that the uncertainties associated with the shape of the concentration-response functions and the potential existence of thresholds for associations between PM and various health endpoints have not been reduced since 1997 (UARG, p. 17).

Response: The EPA notes that, in contrast to the last review when few studies had quantitatively assessed the form of the concentration-response function or the potential for a threshold, several new studies available in this review have used different methods to examine this question, and most have been unable to detect threshold levels in time-series mortality studies. The Criteria Document (EPA, 2004, p. 9-44) recognized that in multi-city and most single-city time-series studies, statistical tests comparing linear and various nonlinear or threshold models have not shown statistically significant distinctions between these models; where potential threshold levels have been suggested in single-city studies, they are at fairly low levels (*Id.* at p. 9-45). Further, the shape of concentration-response functions for long-term exposure to $PM_{2.5}$ was evaluated using data from the ACS cohort, with the HEI reanalysis finding near-linear increasing trends through the range of particle levels observed in this study, and the extended ACS study reporting that the various mortality associations were not significantly different from linear (71 FR at 2635). However, EPA agrees that uncertainties remain in our understanding of the shape of concentration-response functions, and, consistent with the conclusion in the Criteria Document, has concluded that the available evidence does not either support or refute the existence of population thresholds for effects associated with short- or long-term exposures to PM across the range of concentrations in the studies. Even while recognizing that uncertainties remain, EPA believes that the overall understanding of this issue for both short- and long-term exposure studies has been advanced since the last review.

(4) *Comment:* With regard to co-pollutant confounding, these commenters assert that EPA has been "dismissive" of this issue in assessing the epidemiologic evidence of associations between PM and mortality and morbidity endpoints (UARG, p. 18). These commenters asserted that EPA has inappropriately concluded that PM-related mortality

and morbidity associations are generally robust to confounding, which is one of the criteria considered in drawing inferences about the extent to which observed statistical associations are likely causal in nature. The commenters focused on an examination of the extent to which statistically significant $PM_{2.5}$ associations based on one-pollutant models in a number of time-series studies, and in an analysis of associations with long-term exposures in the ACS cohort studies, often did not remain statistically significant in two-pollutant models.

Response: In general, EPA does not believe that the examination of this issue put forward by these commenters reflects the complexities inherent in assessing the issue of co-pollutant confounding. As discussed in section II.A.3 of the proposal (71 FR at 2634) and more fully in the Criteria Document (EPA, 2004, section 8.4.3; chapter 9, section 9.2.2.2.2), although multipollutant models may be useful tools for assessing whether gaseous co-pollutants may be *potential* confounders, such models cannot determine whether in fact they are. Interpretation of the results of multipollutant models is complicated by correlations that often exist among air pollutants, by the fact that some pollutants play a role in the atmospheric reactions that form other pollutants such as secondary fine particles, and by the inherent statistical power of the studies in question. While single-city multipollutant models have received a great deal of attention during this review, the Criteria Document also noted several other approaches to examining the question, including a more careful examination of personal exposures to PM and co-pollutants, the use of factor or principal component analyses, and the use of intervention studies (EPA, 2004, pp. 8-245 to 8-246). The Criteria Document also recognized that it is important to consider the issue of potential co-pollutant confounding in the context of the more recent evidence available about the biological plausibility of associations between the various pollutants and health outcomes, model specification, and exposure error (EPA, 2004, p. 8-254).

An example of other approaches to examining potential co-pollutant confounding is a study of personal exposure to fine particles and copollutant gases conducted in Baltimore (Sarnat et al., 2001). This study found that day-to-day variations in monitored ambient gases were not associated with day-to-day changes in personal exposures to those gases, but they were associated with day-to-day changes in personal exposure to $PM_{2.5}$. One reasonable interpretation of this study is that, for cities like Baltimore, changes in model results when ambient gases are included in multipollutant models may stem from such gases being surrogates for exposures to particles and not confounders at all (EPA, 2004 p. 8-245).

The broader examination of this issue in the Criteria Document included a focus on evaluating the stability of the size of the effect estimates in time-series studies using single- and multi-pollutant models, as illustrated in Figures 8-16 through 8-19 (EPA, 2004, pp. 8-248 to 8-251). This examination found that, for most time-series studies, there was little change in effect estimates based on single- and multi-pollutant models, although recognizing that, in some cases, the PM effect estimates were markedly reduced in size and lost statistical significance in models that included one or more gaseous pollutants. The Criteria Document also noted that PM and the gaseous co-pollutants were

often highly correlated, and it is generally the case that high correlations existed between pollutants where PM effect estimates were reduced in size with the inclusion of gaseous co-pollutants.

With regard to the analysis of multiple pollutants from the ACS cohort, it is important to note that the effects estimates for fine particles actually increased in two pollutant models that incorporated CO, NO_2, and ozone, and were reduced only for models that incorporated SO_2. The Criteria Document recognized, however, that SO_2 is a precursor for fine particle sulfates, which complicates the interpretation of multi-pollutant model results, and that mortality may be associated with not only $PM_{2.5}$ but also with other components of the mix of ambient pollutants in this long-term exposure study.

Far from being dismissive, EPA has examined this issue in detail based on the much more extensive body of relevant evidence available in this review. The Criteria Document concluded that "the most consistent findings from amidst the diversity of multipollutant evaluation results for different sites is that the PM signal most often comes through most clearly" (EPA, 2004, p. 8-254). While acknowledging that these analyses have not fully disentangled the relative role of co-pollutants, EPA believes that this examination provides greater confidence than in the last review that observed effects can be attributed to short- and long-term exposures to $PM_{2.5}$, alone and in combination with other pollutants, while recognizing that potential confounding by co-pollutants remains a very challenging issue to address, even with well-designed studies.

(5) *Comment:* Some commenters raised questions about the role of individual constituents within the mix of fine particles. These commenters pointed out that EPA recognized this issue as an important uncertainty in the last review and did so again in this review. These commenters expressed the view that such continued uncertainty provides no grounds for reconsidering the Agency's 1997 conclusion that the current $PM_{2.5}$ standards provide the requisite protection.

Response: As a general matter, EPA agrees that although new research directed toward the role of individual constituents within the mix of fine particles has been conducted since the last review, important questions remain and the issue remains an important element in the Agency's ongoing research program. The EPA does not agree, however, that continued uncertainty with regard to the relative toxicity of components within the mix of fine particles, in and of itself, provides grounds for not revising the suite of $PM_{2.5}$ standards. Rather, the full body of health effects evidence that has become available since the last review provides a basis for concluding that additional public health protection is warranted to protect against health effects that have been associated with exposure to fine particles measured as $PM_{2.5}$ mass.

At the time of the last review, the Agency determined that it was appropriate to control fine particles as a group, as opposed to singling out any particular component or class of fine particles. This distinction was based largely on epidemiologic evidence of health effects using various indicators of fine particles in a large number of areas that had significant contributions of differing components or sources of fine particles, together

with some limited experimental studies that provided some evidence suggestive of health effects associated with high concentrations of numerous fine particle components. In this review, as discussed in section II.D of the proposal (71 FR at 2643-2645) and in section II.C of the preamble for the final rule, while most epidemiologic studies continue to be indexed by $PM_{2.5}$, some epidemiologic studies also have continued to implicate various components within the mix of fine particles that have been more commonly studied (e.g., sulfates, nitrates, carbon, organic compounds, and metals) as being associated with adverse effects (EPA, 2004, p. 9-31, Table 9-3).

In addition, several recent epidemiologic studies included in the Criteria Document have used $PM_{2.5}$ speciation data to evaluate associations between mortality and fine particles from different sources, and some toxicologic studies have provided evidence for effects associated with various fine particle components or size-differentiated subsets of fine particles.

The available information continues to suggest that many different chemical components of fine particles and a variety of different types of source categories are all associated with, and probably contribute to, effects associated with $PM_{2.5}$. Consequently, there continues to be no basis to conclude that any individual fine particle component *cannot* be associated with adverse health effects (EPA, 2005, p. 5-17). This information is relevant to the Agency's decision to retain $PM_{2.5}$ as the indicator for fine particles (as discussed in section II.C of the preamble for the final rule). The EPA believes that it is relevant to the Agency's conclusion as to whether revision of the suite of $PM_{2.5}$ standards is appropriate. Furthermore, while there remains uncertainty about the role and relative toxicity of various components of fine PM, the current evidence continues to support the view that fine particles should be addressed as a group for purposes of public health protection, and the remaining uncertainty does not call for delaying any increase in public health protection that other evidence indicates may be warranted.

(6) *Comment:* Some commenters identified the issue of model sensitivity as an area in which uncertainty in interpreting epidemiologic evidence has increased since the last review. More specifically, these commenters addressed the issue of the sensitivity of epidemiologic associations to the use of different statistical models and different approaches to model specification used by various researchers. The comments from UARG, Pillsbury et al., the Annapolis Center and others pointed to examples where individual study results are sensitive to the use of alternative models, and to reviews that recommend further exploration of this issue in future research, as a basis for asserting that current modeling approaches are too uncertain to use the available epidemiologic studies as a basis for revising the current $PM_{2.5}$ standards.

Response: The EPA agrees that recent work on model sensitivity has raised new concerns and the Agency has given much attention to this issue. In so doing, EPA recognizes, as does HEI and other researchers, that there is no clear consensus at this time as to what constitutes appropriate control of weather and temporal trends in time-series studies, and that no single statistical modeling approach is likely to be most appropriate in all cases (EPA, 2004, p. 8-238).

While recognizing the need for further research on this issue, EPA believes that the body of time-series epidemiologic studies considered in this review[2] provides an appropriate basis for informing the Agency's decisions on whether to revise the 24-hour $PM_{2.5}$ standard, consistent with the conclusion of the HEI review panel (". . . the revised findings will continue to help inform regulatory decisions regarding PM" HEI, 2003; EPA, 2004, p. 8-237). More specifically, as discussed in section II.A.3 of the proposal (71 FR at 2633-2634), the recent time-series epidemiologic studies evaluated in the Criteria Document have included some degree of control for variations in weather and seasonal variables. However, as summarized in the HEI review panel commentary, selecting a level of control to adjust for time-varying factors, such as temperature, in time-series epidemiologic studies involves a trade-off. For example, if the model does not sufficiently adjust for the relationship between the health outcome and temperature, some effects of temperature could be falsely ascribed to the pollution variable. Conversely, if an overly aggressive approach is used to control for temperature, the result would possibly underestimate the pollution-related effect and compromise the ability to detect a small but true pollution effect (EPA, 2004, p. 8-236; HEI, 2003, p. 266). The selection of approaches to address such variables depends in part on prior knowledge and judgments made by the investigators, for example, about weather patterns in the study area and expected relationships between weather and other time-varying factors and health outcomes considered in the study.

The HEI commentary also reached several other relevant conclusions about the reanalysis of time-series studies: upon reanalysis, the PM effect persisted in the majority of studies; in some of the large number of studies in which the PM effect persisted, the estimates of PM effects were substantially reduced; in the few studies in which further sensitivity analyses were performed, some showed marked sensitivity of the PM effect estimate to the degree of smoothing and/or the specification of weather; and, in most studies, parametric smoothing approaches used to obtain correct standard errors of the PM effect estimates produced slightly larger standard errors than with the use of generalized additive models. However, the impact of these larger standard errors on the level of statistical significance of the PM effect was minor (EPA, 2004, pp. 8-237 to 8-238). While recognizing the need for further exploration of alternative modeling approaches for time-series analyses, the Criteria Document found that the studies included in this part of the reanalysis, in general, continued to demonstrate associations between PM and mortality and morbidity beyond those attributable to weather variables alone (EPA, 2004, pp. 8-340 to 8-341).

For long-term exposure to fine particles, the reanalysis and extended analyses of data from prospective cohort studies have shown that reported associations between mortality and long-term exposure to fine particles are robust to alternative modeling strategies (Krewski et al., 2000). As stated in the reanalysis report, "The risk estimates reported by the Original Investigators were remarkably robust to alternative specifications of the underlying risk models, thereby strengthening confidence in the original findings"

[2] As discussed in section II.A.2.a of the proposal (71 FR at 2629-2630, 2633), these included particular studies that did not use generalized additive models or were reanalyzed using general linear models.

(Krewski et al., 2000, p. 232). In the extended analysis, Krewski et al. (2000) did identify model sensitivities related to education level and spatial patterns in data (e.g., correlation in air pollutant concentrations between cities within a region of the country). However, these model sensitivities do not invalidate the findings of statistically significant associations between long-term exposure to $PM_{2.5}$ and mortality. For example, while the association was stronger for the subset of the ACS cohort with the least education, there was an association with cardiorespiratory mortality in the entire population.[3]

In considering these issues related to uncertainties in the underlying health science, on balance, EPA believes that the available evidence interpreted in light of these remaining uncertainties does provide increased confidence relative to the last review in the reported associations between short- and long-term $PM_{2.5}$ exposures and mortality and morbidity effects, alone and in combination with other pollutants, and generally supports stronger inferences as to the causal nature of the associations. The EPA also believes that this increased confidence, when taken in context of the entire body of available health effects evidence, adds support to its conclusion that the current suite of $PM_{2.5}$ standards needs to be revised to provide increased public health protection. This increased confidence also adds support to the Administrator's decision to place greater reliance on the long-term exposure studies as the basis for the annual $PM_{2.5}$ standard and to place greater reliance on the short-term exposure studies as the basis for the 24-hour $PM_{2.5}$ standard.

(7) *Comment:* In asserting that the estimated risk upon attainment of the current $PM_{2.5}$ standards has decreased since 1997 (UARG, p. 23), some commenters compare results of EPA's risk assessment done in the last review with those from the Agency's risk assessment done as part of this review, and they concluded that risks upon attainment of the current $PM_{2.5}$ standards "are almost surely far below those that were predicted in 1997" (UARG, p. 25). These commenters use this conclusion as the basis for a claim that there is no reason to revise the current $PM_{2.5}$ standards. In particular, UARG and other commenters claimed that, based on this purported reduction in risk estimates, EPA cannot reconcile a decision to provide a greater level of health protection now than that afforded by the current standards with the "not lower or higher than is necessary" standard articulated by the Supreme Court in *Whitman*.

Response: The EPA believes that this claim is fundamentally flawed for three reasons as discussed in turn below: (i) it mischaracterized the use of the quantitative risk assessment in the 1997 rulemaking; (ii) it is factually incorrect in its comparing the quantitative risks estimated in1997 with those estimates in the current rulemaking; and (iii) it fails to take into account that with similar risks, increased certainty in the risks presented by $PM_{2.5}$ implies greater concern than in the last review.

[3] More specifically, in multivariate models, the association found between mortality and long-term PM2.5 exposure was little changed with addition of education level to the model (Krewski et al., 2000, p. 184). This indicates that education level was not a confounder in the relationship between fine particles and mortality, but the relationship between fine particles and mortality is larger in the population subsets with lower education in this study and not statistically significant in the population subset with the highest education (EPA, 2004, p. 8-100).

First, this claim mischaracterizes EPA's use of the risk assessment in 1997 in part by not recognizing that the illustrative risk assessment conducted for portions of two cities (Philadelphia and Los Angeles) in the last review was only used qualitatively to assess the need to revise the then-current PM_{10} standards. The EPA used the 1997 risk assessment estimates to confirm the conclusions drawn primarily from the epidemiologic studies that ambient $PM_{2.5}$ levels allowed under the then current PM_{10} standards presented a serious public health problem. The EPA did not use it as a basis for selecting the level of the 1997 PM standards. See 62 FR at 38656, 65; *ATA III*, 283 F. 3d at 373-74 (noting that EPA did not base the level of the standards on the numerical results of the risk assessment). In so doing, the Administrator concurred with CASAC's judgment that the quantitative risk estimates at the time were too uncertain for EPA to rely on in deciding the appropriate levels for the $PM_{2.5}$ NAAQS. Therefore, the final decision on the level of the NAAQS was not based on the absolute or relative risk reductions estimated in the quantitative risk assessment. Instead, the decision was based on a direct assessment of the available epidemiological studies and the concentration levels observed in urban areas examined in the studies where statistically significant effects had been observed. Since EPA did not rely on the 1997 quantitative risk estimates in setting the level of the 1997 standards, the 1997 estimates associated with those levels do not represent a decision on a requisite level of quantified risk from PM exposure, and, therefore, do not support the argument that a lower estimated risk is more than is necessary to provide the requisite level of protection. As a result, the suggested quantitative comparison between the 1997 estimates and the current estimates of risks at the levels of the current standards is not an appropriate basis for determining whether the current suite of $PM_{2.5}$ standards needs to be revised.

Second, EPA relies on the current risk estimates associated with meeting the current standards in a qualitative manner, as in 1997, to inform the conclusions drawn primarily from the epidemiological studies on whether ambient $PM_{2.5}$ levels allowed under the current suite of $PM_{2.5}$ standards present a serious public health problem warranting revision of the suite of $PM_{2.5}$ standards. The 1997 estimate of these risks, or any comparison to the current estimates, are irrelevant for that purpose, as the 1997 estimates reflect an outdated analysis that has been updated in this review to reflect the current science.

Further, even if the 1997 and current risk assessments were legitimately comparable for decision-making purposes, it would still be factually incorrect to conclude that EPA accepted significantly greater risk in 1997 than is now estimated to be associated with the 1997 standards based on the most recent risk assessment. It is important to note that a very large proportion of the quantitative risks estimated in 1997 and today comes from long-term exposure mortality. The Agency's primary estimates today (which assume a potential threshold of 10 $\mu g/m^3$, as recommended by CASAC for the Agency to use in its primary estimates) result in residual risks in terms of percent of total incidence that are about the same in the current review as they were in the last review for both Philadelphia and Los Angeles. While the separate estimates for annualized short-term mortality risk (which are at least in part subsumed in the larger long-term exposure-related estimates) are somewhat smaller in the more recent analyses for one of the two cities analyzed, the

overall quantitative risk estimates considering PM-related mortality associated with both short- and long-term exposures are about the same.

Third, it is important to take into account EPA's increased level of confidence in the associations between short- and long-term $PM_{2.5}$ exposures and mortality and morbidity effects. In comparing the scientific understanding of the risk presented by exposure to $PM_{2.5}$ between the last and current reviews, one must examine not only the quantitative estimate of risk from those exposures (e.g. the numbers of premature deaths or increased hospital admissions at various levels), but also the degree of confidence that the Agency has that the observed health effects are causally linked to $PM_{2.5}$ exposure at those levels. As documented in the Criteria Document and the recommendations and conclusions of CASAC, EPA recognizes significant advances in our understanding of the health effects of $PM_{2.5}$, based on reanalyses, extended analyses and new epidemiology studies, new human and animal studies documenting effects of concentrated ambient particles, new laboratory studies identifying and investigating biological mechanisms of PM toxicity, and new studies addressing the utility of using ambient monitors to assess population exposures to particles of outdoor origin. As a result of these advances, EPA is now more certain that fine particles, alone or in combination with other pollutants, present a significant risk to public health at levels at or above the range of levels that the Agency had considered for these standards in 1997. From this more comprehensive perspective, since the risks presented by $PM_{2.5}$ are more certain and the overall current quantitative risk estimates are about the same as in 1997, $PM_{2.5}$-related risks are now of greater concern than in the last review.

In sum, quantitative risk estimates were not a basis for EPA's decision in setting a level for the $PM_{2.5}$ standards in 1997, and they do not set any quantified "benchmark" for the Agency's decision to revise the $PM_{2.5}$ standards at this time. In any case, there is not a significant difference in the risk estimates from 1997 to now. Finally, EPA believes that confidence in the causal relationships between short- and long-term exposures to fine particles and various health effects has increased markedly since 1997. Therefore, similar or even somewhat lower quantitative risk estimates today would not be a basis to conclude that no revision to the suite of $PM_{2.5}$ standards is "requisite" to protect public health with an adequate margin of safety. Additional comments on EPA's risk assessment are discussed below in section II.A.4.

(8) *Comment:* Some commenters supporting no revisions to the current $PM_{2.5}$ standards also identified "new" studies that were not included in the Criteria Document as showing "continued erosion of the hypothesis that there is a causal connection between fine PM mass and health effects" and further supporting "the conclusion that more stringent $PM_{2.5}$ standards are not justified" (Pillsbury et al., p. 14). In looking at long-term exposure studies, these commenters cited an update to the Veteran's cohort study (Lipfert et al., 2006a) as showing that traffic density is a better predictor of mortality than any ambient air quality measures, including fine PM. In citing an ACS cohort study in Los Angeles (Jerrett et al., 2005), which the study authors and other commenters interpreted as providing evidence that when exposure is measured with less error, mortality risks associated with $PM_{2.5}$ are higher than previously believed (as discussed above), these

commenters noted that when socioeconomic factors were included in the analyses, associations with fine PM were substantially attenuated. A follow-up to the Six Cities study (Laden et al., 2006), which was cited by other commenters as providing strong evidence that reducing long-term average $PM_{2.5}$ levels improves public health (as discussed above), was viewed by these commenters as reporting implausibly high risk estimates and being flawed in that no co-pollutants or other relevant variables (e.g., income, education) were considered. These commenters also cited a study of mortality among elderly Californians (Enstrom, 2005) as not supporting a current relationship between fine PM and total mortality. These commenters expressed concerns regarding the adequacy of the control of strong potential confounders, such as cigarette smoking, in all of these studies. These commenters also identified what they considered to be the most notable "new" time-series studies, including the ARIES study of mortality in two counties in Georgia (Klemm et al., 2004) and a mortality study including data from nine California counties (Ostro et al., 2006). The results of the ARIES study, which considered constituents of fine PM, are interpreted by these commenters as indicating that the association between air pollution and mortality is complex and cannot be attributed to any single component of the mixture. The Ostro et al. (2006) study, which reports associations between $PM_{2.5}$ and several mortality categories, is interpreted as suggesting that fine PM mortality risk is substantially less than EPA assumed in the last review in areas with relatively high long-term average $PM_{2.5}$ concentrations.

Response: As discussed in section I.C. of the preamble to the final rule, to the extent that these commenters included "new" scientific studies (studies not considered in the Criteria Document) in support of their arguments for not revising the standards, EPA notes that as in past NAAQS reviews, EPA is basing the final decisions in this review on the studies and related information included in the PM air quality criteria that have undergone CASAC and public review and will consider newly published studies for purposes of decision making in the next PM NAAQS review. The EPA reiterates that the provisional assessment of "new" science does not provide the level of analysis and critical assessment provided in the formal process that incorporates review by CASAC and the public. Nonetheless, in provisionally evaluating commenters' arguments, EPA notes that its provisional assessment of "new" science found that such studies did not materially change the conclusions in the Criteria Document.

b. Indicator

The EPA received comparatively few public comments on issues related to the indicator for fine particles. Public comments from all major public and private sector groups received on the proposal were overwhelmingly in favor of EPA's proposal to retain $PM_{2.5}$ as the indicator for fine particles. No public comments were submitted regarding the need for a different size cut for fine particles. In addition to the responses contained in Section II.C of the preamble to the final rule, EPA provides the following responses to specific issues related to the indicator for fine particles.

(1) *Comment:* Some commenters who supported retaining $PM_{2.5}$ as an indicator argued that current scientific evidence does not provide any evidence to identify specific components or sources of concern and, therefore, a mass-based indicator remains the appropriate indicator for fine particles (Engine Manufacturers Association; American Lung Association et al.).

Response: The EPA agrees with these commenters that the current scientific evidence does not support an alternative $PM_{2.5}$ indicator(s) based upon specific components and/or sources of concern at this time. The EPA notes that CASAC concurred with this position during the review of the Staff Paper.

(2) *Comment:* Some commenters emphasized the need to conduct additional research to more fully understand the effect of specific PM components and/or sources on public health. For example, the Electric Power Research Institute highlighted specific new research studies that had been completed since the close of the Criteria Document addressing issues related to fine particle components and source apportionment, and noted its ongoing research on component-related health effects that includes coordinated epidemiology, toxicology, and exposure assessment studies.

Response: The EPA agrees that additional research is important to better understand the role of specific fine particle components and/or sources of fine particles. The EPA also recognizes the ongoing efforts HEI to conduct additional multidisciplinary research targeted at expanding the available data on the health effects associated with specific PM components (HEI, 2005). As new data become available in the peer-review literature, EPA will consider this new evidence for purposes of decision making in the next PM NAAQS review.

(3) *Comment:* One commenter argued that recent studies show that generally PM-related health effects are attributed to several sources including vehicular-related emissions; primary sulfate compounds involving certain metals, such as nickel and vanadium (residual oil emissions); and emissions of carbonaceous and other particles from certain industrial facilities; and not to secondary sulfate or to secondary organic aerosols (comment submitted after close of public comments; docket number OAR-2001-0017-3116). This commenter urged EPA to consider the results of "new" studies that, in the commenter's view, show that vehicular emissions generally, and residual oil emissions in certain localities, are the most important sources contributing to PM-related health effects. This commenter included an extensive discussion of this issue based in large part on an unpublished general review of this body of literature prepared by an individual analyst.

Response: As discussed in section I.C of the preamble of the final rule, EPA conducted a provisional assessment of the most policy-relevant studies published recently which were not included in the Criteria Document. This provisional assessment is included in Appendix A of this document. The EPA notes that with regard to the issue of specific fine particle components, the provisional assessment concluded that "recent analyses continue to indicate that particles related to traffic, residual oil combustion, wood smoke,

and regional sulfate pollution and primary coal burning are associated with increased mortality. A number of "new" studies continue to indicate that traffic-related PM exposures are associated with mortality and morbidity. Recent epidemiologic observations continue to support associations between various fine PM components and both mortality and morbidity effects" (EPA, 2006, p. 38). As discussed in section I.C of the preamble to the final rule, EPA is basing its decisions in this review on studies and related information included in the Criteria Document and Staff Paper which have undergone CASAC and public review. The EPA notes that just as the Agency's provisional assessment of "new" science has not included the level of analysis and critical assessment provided in the formal process that incorporates review by CASAC and the public, neither has the assessment on which the literature review submitted by this commenter. The studies included in the provisional assessment, public comments received on the provisional assessment including additional studies that commenters submitted, as well as more recent scientific evidence will be assessed during the next review of the PM NAAQS.

(4) *Comment:* Some commenters asserted that, because an indicator based on fine particle mass does not differentiate among different fine PM constituents with varying toxicities, the public health ramifications of using a mass-based indicator are unknown. Some of these commenters argued that although EPA recognized the importance of PM speciation in the proposed qualified indicator for coarse particles, EPA failed to differentiate between fine particle species based on toxicity. These commenters generally used this argument to support their overall conclusion that no revisions to the primary $PM_{2.5}$ standards are needed at this time (e.g., American Public Power Association, Class of '85 Regulatory Response Group, American Public Power Association).

In addition, some commenters argued to exclude certain sources from the NAAQS for both fine and coarse particles, specifically agricultural and mining sources (American Farm Bureau Federation, National Mining Association, National Cattlemen's Beef Association). These commenters argued that, as proposed for coarse particles, the scientific evidence does not show that fine particles from these sources are associated with adverse health effects.

Response: As with the last PM NAAQS review, the current review considered the merits of alternative $PM_{2.5}$ indicators including evaluating the available epidemiologic and toxicologic evidence associated with exposure to various PM components (e.g., sulfates or acid aerosols, metals, organic constituents, bioaerosols, diesel particles). The central question of which particle components to regulate has been an issue since the inception of the first PM standards. As discussed in Chapter 9 of the Criteria Document, the available scientific evidence suggests that many different chemical components of fine particles and a variety of different types of source categories are all associated with, and probably contribute to, mortality, either independently or in combinations" (EPA, 2004, p-9-31). Conversely, as noted in section 5.3.2 of the Staff Paper, the Criteria Document states that the available evidence "provides no basis to conclude that any individual fine particle component *cannot* be associated with adverse health effects (EPA, 2005, p-5-17)."

As discussed in section III.C of the preamble to the final rule, EPA received a large number of comments on its proposed decision to consider a qualified indicator for coarse particles. The practical difficulties and imprecision associated with a qualified indicator, as well as the substantial scientific uncertainty regarding the health effects associated with different components and mixes of coarse particles as well as other factors have convinced the Administrator that it is inappropriate to adopt a qualified coarse particle indicator at this time. Similarly, as discussed in Section II.C of the preamble to the final rule, EPA does not believe there is sufficient evidence that would lead toward the selection of one or more PM components as being primarily responsible for effects associated with fine particles, nor is there any component that can be eliminated from consideration. Therefore, EPA believes that a mass-based indicator for fine particles remains appropriate at this time. Further, for the reasons outlined above in responding to a similar comment in section II.A.2.a.ii of this document, EPA does not agree that continued uncertainty with regard to the relative toxicity of components within the mix of fine particles, in and of itself, provides grounds for not revising the suite of $PM_{2.5}$ standards.

The EPA recognizes that the identification of specific components, properties, and sources of fine particles that are linked with health effects remains an important research need. Specifically, EPA acknowledges that "continued source characterization, exposure, epidemiologic, and toxicologic research is needed to help identify components, characteristics, or sources of particles that may be more closely linked with various specific effects to aid in our understanding of causal agents and in the development of efficient and effective control strategies for reducing health risks. Conducting human exposure research in parallel with such health studies will help reduce the uncertainty associated with interpreting health studies and provide a stronger basis for drawing conclusions regarding observed effects" (EPA 2005, p. 5-73).

(5) *Comment:* Some commenters argued that, with a 2.5 μm cutpoint for fine particles, there can be considerable intrusion of the smallest fraction of coarse particles into the $PM_{2.5}$ category. These commenters argued that "such inclusion will undermine and confound the fine particle standard by including coarse particles that are without substantial health or welfare effects, and likewise misdirect control efforts" (National Mining Association, p. 43; National Cattlemen's Beef Association, p. 43). Some of these commenters argued that "EPA has the opportunity to retain the $PM_{2.5}$ indicator, while supplementing it with a mechanism to eliminate coarse particles prior to making nonattainment determinations" and provided additional information on a technique for excluding coarse particle intrusion from $PM_{2.5}$ measurements (American Farm Bureau Federation, p 45, National Mining Association, p. 46).

Response: The EPA recognized the potential for coarse particle intrusion in the 1997 review of the standards (62 FR at 38667 to 38668). As discussed in section 9.2.1 and illustrated in Figure 2-18 of the Criteria Document, the ranges of fine and coarse particles overlap for sizes between 1 and 3 μm (EPA, 2004, p 9-10; p. 2-18). As discussed in section III.C of the preamble, EPA considered an alternative cutpoint of 1 μm as well as 2.5 μm in this review. After reconsidering the issue, EPA continues to believe that 2.5

μm is the more appropriate size cut because the greatly expanded epidemiologic evidence is largely based on $PM_{2.5}$ and because EPA believes it is more important from a regulatory perspective to capture fine particles more completely under all conditions than to avoid some coarse-mode intrusion into the fine fraction in some areas. The Staff Paper recognized that particles can act as carriers of water, oxidative compounds, and other components into the respiratory system, which adds to the importance of ensuring that larger accumulation-mode particles are included in the fine particle size cut (EPA, 2005, p. 5-18).

The EPA recognizes that the choice of indicator does permit some coarse particle intrusion into the fine particle measurement, but that the contribution of such particles to this mass is generally quite limited. In some conditions, however, the contribution may be more significant. Because the major focus of the fine particle standard is to address fine particles smaller than 2.5 μm, EPA believes it is appropriate to minimize the intrusion of coarse particles larger than this size into the catch. In part for this reason, as discussed in section VI of the preamble, EPA the use of a new "Very Sharp Cut Cyclone Separator" (VSCCS) as an alternative inlet for the $PM_{2.5}$ Federal Reference Method (FRM). In addition to reduced maintenance, the VSCCS $PM_{2.5}$ inlet should serve to reduce the intrusion of larger coarse particles into the fine filter, particular in high coarse particle conditions. EPA encourages the use of this inlet in areas with higher coarse particle levels. As discussed in section 9.2.1 and illustrated in Figure 2-18 of the Criteria Document, there are overlapping ranges of fine and coarse particles between 1 and 3 μm (EPA, 2004, p 9-10; p. 2-18). In section II.C of the preamble to the final rule, EPA acknowledges that size cuts of both 1 μm and 2.5 μm were considered in this review and that EPA continues to believe that 2.5 μm is the appropriate size cut for fine particles because the epidemiologic evidence is largely based on $PM_{2.5}$ and because EPA believes it is more important from a regulatory perspective to capture fine particles more completely under all conditions than to avoid some coarse-mode intrusion into the fine fraction in some areas. The Staff Paper recognized that particles can act as carriers of water, oxidative compounds, and other components into the respiratory system, which adds to the importance of ensuring that larger accumulation-mode particles are included in the fine particle size cut (EPA, 2005, p. 5-18).

As discussed below in response to a similar comment with regard to excluding crustal materials from the indicator for coarse particles, EPA does not agree that there is sufficient evidence to conclude that crustal particulate matter in the coarse mode is benign or to exclude crustal materials from the indicators for either coarse or fine particles. In addressing this general comment below, EPA notes that studies by Mar et al. (2003) and Laden et al. (2000), which was reanalyzed by Schwartz (2003), examined the associations of crustal materials in the fine particle fraction, which typically makes up just a small fraction of fine particle mass. Based on an assessment of these studies and all the available evidence, as discussed below, EPA believes that it is inappropriate to exclude the tail of the coarse mode particles from the $PM_{2.5}$ indicator.

To the extent that these commenters based their views on the anticipated burden that the use of the $PM_{2.5}$ indicator may have, EPA notes that such implementation-related issues

are legally irrelevant in determining which standards are requisite to protect public health with an adequate margin of safety and was therefore not considered in its decision making process.

(6) *Comment:* Two commenters state that EPA should instruct States to effectively distinguish between urban and agricultural sources of $PM_{2.5}$ and to exclude agricultural sources from the Clean Air Act controls to implement the NAAQS. They also suggest differentiating counties by urban or non-urban dominance of $PM_{2.5}$ using the same five-step test as for locating monitors for the proposed $PM_{10-2.5}$ network. The $PM_{2.5}$ monitors would be designated as subject to either the 2006 standard (35 μg/m3) (for urban sources) or 1997 standard (65 μg/m3) (for rural sources).

Response: These commenters fail to recognize the significant differences in the underlying character of urban and rural fine particles, as compared to coarse particles. Because of their wider transport and secondary origin, the composition of fine particles in rural areas can contain substantial fractions of materials from anthropogenic combustion sources, including secondary aerosols from coal combustion. As discussed above in this document and in Section II.C of the preamble, the scientific evidence provides no basis for excluding any component of fine particles from the indicator. Accordingly EPA can see no rational basis for developing different standard levels of $PM_{2.5}$ either for different sources or for application to different areas.

c. Averaging Time

The EPA received very limited public comments on the issue of averaging time for the $PM_{2.5}$ primary standards. A group of public health and environmental organizations agreed that "the EPA has selected the appropriate averaging times for the fine particle standards" (American Lung Association, et al.). In addition to the discussion contained in Section II.D of the preamble to the final rule, EPA provides the following response to a specific issue related to the averaging time for fine particles.

Comment: Two commenters expressed support for a fine particle standard with an averaging time less than 24 hours (Save Our Summers, Safe Air for Everyone). These commenters argued that a 24-hour standard is not adequate to protect individuals and communities who are unusually vulnerable to sudden, acute exposures to $PM_{2.5}$ pollution citing concerns associated with PM exposures associated with agricultural burning that can cause very high spikes in $PM_{2.5}$ concentrations (for an hour or more). Specifically, these commenters argued that adverse health effects may be associated with short-term peak $PM_{2.5}$ exposures, that, when averaged over a 24-hour period would be at or below the proposed level of the 24-hour $PM_{2.5}$ standard. These commenters argued that fine particles in the form of smoke from grass residue burning is a serious danger to public health, especially to farm workers and motorists exposed at or near fields where agricultural burning is occurring, and that these types of exposures must be accounted for in revising the PM standards (see evidentiary submission from local physicians in support of the commenter's motion for preliminary injunction, pp. 12-14 of comment letter, Safe Air For Everyone, 2326; Save Our Summers, 2030).

Response: As discussed in section II.D. of the preamble to the final rule and in section 5.3.3 of the Staff Paper, EPA has considered the appropriate averaging time(s) supported by the information available in this review and, specifically, whether this information supported consideration of different averaging times in addition, or in place of the 24-hour and annual averaging times used for the current $PM_{2.5}$ standards. The EPA recognizes that most time-series epidemiological studies use 24-hour average PM measurements; however, there is a growing body of scientific studies that provide evidence of effects associated with exposure periods shorter than 24 hours. These studies are summarized in section 3.6.5.3 of the Staff Paper (EPA, 2005, p 3-52 to 3-53). The EPA concludes that the available data are too limited to serve as a basis for establishing a shorter-than 24-hour fine particle primary standard at this time but that these data do add weight to the importance of a 24-hour standard. The EPA recognizes that data on effects linked with very short, peak $PM_{2.5}$ exposures, such as those related to wildfires, agricultural burning, or other episodic events, would provide valuable information both for the standard-setting process and for risk communication and management efforts (EPA, 2005, p-5-74).

d. Forms

The EPA received a limited number of public comments on the appropriate forms for the PM2.5 standards. Incorporating responses contained in sections II.A.2.d of the preamble to the final rule, EPA provides the following responses to specific comments related to the form of (i) the 24-hour $PM_{2.5}$ standard and (ii) the annual $PM_{2.5}$ standard.

i. 24-hour standard

None of the public commenters raised objections to continuing the use of a concentration-based form for the 24-hour standard. Many of the individuals and groups who supported a more stringent 24-hour $PM_{2.5}$ standard noted in Section II.B of the preamble to the final rule also recommended a more restrictive concentration-based percentile form, specifically a 99^{th} percentile form. The EPA received comparatively few public comments from State and local air pollution control authorities and tribal organizations on the form of the 24-hour $PM_{2.5}$ standard. Of the limited number of state air pollution control authorities that commented on the form of the 24-hour $PM_{2.5}$ standard, all supported retaining the 98^{th} percentile form. Of the limited number of local air pollution control authorities and tribal organizations that commented on the form of the 24-hour $PM_{2.5}$ standard, some supported retaining the 98^{th} percentile form while others supported the 99^{th} percentile form. Beyond their support for retaining the current 24-hour $PM_{2.5}$ standard, which has a 98^{th} percentile form, commenters representing industry associations and businesses provided no specific comments regarding the form of the 24-hour $PM_{2.5}$ standard. In addition to the discussion contained in Section II.E.1 of the preamble to the final rule, EPA provides the following responses to specific issues related to the form for 24-hour $PM_{2.5}$ standard.

(1) *Comment:* The limited number of commenters who provided a specific rationale for their recommendation in support of a 99th percentile form generally expressed their concern that the 98th percentile form could allow too many days where concentrations exceeded the level of the standard, and thus fail to adequately protect public health.

Response: In considering this issue, as discussed in section II.F of the preamble to the final rule, the Staff Paper took into consideration the relative risk reduction afforded by alternative forms at the same standard level, the relative year-to-year stability of the air quality statistic to be used as the basis for the form of a standard, and the implications from a public health communication perspective of the extent to which either the 98th or 99th percentile form allows different numbers of days in a year to be above the level of the standard in areas that attain the standard. Based on their review, most CASAC Panel members favored continued use of the 98th percentile form because it is more robust than the 99th percentile, such that it would provide more stability to prevent areas from bouncing in and out of attainment from year to year (Henderson, 2005a). In retaining the 98th percentile form, the Administrator focused on the relative stability of the 98th and 99th percentile forms as a basis for his decision, while recognizing that the degree of public health protection likely to be afforded by a standard is a result of the combination of the form and the level of the standard.

(2) C*omment:* Several state air pollution control agencies that otherwise supported EPA's proposal to retain the 98th percentile form of the 24-hour $PM_{2.5}$ standard raised concerns regarding a technical problem associated with a potential bias in the method used to calculate the 98th percentile concentration for this form. NESCAUM, in particular, noted that "the existing and proposed methodology yields a lower (i.e., less stringent) value on average for a 1 in 3 day frequency sample data-set compared to a daily sample data-set by approximately 1 $\mu g/m^3$" (NESCAUM, p. 3), and recommended revisions to the methodology such that "the calculation becomes insensitive to data capture rate or sampling frequency" (NESCAUM, Attachment A, p.7). Another state commenter suggested the issue could be addressed by "the addition of language that requires areas that are near the daily NAAQS to continue to use every day FRM/FEM sampling" (Delaware Department of Natural Resources, p. 4).

Response: The EPA agrees with these commenters that the potential bias in calculating the design value of the 24-hour $PM_{2.5}$ standard is a concern. To reduce this bias, EPA had proposed to increase the sampling frequency for monitoring sites that were within 10 percent of the standard to 1 in 3 day sampling (40 CFR Part 58 section 12(d)(1); 71 FR at 2780). The EPA is persuaded by these commenters that it is appropriate to adjust the proposed sampling frequency requirements in order to further reduce this bias. Accordingly, as discussed in section II.E.1 of the preamble to the final rule, EPA is modifying the final monitoring requirements such that areas that are within 5 percent of the standard will be required to increase the frequency of sampling to every day (40 CFR Part 58 section 12(d)(1)).

ii. Annual standard

As discussed in section II.E.2 of the preamble to the final rule, relatively few public comments were received on the form of the annual $PM_{2.5}$ standard.

(1) *Comment:* Of the commenters noted above in Section II.B who supported a more stringent annual $PM_{2.5}$ standard, those who commented on the form of the annual $PM_{2.5}$ standard argued that the EPA analyses described above demonstrated that the current form of the standard results in uneven public health protection leading to disproportionate impacts on potentially vulnerable subpopulations, and thus a change in the form of the standard is needed. However, these commenters argued that the proposed modifications to the spatial averaging criteria were not stringent enough and, in order to reduce the possibility of pollution hotspots and disproportionate impacts, especially in areas meeting the annual $PM_{2.5}$ standard, spatial averaging should be eliminated (American Lung Association et. al., 2006, pp. 44-47; Schwartz, 2005, p.2). Of the commenters noted above in Section II.B who supported retaining the current annual $PM_{2.5}$ standard, those who commented specifically on the form of the standard supported retaining the current spatial averaging criteria. These views are most extensively presented in comments from UARG who argued that changes to the spatial averaging criteria, effectively increasing the stringency of the standard, are not needed as the current standards provide the requisite degree of public health protection (UARG, 2006. pp. 33-36). In addition, one state air pollution control agency supported a more stringent level for the annual $PM_{2.5}$ standard in the range recommended by CASAC but also supported retaining the option for spatial averaging for the form of the standard arguing that "rarely is one monitor representative of an entire nonattainment area" especially in the western U.S. (Utah Department of Environmental Quality, 2006, p. 2).

Response: In responding to these comments, EPA emphasizes that the intent of the current spatial averaging criteria, as defined in 1997 based on a limited set of $PM_{2.5}$ air quality data, was to ensure that spatial averaging would not result in inequities in the level of protection provided by the $PM_{2.5}$ standards against health effects associated with short- and long-term exposures to $PM_{2.5}$. Based on the analyses described above (Schmidt et al., 2005), which are based on the much larger set of air quality data that has become available since the last review, EPA now believes that tighter constraints on spatial averaging are necessary to address concerns over potential disproportionate impacts on the populations that EPA has identified as being potentially vulnerable to $PM_{2.5}$-related health effects. The EPA believes that current information and analyses indicate that application of the current form has the clear potential to result in disproportionate impacts on potentially vulnerable subpopulations in some areas. The EPA recognizes that the proposed constraints have the potential to increase the stringency of the annual $PM_{2.5}$ standard in some areas in which a State might choose to use spatial averaging. The EPA believes that in such cases this increased stringency is warranted so as to address possible disproportionate impacts on potentially vulnerable populations and more generally to avoid inequities across all population groups. The EPA disagrees with those commenters who support eliminating spatial averaging altogether. The EPA believes that the proposed narrowing of the spatial averaging criteria will adequately

address the concerns about disproportionate impact raised by some commenters, as analyzed in the Staff Paper, by substantially reducing the amount of spatial variation in long-term ambient levels that will be allowed to be averaged together in determining compliance with the standard.

(2) *Comment:* Some commenters argued that the reasons for allowing spatial averaging relate to consideration of cost and feasibility and thus serve no purpose related to protecting public health. The proposal thus violates fundamental tenets of the Clean Air Act (American Lung Association et al.).

Response: These commenters do not identify the basis for their view that the proposal reflects consideration of cost and feasibility. The EPA may not, and did not, consider issues of cost and feasibility in adopting the provisions on spatial averaging.

e. Levels

A large number of comments on the proposed levels for the primary standards for $PM_{2.5}$ basically expressed one of two substantively different views: (1) support for more health protective standards at or below the levels proposed by EPA or (2) opposition to any modification of the current $PM_{2.5}$ standards. Many of these commenters simply expressed their views without stating any rationale, while others gave general reasons for their views but without reference to the factual evidence or rationale presented in the proposal notice as a basis for the Agency's proposed decision regarding the levels of the primary $PM_{2.5}$ standards. A number of commenters, including many States and Tribes, who supported the proposed level generally placed great weight on the recommendation of CASAC. Section II.F of the preamble to the final rule presents the Agency's response to these very general views. In addition to the discussion contained in that section, EPA provides the following responses to specific issues related to the levels for the primary $PM_{2.5}$ standards.

i. 24-hour standard

Many commenters expressed disagreement with the proposed level of the 24-hour $PM_{2.5}$ standard. As noted in section II.B. of the preamble for the final rule, these commenters were in two distinct groups that expressed sharply divergent views on their interpretations of the science (in some cases taking into consideration "new" science not included in the Criteria Document) and the appropriate policy response based on the science and their views on how the quantitative risk assessment should factor into a decision on the standard level.

(a) Support for Retaining the Current Level

(1) *Comment:* In interpreting the available scientific information, including consideration of "new" science, and advocating a policy response based on the science, one group of commenters focused strongly on the uncertainties they saw in the scientific evidence as a basis for concluding that no change to the current level of the 24-hour $PM_{2.5}$ standard was warranted. This group included virtually all commenters representing industry associations and businesses. In commenting on the proposed level, these commenters

most generally relied on the same arguments presented in section II.B.2 of the preamble for the final rule as to why they believed it was inappropriate for EPA to make any revisions to the suite of primary $PM_{2.5}$ standards. That is, they asserted that the health effects of concern associated with short-term exposure to $PM_{2.5}$ have not changed significantly since 1997; that the uncertainties in the underlying time-series epidemiologic studies are as great or greater than in 1997; that the estimated risk upon attainment of the current $PM_{2.5}$ standards is lower now that it was when the $PM_{2.5}$ standards were set in 1997; and that "new" science not included in the Criteria Document continues to increase uncertainty about possible health risks associated with exposure to $PM_{2.5}$.

Response: These general comments are addressed above in section II.A.2.a.ii and in section II.B.2 of the preamble for the final rule.

(2) *Comment:* More specifically, UARG's comments in particular (which were referenced by some other commenters representing industry associations and business as well) called into question EPA's rationale for the proposed level of 35 $\mu g/m^3$. Many of these commenters primarily relied on an examination of this rationale contained in an attachment to UARG's comments as the basis for concluding that the available studies do not support EPA's view of the overall pattern of statistically significant associations in studies of short-term exposure to $PM_{2.5}$ across a wide range of 98^{th} percentile $PM_{2.5}$ values. This examination concluded that there is no consistent pattern of associations at levels up to (and above) the 65 $\mu g/m^3$ 98^{th} percentile level of the current standard. This examination was based on an individual consultant's ranking of a set of short-term exposure studies by what was characterized as the "overall significance" of each study's results. A number of studies were included in this examination that were not included among the studies that EPA considered in looking at the pattern of associations.

Response: In considering the approach used in this examination of short-term exposure studies, EPA concludes that the categorical rankings were defined in a very restrictive way, emphasizing results from multi-pollutant models and alternative model specifications, which had the effect of discounting statistically significant results in some studies. More specifically, in this examination, the consultant ranked each study into one of three categories: "no overall significant association," "mixed significance," and "overall significant association." A study was only considered to have an "overall significant association" if a majority of the regressions in the paper produced statistically significant associations, and, if a two-pollutant model result is provided, it must also be statistically significant (unless there is evidence of multicollinearity problems in the two-pollutant model, which is considered to exist only when both the PM and gaseous pollutant would become insignificant in a two –pollutant model even though both are significant in their respective one-pollutant models). A ranking of "no overall significant association" was assigned if the majority of the results in the paper are insignificant, even if statistically significant results exist in the paper, and, if there is only one one-pollutant and one two-pollutant model result reported and the two-pollutant model result is not statistically significant (unless there is evidence of multicollinearity).

In considering this categorical ranking approach, EPA reiterates that it believes in the importance of a comprehensive evaluation that considers and weighs a variety of evidence, including biological plausibility of associations between the various pollutants and health outcomes, and focuses on the stability of the size of the effect estimates in time-series studies considering both single- and multi-pollutant models, rather than just looking at statistical significance in a large number of alternative models as a basis to delineate between real and suspect associations, as discussed above in section II.A.2.a.ii (and in section II.B.2 of the preamble to the final rule). The EPA finds that in some cases the approach used in the consultant's evaluation does not give adequate weight to important statistically significant results as a consequence of simply counting the number of statistically significant results across all models presented. This has the effect of weighing all models equally, regardless of plausibility or statistical power, and it allows a lack of statistically significant results for one lag structure to essentially cancel out statistically significant results based on another lag structure. That is, EPA does not agree, for example, that a statistically significant association between mortality and same-day exposure to $PM_{2.5}$ should be completely discounted by a finding in the same study that an association between mortality and $PM_{2.5}$ exposure several days prior to death is not statistically significant. Health effects associated with relatively more immediate exposures could well be the consequence of a biological mechanism that would not reasonably be expected to result in the same health effect several days after exposure. Thus, EPA does not believe that it is appropriate to simply average out statistically significant and nonsignificant results derived from models with different lags.

Further, EPA disagrees with some of the underlying assumptions in this commenter's analysis. One key assumption is that, in selecting from several model results, the author has selected GLM results preferentially over GAM analysis results. The EPA disagrees that one approach is necessarily better than the other. The Criteria Document included an extensive discussion of the results of reanalyses of time-series epidemiologic studies, and observed that there are advantages and disadvantages with the different modeling approaches (Section 8.4.2). As observed by authors in the reanalysis of the NMMAPS morbidity study, "The wide use of GAMs in epidemiologic studies is due to flexibility in modeling nonlinear parameters such as season and weather" in allowing researchers to evaluate relationships with nonlinear variables without having to make assumptions about the form of the relationship (Schwartz et al., 2000, p. 25). In the reanalyses to address the issues identified with the default specifications for the initial GAM software, one approach was to use GLM with natural splines for the nonlinear parameters, an approach that had been used prior to the development of GAM. The use of GLM with natural splines requires the investigator to select "degrees of freedom" for the form of the nonlinear parameters, and investigators have not identified any one optimal approach for selecting degrees of freedom in these models. In short, EPA found that "[t]he GLM/natural splines may produce correct standard errors but cannot guarantee "correct" model specifications" (EPA, 2004, p. 8-231). A key conclusion in the HEI Review Committee report was that no one model could be recommended "as being strongly preferred over another at this point" (EPA, 2004, p. 8-238). EPA does not agree that either GLM or GAM is the single best modeling approach. For the presentation of results from the body of U.S. and Canadian studies in Figures 3-1 and 3-2 of the Staff Paper,

EPA chose results from GLM models, placing emphasis on characterization of the standard errors for the associations. In quantifying health risk, EPA selected results from GAM models using more stringent convergence criteria, recognizing the potential for understatement of standard errors around the central risk estimates (EPA, 2005, p. 4-19).

In addition, this examination included several studies that, for a variety of reasons, EPA does not believe are appropriate for such an analysis. The addition of such studies, some of which had relatively low statistical power, served to dilute the pattern of associations seen in studies considered by EPA as providing a more appropriate basis for this type of examination. For example, several studies used air quality measures that are not appropriate for comparison to a 98^{th} percentile value based on a distribution of 24-hour average $PM_{2.5}$ concentrations measured at population-oriented monitoring sites. In particular, Linn et al. (1999), was an exposure study that only measured $PM_{2.5}$ outside of individual study participants' homes and indoors over 4-day intervals, and did not report any $PM_{2.5}$ effect estimates. Studies by Ostro in Denver (Ostro et al., 1991) and Los Angeles (Ostro et al., 2001) used less than 24-hour average $PM_{2.5}$ concentrations; 7-hour average concentrations were used in the Denver study, and 12-hour average $PM_{2.5}$ concentrations were used in Los Angeles, which were described as "problematic" by the authors (being greater than measured PM_{10} concentrations on a number of days), leading to only a limited $PM_{2.5}$ analysis. In Korrick et al. (1998), which was a study of mountain hikers in New Hampshire, $PM_{2.5}$ concentrations were measured only at the bottom of the mountain, whereas ozone, which was the primary focus of the study, was measured both at the bottom and top of the mountain to provide a more representative measure of exposure. Further, the study by Zhang et al. (2000) did not report any quantitative $PM_{2.5}$ effect estimates. The panel study by Delfino et al. (1996) included only 12 subjects. The study by Tolbert et al. (2000) was a preliminary study that reported only interim results. The study by Tsai et al. (2000) was a source apportionment study with low statistical power. EPA was not able to obtain air quality data from the author for the study by Moolgavkar (2003). For these reasons, EPA appropriately did not include these studies when assessing the pattern of results from relevant short-term exposure studies.

Further, EPA notes that even if this examination were to be accepted at face value, it still would support a distinction between the patterns of associations above and below the proposed level, in that over half of the cited studies with 98^{th} percentile values above 35 $\mu g/m^3$ were characterized as being of overall or mixed significance, and more than half of the cited studies with 98^{th} percentile values below 35 $\mu g/m^3$ were characterized as having no overall significant association.

(b) Support for Revising the Level

(1) *Comment:* A group of commenters, including many medical groups, numerous physicians and academic researchers, many public health organizations, some States, and a large number of individual commenters, viewed the epidemiologic evidence and other health studies as strong and robust and expressed the belief that a much stronger policy response is warranted, generally consistent with a standard level at or below 25 $\mu g/m^3$. American Lung Association et al. and other commenters noted three studies included in

the Criteria Document with 98th percentile values below 35 μg/m^3, including a mortality study in Phoenix (Mar et al., 2000; reanalyzed in Mar et al., 2003) with a 98th percentile value of 32 μg/m^3, a study of emergency department visits in Montreal (Delfino et al., 1997) with a 98th percentile value of 31 μg/m^3, and a study of increase in myocardial infarction in Boston (Peters et al., 2001) with a 98th percentile value of 28 μg/m^3. Further, these commenters expressed the view that EPA's proposed approach to selecting a level of the 24-hour $PM_{2.5}$ standard is fundamentally flawed because it "relies unreasonably on point estimates of statistical significance at various concentrations, rather than on trends, and because it completely fails to consider issues of statistical power" (American Lung Association et al., p. 57). In addition, these commenters found EPA's justification for the proposed level to be "simply irrational" in that it "essentially fabricates uncertainty" as a basis for avoiding setting a standard that the evidence "clearly indicates is necessary" (*Id.*).

Response: In considering these comments, the Administrator first notes that he generally agrees with CASAC's view that selecting a level within the range of 30 to 35 μg/m^3 is a public health policy judgment and that the science does not dictate the selection of any specific level within this range. The Administrator also believes that this policy judgment should take into consideration the important uncertainties that remain in issues that are central to interpreting these types of time-series epidemiologic studies. While the Administrator believes that progress has been made since the last review in addressing key uncertainties, as discussed in section II.B.2 of the preamble for the final rule, EPA and the scientific community, including CASAC and the National Research Council (NRC), recognize that important uncertainties remain that warrant further research (e.g., see NRC, 2004). Thus, the Administrator does not agree that the Agency is "fabricating" nonexistent uncertainties.

More specifically, in considering the studies cited in these comments as a basis for a standard level below 35 μg/m^3, the Administrator continues to believe that it is necessary to consider not only the results of these studies and the inherent uncertainties in such studies, but also the pattern of results from other studies with similar air quality values. In so doing, EPA notes that the statistically significant results in Peters et al. (2001) were uniquely associated with 1 to 2 hour lag times, but not with 24-hour average $PM_{2.5}$ concentrations, such that it would provide a very tenuous basis for the level of a 24-hour average national standard. While the studies in Phoenix and Montreal do provide some evidence of statistically significant associations within the range of 30 to 35 μg/m^3, several other studies within this range of air quality that generally have somewhat greater statistical power and narrower confidence ranges do not provide such evidence. In making the public health policy judgment inherent in selecting a standard level, the Administrator believes that it is necessary to weigh the evidence and related uncertainties against the requirement that the standard is to be neither more nor less stringent than necessary to protect public health with an adequate margin of safety. See *NRDC v. EPA*, 902 F. 2d 962, 971 (D.C. Cir. 1990) (in considering level of a NAAQS, EPA is required to take into account all of the relevant studies in the record and rationally determine what weight to give each study); *API v. Costle*, 665 F. 2d 1176, 1187 (D.C. Cir. 1981) (same).

In so doing, the Administrator does not agree that this evidence presented by the American Lung Association et al. warrants a level below 35 $\mu g/m^3$.

(2) *Comment:* Some commenters identified several "new" studies in support of their arguments for a lower level, including the large multi-city John Hopkins study (Dominici et al., 2006) and two other morbidity studies in Vancouver (Chen et al., 2004) and Atlanta (Peel et al., 2005), as well as a recent study of mortality in California (Ostro et al., 2006). The comments from the American Lung Association et al. included an excerpt from comments separately provided by the principal investigator in the Johns Hopkins study (Dominici), reporting that an additional, as yet unpublished, analysis that considered only days with $PM_{2.5}$ concentrations below 35 $\mu g/m^3$ found statistically significant $PM_{2.5}$ associations with hospital admissions for various causes.

Response: As noted in Section I.C of the preamble for the final rule, as in past NAAQS reviews, EPA is not relying on "new" studies as a basis for its final decisions in this review. The EPA reiterates that the provisional assessment of "new science" does not provide the level of analysis and critical assessment provided in the formal process that incorporates review by CASAC and the public. Nonetheless, in provisionally evaluating commenters' arguments concerning the implications for the level of the 24-hour $PM_{2.5}$ standard of the Johns Hopkins study and the additional analysis of data from that study presented in comments, EPA first notes that while the study may provide may provide additional strong support for the link between short-term $PM_{2.5}$ exposure and morbidity and interesting insights that advance our understanding of $PM_{2.5}$ effects, EPA believes that such an assessment would, even if fully reviewed and considered, have limited value as a basis for selecting a standard level. Further, EPA notes that it is unclear what conclusions should be drawn from an analysis that simply eliminates days above a certain level. The EPA did not propose a 24-hour standard with a 98^{th} percentile based on a view that only days above 35 $\mu g/m^3$ present a risk from short-term exposure to $PM_{2.5}$. The EPA focused on the 98^{th} percentile value of 35 $\mu g/m^3$ as a way to identify a distribution of daily air quality levels over a year that was somewhat below the distribution of daily air quality levels expected to be associated with serious health effects. Eliminating days in the year above 35 $\mu g/m^3$ from a study does not identify any expected distribution of daily levels across a year with a 98^{th} percentile below 35 $\mu g/m^3$. It also does not take into account the differences across the broad distribution of air quality values that would realistically occur in an area that naturally had a 98^{th} percentile value at a level of 35 $\mu g/m^3$. This type of truncated analysis would likely include many more days with $PM_{2.5}$ levels near the cut-off value than would a naturally occurring distribution. Thus, EPA believes that such an assessment would, even if fully reviewed and considered, have limited value as a basis for selecting a standard level. See 62 FR 38670 (strength of associations in data from short-term epidemiologic studies "is demonstrably in the numerous 'typical' days in the upper to middle portion of the annual distribution, not on the peak days").

With regard to the other "new" studies cited, EPA notes that neither the Vancouver (Chen et al., 2004) nor Atlanta(Peel et al., 2005) studies found statistically significant associations with $PM_{2.5}$, and that the Atlanta and California (Ostro et al., 2006) studies

were conducted in areas with 98th percentile $PM_{2.5}$ values well above the proposed level. Thus, EPA concludes that, taken at face value, these studies would provide no basis for commenters' claim that they would require a lower standard level than one based on the science included in the Criteria Document.

(3) *Comment:* Commenters who argued for or against changing the level of the primary $PM_{2.5}$ standards submitted comments regarding how the quantitative risk assessment should factor into a decision on the standard level. The EPA notes that both groups of commenters generally consider the risk assessment in their comments on the standard level, but they reach diametrically opposed conclusions as to what standard level is supported by the assessment. The general views of both groups on the implications of the risk assessment are presented in section II.B.2 of the preamble for the final rule, with one group arguing that it supports a decision not to revise either of the current $PM_{2.5}$ standards, and the other group arguing that it supports a decision to revise both $PM_{2.5}$ standards. More specifically, some of the medical/environmental health commenters consider the magnitude of risk estimated to remain upon meeting the proposed 24-hour standard as a strong reason to select a lower level. These commenters generally assert that the risks are likely even higher than EPA's primary estimates in part because EPA incorporated a surrogate threshold of 10 $\mu g/m^3$ even though there is no clear evidence of a threshold in the relevant time-series studies. On the other hand, the industry/business commenters generally assert that the risks are likely lower than EPA's primary estimates in part because EPA did not base its primary estimates on an assessment that included all statistical model results presented in the studies.

Response: Having considered comments based on the quantitative risk assessment from both groups of commenters, the Administrator finds no basis to change the position on the risk assessment that was taken at the time of proposal. That is, as discussed in section II.F of the preamble for the final rule, while the Administrator recognizes that the risk assessment rests on a more extensive body of data and is more comprehensive in scope than the assessment conducted in the last review, he is mindful that significant uncertainties continue to underlie the resulting quantitative risk estimates. Further, in the Administrator's view, this risk assessment, which is based on studies that do not resolve the issue of a threshold, has important limitations as a basis for standard setting in this review, since if no threshold is assumed the assessment necessarily predicts that ever lower standards result in ever lower risks. This has the effect of masking the increasing uncertainty that exists as lower levels are considered, even when a range of assumed thresholds are considered. As a result, the Administrator judges that the quantitative risk assessment does not provide an appropriate basis for selecting the level of the 24-hour $PM_{2.5}$ standard.

(4) *Comment:* In its consideration of a level for the 24-hour standard for $PM_{2.5}$, EPA relies too heavily on studies which are statistically significant and ignores the overall pattern of the evidence which shows effects at lower concentrations. Among other things, this approach is at odds with case law indicating that the requirement that standards provide an adequate margin of safety refutes any suggestion that the Administrator can act only to

protect against health effects that are known to be clearly harmful (citing Lead Industries, 647 F. 2d at 1154-55).

Response: As discussed in section II.F.1 of the preamble to the final rule, in choosing the level for the 24-hour $PM_{2.5}$ standard, the Administrator did not ignore the short-term $PM_{2.5}$ epidemiologic studies which showed effects but were not statistically significant. Nor did the Administrator ignore the short-term studies which showed no effects (including a number of studies with 98th percentile levels which were higher than the 35 ug/m3 level selected for the 24-hour standard). In short, far from unreasonably exalting the importance of statistical significance, the Administrator made an informed judgment after considering all of the relevant short-term epidemiologic studies, consistent with his legal obligations. API, 665 F. 2d at 1187; NRDC v. EPA, 902 F. 2d 962, 970. See also ATA III, 283 F. 3d at 372 (reasonable for EPA to set level of $PM_{2.5}$ NAAQS just below the mean annual $PM_{2.5}$ concentrations in studies showing a statistically significant association between fine particulate matter and health effects). While EPA agrees that the margin of safety calls for EPA to take into consideration uncertainty over whether an effect will occur, EPA has done so here as explained in section II.F to the preamble to the final rule. Lead Industries addresses a different issue – whether an effect that does occur should be considered adverse, not the issue here of whether an effect will occur at various ambient levels.

ii. Annual Standard

As noted in section II.B of the preamble to the final rule, EPA received comments on the proposal from two distinct groups of commenters. One group that included virtually all commenters representing industry associations and businesses agreed with the Agency's proposed decision not to revise the level of the annual $PM_{2.5}$ standard. The other group of commenters included many medical groups, numerous physicians and academic researchers, many public health organizations, many States, and a large number of individual commenters.

(a) Support for retaining the current level

(1) *Comment: S*ome commenters (e.g., Pillsbury et al; Annapolis Center; UARG) emphasized that uncertainties remain in interpreting key long-term $PM_{2.5}$ exposure studies with regard to issues such as potential confounding by co-pollutants, especially SO_2, modeling to address spatial correlations in the data, and effect modification by education level or socioeconomic status.

Response: While recognizing the uncertainties that remain in interpreting key long-term exposure studies, the Administrator continues to believe that these studies provide strong evidence of an association between long-term exposure to $PM_{2.5}$ and mortality. Nonetheless, as discussed in section II.F.2 of the preamble to the final rule, EPA agrees that the remaining uncertainties weigh against reaching the conclusion that the level of the annual $PM_{2.5}$ standard should be lowered on the basis of these studies.

(2) *Comment:* Some commenters cited "new" studies supporting their argument that the level of the annual $PM_{2.5}$ standard should not be revised. Pillsbury et al. and the Annapolis Center identified the Laden et al. (2006) and Jerrett et al. (2005) studies emphasized specific aspects of the studies supporting their point of view, such as noting that there was a poor fit in the $PM_{2.5}$ association in the later period in the Laden et al. study and that the $PM_{2.5}$ associations were substantially attenuated when socioeconomic variables were added to the model in the Jerrett et al. study. These commenters further argued that appropriate co-pollutant modeling was not done in either study, and that, in their view, the risk estimates in both studies are implausibly large. Other "new" studies were identified by Pillsbury et al. and other industry commenters as ones that provide stronger evidence for traffic emissions or traffic-related factors than for $PM_{2.5}$ (Lipfert, 2006) or that provide results that do not support a current relationship with fine particles, but do not rule out a relationship with a much earlier time period (Enstrom, 2005). These commenters generally concluded that these "new" studies continue to show a lack of consistency regarding associations between fine particles and health effects.

Response: As noted in Section I.C. of the preamble for the final rule, as in past NAAQS reviews, EPA is not relying on such "new" studies as a basis for its final decisions in this review. The EPA reiterates that the provisional assessment of "new science" does not provide the level of analysis and critical assessment provided in the formal process that incorporates review by CASAC and the public. Nonetheless, in provisionally evaluating commenters' arguments concerning the implications of these "new" mortality studies, EPA notes that these and other "new" long-term exposure mortality studies yield a pattern of results that is generally similar to those available previously, assuming their results were accepted following a full critical review. In looking at the Laden et al. (2006) and Jerrett et al. (2005) studies in particular, EPA notes that these two studies, taken at face value, appear to suggest that previous mortality studies may underestimate the magnitude of risks associated with long-term $PM_{2.5}$ exposure. However, in neither of these two studies was the cross-city long-term average $PM_{2.5}$ concentration reported, and in the Laden et al. (2006) study the $PM_{2.5}$ concentrations for recent years were estimated from visibility data, which introduces uncertainty in interpreting the results of this study. The EPA notes that the early period of the Enstrom (2005) study was done in areas with long-term average $PM_{2.5}$ concentrations appreciably higher than the level of the current standard.

(b) Support for revising the current level

(1) *Comment:* Some commenters expressed the view that EPA has downplayed the results of the key long-term exposure $PM_{2.5}$ mortality studies discussed in section II.A. of the preamble for the proposal, including the original analyses and reanalyses of the ACS and Six Cities cohorts and the extended ACS cohort study to the extent that these studies provide evidence of effects below the level of the current standard. For example, American Lung Association et al. and Schwartz (2006) asserted that the ACS cohort study and the HEI reanalysis provide direct evidence of premature mortality associated with annual exposures below 15 $\mu g/m^3$ based on plots of the concentration-response function between long-term exposure to $PM_{2.5}$ and risk of dying across 50 U.S.

metropolitan areas that show no substantial deviation from linear, non-threshold relationships down through levels well below 15 $\mu g/m^3$. These commenters do not, however, discuss the uncertainties inherent in this type of epidemiologic study or the implications of these uncertainties on their interpretation of the results.

Response: In considering these commenters' assessments of these mortality studies, the Administrator continues to believe that these studies provide strong evidence of an association between long-term exposure to $PM_{2.5}$ and mortality. However, the Administrator believes that the remaining uncertainties weigh against reaching the conclusion that the level of the annual $PM_{2.5}$ standard should be lowered on the basis of these studies. In reaching this conclusion, the Administrator notes that even though the long-term average $PM_{2.5}$ concentration across the cities in the extended ACS study (17.7 $\mu g/m^3$) is lower than in the original study (21 $\mu g/m^3$), the level of the current standard is still appreciably below the long-term average of the extended ACS study and that of the Six Cities study (18 $\mu g/m^3$).

(2) *Comment:* In commenting on alternative approaches to interpreting the results of the long-term $PM_{2.5}$ exposure studies as a basis for setting a standard level, American Lung Association et al. expressed the view that the level of the standard should be based on a concentration that is one standard deviation below the cross-city long-term average in each relevant long-term exposure study.

Response: In considering such an approach, the Administrator notes that while that approach would by definition lead to a more precautionary standard, there is no basis for concluding that it is a more scientifically defensible approach or that it is more appropriate in this case where a number of key uncertainties in the evidence remain to be addressed in future research, and where the basic decision is a judgment by the Administrator as to what level is neither more nor less stringent than is necessary to protect public health with an adequate margin of safety. As discussed in section II.G.2 of the preamble for the proposed rule, the Administrator continues to believe that it is reasonable to base the decision on the standard level on long-term average $PM_{2.5}$ concentrations in the key long-term exposure studies, because the evidence of an association in any such study is strongest at and around the long-term average $PM_{2.5}$ concentration where the data in the study are most concentrated (71 FR at 2651). See also *ATA III*, 283 F. 3d at 372 (holding that EPA reasonably established the level of the annual PM2.5 standard "just below the range of mean annual PM2.5 concentrations" in the critical epidemiological studies).

(3) *Comment*: The American Lung Association et al. and the California Air Resources Board (CARB) cited "new" studies to support their conclusion that the level of the annual $PM_{2.5}$ standard should be revised. These commenters concluded that these "new" mortality studies strengthen the evidence of mortality associated with long-term exposure to $PM_{2.5}$ and provide additional support for a lower annual $PM_{2.5}$ standard level. Specifically, these commenters identified an intervention study by Laden et al. (2006) as one that provides evidence of a decrease in $PM_{2.5}$-related deaths in response to decreased exposure levels and that reports greater risk than previously believed and at lower $PM_{2.5}$ levels; a

study of the ACS cohort in Los Angeles by Jerrett et al. (2005) as one that provides evidence of greater risk when improved measures of exposure are used; a study by Chen et al. (2005) as providing evidence of cardiac-related mortality in women, but not men, and a study by Woodruff et al. (2006) providing evidence of respiratory mortality in infants.

Response: As noted in Section I.C. of the preamble for the final rule, as in past NAAQS reviews, EPA is not relying on such "new" studies as a basis for its final decisions in this review. The EPA reiterates that the provisional assessment of "new science" does not provide the level of analysis and critical assessment provided in the formal process that incorporates review by CASAC and the public. Nonetheless, in provisionally evaluating commenters' arguments concerning the implications of these "new" mortality studies, EPA notes that these and other "new" long-term exposure mortality studies yield a pattern of results that is generally similar to those available previously, assuming their results were accepted following a full critical review. In looking at the Laden et al. (2006) and Jerrett et al. (2005) studies in particular, EPA notes that these two studies, taken at face value, appear to suggest that previous mortality studies may underestimate the magnitude of risks associated with long-term $PM_{2.5}$ exposure. However, in neither of these two studies was the cross-city long-term average $PM_{2.5}$ concentration reported, and in the Laden et al. (2006) study the $PM_{2.5}$ concentrations for recent years were estimated from visibility data, which introduces uncertainty in interpreting the results of this study. With regard to the Chen et al. (2005) and Woodruff et al. (2006) studies, EPA notes that these studies were done in areas with long-term average $PM_{2.5}$ concentrations appreciably higher than the level of the current standard. as was the early period of the Enstrom (2005) study.

(4) *Comment:* Some commenters who supported a lower annual standard level also asserted that EPA failed to adequately consider long-term exposure $PM_{2.5}$ morbidity studies, especially studies of effects in children. For example, the Children's Health Protection Advisory Committee (2006) and other commenters noted that studies by Razienne et al. (1996) and Gauderman et al. (2002, 2004) showed effects on children's lung function at long-term cross-city average $PM_{2.5}$ concentrations of 14.5 $\mu g/m^3$ and 15 $\mu g/m^3$, respectively. In addition, the Children's Health Advisory Committee also points to a few studies of "traffic-related" pollution (van Vliet et al., 1997; Brunekreef et al., 1997; Kim et al., 2004) that they assert have shown associations between fine particles and adverse respiratory outcomes, including asthma in children who live near major roadways, with mean annual average fine particle concentrations near and below 15 $\mu g/m^3$.

Response: Section II.G.2 of the preamble for the proposed rule included a careful discussion of the 24-Cities study (Razienne et al., 1996) and the earlier Southern California children's health study (Gauderman et al., 2000, 2002), studies which were included in the Criteria Document, and explained the basis for the Administrator's provisional conclusion that these studies provide an uncertain basis for establishing the level of a national standard (71 FR at 2651).

With respect to studies of traffic-related pollution, EPA notes that these studies generally do not disentangle potential effects of fine particles from those of other traffic-related pollutants, and thus provide an uncertain basis for establishing the level of a $PM_{2.5}$ standard. Further, two of the studies cited by this commenter are "new" studies not included in the Criteria Document. As discussed in section I.C of the preamble for the final rule, EPA is not relying on such "new" studies as a basis for its final decisions in this review. Nonetheless, in provisionally evaluating commenters' arguments concerning the implications of these "new" studies, EPA notes that while the Gauderman et al. (2004) Southern California children's health study appears to add support to the previous Gauderman et al. (2002) study, it reports associations not only with fine particles and components, but also acid vapor and NO_2 and it does not extend the scope of the original study beyond the southern California area, which was an important consideration in the Administrator's view at the time of proposal that this study provided an uncertain basis for establishing the level of a national standard (71 FR at 2651). With regard to the Kim et al. (2004) study, EPA notes that the study reports positive effect estimates suggestive of an association with black carbon and other primary traffic emissions. Thus, taken at face value, these "new" morbidity studies would seem to have limited value as a basis for selecting a level of the annual $PM_{2.5}$ standard, and without further analysis and critical, integrative assessment of these and other long-term exposure morbidity studies, including review by CASAC and the public, these studies do not appear to provide a basis for the commenters' claims that they would require a lower standard level than one based on the science included in the Criteria Document.

(5) *Comment:* The CARB and some other commenters who supported a lower annual standard level discussed the rationale used by the CARB in deciding to set the State's annual $PM_{2.5}$ standard at a level of 12 $\mu g/m^3$. Some of these commenters also pointed to the World Health Organization's annual $PM_{2.5}$ guideline value of 10 $\mu g/m^3$ in support of their view that the scientific evidence supports an annual $PM_{2.5}$ standard in the U.S. at a level no higher than 12 $\mu g/m^3$.

Response: In considering these comments, the Administrator notes that his decision is constrained by the provision of the CAA that requires that the NAAQS be requisite to protect public health with an adequate margin of safety. This requires that his judgment is to be based on an interpretation of the evidence that neither overstates nor understates the strength and limitations of the evidence, or the appropriate inferences to be drawn from the evidence. This is not the same legal framework that governs the standards set by the State of California or the guidelines established by a working group of scientists within the World Health Organization.[4] Thus, the Administrator does not agree that the California standard or the WHO guideline provide an appropriate basis for setting the level of the annual $PM_{2.5}$ NAAQS in the U.S.

[4] For example, the California statute does not refer to setting a standard that is "requisite" to protect, as that term is used in the CAA, and California, unlike EPA, may take economic impacts into consideration in setting air quality standards. In addition, as with the WHO guidelines, the standards appear to be more in the nature of goals as compared to binding requirements that must be met

3. Specific Comments on the Interpretation of Scientific Evidence

The EPA received many comments on the Agency's interpretation of the scientific evidence for fine particles. Some of these comments are addressed above, as appropriate, in section II.A.2. Incorporating responses contained in Section II of the preamble to the final rule, EPA provides the following responses to specific issues related to the interpretation of the scientific evidence for fine particles.

(1) *Comment:* Some commenters asserted that EPA's justification for revising the suite of $PM_{2.5}$ standards "cherry picks" results from epidemiologic studies and accepts without critical evaluation the findings of studies that ostensibly support its proposal, and downplays important uncertainties and results of studies that do not support its proposal (e.g., Pillsbury et al., especially attached comments by Moolgavkar).

Response: The EPA disagrees with these commenters approach to assessing health effects evidence as well as their conclusion regarding the lack of a scientific basis to support the continuation of NAAQS to protect against the health effects of thoracic coarse particles. The EPA contrasts these commenters' narrow focus on counting the numbers of epidemiological studies that achieve statistical significance, without regard to other considerations that are important to consider in a comprehensive appraisal of the evidence. Moreover, as discussed in response to comments regarding multiple pollutant studies and models in section III.B of the preamble and in this document, EPA has not focused solely on the results of single pollutant models, but has also carefully examined the implications of multiple pollutant results.

As discussed below, EPA has recognized the distinction between evaluation of the relative scientific quality of individual study results, and evaluation of the pattern of results in a body of evidence. The EPA has done both. The more detailed discussions of individual studies include assessment of the quality of the study, based on criteria for assessment of the epidemiologic studies that are described in Section 8.1.1 of the Criteria Document. Statistical significance is an indicator of the precision of that study's results, which is influenced by the size of the study, as well as exposure and measurement error and other such factors.

In developing an integrated assessment of the health effects evidence for both $PM_{2.5}$ and $PM_{10-2.5}$, EPA's has emphasized the importance of examining the pattern of results across various studies, and not focusing solely on statistical significance as a criterion. In doing so, EPA recognizes the distinction between evaluation of individual study results and integration of a body of evidence. Individual studies are discussed and evaluated to assess their relative scientific quality; the criteria EPA used for assessing the epidemiologic studies are described in Section 8.1.1 of the Criteria Document. Statistical significance is an indicator of the strength of the relationship between PM and the health outcome reported in an individual study. However, it is important not to focus the on results of statistical tests to the exclusion of other information. As observed by Rothman (1998):

> Many data analysts appear to remain oblivious to the qualitative nature of significance testing. Although calculations based on mountains of valuable quantitative information may go into it, statistical significance is itself only a dichotomous indicator. As it has only two values, significant or not significant, it cannot convey much useful information. . . . Nevertheless, P-values still confound effect size with study size, the two components of estimation that we believe need to be reported separately. Therefore, we prefer that P-values be omitted altogether, provided that point and interval estimates, or some equivalent, are available. (Rothman, 1998, p. 334)

The concepts underlying EPA's approach to integrated assessment of statistical associations reported for the health effects of PM have been discussed in numerous publications, including a recent report by the U.S. Surgeon General on the health consequences of smoking (Centers for Disease Control and Prevention, 2004). This report also cautions against over-reliance on statistical significance in evaluating the overall evidence for an exposure-response relationship.

> Hill made a point of commenting on the value, or lack thereof, of statistical testing in the determination of cause: "No formal tests of significance can answer those [causal] questions. Such tests can, and should, remind us of the effects the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond that, they contribute nothing to the 'proof' of our hypothesis" (Hill 1965, p. 299).
>
> Hill's warning was in some ways prescient, as the reliance on statistically significant testing as a substitute for judgment in causal inference remains today (Savitz et al., 1994; Holman et al., 2001; Poole 2001). To understand the basis for this warning, it is critical to recognize the difference between inductive inferences about the truth of underlying hypotheses, and deductive statistical calculations that are relevant to those inferences, but that are not inductive statements themselves. The latter include p values, confidence intervals, and hypothesis tests (Greenland 1998; Goodman 1999). The dominant approach to statistical inference today, which employs those statistical measures, obscures this important distinction between deductive and inductive inferences (Royall 1997), and has produced the mistaken view that inferences flow directly and inevitably from data. There is no mathematic formula that can transform data into a probabilistic statement about the truth of an association without introducing some formal quantification of external knowledge, such as in Bayesian approaches to inference (Goodman 1993; Howson and Urbach 1993). Significance testing and the complementary estimation of confidence intervals remain useful for characterizing the role of chance in producing the association in hand (CDC, pp. 23-24).

Accordingly, the statistical significance of individual study findings has played an important role in EPA's evaluation of the study's results, and EPA has placed greater

emphasis on studies reporting statistically significant results. However, in the broader evaluation of the evidence from many epidemiologic studies, EPA has also emphasized the *pattern* of results for drawing conclusions on the relationship between PM indicators and health outcomes, as well as consideration of the integration of epidemiologic evidence with findings of laboratory studies.

The EPA considered the results of studies conducted in many different countries to draw conclusions about the likelihood of a causal relationship between various PM indicators and health outcomes. Because EPA places greater weight on US and Canadian studies in determining standard levels, for presentation purposes, the Criteria Document, Staff Paper and proposal notice present graphical results from epidemiologic studies in these two countries, standardized to a common increment of PM, and based on similar analytic strategies (i.e., single-pollutant results). EPA believes that the examination of multi-pollutant model results and the inherent instability that often occurs in effects estimates for correlated pollutants in such studies justifies the use of single pollutant model results as the most appropriate basis for comparing effects estimates across the three major pollutant indicators (EPA, 2004, section 8.4.3; EPA 2005, p 3-46).

As discussed in section 9.2.2 of the Criteria Document, the comparisons across studies and PM indicators in these figures begins with an evaluation of the overall pattern of excess risk results – whether generally positive or centered around zero, the consistency in size of effects estimates, the precision of the studies evidenced in the width of the confidence intervals, with special attention to comparisons of similar effects categories across different pollutant indicators. For example, in comparing effects estimates for PM, $PM_{2.5}$, and $PM_{10-2.5}$, the Criteria Document noted that the effects estimates for the $PM_{2.5}$ and $PM_{10-2.5}$ are generally larger for than those for equal amounts of PM_{10}, "which is consistent with $PM_{2.5}$ and $PM_{10-2.5}$ having independent effects" (EPA, 2004, p 9-25).

Finally, it is important to reiterate that the EPA's evaluation of the scientific evidence used in the current PM NAAQS review was the subject of exhaustive and detailed review by the CASAC and the public. Four drafts of the Criteria Document were released for CASAC and public review at public meetings, several additional teleconference meetings were held with the CASAC for review of specific chapters or sections, and a special workshop was convened with numerous independent experts as well as some CASAC members to discuss issues that arose regarding statistical modeling using GAM for time-series epidemiologic studies. Evidence related to the substantive issues raised by these commenters were evaluated in the Criteria Document drafts, and discussed at length in public CASAC meetings. This process ensured that overemphasis or underemphasis on any study or group of studies was addressed. Following the final meeting of the CASAC on the Criteria Document, the consensus letter from the CASAC panel stated "We are pleased that we have been able to complete the review and achieved closure on the Criteria Document for PM. . ." (Hopke, 2004) indicating that the CASAC panel found the coverage of the literature in the Criteria Document to be appropriate. Further, CASAC found that the Staff Paper, which presented the most policy-relevant scientific information drawn from the Criteria Document, adequately reviewed advances in

understanding PM-related effects and was "scientifically well-reasoned" (Henderson, 2005a).

(2) *Comment:* Some commenters provided a specific example of what they considered to be "cherry-picking" studies from the epidemiologic literature. As an example, these commenters argued that EPA focused on the results from Mar et al. (2003) but not on other studies conducted in Phoenix using the same air quality data set (Smith et al., 2000; Clyde et al., 2000) (e.g., UARG).

Response: The EPA disagrees with this comment on two points: (1) EPA discussed all three studies in detail in the Criteria Document (EPA, 2004, Table 8-2, p. 8-58 and pp. 8-62 to 8-63), and (2) EPA does not agree that these three studies provide conflicting evidence on the relationship between PM and mortality in Phoenix. The study by Mar and colleagues (2003) was focused primarily on evaluating the relationship between PM and mortality in Phoenix. Smith et al. (2000) used the Phoenix data set to assess potential threshold levels, and Clyde et al. (2000) used a Bayesian modeling averaging approach. Smith et al. (2000) and Clyde et al. (2000) both identified associations between mortality and $PM_{10-2.5}$ that were consistent with the results of the first study. For $PM_{2.5}$, Clyde et al. (2000) reported positive associations with mortality, but found that the association with $PM_{10-2.5}$ was considered stronger than the association with $PM_{2.5}$. Smith et al. (2000) reported an association with $PM_{2.5}$ that was nonlinear in form, and suggested that a threshold level could be found in the range of 20-25 μg/m3 for $PM_{2.5}$. The EPA observes that most of the epidemiologic studies that evaluated the form of the concentration-response function did not find a threshold level in the relationship between PM and mortality (EPA, 2004, section 8.4.7).

(3) *Comment:* One commenter argued that the available toxicology data contradicts the conclusion that $PM_{2.5}$ is causally related to mortality effects (International Truck & Engine Corporation).

Response: The EPA acknowledges that there are limited data demonstrating mortality in rodents exposed to PM, but recognizes a limited number of studies that do report deaths following PM exposure. Killingsworth et al. (1997) exposed monocrotaline-treated rats (as a model of pulmonary hypertension) to residual oil fly ash (ROFA) for 3 consecutive days and reported 42% lethality. In a similar study employing a rodent model of pulmonary hypertension, 50% of the animals died following exposure to ROFA (Watkinson et al., 1998). Lethalities were observed with all dose groups and were ascribed to either a slow failure of the myocardium or fatal arrhythmia based on electrocardiogram (ECG) data. In another toxicological study utilizing rodent models of pulmonary hypertension or chronic bronchitis, 19 and 37% mortality was observed, respectively, in animals exposed to concentrated ambient particles (CAPs) (Godleski et al., 1996). The CAPs concentration averaged 228 and 288 $\mu g/m^3$ over a 3-day exposure period; deaths occurred both during exposure and overnight. These studies provide evidence for biological plausibility of PM-induced health effects that supports the epidemiological findings.

It is not surprising that lethality is not induced in more toxicological research, as these types of studies do not readily lend themselves to this endpoint. Epidemiologic studies have observed associations between PM and mortality in communities with populations in the range of many thousands to millions of people. Clearly, it is not feasible to expose hundreds (if not thousands) of animals to ambient PM (potentially over many years) in a laboratory setting to induce enough lethalities to distinguish between natural deaths and those attributable to PM. Furthermore, the heterogeneous human populations sampled in epidemiological studies are comprised of individuals with different physical, genetic, health, and socioeconomic backgrounds which may impact the outcome. However, in toxicological studies, the rodent groups are typically inbred, such that inter-individual variability is minimized. Thus, if the rodent strain used is quite robust, PM-induced effects may not be observed at low exposure concentrations.

The EPA disagrees that toxicology studies are done to replicate the mortality observed in human populations. The strength of toxicology studies is the "ability to define and reasonably titrate the attribute of interest in an otherwise well-defined study situation in which subject genetics, husbandry, and personal exposure scenarios are well controlled" (Kodavanti et al., 1998). Furthermore, toxicology enables one to examine dose-response relationships and assess possible modes of action for observed adverse effects.

(4) *Comment:* Some commenters stated that EPA downplays the uncertainty in the available epidemiologic evidence, and argued that publication bias is likely to have inflated the magnitude and consistency of the epidemiological associations (e.g., Annapolis Center).

Response: The EPA recognizes the possibility of publication bias, which can potentially occur in any field of study. In the discussion of multi-city mortality studies, EPA observed that one of the advantages of multi-city studies is that "they clearly do not suffer from potential omission of negative analyses due to 'publication bias'" (EPA, 2004, p. 8-30).

Some of these commenters referred to a commentary by Goodman (2005) as highlighting a major discrepancy between the results of multi-city results and a meta-analysis of single-city results. This commentary discussed the results of several studies that report results of meta-analyses and multi-city analyses for the relationship between short-term exposure to ozone and mortality. The author states, "Although the NMMAPS analysis does not qualitatively contravene the meta-analytic results, in that it still shows an ozone hazard, it does point strongly to a smaller effect – less than one third of the risk" (Goodman, 2005, p. 430). Thus, in the multi-city study, a statistically significant association is found between ozone and mortality, but the magnitude of the effect estimate is smaller than those reported in single-city studies.

The EPA observes that a recent publication has also evaluated evidence related to publication bias in studies of PM-related health effects. Anderson et al. (2005) evaluated results from several multi-city studies and conducted meta-analyses for both mortality and morbidity outcomes. The authors reported that adjustment for publication bias reduced effect estimate size by as much as 40%. However, the authors report "after

correcting for publication bias statistically, associations between particles and adverse health effects remained positive and precisely estimated" (Anderson et al., 2005, p. 155).

The EPA does not agree that reported associations between PM and health effects are an artifact of publication bias. The EPA acknowledges that publication bias can result in potential overestimation of the estimated risk in a body of literature. However, for an individual study, factors such as exposure error or selection of results from an individual lag period from among several positive associations can result in underestimation of an effect estimate.

(5) *Comment:* One commenter questioned the basis for calculating a combined 98th percentile PM concentrations for the 8 Canadian cities evaluated in Burnett and Goldberg, 2003 (UARG).

Response: Burnett et al. (2000, reanalyzed Burnett and Goldberg, 2003) reported associations between PM and mortality in eight large Canadian cities. The authors did not report city-specific associations, but reported effect estimates for all cities together. For this reason, EPA staff calculated descriptive statistics using air quality data for all eight cities from the study period evaluated (Ross and Langstaff, 2005).

Several commenters submitted a review article critiquing EPA's rationale for a fine particle standard (Moolgavkar, 2005) (e.g., Annapolis Center, Alliance of Automobile Manufacturers, International Truck & Engine Corporation, Pillsbury et al). In considering these comments, EPA agrees that the issues discussed in this article are important considerations in the interpretation of epidemiologic evidence. The article highlights issues such as potential confounding of associations between PM and health outcomes by copollutants or other variables, the influence of model specification on epidemiologic study results, and the shape of exposure-response relationships in pollution epidemiologic study results. The EPA agrees that these are key issues to consider in evaluating evidence from a body of epidemiologic studies. In fact, such issues have been extensively evaluated by EPA in both the 1996 and the Criteria Documents (EPA, 1996a; EPA, 2004). Detailed discussions of a range of issues related to epidemiologic studies have been included in the Criteria Document, and reviewed by CASAC (see EPA, 2004, sections 8.1.3 and 8.1.4 pp. 8-8 to 8-18 and section 8.4, pp. 8-222 to 8-335). While agreeing that these issues are important, EPA's conclusions regarding a number of these issues – also reviewed by CASAC – differ from the conclusions presented in the article. These issues are addressed in the following responses to specific comments.

(6) *Comment***:** These commenters raised issues regarding the adequacy of model specification and control of temporal or weather variables in time-series epidemiologic studies. Specifically, concerns were expressed regarding the following issues: (1) "The revised analyses necessitated by the S-plus problems, . . . clearly indicate that methods used for controlling temporal trends and weather can have profound effects on the results of time-series analyses of air pollution data..." (2) ". . . relatively few studies have examined effect modification by season. The few that have done so, reported strong effect modification of air pollution effects by season (e.g., Moolgavkar et al., 1995)" and

(3) " . . . control of weather has, once again, surfaced as an important issue" (Moolgavkar, 2005 pp. 127 to 128).

Response: First, EPA does not agree that the results of reanalyses to address issues related to the use of generalized additive models (GAMs) calls into question reported associations between PM and health outcomes. The EPA evaluated the results of these reanalyzed studies, and recognized that there remains no altogether satisfactory way to choose the most appropriate degrees of freedom. Nonetheless, the HEI Review Panel concluded that while the number of studies showing an association of PM with morality was slightly smaller, the PM association persisted in the majority of studies. The EPA recognizes that in some of the large number of studies in which the PM effect persisted, the estimates of PM effect were substantially reduced" (HEI, 2003, p. 269).

Second, the author cited one of his own studies as the basis for a conclusion that PM effects are strongly modified by season. The EPA agrees that seasonal models have not been widely used. The EPA also recognizes that the use of smaller data subsets will markedly reduce statistical power to detect associations and also reduce the precision of any findings, however, EPA observes that a number of the studies included in the Criteria Document did report results from seasonal models. Some reported significant associations with mortality or morbidity with PM_{10} or $PM_{2.5}$ in all seasons tested (e.g., Schwartz et al., 2003, 10 U.S. cities; Fairley, 2003, Santa Clara County, CA; Kinney et al., 1995, Los Angeles; Stieb et al., 2000, St. John, Canada) while others reported some differences between seasons (e.g., Sheppard et al., 1999, Seattle; Ostro et al., 1995, Southern California). The EPA disagrees that the available studies can support a conclusion that air pollution effects are consistently and strongly modified by season.

Lastly, EPA agrees that control of different variables, such as weather, remains important. As discussed in section 5.5 of the Staff Paper, " …investigation of recently discovered questions on the use of generalized additive models in time-series epidemiologic studies has again raised model specification issues. While reanalyses of studies using different modeling approaches generally did not result in substantial differences in model results, some studies showed marked sensitivity of the PM effect estimate to different methods of adjusting for weather variables. There remains a need for further study on the selection of appropriate modeling strategies and appropriate methods to control for time-varying factors, such as weather" (EPA, 2005, pp 5-73 to 5-74).

(7) *Comment:* These commenters argued that EPA has not adequately addressed potential confounding by copollutants. Specific comments include:

- "If, as seems highly likely, individual criteria pollutants are indicators of a complex pollution mix, then different pollutants may be confounders of PM in different parts of the country" (Moolgavkar, 2005, p. 128)
- " . . a low concentration of a specific pollutant does not exonerate that pollutant, but it indicates that the pollution association with health effects may persist in the

absence of that specific pollutant . . . it is clear that different pollutants appear to be important in different geographic areas" (Moolgavkar, 2005, p. 129).

- "For example, CO is probably the best marker of air pollution effects in LA; it is less important in Chicago, where SO_2 appears to be a better marker" (Moolgavkar, 2005, p. 131).
- ". . . individual pollutants are best regarded as indices of the pollution mix, with no single pollutant being the best index in all areas" (Moolgavkar, 2005, p. 138)
- "… in some areas that marker is PM in others it is one or more of the gases. While the Agency acknowledges that the gases, such as CO, are probably markers of sources of pollution, such as emissions from motor vehicles, it fails to acknowledge that the same is true of PM. On the contrary it tries to make the case that PM, as measured by its mass concentration, is directly responsible for effects on human health" (Moolgavkar, 2005, p. 138).

Response: The EPA strongly disagrees that the Agency has tried to "make a case" that PM is the sole contributor to health effects associated with ambient air pollutant exposure. The EPA consistently recognizes that other pollutants are also associated with health outcomes, as is reflected in the fact that EPA has established regulations to limit emissions of the gaseous criteria pollutants as well as numerous other air pollutants. In its assessment of the health evidence regarding PM, EPA has carefully evaluated the potential for confounding, effect modification or other interactions between PM and gaseous air pollutants, and concluded: "It is also the case that the most consistent findings from amidst the diversity of multi-pollutant model evaluation results for different sites is that the PM signal comes through most clearly" (EPA, 2004, p. 8-254).

The EPA agrees that air pollution mixtures can differ from one location to another, as reflected in some apparent heterogeneity in PM-health relationships between cities. However, EPA does not agree that one can characterize CO as the most important pollutant in one city, but SO_2 as the most important pollutant in another. The conclusions on which pollutants are the most important markers of the air pollution mixture appear to be drawn from the results of the studies the author conducted in Los Angeles and Cook Counties, California (Moolgavkar, 2000a,b,c; reanalyzed 2003). In Los Angeles, two-pollutant model results showed associations between several health outcomes (total, cardiovascular and COPD mortality, and cardiovascular hospital admissions) generally remained significant for CO, but associations with PM_{10} or $PM_{2.5}$ did not. In Cook County compared to Los Angeles County, the results varied more between health outcomes, with PM_{10} being robust to adjustment for copollutants in some models (e.g., total mortality at 1-day lag) but not in others; however, more robust associations were reported with SO_2 than with PM_{10} for COPD hospitalization and cardiovascular mortality.

However, EPA does not agree that these findings characterize the general pattern of results across all studies. For example, in an earlier study conducted in Los Angeles, Kinney et al. (1995) reported associations with total mortality that were statistically significant for CO and marginally significant for PM_{10} and O_3. In two-pollutant models, the effect estimates for both "dropped somewhat when both were included in the model, suggesting a similar strength of association with mortality for the two pollutants" (Kinney

et al., 1995, p. 66). In another study conducted in Cook County, Ito and Thurston (1996) reported that PM_{10} and O_3 were most consistently associated with total mortality, and in two-pollutant models both effect estimates were reduced slightly but remained statistically significant.

(8) *Comment***:** Specific issues were included regarding the reanalyses of the NMMAPS study. These comments included the following:

- "In 11 cities that showed positive and statistically significant associations in the original analyses, these associations became insignificant in the revised analyses. By contrast, no cities with statistically insignificant associations in the original analyses showed significant coefficients in the revised analyses. Third, only two cities, New York and Oakland, show positive and statistically significant associations between PM and mortality in the revised analyses, with one city, Little Rock, showing a significant negative association" (Moolgavkar, 2005, p. 130).
- "With the exception of New York, none of the largest metropolitan areas in the US show statistically significant associations between PM_{10} and mortality despite 8 years of data… thus, significance is clearly not an issue of power alone, since one would expect adequate power in the Chicago time-series to detect an effect if there is one" (Moolgavkar, 2005, p. 130).
- "A glance at the results of NMMAPS shows considerable heterogeneity of the estimates, although the heterogeneity is not statistically significant" (Moolgavkar, 2005, p. 137).

Response: In the Criteria Document, EPA recognized that in the expanded body of literature, especially in the multi-city studies, there appears to be greater spatial heterogeneity in city-specific excess risk estimates for relationships between short-term ambient PM_{10} concentrations and acute health effects than was previously evident (note that most multi-city studies used PM_{10}). As observed by Moolgavkar, NMMAPS did not find statistically significant evidence for heterogeneity in associations between PM_{10} and mortality. The EPA agrees that there is more apparent variation in effect estimate size than was seen in the studies available in the previous PM NAAQS review.

The Criteria Document discussed the evidence related to heterogeneity in section 8.4.8, and observed that the reasons for variation in effects estimates are not well understood (EPA, 2004 pp. 8-323 to 8-327). Factors likely contributing to the apparent heterogeneity include geographic differences in air pollution mixtures, composition of ambient PM components, and personal and sociodemographic factors potentially affecting PM exposure (such as use of air conditioning), as well as differences in PM mass concentration (EPA, 2004, p. 8-343).

Another key factor that contributes to heterogeneity or variation between areas is statistical power. Many multi-city studies have combined results from communities with fewer available data that would likely not have been considered adequate for use in single-city analyses. For example, using the NMMAPS results, EPA found that, with increasing statistical power as indicated by the extent of the PM time series data and

number of deaths per day, the effect estimates were more consistent in size and standard errors decreased (EPA, 2004, p. 8-324).

The EPA observes that the author recognized the importance of statistical power for interpreting these results, and EPA agrees that it is reasonable to focus on results from areas with greater power. However, EPA recognizes that the NMMAPS research team urged "caution against attempts to interpret estimates for any specific city" as the focus of the analyses was on evaluating relationships between PM_{10} and health outcomes in the combined dataset (Samet et al., 2000, p. 43). The review article submitted by these commenters focused on single-city results, and raised a series of technical issues with the analytical approach used, including the use of a standard analytical approach that did not allow for city-specific modeling of factors such as meteorology that likely vary from city to city. The EPA does not agree that the issues raised diminish the value of the NMMAPS analyses.

The HEI Health Review Committee also recognized some apparent heterogeneity in the NMMAPS results but concluded:

> The investigators use the term *strong* to characterize the degree to which their results provide evidence of an effect of increasing PM_{10} on morbidity and mortality. The Panel also concludes that the evidence for PM_{10} effects on both number of deaths and hospitalizations can be regarded as compelling and consistent. . . . The results relating to mortality and particulate air pollution also can be said to be strong in that they are robust: results were essentially the same regardless of the manner in which the statistical models were specified. . . The heterogeneity of effect across cities offers the potential to identify factors that could influence the effect of PM_{10} on health and thus provide valuable insights into the mechanisms by which PM_{10} causes adverse health effects." (HEI, 2000, p. 78)

Despite there being some evidence for greater variation in magnitude and precision of PM-health associations between geographic areas, EPA concluded in the Criteria Document that the extensive body of epidemiology evidence provided strong evidence that "ambient thoracic particles, acting alone and/or in combination with gaseous co-pollutants, are likely causally related to various human health endpoints" (EPA, 2004, p. 8-337)

(9) *Comment:* In discussing the long-term $PM_{2.5}$ exposure studies, the issue of residual confounders was raised. Two strong possible confounders identified in these comments were changing smoking habits and changing life-style factors. Specifically, "these life-style changes are more likely to be adopted by the more affluent, better-educated communities, which are also exposed to less air pollution" (Moolgavkar, 2005, p. 135).

Response: The EPA believes for smoking and life-style factors to be a confounder in the relationship between PM and mortality, the patterns in these factors would need to be

correlated with PM concentrations. The reanalysis of the data from the ACS study used available data on individual health factors, and none were found to be confounders of the relationship between $PM_{2.5}$ and mortality. Taken a step further, the commenters have speculated that changes in personal life-style factors may be correlated with changes in $PM_{2.5}$ concentrations across the U.S. In other words, areas that saw greater reductions in $PM_{2.5}$ also had greater reductions in smoking or other personal risk factors at the population level. No evidence has been offered that such correlations exist.

(10) *Comment:* The commenters asserted that EPA did not place adequate weight on an important long-term study, the Washington University-EPRI Study. Specifically, these comments asserted that perhaps EPA "paid short shrift" to this study "because the study reported no increased risk of mortality associated with exposure to PM" and the "strongest associations were seen with NO_2 and peak ozone" (Moolgavkar, 2005, p. 133). The study authors point out that ". . . those pollutants that are included should be considered as indices of the overall urban pollution mix" (Lipfert et al, 2000).

> *Response:* The EPA's determination of which studies merited being given the greatest weight is discussed in Criteria Document, and the basis for the determination was also discussed repeatedly in CASAC meetings. The EPA compared the long-term exposure studies in Section 8.2.3.2.5 of the Criteria Document using several key issues for consideration which were clearly stated: (1) cohort size and characteristics; (2) study design; and (3) air quality data used in exposure characterization (EPA, 2004, pp. 8-116 to 8-121). The relative merits of the different long-term exposure studies were discussed in detail at public CASAC meetings, and the weights that EPA placed on the various long-term exposure studies, including the study cited by this commenter, reflect the general consensus advice provided by CASAC during those meetings (see, e.g., April 6, 2005 transcript).

(11) *Comment:* Regarding distributed lag model results, these commenters stated that:

> Although the Agency deliberately chooses to present the coefficients from lags that maximize the PM associations, it contends that even these might underestimate the PM effects, asserting in the "integrative Summary (chapter 9) of the current Criteria Document… that distributed lag models would yield higher effect estimates. The Agency presents no evidence to back up this claim. In fact, it is not clear under what circumstances distributed lag models would yield higher risks than the traditional lag models. It is also clear that if distributed lags are used for PM effects, then similar distributed lag models should be considered simultaneously to control weather and co-pollutants (Moolgavkar, 2005, p. 135).

*Response***:** The EPA believes that the results of numerous studies clearly indicate that distributed lag models can be the more appropriate choice for numerous health outcomes. The evidence related to lag periods between pollution exposure and health outcome is discussed in detail in Section 8.4.4 of the Criteria Document (EPA, 2004, pp. 8-269to 8-

281). In a study of 10 U.S. cities, consistently larger risk estimates were reported from models using a distributed lag approach when compared with results of single-day lag models (Schwartz, 2003). Similarly, the results of the NMMAPS analyses for mortality showed larger associations when a distributed lag approach was used.

The EPA observes that if one chooses the most significant single-lag day only, and if more than one lag day shows positive (significant or otherwise) associations with mortality, then reporting a RR for only one lag would also underestimate the pollution effects. The EPA believes that where a pollution-related health effect may be observed over several days following an exposure period, a distributed lag approach more appropriately characterizes the exposure-effect relationship. However, in the NMMAPS results for cardiovascular and respiratory hospital admissions in the elderly, risk estimates from distributed lag models were larger than those from single-day models, but not markedly different from those reported in models using a 2-day moving average of PM_{10} (Samet et al., 2000; Schwartz, 2003).

The results presented for associations between PM_{10} and mortality in Cook County are an example where there is no apparent pattern in results at different lag periods. As summarized in Section 3.6.5 of the Staff Paper, in selecting quantitative results for presentation or use in quantitative risk assessment, staff considered the pattern of results that is seen across the series of lag periods (EPA, 2005 p. 3-47). In the majority of studies, if an association with PM was reported, there was evidence of some reasonable pattern in lag period results. In the few situations when such a pattern was not apparent (e.g., results from Cook County analyses in Moolgavkar, 2003) those findings were found to not be appropriate for use in quantitative risk assessment. The EPA believes that the epidemiologic studies fully support the conclusion drawn in the Criteria Document:

> One would then expect to see different best-fitting lags for different effects, based on potentially different biological mechanisms as well as individual variability in responses. If various health effects are substantiated by toxicological evidence as likely occurring at different lag days, so that the risks for each lag day should be additive, then higher overall risks may exist that than are implied by maximum estimates for any given single day lag. In that case, multi-day averages or distributed lag models should be used to project more fully any potential PM-related public health risks (EPA, 2004, p. 8-342).

(12) *Comment:* With regard to "intervention" studies in Dublin and Hong Kong, the commenters asserted that "that the relationship between air pollution and health effects is more complex than suggested by the Agency" (Moolgavkar, 2005, p. 137)

Response: The EPA does not believe that the relationship between health effects and air pollutants is simple, and does not agree that the Agency has ever characterized it in that way. In the evaluation of the intervention study results contained in the Criteria Document, EPA discussed the changes in various pollutants, including PM indices and SO_2, that followed the different regulatory changes (EPA, 2004, section 8.2.3.4, pp. 8-

131 to 8-135). In summing up this evaluation, EPA concluded: "As such, these specific intervention studies are valuable in drawing qualitative conclusions that imply likely causal relationships underlying the observed mortality decrements occurring in concert with declines in ambient PM and/or SO_2 levels" (EPA, 2004, p. 8-135).

(13) *Comment:* Some commenters questioned the use of the Cox proportional hazards model in the prospective cohort studies (e.g., American Cancer Society and Six Cities studies). The commenters cite a recent article that raises questions about the results of prospective cohort studies, one being whether the Cox proportional hazards model is the appropriate tool for these analyses (Moolgavkar, 2006).

Response: The Cox proportional hazards model has been widely used in prospective cohort studies, and its use was evaluated in the extensive reanalyses of the Six Cities and American Cancer Society studies by Krewski et al. (2000). The reanalysis investigators used numerous alternative models and methods to assess relationships. Overall, they report that the Cox proportional hazards assumption appeared appropriate in general, though there was some evidence that the effects of both fine particles and sulfate varied somewhat with time (Krewski et al., 2000, p. 220). For example, in the Six Cities study reanalyses, the authors report positive, statistically significant associations between mortality and fine particle exposures from the Cox proportional hazards model and five alternative models based on the use of Poisson regression and different potentially time-varying covariates (Krewski et al., 2000, p. 149). In these alternative models, the relative risk estimates were slightly larger than those from the Cox proportional hazards model, except for the model in which changes in $PM_{2.5}$ concentrations over time were incorporated; in this last model the relative risk estimate was 1.16 (95% CI: 1.02-1.32) per 18.6 $\mu g/m^3$ $PM_{2.5}$ [compared with 1.26 (95% CI: 1.08-1.45) from the original Cox proportional hazards model]. The associations between long-term exposure $PM_{2.5}$ and mortality remained statistically significant even in Poisson regression models that incorporated changes in cigarette smoking habits, one of the potential sensitivities raised by Moolgavkar (2006). While EPA has recognized the need for continued research into alternative modeling strategies, the existing studies have extensively evaluated the relationship between $PM_{2.5}$ and health, and continue to indicate that long-term exposure to $PM_{2.5}$ is associated with increased mortality risk.

4. Specific Comments on the Health Risk Assessments

Comments related to the health risk assessments conducted for $PM_{2.5}$ are addressed in this section. Incorporating responses contained in Section II of the preamble to the final rule, EPA provides the following responses to specific issues related to the quantitative health risk assessments.

(1) *Comment*: Some commenters argued that the Agency's risk assessment is arbitrary and biased upwards by selective use of model results that have the largest and most significant findings in each source study. This bias is introduced by EPA's decisions to rely only on single pollutant results, its use of GAM-based analyses rather than GLM-

based estimates, and its use of model formulations with the least amount of controls of those reported in each paper.

Further, these commenters argued that EPA's risk estimates included in the Risk Assessment Technical Support Document (TSD) (Abt Associates, 2005b) and reported in Chapter 4 of the Staff Paper (EPA, 2005) do not reflect the full range of effect estimates developed for each city and included in the Criteria Document (EPA, 2004). Instead, for purposes of estimating risk, these commenters (e.g., UARG) argued that EPA selected a single regression model to estimate risk for each of the cities based on EPA's judgment of the "best" effect estimate to use out of all those available in each study. These commenters argued that this approach must be considered arbitrary because it fails to give any weight to the other effect estimates developed for each of the cities, despite the fact that the ignored estimates are preferred from a scientific viewpoint because they have employed additional statistical treatments to address confounders such as weather, co-pollutants, or model biases.

In addition, one commenter argued that "the tendency toward overstatement of risks in EPA's approaches to handling uncertainty can be averted merely by more complete and clear representation of the evidence, without any formal uncertainty analysis. … merely providing complete and quantitative information from the full body of epidemiological evidence can provide a far clearer synopsis of the evolution of confidence in the associations" (UARG, Attachment 2, p. 14).

Response: The risk assessment did not rely exclusively on single-pollutant or multi-pollutant concentration-response functions, but showed the results from both for risk estimates associated with recent PM air quality levels (e.g., see EPA, 2005, figures 4-5 through 4-7, pp. 4-39 to 4-41) and for various sensitivity analyses (e.g., see Abt Associates, 2005b, Exhibits E.33 through E.36 pp. E-64 to E-67). As stated in the Risk Assessment TSD, "given that single and multi-pollutant models each have both potential advantages and disadvantages, with neither type clearly preferable over the other in all cases, we report risk estimates based on both single and multi-pollutant models where both are available" (Abt Associates, 2005b, p. 46). The single- and multi-pollutant model results for short-term exposure mortality are shown side by side in Figure 7.2 of the TSD and Figure 4-5 of the final Staff Paper (Abt Associates, 2005b, p. 79; EPA, 2005, p. 4-39). The single- and multi-pollutant model results for long-term exposure mortality (Krewski et al., 2000) are shown side by side in Figure 7.6 of the TSD (Abt Associates, 2005b, p. 83) and Figures 4-6 and 4-7 of the final Staff Paper (EPA, 2005, pp. 4-40 to 4-41).

The Staff Paper discussed the multi-pollutant risk estimates, noting that "in two cases there is relatively little difference in the risk estimates between single-pollutant and multi-pollutant models (i.e., Pittsburgh and San Jose), while in the third case (Los Angeles) there are larger differences when either CO or NO_2 are added to the model along with $PM_{2.5}$"(EPA, 2005, p. 4-42). With respect to risks associated with longer-term exposures, the final Staff Paper also states, "As shown in Figure 4-7, the risk estimates based on multi-pollutant models, involving addition of different single co-pollutants in the ACS study, show generally greater risk associated with $PM_{2.5}$, when CO, NO_2, or O_3

were added to the models and lower risk associated with $PM_{2.5}$ when SO_2 was added" (EPA, 2005, p. 4-42). Location-specific exhibits generally include results from both single- and multi-pollutant models.

The GAM model was selected for the base case analysis, because that was the model preferred by most of the original study authors. However, the results from many different model specifications were shown for Los Angeles (based on Moolgavkar (2003)) in Exhibits 7.12a and b and were summarized in the final Staff Paper (Abt Associates, 2005b, pp. 100-103).

While it is certainly possible to present risk estimates based on each and every concentration-response function available, EPA believes this approach has two major drawbacks: (1) it gives equal weight to all concentration-response functions, regardless of their merit, and (2) it is extremely difficult to infer any conclusions from such a presentation. Instead, EPA established reasonable criteria for selecting concentration-response functions to use in the risk assessment, and clearly stated these criteria. One of the main motivations for doing this was specifically to avoid arbitrariness in the selection of concentration-response functions. In those cases in which one concentration-response function was not clearly preferable over another – e.g., single-pollutant vs. multi-pollutant models or single-city vs. multi-city models – EPA presented results from both for the estimates associated with recent air quality to provide a sense of how much difference these choices made in the estimates. The reasons EPA excluded some models are clearly stated in the TSD and Staff Paper.

A vast array of models of the relationship between PM and a given health endpoint can be created, for example, by using different lag structures and/or different co-pollutants and/or different methods of adjusting for temporal and weather effects. The EPA believes that the fact that in some such models the PM effect is not statistically significant does not, in and of itself, indicate much – particularly if many of these models are mis-specifications of the relationship of interest. For example, it is likely that not all lag structures are equally valid models of the relationship between PM and mortality. Further, EPA believes that using all possible models in the risk assessment, including those that were basically mis-specifications of the relationship being estimated, would serve only to falsely inflate the perception that there is no relationship. Similarly, while there are advantages to including co-pollutants in a model, there are also disadvantages, as has been noted in the Criteria Document in sections 8.4.3.2 and 8.4.3.3 (EPA, 2004, pp. 8-240 to 8-254). While omitting a co-pollutant can produce a biased estimate, including a co-pollutant with which the pollutant of interest is highly correlated can serve to mask a true relationship by inflating the variance of the estimator.

Similarly, there appears to be a presumption in these comments that the more "controlling" variables in a model the better, but this is not true. It is possible to "over-control" for potentially confounding effects, so that real but small effects of the variable of interest get washed out – i.e., more controls are not always better in statistically estimated models. As noted in the HEI Special Report ("Revised Analyses of Time-Series Studies of Air Pollution and Health," May 2003), in its discussion of modeling

time effects (where time is a surrogate measure for unknown or unmeasured factors that affect daily mortality or morbidity), "Unfortunately, if control is too strict, which in this case consists of modeling time effects too finely, the estimate of air pollution effect can become imprecise and part of a true pollution effect can be absorbed into the time effect. … Effects of weather (typically temperature and relative humidity in these studies) have similar potential pitfalls when modeled in a fashion similar to time" (HEI, 2003, p. 63).

(2) *Comment*: Some commenters argued that the majority of the individual model results used in the risk assessment continued to show no significance and that when increased statistical controls are applied in both time series and longer-term studies, the relative risk often declines (Exxon-Mobil, UARG – attachment 2). These commenters also argued that this is also true when co-pollutants are evaluated with exposures to $PM_{2.5}$ and asserted that of the 56 individual short-term $PM_{2.5}$ mortality risk coefficients [used in the risk assessment], 31 of them are insignificant, while 25 of them are significant. These commenters asserted that EPA was arbitrary in selecting the results of individual studies to include in the risk assessment.

Response: First, it is important to recognize that EPA's criteria for selection of studies and concentration-response relationships were described in the draft "Particulate Matter NAAQS Risk Analysis Scoping Plan" (EPA, 2001) and in draft Risk Assessment TSD reports (Abt Associates, 2002; Abt Associates, 2003; Abt Associates, 2005a) and drafts of the Staff Paper that were reviewed by the CASAC and made available to the public for comment at several stages during the review. The CASAC did not express any concerns about EPA's selection of studies to be included in the $PM_{2.5}$ risk assessment and in its March 2006 letter to the EPA Administrator stated, "While the risk assessment is subject to uncertainties, most of the PM Panel found EPA's risk assessment to be of sufficient quality to inform its recommendations" (Henderson, 2006).

Second, we count 54 short-term exposure mortality $PM_{2.5}$ risk coefficients (including both non-accidental and cause-specific mortality) in Appendix C.1 of the risk assessment Technical Support Document (TSD) (Abt. Associates, 2005b), not 56. Of these, 49, or 90.7%, are positive and 22, or 40.7%, are statistically significant. The comment seems to be implying that "only" 22 out of 54 estimates being statistically significant is an rgument against an effect existing, and this is not the case. Particularly for a small but real effect, which is difficult to detect above a lot of "noise," having as great a percentage as 40% of estimates be statistically significant (to say nothing of over 90% of these estimates being positive) argues for an effect existing. Lack of statistical significance doesn't necessarily imply that the risks are not real. Particularly for a small effect that may be difficult to detect above a lot of "noise," lack of statistical significance of an estimate may reflect only insufficient statistical power to detect a small but real effect. Given this, it is telling that such a high percentage of effect estimates are positive, since if there were truly no effect EPA would expect to see only about half the effect estimates be positive. The comment that "EPA was arbitrary in selecting the results of individual studies to support its position" is not supported, since EPA clearly stated criteria for selection of concentration-response functions to use in the risk assessment in drafts of the Staff Paper

and Risk Assessment TSD, which were reviewed by the CASAC and the public at several stages in the review.

(3) *Comment:* Some other commenters argued that EPA's risk assessment underestimated the risks associated with $PM_{2.5}$ because the assessment only looked at a few cities and a few health endpoints. They noted that most of the nation's largest cities were not covered in EPA's risk assessment. Some of these commenters also argued that the risk assessment underestimated risks because EPA incorporated an assumed "cutpoint" in its assessment that is not supported by studies that find no evidence of a threshold (American Lung Association et al.).

Response: The EPA has consistently acknowledged that the risk assessment does not address all of the various health effects for which there is some evidence of association with exposure to $PM_{2.5}$, nor has EPA every claimed that the risk assessment represents a national estimate of health risks associated with meeting the current or alternative $PM_{2.5}$ standards. As stated in the 2001 draft "Particulate Matter NAAQS Risk Analysis Scoping Plan," which was reviewed by the CASAC, "both the prior and current proposed PM risk analyses estimate risks for sample urban areas, rather than attempt a nationwide analysis" (EPA, 2001, p.2).

With respect to the comment about use of an assumed cutpoint, consistent with the Criteria Document, EPA concludes that the available evidence does not either support or refute the existence of population thresholds for the effects of PM across the range of concentrations in the studies (EPA, 2004, pp. 8-345 to 8-346). The EPA included in the risk assessment estimates based on alternative cutpoints, including estimates down to the lowest measured level in the various studies, but consistent with the advice from CASAC, EPA placed greater weight on the estimates associated with a cutpoint of 10 $\mu g/m^3$. As discussed in section II.B of the preamble to the proposed rule, the Administrator believes that unusually large uncertainties continue to underlie the resulting quantitative risk estimates, and that this risk assessment has important limitations as a basis for setting a standard level in this review, in part because the available studies do not resolve the questions related to potential effect thresholds.

(4) *Comment:* One commenter specifically asserted that EPA's presentation of risk assessment results in Chapter 5 of the Staff Paper (EPA, 2005), and thus to CASAC, was biased and undermined CASAC's ability to provide objective advice by only including estimated percent reductions from the current standards in a series of 3-dimensional figures and not presenting information about the uncertainties in these estimates (ExxonMobil, pp. 48-59).

Response: It is not correct that EPA only included estimated percent reductions in risks for alternative standards from the current standards in the series of 3-dimensional figures presented to the CASAC and included in Chapter 5 of the final Staff Paper. The figure included in the commenter's comment showing a recreation of Figure 5-1(a) from the Staff Paper leaves out the information presented by EPA of the estimated incidence and incidence rate (and associated 95% confidence ranges) associated with meeting the

current standards for each of the five locations. The EPA included in the figure title the following, "Risk associated with meeting current $PM_{2.5}$ standard, based on the ACS extended study, is shown in figures in terms of estimated annual incidence rate and annual incidence (and 95% confidence ranges)" (EPA, 2005, p. 5-25). In fact, all of the 3-dimensional figures included in Chapter 5 of the Staff Paper presented risk estimates including the incidence and incidence rate estimates associated with the current standards. The Staff Paper states, "To put the estimated percentage reductions in perspective, these figures also include the estimated $PM_{2.5}$-related annual incidence rate (in terms of deaths/year/100,000 general population) and annual incidence (in terms of deaths/year) of total mortality associated with long-term exposure associated with just meeting the current $PM_{2.5}$ standards"(EPA, 2005, p.5-24). Contrary to the claim made by the commenter that EPA totally ignored the statistical uncertainty in its presentation in Chapter 5, the 3-dimensional figures did include 95% confidence ranges for the estimates associated with just meeting the current standards.

In addition, the introductory discussion of risk-based considerations (Section 5.3.1.2) of the Staff Paper discussed the most significant uncertainties and noted that "the risk assessment discussed in Chapter 4 addresses a number of key uncertainties through various base case analyses, as well as through several sensitivity analyses"(EPA, 2005, p.5-10). Because assumptions about the form of the concentration-response function had the greatest impact on the risk estimates, EPA staff included 3-dimensional figures showing estimates "not only with the reported linear or log-linear concentration-response functions, but also with modified functions that incorporate alternative assumed cutpoints as surrogates for potential population thresholds"(EPA, 2005, pp.5-10 to 5-11). Thus, EPA does not agree with the commenter's claim that uncertainties were ignored in the presentation of the results of the risk assessment in the Staff Paper.

(5) *Comment:* Some commenters argued that EPA's evaluation of the sensitivity of the risk estimates to alternative plausible concentration-response functions is limited to consideration of a threshold model and does not encompass consideration of any equally plausible sigmoidal model. These commenters asserted that the correct way to assess thresholds is to estimate different threshold models, or sigmoidal models, using the original data used in the epidemiological study.

One commenter (API) argued that the threshold (or "hockeystick") model the Agency used to examine the effect of alternative concentration-response relationships was incorrectly matched to the linear concentration-response model originally fit to the data. The argument presented for this relation between the linear and hockeystick models is that the linear model b is a weighted average of the zero slope below c and the slope b^T above c. The commenter further argued that this weighting completely ignored the frequency distribution of concentrations between zero and highest measured level (HML) and has the undesirable consequence that the hockeystick response model lies entirely below the linear model between zero and HML, when considering incremental effects above background. This commenter argued that all subsequent calculations based on this incorrect matching of concentration-response functions needed to be re-evaluated (API).

Response: The EPA does not agree that its role during the review of a NAAQS is to refit the original data that were used in analyses contained in published, peer-reviewed epidemiologic studies to alternative models. The EPA has repeatedly acknowledged that uncertainties remain in the understanding of the shape of concentration-response functions, and, whether or not thresholds exist. Consistent with the conclusion in the Criteria Document, EPA concludes that the available evidence does not either support or refute the existence of population thresholds for the effects of PM across the range of concentrations in the studies. However, EPA notes that, in contrast to the last review when few studies had quantitatively assessed the form of the concentration-response function or the potential for a threshold, several new studies available in this review have used different methods to address this question, and most have been unable to detect threshold levels in time-series mortality studies.

The Criteria Document (EPA, 2004, p. 9-44) recognized that in multi-city and most single-city time-series studies, statistical tests comparing linear and various nonlinear or threshold models have not shown statistically significant distinctions between these models. Where potential threshold levels have been suggested in single-city studies, they are at fairly low levels (*Id.* at p. 9-45). Further, the shape of concentration-response functions for long-term exposure to $PM_{2.5}$ was evaluated using data from the ACS cohort, with the HEI reanalysis finding near-linear increasing trends through the range of particle levels observed in this study, and the extended ACS study reporting that the various mortality associations were not significantly different from linear (71 FR at 2635).

The use of a "hockeystick" model in the risk assessment is intended only as an approximation to a sigmoidal model, whose exact shape EPA did not know. However, the hockeystick model has the main features, relative to the log-linear or linear model, of a sigmoidal curve: (1) there is a point below which there is either no effect or a greatly attenuated effect, and (2) the slope above the threshold (or the slope of the "middle portion" of the sigmoidal model) is greater than the slope of the corresponding log-linear or linear curve. If the original concentration-response function was estimated based on a mis-specified model (e.g., the "truth" is some type of threshold or sigmoidal relationship), then the estimated slope of the linear or log-linear model would be downward biased relative to the slope above the threshold (or the slope of the "middle portion" of the sigmoidal model), and thus the estimated slope should be adjusted upward when the hockeystick model is used.

The comenters' conclusion that EPA's method "has the undesirable consequence that the hockeystick response model lies entirely below the linear model between zero and HML" is not true, however, unless EPA anchored the intercept in the hockeystick model to the intercept in the original estimated log-linear function, which was not done (as illustrated in Figure 2-1, Abt Associates, 2005b). The EPA method does not require that a value be specified for the intercept of the hockeystick model, and, in fact, EPA believes it does not make sense for that intercept to be the same as the intercept of the original log-linear model, since the basic idea behind the method used was to find a hockeystick model that would have been estimated from the same data that were used to estimate the original log-linear model. The EPA notes, however, that the closer the threshold is to the lowest

measured (PM) level (LML) in the study, the less of a difference the frequency distribution of PM concentrations will make. The relative weight of the horizontal portion of the "true" hockeystick concentration-response function in affecting the slope of an estimated (mis-specified) log-linear concentration-response function will depend not only on the frequency distribution of PM concentrations in the study (the distribution of points along the x-axis) but also on the width of the range of PM concentrations below the threshold versus above it. In the absence of any actual data, it was this second influence on the estimated slope in the concentration-response function from the epidemiological study that EPA relied upon.

(6) *Comment:* Some commenters argued that EPA considered a narrow range of hockeystick models with a maximum threshold or cutpoint at 20 $\mu g/m^3$ without adequate justification, thus ignoring the consequences of higher thresholds in its sensitivity study (e.g., API).

Response: The EPA presented its plans for alternative cutpoints for both short-term and long-term exposure effects in its draft "Particulate Matter NAAQS Risk Analysis Scoping Plan" (EPA, 2001) and in draft Risk Assessment TSD reports (Abt Associates, 2002; Abt Associates, 2003; Abt Associates, 2005a) that were reviewed by the CASAC and made available to the public for comment at several stages during the review. The CASAC did not suggest that the range of cutpoints included in the risk assessment was inappropriate. Rather, CASAC stated that "the Panel favored the primary use of an assumed threshold of 10 $\mu g/m^3$. The original approach of using background or LML as well as the other postulated thresholds, could still be used in a sensitivity analysis of threshold assumptions" (Henderson, 2005, p. 6). Nowhere in CASAC's comments was there any suggestion that higher thresholds, beyond those considered in EPA's assessment, should be considered.

(7) *Comment*: Some commenters argued that, in developing estimates of risk based on a small subset of studies, EPA failed to comply with federal guidance on risk assessment and the National Academy of Sciences' recommendations (NAS, 2002). As noted in the final Staff Paper, EPA clearly states that the uncertainties incorporated quantitatively in the risk assessment reflect only the statistical standard error of the estimated linearized effect coefficient, as derived from the epidemiologic modeling -- assuming a true linear concentration-response relationship. Since the reported uncertainties ignore the concentration-response specification uncertainty and may be dwarfed by the specification uncertainty, they are not useful as reported and are possibly deceptive. An alternative would be to integrate the results of the sensitivity study, possibly using Bayesian methods, to obtain measures of risk estimation uncertainty that more realistically reflect the available information (API).

Response: The point that the uncertainty ranges reported in the risk assessment do not reflect all of the uncertainty in the risk estimates is discussed in the Staff Paper (EPA, 2005, Section 4.3.4, pp.4-26 to 4-35). As indicated in the Staff Paper, statistical uncertainty surrounding the estimated PM coefficients in the reported concentration-response functions is reflected in the confidence intervals and additional uncertainties are "addressed quantitatively through sensitivity analyses and/or qualitatively. … Given the

existing data gaps in the scientific evidence and associated uncertainties, a more comprehensive integrated assessment of uncertainties, would be desirable, but in the staff's judgment would require use of techniques involving elicitation of probabilistic judgments from health scientists. While the Agency is currently developing these approaches, such comprehensive assessments of uncertainty are not available for the current risk assessment for this PM NAAQS review."(EPA, 2005, p.4-31)

The EPA believes that the approach proposed by the commenter of considering all or most models in an "integrated uncertainty analysis" can produce highly misleading results. Suppose, for example, that five different lag structure concentration-response functions have been estimated, but that the "true" lag is 0-day. The other concentration-response functions are, then, mis-specified. Suppose that, as a result, they show a "statistically insignificant" relationship between PM and the health endpoint. If those models are included in an "integrated uncertainty analysis" they will inflate the apparent probability that there is no relationship between PM and the health effect, when in fact they have only mis-specified the relationship. Even if EPA knew that all the models that were going to be included in an Agency "integrated uncertainty analysis" were correctly specified, EPA would still have to select weights for the concentration-response functions included. Because the results of an "integrated uncertainty analysis" conducted in this manner are heavily dependent on the weights used, this exercise would give the appearance of a quantitative answer to something that is, in fact, a subjective assessment. The EPA believes that it could, thus, be more misleading than clarifying.

(8) *Comment*: Some commenters argued that none of the newly available studies on short-term exposure mortality in the risk assessment cities finds a $PM_{2.5}$-mortality association that is statistically significant in all of the formulations that are reported in those studies (ExxonMobil, UARG, attachment 2). These commenters further argued that these studies thus provide strong evidence that the $PM_{2.5}$-mortality associations are not "robustly statistically significant" – i.e., statistical significance is eliminated in the face of a variety of "reasonable alternative statistical modeling methods and formulations."

Response: This comment seemed to imply that unless the $PM_{2.5}$-mortality associations remain statistically significant over a wide variety of alternative models, or even all models, they are "suspect." The lack of statistical significance in a particular model does not imply that the relationship is no longer likely. There are several ways in which the statistical significance of a small but real effect can be lost – if, for example, (1) a covariate with which the variable of interest is highly correlated is added to the model; or (2) the model has been essentially mis-specified (e.g., by incorrectly specifying the lag structure); or (3) potentially confounding effects such as weather variables have been "over-controlled" for in the analysis. The yardstick of "statistical robustness" implied by this commenter is unreasonable.

(9) *Comment*: These commenters (UARG – attachment 2, Exxon-Mobil, API, Alliance of Automobile Manufacturers) further argued that considering the ACS study finding that the association between long-term exposure to $PM_{2.5}$ and mortality is found largely among individuals with no more than a high school education that:

- this finding should be reflected in the risk assessment;
- only within this sub-population was the association statistically significant, increasing the uncertainty about the dimensions of the reported association between $PM_{2.5}$ and mortality in the whole ACS dataset; and
- all hypotheses about what this result means lead to conclusions that either the relative risk (RR) estimates being used in the risk assessment are biased, or that the association with $PM_{2.5}$ is actually due to some other confounder and is not causal – i.e., this finding strongly suggests that mortality is not the result of ambient air quality exposure, but rather due to some socioeconomic factor or some specific type of pollution that is more prevalent in specific environments, in contrast to the ambient air in general.

Response: The EPA believes that the fact that the association was not statistically significant among the sub-population with more than a high school education doesn't increase the uncertainty about the association over the whole population, which was itself statistically significant and is effectively a weighted average of the RRs for the two sub-populations; nor does it imply that it is biased.

As noted above, the RR for the whole population is effectively a weighted average of the RRs for the two sub-populations -- those individuals with no more than a high school education and those with more than a high school education. The EPA's application of the RR based on the whole ACS population to the whole population in each risk assessment location should yield an unbiased estimate of risk over the whole population, unless the composition of the assessment population is substantially different from that of the ACS study population -- i.e., unless the percentages of individuals in the two sub-populations are substantially different from those in the ACS study population. (This is a particular example of the more general issue of whether the assessment population is sufficiently similar to the study population on which a RR or concentration-response function is based.)

The lack of statistical significance for the sub-population with more than a high school education in the ACS study does not imply that "mortality is not the result of ambient air quality exposure, but rather due to some socioeconomic factor or some specific type of pollution that is more prevalent in specific environments, in contrast to the ambient air in general" as the commenters suggested. It is likely that the impact of air pollution on health is more readily detectable among the sub-population with less education because less education is correlated with lower socioeconomic status, which in turn is correlated with less access to medical care. The result observed in the ACS study may mean only that among those with less access to medical care, the effects of air pollution on health are not dealt with as readily and, therefore, are translated more readily into premature death.

(10) *Comment:* One commenter asserted that the risk assessment completely ignores the Veterans' Cohort study (Lipfert et al., 2000) (UARG – attachment 2).

Response: The reasons for not including the Veteran's Cohort study are provided in the Risk Assessment TSD which notes that the Criteria Document concluded:

> In considering the results of these studies together, statistically significant associations are reported between fine particles and mortality in the ACS and Six Cities analyses, inconsistent but generally positive associations with PM were reported in the AHSMOG analyses, and distinctly inconsistent results were reported in the VA study. Based on several factors, the larger study population in the ACS study, the larger air quality data set in the Six Cities study, the more generally representative study populations used in the Six Cities and ACS studies, and the fact that these studies have undergone extensive reanalyzes – the greatest weight should be placed on the results of the ACS and Six Cities cohort studies in assessing relationships between long-term PM exposure and mortality (U.S. EPA 2004, pp.8-120 to 8-121).

The Risk Assessment TSD goes on to note (Abt Associates, 2005b, p.50) that only the results of the ACS and Six Cities studies are included in the quantitative risk assessment and that the AHSMOG and Veteran's studies are discussed in the Criteria Document and Staff Paper. As noted in the Staff Paper (EPA, 2005, p.4-25), EPA's reliance on the ACS and Six Cities studies for the purposes of quantitative estimates is consistent with the views expressed in the NAS 2002 report and the SAB Clean Air Act Compliance Council review of the proposed methodology to estimate the health benefits associated with the Clean Air Act (SAB, 2004). Also, the CASAC in its review of drafts of the Risk Assessment TSD and Staff Paper did not express any disagreement with the choice of studies used in the final Risk Assessment TSD.

(11) *Comment:* Some commenters argued that toxicologic evidence strongly indicated that the composition of particulate matter is important, and that the assumption of equal toxicity by mass used in the risk assessment is not supported. This uncertainty [about the relative toxicities of $PM_{2.5}$ constituents] affects the Agency's assessment of risk from exposure to $PM_{2.5}$, as well as the effectiveness of any specific control strategy to reduce $PM_{2.5}$ emissions. The EPA's primary risk estimates assume that every control strategy to meet a tighter standard will always reduce the species that might actually affect health in the same proportion as the reduction of total PM mass. These commenters argued that there is no evidence to support this assumption, and alternative assumptions could produce larger or smaller health benefit, therefore, they argued that it is possible that actual PM control strategies might not control the potent species of PM at all, producing no health benefit. (Alliance of Automobile Manufacturers, ExxonMobil)

Response: The EPA believes this comment addresses two issues: (1) Are the pollutant species within $PM_{2.5}$ equally toxic?, and (2) if they are not, would every control strategy to meet a tighter standard always reduce the species that might actually affect health in the same proportion that all $PM_{2.5}$ mass is reduced?

At the time of the last PM NAAQS review, the Agency determined that it was appropriate to assess health risks and control fine particles as a group, as opposed to singling out any particular component or class of fine particles. This distinction was based largely on epidemiologic evidence of health effects using various indicators of fine particles in a large number of areas that had significant contributions of differing components or sources of fine particles, together with some limited experimental studies that provided some evidence suggestive of health effects associated with high concentrations of numerous fine particle components.

In this review, as discussed in section II.D of the preamble for the proposal (71 FR at 2643-2645) and in section II.C of the preamble for the final rule, while most epidemiologic studies continue to be indexed by $PM_{2.5}$, some epidemiologic studies also have continued to implicate various components within the mix of fine particles that have been more commonly studied (e.g., sulfates, nitrates, carbon, organic compounds, and metals) as being associated with adverse effects (EPA, 2004, p. 9-31, Table 9-3). In addition, several recent epidemiologic studies have used $PM_{2.5}$ speciation data to evaluate associations between mortality and fine particles from different sources, and some toxicologic studies have provided evidence for effects associated with various fine particle components or size-differentiated subsets of fine particles. The available information continues to suggest that many different chemical components of fine particles and a variety of different types of source categories are all associated with, and probably contribute to, effects associated with $PM_{2.5}$ exposures. Consequently, there continues to be no basis to conclude that any individual fine particle component *cannot* be associated with adverse health effects (EPA, 2005, p. 5-17).

Thus, while the Agency recognizes that it is unlikely that all components of $PM_{2.5}$ are equally toxic, there is insufficient evidence to explicitly take into account differences in relative toxicity based on compositional differences. It is true that, if the pollutant species are not equally toxic and if the proportion of those species within PM varies from one location to another, then applying a concentration-response function estimated in one location to another location could lead to either underestimation or overestimation of risks. This is one of the reasons EPA generally limited the application of single-city concentration-response functions to the urban area in which the function was estimated. If the proportions of the species within $PM_{2.5}$ are the same in the assessment location as in the study location, then even if there are differential species toxicities, estimates of health risk attributable to "as is" $PM_{2.5}$ above background concentration should be unbiased.

On the second point, EPA implicitly assumed in the risk assessment that reductions in $PM_{2.5}$ to just meet a standard would reduce all constituent pollutant species in the same proportion. The EPA made this assumption in the absence of any information to do otherwise. As noted above, uncertainties about relative toxicity and disproportionate reductions among various components could lead to either higher or lower risk estimates. A more refined risk assessment awaits the results of future research that would allow EPA to make reasonable estimates of the relative toxicities of the pollutant species and

the location-specific disproportionate changes in species that are likely to occur when alternative standards are just met

(12) *Comment:* Some commenters contended that the air quality rollback method used by EPA to estimate risks associated with the current and alternative standards overstated the amount by which the worst case monitor would have to be reduced in order to just attain either a daily or annual standard. The commenters provided figures showing an alternative approach which assumed both that the effect of a controlling daily standard would be to reduce $PM_{2.5}$ levels only on the peak days that would stand in the way of attainment and that $PM_{2.5}$ levels would be reduced to a level that exactly attains the standard, but not any further, in contrast to EPA's methodology which these commenters contend assumes an arbitrary degree of further reduction in $PM_{2.5}$ (ExxonMobile, UARG – attachment 2).

Response: The approach used by EPA to adjust air quality to simulate just meeting the current suite and alternative suites of annual and daily standards proportionally rolls back $PM_{2.5}$ concentrations in excess of estimated policy-relevant background levels. For the base case risk estimates the amount of reduction is based on the design value which, consistent with the current form of the standard, is defined in terms of the 3-year averages (of annual means or 98^{th} percentiles) based on the maximum monitor within an urban area.

As indicated in the Staff Paper, the use of a proportional rollback of $PM_{2.5}$ levels in excess of background is supported by "both the 1996 assessment (see Abt Associates, 1996, section 8.2) and a more recent analysis of historical air quality data (see Appendix B in Abt Associates, 2005b) have found that $PM_{2.5}$ levels in excess of estimated background concentrations in general have historically decreased in a roughly proportional manner" (EPA, 2005, p.4-18). The Staff Paper and Risk Assessment TSD discuss sensitivity analyses using an alternative air quality adjustment approach that reduces the top 10% of daily $PM_{2.5}$ concentrations more than the lower 90% (EPA, 2005, p.4-52 and 4-56, Abt Associates, 2005b, p.131). The EPA believes that the commenters' alternative approach of only reducing peak days exceeding the daily standard level is unrealistic in that most PM-related air pollution control measures are continuous in nature. With respect to the second altered assumption, the commenters appear to interpret attainment of the standard on the basis of a single year, which is not consistent with the form of the current standard or the alternative standards that EPA analyzed. Thus, EPA does not agree that its approach assumed an arbitrary degree of further reduction, but rather EPA's approach reflects that the reductions required are based on a three-year period, not just a single year.

5. Specific Comments Related to Data Handling (Appendix N)

The final rule for PM revises Appendix N to 40 CFR Part 50 for the annual and 24-hour $PM_{2.5}$ standards to address specific data handling procedures including data assimilation, data completeness, and missing data adjustments. All of the comments submitted on the proposed revisions to Appendix N were submitted by State air pollution control agencies. In reviewing the

public comments on data handling, EPA observed that the proposed Appendix N does not clearly state how quarterly data capture rates are calculated, especially in the context of "make-up" sampling. The EPA has encouraged the practice of make-up sampling in order to increase data capture rates. The EPA issued guidance in 1999 detailing the appropriate make-up procedures (EPA, 1999) and since then, EPA has implemented the guidance protocol into their annual design value calculation activities. The final Appendix N defines a new term, "creditable samples," to simplify the calculation of data capture rates and also to facilitate calculation of annual 98^{th} percentile values (see response to comment (5) below). Creditable samples are simply the sum of completed scheduled samples plus valid make-ups. The final appendix explicitly stipulates the procedure for calculating quarterly data capture rates: "Quarterly data capture rates (expressed as a percentage) are specifically calculated as the number of creditable samples for the quarter divided by the number of scheduled samples for the quarter, the result then multiplied by 100 and rounded to the nearest integer" [40 CFR Part 50, App. N 3.1(b)].

Incorporating responses contained in sections II.E and V.A of the preamble to the final rule, EPA provides the following responses to specific comments related to interpretation of the NAAQS for $PM_{2.5}$.

(1) *Comment:* One commenter argued that the proposed Appendix N is not clear on the procedure for augmenting the primary monitor data record with data from collocated Federal Reference Method/Federal Equivalent Method (FRM/FEM) instruments. Also, this commenter argued that EPA must have the associated mechanisms integrated and tested in the Air Quality System (AQS) (South Carolina Department of Health and Environmental Control).

Response: Several comments were received on the composite site record approach and most deemed it a worthwhile improvement. However, as this commenter noted and as EPA agrees, there was some ambiguity in the proposed language as to when the substitutions would be implemented. The final Appendix N clarifies the procedure by replacing the words "as necessary" with "as much as possible" in the following sentence, "Data for the primary monitor shall be augmented *as much as possible* with data from collocated FRM/FEM/ARM monitors." The final appendix further stipulates that the replacement will be made on all days that a primary monitor measurement is not recorded, and not just (unrecorded) scheduled sampling days. The appendix calls the substituted collocated values "daily values," just like all measurements emanating from the primary monitor. The impending usage of "daily values" is addressed in new and/or enhanced descriptions in the final appendix for "creditable samples," "daily values," "extra samples" and "make-up samples." The EPA is pursuing the incorporation of the composite site record logic into the AQS.

(2) *Comment:* A limited number of comments were received in regards to the explicit addition of language to consider 11 samples per quarter to be sufficient if the corresponding 3-year design value was over the NAAQS level. Two of the three commenters approved of the proposed modification; the third commenter voiced the general concern that EPA needs to set a uniform standard for data completeness that

remains consistent regardless of design value level or intended use of the data (Texas Commission on Environmental Quality).

Response: The EPA considers it appropriate to have different completeness criteria for different uses of data. Consistent with the objective of protecting the public health, EPA supports a higher hurdle to prove attainment than to show nonattainment. For $PM_{2.5}$, EPA has set a general minimum completeness guideline of 75% data capture per quarter [40 CFR Part 50, App. N 4.1(b); 1997 40 CFR Part 50, App. N 2.1(b)]. In recognition that the reference sampling method is manually intensive, EPA has permitted, in rule and in guidance, the use of less complete data. Eleven samples per quarter were previously established by EPA as an acceptable minimum whenever the corresponding annual average was over the level of the standard. [1997 40 CFR Part 50, App. N 2.1(b)] In this PM NAAQS review, EPA proposed to modify the criterion to also consider 11 samples per quarter sufficient if the corresponding design value was over the NAAQS level and solicited comment on this proposed change (71 FR at 2685-86). This proposed change was precipitated, in part, by a comment received during the previous PM NAAQS review which posed a hypothetical situation where during a 3-year period, the annual means for years 1 and 3 could exceed the level of the standard and thus 11 samples per quarter would be sufficient but the annual mean for year 2 would not exceed the level of the standard and therefore 11 samples per quarter would be insufficient for that year (assuming 75% each quarter was not achieved) (EPA 1997, p. 47). The EPA responded to this comment by noting that Appendix N allows some flexibility in the use of incomplete data, "subject to the approval of the Regional Administrator" [1997 40 CFR Part 50, App. N 2.1(c)]. The EPA believes that for this particular example, the 75% requirement should be waived for year 2 and the 11 sample criterion used instead. Therefore, in the absence of significant dissent, the EPA has incorporated the proposed change in the final Appendix N; 11 samples are now considered sufficient for years where a resulting design value exceeds the NAAQS. The EPA believes that this explicit change will help promote national consistency.

(3) *Comment:* Some commenters argued that the proposal to allow (for nonattainment purposes) a data substitution method to validate quarters that had less than 11 samples was flawed because it did not set a limit on the number of quarters in which the substitution could be implemented. (NESCAUM, New York Department of Environmental Conservation). Further, one commenter thought that if such an approach was allowed for nonattainment purposes it should also be permitted for attainment purposes. (Texas Commission on Environmental Quality).

Response: The concept of using 'less than complete' data for regulatory purposes is already authorized by existing Appendix N section 2.2 (b) ("Situations may arise in which there are compelling reasons to retain years containing quarters which do not meet the data completeness requirement of 75 percent or the minimum number of 11 samples. The use of less than complete data is subject to the approval of the appropriate Regional Office.") Data handling guidance, issued in 1999, documented several example methods by which 'less than complete' data could be considered sufficient to show attainment or nonattainment (EPA, 1999). The EPA has utilized three of the suggested methods in its

annual $PM_{2.5}$ design value updates. The rule change adopted in this proceeding merely codifies the single most important of these three methods, the one utilized to verify nonattainment. Making the nonattainment substitution method part of the rule will help ensure national consistency. The logic of the data substitution technique is self-policing in that the more data that are missing, the greater the likelihood that the substitutions of the 'historically low' value will yield a test design value below the level of the standard and, if that occurs, the design valid will not be considered complete and valid. In regard to there being an explicit limit on the number of quarters in which the substitution could be implemented, the 1999 $PM_{2.5}$ data handling guidance actually stated that because substitution of low values is such "a compelling argument" that use of the approach be considered "for several quarters with no data." Therefore, EPA is not persuaded by these comments to implement a limitation on the number of quarters in which the substitution can occur. In regard to the issue of allowing a data substitution approach for attainment, EPA notes that it will issue data handling guidance that addresses the two attainment data substitution techniques currently in practice.

(4) *Comment:* A limited number of commenters argued that the "applicable number" concept (utilized in the regular non-seasonal 98^{th} percentile formula) has merit but is complex, confusing, and difficult to program. Also, two commenters noted that the "applicable number" method should give credit to "extra" samples taken at the end of the month or quarter (NESCAUM, New York Department of Environmental Conservation).

Response: The EPA discussed the "applicable number" concept in the 1999 Guideline on Data Handling for the PM NAAQS (EPA, 1999). As stated in that document, the applicable number for a year is the sum of the corresponding quarterly applicable numbers, and a quarterly applicable number is the lower of the actual number of samples and the scheduled number of samples. The EPA's original and still-applicable intent, is to exclude "extra" samples from being included in the "applicable number" count. "Extra" samples are ones taken on non-scheduled days that cannot be used as "make-ups" for missed (or invalidated) scheduled day samples.

The Guidance also contains instructions as to when a "make-up" sample could be made. Apparently, some States misinterpreted the "applicable number" concept intent and may have taken extra samples at the end of the quarter in order to raise their applicable number. A rise in the applicable number can cause a 98^{th} percentile value selection further down the (descending) data distribution (i.e., making it a lower value). Technically, under the guideline approach, extra samples (at the end of the quarter) can be included in the applicable number count up to the same extent (number) that samples are missed (or invalidated) earlier in the quarter and not made up. As previously stated, this was not EPA's intent. [Example: A site is sampling every third day. This site misses its first three scheduled samples of the quarter and does not make them up as permitted. However, three extra samples are taken at the end of the month. These three samples would have been included in the quarterly applicable number.] The EPA has therefore modified the applicable number concept in a way which addresses both stated comments: (1) the procedure has been simplified and (2) the unintended loophole closed by regulatory language. The applicable number of samples for a year is now defined as the

sum of completed scheduled samples plus valid make-ups. [40 CFR Part 50, App. N 4.5(a)(1)].

Furthermore, the "applicable number" term has now been replaced with a more intuitive term, "creditable samples," which refers to the collective sum of these two types of samples (completed scheduled samples plus valid make-ups). For $PM_{2.5}$, the EPA has always calculated quarterly data completeness using "creditable samples" (though not referred to as that) as the numerator and number of scheduled samples as the denominator. Thus, in addition to simplifying the "applicable number" (or "creditable number") procedure, the EPA has also united the concept with data capture.

(5) Comment: Some commenters argued that there is a bias in EPA's current method of calculating 98th percentiles which can produce a lower value for 1 in 3 day sampling schedules compared to one calculated for daily sampling schedules (NESCAUM, Delaware Department of Natural Resources and Environmental Control).

Response: The EPA acknowledges a slight bias in the prescribed calculation of annual 98th percentile values for periodic (i.e., 1 in 3 day) sampling schedules. According to recent analyses of 2003-2005 data, the EPA estimates the bias to be about 0.8 µg/m3. The EPA agrees that this bias is a concern, especially for controlling sites in an area that have design values close to the NAAQS. As discussed in sections II.E.1 of the preamble to the final rule, EPA proposed to reduce this bias by increasing the sampling frequency for monitoring sites that are within 10 percent of the standard to 1 in 3 day sampling. The EPA is persuaded by these comments that it is appropriate to adjust the proposed sampling frequency requirements in order to further reduce this bias. Therefore, the EPA has instituted a new monitoring rule that requires key sites (i.e., controlling ones) that operate on a 1 in 3 day schedule that have a 24-hour (98th percentile) design value within 5% of the level of the NAAQS (approximately 33-37 µg/m^3) to convert to daily sampling (40 CFR Part 58 section 12(d)(1)).

Another point worth noting in regard to this bias issue is the anticipated impending shift from manual FRMs for $PM_{2.5}$ to continuous FEMs. With revised monitoring rules there is now an available framework for continuous $PM_{2.5}$ methods to be granted federal equivalency. The EPA anticipates that many States will soon (or eventually) be making a gradual shift from filter-based methods to less expensive continuous methods thus making the sampling frequency a moot issue. Continuous samplers usually operate every day.

(6) *Comment:* One commenter argued that the revised requirements for spatial averaging are excessively restrictive and, due to the criterion virtually requiring speciation sampling at all candidate sites, are thus unreasonably burdensome for any monitoring organization (South Carolina Department of Health and Environmental Control).

Response: Appendix N stipulates three key criteria that must be met in order for a set of sites to qualify for spatial averaging. With respect to the first two spatial averaging criteria, EPA notes that the original, similar but less restrictive constraints on spatial

averaging were adopted before data were widely available on spatial distributions of $PM_{2.5}$ air quality levels. Section 2.4.1 of the Staff Paper presented results of an analysis of recent air quality data on the mean differences and correlations between monitor pairs in metropolitan areas across the country (Schmidt et al., 2005). The previous criterion that differences in annual means between individual monitors and the corresponding multi-site spatial average not exceed 20 percent on an annual basis was met by over 90 percent of monitor pairs, while the actual annual median and mean differences for all monitor pairs were 5 percent and 8 percent, respectively. For all pairs of $PM_{2.5}$ monitors, the median correlation coefficient based on annual air quality data is approximately 0.9, which is substantially higher than the previous spatial averaging criterion of a minimum correlation of at least 0.6, which was met by nearly all monitor pairs.

This analysis also showed that in some areas with highly seasonal air quality patterns (e.g., due to seasonal wood smoke emissions), substantially lower seasonal correlations and larger seasonal differences can occur relative to those observed on an annual basis. Based on this analysis, EPA decided to tighten the first two criteria. With the tightened criteria, the analysis showed that a dozen different areas, ten more than now use spatial averaging, could meet them.

The third criterion for spatial averaging, that all of the monitoring sites should principally be affected by the same major emission sources of $PM_{2.5}$, is essentially unchanged from the 1997 regulations. Unlike the first two criteria, EPA is granting some flexibility in how the third criterion could be met The EPA added the additional text to this criterion, suggesting comparison of quarterly speciation profiles, as an illustration of the type of evidence that would support such a claim. The EPA recognizes that there are various additional methods by which the assertion could be corroborated and not all of the methods require speciation data. For instance, a detailed bottom-up emission inventory analysis of the proximate areas of the candidate sites could also affirm the third criterion supposition. Hence, speciation sampling is not necessarily required at candidate sites. The EPA plans to issue guidance describing several methods by which this third criterion could be demonstrated. For clarification, the final Appendix N inserts the words "For example" before the suggested technique. ["(3) All of the monitoring sites should principally be affected by the same major emission sources of $PM_{2.5}$. For example, this could be demonstrated by site-specific chemical speciation profiles confirming all major component concentration averages to be within 10 percent for each calendar quarter."]

B. Primary Thoracic Coarse Particle Standards

1. General Comments on Proposed Primary $PM_{10-2.5}$ Standards

A large number of comments on the proposed primary standards for thoracic coarse particles were general in nature, basically expressing one of two substantively different views: 1) support for retaining a standard for thoracic coarse particles based on an unqualified indicator, rather than the qualified indicator proposed by EPA; and 2) opposition to retaining any coarse particle standard at this time, pending further research. A number of the commenters expressing the second viewpoint provided conditional support (if any standard were to be adopted) for a coarse particle standard based on the kind of qualified indicator EPA proposed. Many commenters simply expressed their views without stating any rationale, while others gave general reasons for their views but without reference to the factual evidence or rationale presented in the proposal notice as a basis for the Agency's proposed decision.

The preamble to the final rule presents the Agency's full response to these views, expressly identifying: 1) the strengths and limitations of the scientific evidence on the effects of thoracic coarse particles; 2) the need for and appropriateness of a primary standard to protect against the effects of thoracic coarse particles; 3) the advice of CASAC on the adequacy of the scientific evidence available for making a decision on the standards; and 4) the appropriate indicator, level and form for a standard designed to protect against adverse effects associated with exposure to coarse particles. See sections III.B, III.C and III.D of the preamble to the final rule.

2. Specific Comments on Proposed Primary $PM_{10-2.5}$ Standards

A large number of comments addressed the specific elements of the proposed primary coarse particle standards, the strength of scientific evidence available to support continued protection from thoracic coarse particles, the type of indicator that would be most appropriate to protect against the effects of thoracic coarse particles, the appropriate averaging time, level, and form of the standard(s), and the handling of the transition between current and revised standards. Responses to key issues raised on these topics are generally summarized in sections III.B.2, III.C.2, III.D, and VII of the preamble. Below, EPA provides more detailed responses to the full range of significant issues raised in these comments. It is important to note that because the Administrator's final decision regarding the primary coarse particle standard differs from what was proposed, a number of issues raised by commenters are now moot. Specifically, since the Administrator is retaining the current 24-hour PM_{10} standard, rather than adopting a new standard for coarse particles based on a qualified $PM_{10-2.5}$ indicator, concerns about various aspects of the proposal, such as the scope of the proposed qualified indicator, the monitoring site-suitability test and the exclusion of agricultural and mining sources from the indicator (including concerns that these provisions were inconsistent not only with the Clean Air Act but also with the Equal Protection and Due Process clauses of the United States Constitution), are moot. Though EPA has summarized many of these issues below, it does not respond to them in detail since they pertained to specific aspects of the proposal that were not adopted in the final rule.

a. Need for Revision

In the current review of the primary PM_{10} standards, EPA focused on whether to revise the indicator for thoracic coarse particles. Most public comments on coarse particles addressed the proposed revisions to the indicator, particularly the proposal to adopt a new $PM_{10-2.5}$ indicator that was qualified to focus on particles associated with particular types of emissions sources and to impose stringent monitor site-suitability criteria for NAAQS-comparable monitors. These comments are addressed in section III.C.2 of the preamble to the final rule and discussed more fully below in section II.B.2.b. This section addresses those comments that, directly or indirectly, addressed the need to continue the kind of protection against coarse particles that is provided by the current PM_{10} standards.

As discussed in section III.B.2 of the preamble to the final rule, EPA is in general agreement with those commenters who believed that the current scientific evidence requires retention of a national standard to protect against the effects of coarse particles. These commenters stressed the availability of numerous studies showing associations between thoracic coarse particles and adverse health effects. A number of other commenters recommended revising the PM_{10} standards by revoking both the 24-hour and annual standards. These groups argued that the current body of scientific evidence is insufficient to justify either retaining the current PM_{10} standards or setting a revised standard for thoracic coarse particles at this time. Emphasizing the uncertainties in the currently available scientific evidence, these commenters generally expressed the view that EPA had failed to demonstrate that a coarse particle standard is necessary to protect public health. These commenters recommended deferring the decision on the appropriateness of setting a coarse particle standard pending additional monitoring and scientific research on health effects associated with exposure to coarse particles. The EPA has responded to these comments in section III.B.2 of the preamble to the final rule, and provides additional details in response to specific issues below.

i. Comments supporting continued protection from coarse particles

(1) *Comment*: Most commenters supported the Administrator's proposed decision to maintain a standard to continue protection against the adverse health effects associated with short-term exposure to thoracic coarse particles. In arguing that continued protection is necessary, commenters expressed the following specific views:

- Coarse particles penetrate to and deposit deep in the lungs, similar to fine particles.
- The epidemiological evidence demonstrates that coarse particles are associated with morbidity and mortality, and that coarse particles may even have stronger effects than fine particles in some instances. Some commenters took particular exception to the alternative view of the epidemiological evidence that was included in section III.E of the proposal, noting that this view is in conflict with the assessment of the same studies in the Criteria Document, Staff Paper and section II.A. of the proposal. For example, the American Lung Association et al. cited Ostro's remarks to CASAC regarding the results of his Coachella Valley study in rebuttal of this alternative view.

- The EPA cannot provide justification for declining to set such a standard given the "voluminous evidence based on the latest scientific knowledge indicating that coarse particles cause adverse health impacts," including respiratory- and cardiac-related hospital admissions and respiratory symptoms in adults, and hospital admissions for asthma in children (American Lung Association et al., p. 115).
- In a systematic review of more than 30 studies, many of which were included in the Criteria Document, Brunekreef and Forsberg (2005) reinforce many of the conclusions of the final Staff Paper and the strength of the associations for coarse particles. The conclusions of this review are supported by Sandström et al., 2005.
- New studies published too late for inclusion in the Criteria Document, including Mar et al. (2004), Lin et al. (2005), Chen LH et al. (2005); Becker et al. (2005), and Chen Y et al. (2005), support the need for continued regulation of coarse particles.
- CASAC explicitly recommended adopting a short-term standard for coarse particles, as supported by the conclusions in the Criteria Document and Staff Paper.
- The standard(s) for coarse particles should continue to provide protection from every type of coarse particle everywhere in the country—that is, EPA should retain a national standard based on an unqualified indicator. (See section II.B.2.b.i on indicator for a complete discussion of these comments.)
- Based on essentially the same body of evidence, the World Health Organization determined it was appropriate to maintain PM_{10} standards to protect against effects associated with exposure to coarse particles.

Response: As noted in section III.B.2 of the preamble to the final rule, EPA generally agrees with these commenters regarding the need to provide continued protection from short-term exposure to the types of coarse particles represented in these studies, although not with every specific point made by the commenters. The scientific evidence cited by these commenters was generally the same as that discussed in the Criteria Document and the Staff Paper and the commenters' recommendations for retaining a coarse particle standard are broadly consistent with staff and CASAC recommendations on this issue. To the limited extent that some commenters cited "new" scientific studies in support of their arguments in favor of retaining a coarse particle standard, EPA notes that it is basing the final decisions in this review on the studies and related information included in the PM air quality criteria that have undergone CASAC and public review, and will consider the newly published studies for purposes of decision making in the next PM NAAQS review, as discussed in section I.C of the preamble to the final rule. Nonetheless, in provisionally evaluating commenters' arguments concerning the implications of the scientific evidence on the health effects of coarse particles, EPA notes that the evidence it did consider in this review is more than adequate to support the continuation of standards to protect against the effects of coarse particles, without considering the "new" science. The Agency also notes that its preliminary analysis suggests such studies would not materially change the conclusions in the Criteria Document. Nonetheless, throughout this document, EPA discusses certain conclusions from some of the "new" science. All of these conclusions are, of course, provision and subject to change pending additional peer review that will take place in the context of the next round of standard setting. With respect to these commenters' recommendations regarding the type of indicator that EPA should adopt to provide continued protection from coarse particles, EPA notes that its

responses to these comments are given in section II.B.2.b below, in the context of discussing more detailed comments on indicator.

ii. Comments opposing continued protection from coarse particles

Some commenters argued that the current body of scientific evidence is insufficient to justify either retaining the current PM_{10} standards or setting a revised standard for thoracic coarse particles at this time. The EPA responded to these comments in section III.B.2 of the preamble and provides more detailed responses below.

(1) *Comment:* Some commenters expressed concern over what they viewed as the general lack of scientific support for a coarse particulate matter standard and the failure of EPA to appropriately address that deficiency. The National Mining Association and National Cattlemen's Beef Association submitted comments to this effect, and also provided a more detailed assessment of specific studies, done by a consultant. The consultant commented that EPA repeatedly acknowledges the deficiencies in the evidence regarding coarse particles, and never describes it as sufficient or adequate. In his view, EPA has overstated the informational value of the data from cited studies, and that the preamble to the proposal was constructed to obscure deficiencies and minimize objections that might have been raised regarding the lack of scientific justification for the proposed coarse particle standard. According to the consultant, a detailed, balanced reading of the evidence indicates no basis to justify regulating $PM_{10-2.5}$, only arguments and hypotheses that mainly reflect biological plausibility rather than empirical findings. Echoing this comment, the National Mining Association claimed that a "fair and sound" assessment of evidence would not conclude coarse particles have effects at ambient concentrations (p. 14).

Response: The rationale for these commenters' conclusions does not consider important aspects of the rationale for retaining coarse particle protection and are inconsistent with CASAC and other recent reviews of the scientific evidence. As summarized in section III.A of the proposal preamble, the scientific evidence contained in the Criteria Document and Staff Paper, both of which have been reviewed and found acceptable for use in regulatory decision making by CASAC, supports the need for a standard to provide continued protection from at least some coarse particles.

Even in the NAAQS reviews that concluded in 1987 and 1997, EPA found that the scientific evidence then available supported the need to continue regulation of thoracic coarse particles through appropriate NAAQS. This evidence included mechanistic considerations developed from particle dosimetry and toxicology, as well as an integrated assessment of particle composition and both community and occupational epidemiologic studies. By 1997, EPA judged the evidence to be strong enough to propose separate standards for fine and coarse particles. While the D.C. Circuit found problems with the indicator for thoracic coarse particles promulgated in 1997, the court upheld EPA's determination that a standard was needed (ATA I, 175 F.3d at 1054). In EPA's judgment, the more recent studies included in the 2004 Criteria Document serve to add to, not reduce, the concern present in previous reviews over ambient exposures to coarse

particles, particularly in urban areas. While they are subject to recognized limitations, particularly in terms of providing quantitative assessments of effect levels, the collective evidence from the additional scientific studies included in the Criteria Document demonstrates that protection against the health effects associated with ambient coarse particles is appropriate. The EPA responds to the consultant's more detailed comments on specific studies in a subsequent section of this document.

These commenters' claims regarding the weight of evidence are also countered by the comments and assessments provided by other commenters. Chief among these is the published review of the health effects literature on coarse particles (Brunekreef and Forsberg, 2005) submitted by a number of commenters. This paper is a comprehensive review of studies—most of which are included in the Criteria Document— that have analyzed the effects of both fine and coarse particles. The authors reached the following conclusions regarding effects of ambient coarse particles on morbidity and mortality:

> In studies of chronic obstructive pulmonary disease, asthma and respiratory admissions, coarse PM has a stronger or as strong short-term effect as fine PM, suggesting that coarse PM may lead to adverse responses in the lungs triggering processes leading to hospital admissions. There is also support for an association between coarse PM and cardiovascular admissions. Time series studies relating ambient PM to mortality have in some places provided evidence of an independent effect of coarse PM on daily mortality, but in most urban areas, the evidence is stronger for fine particles (Brunekreef and Forsberg, 2005, p. 309).

The overall conclusions of this review paper, as well as the relative weight given to morbidity and mortality effects, are consistent with EPA and CASAC conclusions.

The EPA specifically notes that there was unanimous agreement among CASAC Panel members that "there was a need for a specific primary standard to address particles in the size range of 2.5 to 10 microns" (Henderson, 2005b, p. 4). In making this recommendation, CASAC indicated its agreement with the summary of the scientific data regarding the potential adverse health effects from exposures to thoracic coarse particles in section 5.4 of the Staff Paper which form the basis for EPA's decision to retain a coarse particle standard.

(2) *Comment*: Several commenters stated that there has never been a valid coarse particle standard.

Response: The EPA disagrees with the underlying premise of this comment, which ignores the 35 year history of the NAAQS for particulate matter. Over this period, EPA has continued to maintain and implement PM standards with indicators that included substantial contributions of coarse particulate matter. The original total suspended particulate matter standards included coarse particles up to a nominal 35 μm, and remained a valid particulate matter standard through 1987 when it was replaced by the PM_{10} standards. While, as some commenters have noted, EPA developed policies to place higher priority on meeting the TSP standard in populated areas, the standard was

implemented through strategies that placed controls on direct emissions of both coarse and fine particles.

The PM standards review that was completed in 1987 placed primary attention on developing and selecting the most appropriate indicator that would include particles of greatest concern to health (EPA, 1982). Based on a consideration of the available scientific information, EPA staff and CASAC determined that ambient fine and coarse particles that presented the greatest risk were those that penetrate to the tracheobronchial and alveolar region; based on dosimetric data, this was determined to be those less than 10 μm. In that review, some commenters, including the American Mining Congress, argued for the exclusion of coarse particles or alternative definitions. The EPA gave explicit consideration to many of the same arguments advanced by some commenters (e.g. National Mining Association, pp. 34-6) in this review, and decided to include thoracic coarse particles in the PM_{10} indicator. In responding to these comments EPA rejected the suggestion of an alternative smaller thoracic particle indicator or the idea of excluding coarse particles altogether (52 FR 24648-49). With regard to the latter point, EPA noted:

> Coarse dusts have been associated with responses such as broncoconstriction, altered clearance, and alveolar tissue damage (SP, Table 5-2). Given current information, it would be premature to ascribe all of the effects in the British, U.S., and other epidemiological studies to the fine fraction (52 FR at 24649).

It is therefore clear from the record that EPA understood and intended the 1987 PM_{10} primary and secondary standards to regulate coarse as well as fine particles. The EPA recognized that, in some areas, PM_{10} violations could be dominated by coarse particles. Accordingly these standards must be considered as valid coarse, as well as fine, particle standards.

Information developed following the 1987 review made it possible to add separate standards for fine particles in 1997, but based on their evaluation of the available science, EPA staff and CASAC both strongly recommended retention of PM_{10} standards, in this case solely to provide protection against the health and welfare effects of coarse particles. As discussed more fully in section III.B of the preamble to the final rule, the core legal questions regarding the validity of those standards had nothing to do with doubts about the health effects of ambient thoracic coarse particles.

In this review, EPA has concluded that the additional information developed since the 1997 review has increased the specificity and added to the epidemiological support for concerns over the health effects of thoracic coarse particles. In making a final decision not to revise the 24-hour PM_{10} standard, the Administrator has considered the totality of the evidence before him in this review, considered alternative approaches, and justified the level and form of the 24-hour primary standard on consideration of that evidence, and not on the preexisting standard itself. In this sense, the validity or lack thereof of past standards for coarse particles is largely irrelevant.

(3) *Comment:* Commenters criticized EPA's interpretation of the available epidemiologic studies, with particular emphasis on whether EPA had adequately considered the role of many acknowledged confounders that undermine the significance of coarse particle associations. Some of these commenters placed extensive reliance on the alternative views of the epidemiological evidence contained in the proposal. According to the commenters, these associations may actually be attributable to $PM_{2.5}$, criteria co-pollutants, non-criteria co-pollutants, uncorrected time trends, weather changes, and model choices. These commenters were also highly critical of EPA's reliance on study results based on single-pollutant models.

Response: As noted in section III.B.2 of the preamble to the final rule, EPA disagrees with the arguments advanced by these commenters. The alternative interpretation of the evidence espoused by these commenters essentially argues that it is more reasonable to presume that the positive results from one-pollutant $PM_{10-2.5}$ statistical models are the result of bias associated with omitting co-pollutants, especially $PM_{2.5}$, for which the evidence is much stronger. The EPA does not accept this argument for both technical and public health policy reasons. The Criteria Document and Staff Paper explain the rationale for reliance on single pollutant models in these studies, while recognizing the significant uncertainties in the limited number of studies available (EPA, 2004, section 8.4.3; EPA, 2005a, p. 3-46). These documents illustrate the results of a number of studies that examined co-pollutants (Figures 8-16 through 8-18 of the Criteria Document), where it can be seen that, in most cases, the inclusion of gaseous co-pollutants does little to change the effects estimate for $PM_{10-2.5}$, although in some cases it does. Though recognizing the uncertainties involved in measuring coarse particles, these documents further note the importance of the relative consistency in the size of effects estimates for coarse particles as well as the pattern of generally positive associations, and the need for considering the results of recent statistically significant associations found in PM_{10} studies where it is reasonable to expect that the coarse fraction dominated the distribution. It would be unwise to presume, in the face of this evidence, that the single pollutant result for coarse particles is generally the result of omitted gases in the model.

The EPA also believes that it is inappropriate to presume that coarse particle or PM_{10} associations in single or multipollutant models can be wholly explained by fine particles. In studies where $PM_{2.5}$ and $PM_{10-2.5}$ have similar effect estimates, it is difficult to determine whether one or both contribute to the result (e.g. EPA, 2004, p. 8-61). The comparison of $PM_{2.5}$ and $PM_{10-2.5}$ is further complicated by the differential measurement error between the two pollutants, which is generally greater for coarse particles (as discussed below). When both pollutants have similar effect estimates, it is difficult to determine whether one or both contribute to the result (e.g. EPA, 2004, p. 8-61). Some studies conducted in urban areas, however, have found significant associations for coarse particles, but not fine particles. The Criteria Document summarizes a case cross-over study (Lin et al., 2002) that found a significant association of $PM_{10-2.5}$ with asthma hospital admissions that was robust to the inclusion of gaseous co-pollutants, but did not report significant associations for $PM_{2.5}$. Unlike more commonly used time series studies, the design used in this study has the advantage of controlling for confounding by having each case serve as its own control. The Criteria Document notes limitations in

available measurement information and adjustment for season that may have influenced the relative results for fine and coarse particles (EPA, 2004, p. 185-186).

For these reasons, and as explained further in section II.B.3 below, EPA believes that it would be inappropriate to presume that all of the effects associated with coarse particles in single pollutant models are actually the result of confounding by fine particles or gaseous pollutants (see also response to similar comments regarding confounding in fine particle studies in section II.A, above).

(4) *Comment:* Some commenters stated that the vast majority of epidemiological studies using $PM_{10-2.5}$ indicator found no statistically significant association with either mortality or morbidity. In the view of these commenters, the evidence of such associations is both extremely limited and subject to serious questions and uncertainties, and the commenters concluded that the record provides no sound basis for establishing a $PM_{10-2.5}$ NAAQS. One commenter stated that even considering only single-pollutant models, 24 of the 32 excess risk estimates for coarse particles plotted in Figure 2 of the proposal (71 FR 2656) fail to achieve statistical significance, and that about half of the statistically significant effects identified in the remaining 6 studies represent an over-interpretation of the author's results by EPA (e.g., Fairley et al., 2003) (Engine Manufacturers Association).

Response: The EPA disagrees with these commenters' approach to assessing health effects evidence as well as their conclusion regarding the lack of a scientific basis to support the continuation of NAAQS to protect against the health effects of thoracic coarse particles. The EPA believes these commenters have focused too narrowly on counting the numbers of epidemiological studies that achieve statistical significance, without regard to other considerations that are important to consider in a comprehensive appraisal of the evidence. Moreover, as discussed in response to comments regarding multiple pollutant studies and models in section III.B of the preamble and in this document, EPA has not focused solely on the results of single pollutant models, but has also carefully examined the implications of multiple pollutant results.

As discussed below, EPA has recognized the distinction between evaluation of the relative scientific quality of individual study results, and evaluation of the pattern of results in a body of evidence. The EPA has done both. The more detailed discussions of individual studies include assessment of the quality of the study, based on criteria for assessment of the epidemiologic studies that are described in Section 8.1.1 of the PM Criteria Document (EPA, 2004). Statistical significance is an indicator of the precision of that study's results, which is influenced by the size of the study, as well as exposure and measurement error and other such factors.

In developing an integrated assessment of the health effects evidence for both $PM_{2.5}$ and $PM_{10-2.5}$, EPA's has emphasized the importance of examining the pattern of results across various studies, and not focusing solely on statistical significance as a criterion. In doing so, EPA recognizes the distinction between evaluation of individual study results and integration of a body of evidence. Individual studies are discussed and evaluated to assess their relative scientific quality; the criteria EPA used for assessing the

epidemiologic studies are described in Section 8.1.1 of the Criteria Document. Statistical significance is an indicator of the strength of the association between PM and the health outcome reported in an individual study. However, it is important not to focus on the results of statistical tests to the exclusion of other information. As observed by Rothman:

> Many data analysts appear to remain oblivious to the qualitative nature of significance testing. Although calculations based on mountains of valuable quantitative information may go into it, statistical significance is itself only a dichotomous indicator. As it has only two values, significant or not significant, it cannot convey much useful information. . . . . Nevertheless, P-values still confound effect size with study size, the two components of estimation that we believe need to be reported separately. Therefore, we prefer that P-values be omitted altogether, provided that point and interval estimates, or some equivalent, are available (Rothman, 1998, p. 334).

The concepts underlying the EPA's approach to integrated assessment of statistical associations reported for the health effects of PM have been discussed in numerous publications, including a recent report by the U.S. Surgeon General on the health consequences of smoking (Centers for Disease Control and Prevention, 2004). This report also cautions against over-reliance on statistical significance in evaluating the overall evidence for an exposure-response relationship.

> Hill made a point of commenting on the value, or lack thereof, of statistical testing in the determination of cause: "No formal tests of significance can answer those [causal] questions. Such tests can, and should, remind us of the effects the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond that, they contribute nothing to the 'proof' of our hypothesis" (Hill, 1965, p. 299).
>
> Hill's warning was in some ways prescient, as the reliance on statistically significant testing as a substitute for judgment in causal inference remains today (Savitz et al., 1994; Holman, et al., 2001; Poole, 2001). To understand the basis for this warning, it is critical to recognize the difference between inductive inferences about the truth of underlying hypotheses, and deductive statistical calculations that are relevant to those inferences, but that are not inductive statements themselves. The latter include p values, confidence intervals, and hypothesis tests (Greenland, 1998; Goodman, 1999). The dominant approach to statistical inference today, which employs those statistical measures, obscures this important distinction between deductive and inductive inferences (Royall, 1997), and has produced the mistaken view that inferences flow directly and inevitably from data. There is no mathematic formula that can transform data into a probabilistic statement about the truth of an association without introducing some formal quantification of external knowledge, such as in Bayesian approaches to inference (Goodman, 1993; Howson and Urbach, 1993). Significance testing and the complementary estimation of confidence intervals remain useful for

characterizing the role of chance in producing the association in hand (CDC, pp. 23-24).

Accordingly, the statistical significance of individual study findings has played an important role in EPA's evaluation of the study's results, and EPA has placed greater emphasis on studies reporting statistically significant results. However, in the broader evaluation of the evidence from many epidemiologic studies, EPA has also emphasized the *pattern* of results for drawing conclusions on the relationship between PM indicators and health outcomes, as well as consideration of the integration of epidemiologic evidence with findings of laboratory studies.

Because EPA places greater weight on US and Canadian studies in making quantitative decisions on U.S. standards, for presentation purposes, the Criteria Document, Staff Paper and proposal notice present graphical results from epidemiologic studies in these two countries, standardized to a common increment of PM, and based on similar analytic strategies (i.e., single-pollutant results). The EPA believes that the examination of multi-pollutant model results and the inherent instability that often occurs in effects estimates for correlated pollutants in such studies justifies the use of single pollutant model results as the most appropriate basis for comparing effects estimates across the three major pollutant indicators (EPA, 2004, section 8.4.3; EPA, 2005a, p. 3-46). This approach was reviewed by CASAC in their review of EPA's Criteria Document and Staff Paper.

As discussed in section 9.2.2 of the Criteria Document, the comparisons across studies and PM indicators in these figures begins with an evaluation of the overall pattern of excess risk results – whether generally positive or centered around zero, the consistency in size of effects estimates, the precision of the studies evidenced in the width of the confidence intervals, with special attention to comparisons of similar effects categories across different pollutant indicators. For example, in comparing effects estimates for PM, $PM_{2.5}$, and $PM_{10-2.5}$, the Criteria Document noted that the effects estimates for the $PM_{2.5}$ and $PM_{10-2.5}$ are generally larger for than those for equal amounts of PM_{10}, "which is consistent with $PM_{2.5}$ and $PM_{10-2.5}$ having independent effects" (EPA, 2004, p. 9-25).

As discussed more fully in section III.B of the preamble to the final rule, in the next comment response and elsewhere in this document, and by a number of commenters, $PM_{10-2.5}$ data are generally subject to greater exposure measurement error than $PM_{2.5}$ and the pollutant gases. In general, this additional 'noise' in the data serves to increase the uncertainty in effects estimates and makes it more difficult to achieve statistical significance for a pollutant that is, in fact, causally linked to health effects (EPA, 2004, p. 5-126). This makes it even more important to examine the overall pattern of results for a pollutant like $PM_{10-2.5,}$ as well as the level of significance This bias is one directional, hence it also means that the evidence is more likely to underestimate the likelihood of causality and the effect estimate than over estimate (EPA, 2005a, p. 3-42).

The EPA's integrative assessment of the evidence on health effects of $PM_{10-2.5}$ is based on the pattern of results from epidemiologic studies conducted in urban areas, and supported by some evidence, albeit limited, from toxicologic studies. The EPA found the

health evidence on $PM_{10-2.5}$ provided support for morbidity effects, with some suggestive evidence for associations with mortality. From the findings of U.S. and Canadian studies (as shown in Figure 2 of the preamble to the proposed rule), the Criteria Document observed: "Associations between $PM_{10-2.5}$ and hospitalization for cardiovascular and respiratory diseases are positive, and the effect estimates are of the same general magnitude as for PM_{10} and $PM_{2.5}$. In general, as was the case for mortality, the confidence intervals for the $PM_{10-2.5}$ estimates are broader than those for associations with PM_{10} or $PM_{2.5}$ and some, but not all, of the associations are statistically significant" (EPA, 2004, p. 9-28). Positive and statistically significant associations were reported with hospitalization for cardiovascular and respiratory diseases, including ischemic heart disease and pneumonia.

Figure 2 also includes positive, but not statistically significant associations with hospitalization for heart failure and stroke, and a nearly significant association with asthma hospitalization (in a GLM model – a significant association was reported in a GAM/natural splines model). A series of positive associations was also reported with cardiovascular mortality; the associations were statistically significant in two studies, and of similar magnitude but not reaching significance in the other three studies. As observed in the preamble, associations with total mortality were not as consistently positive. Considering also the evidence from studies of respiratory symptoms as well as those conducted in countries outside the U.S. and Canada, EPA believes that the findings represent a pattern that clearly links short-term exposures to urban/industrial $PM_{10-2.5}$ with morbidity and cardiovascular mortality.

Thus, EPA disagrees with the commenters' assertion that the available evidence provides "no sound basis" for a $PM_{10-2.5}$ standard. The fact that a number of the effect estimates are not statistically significant, particularly for total mortality, does not undermine this conclusion. This conclusion reflects an overly narrow view of how to evaluate the evidence, as compared to EPA's more integrated view of an entire body of evidence.

(5) *Comment:* Some commenters expressed the view that the epidemiologic studies were flawed by the reliance on data from central monitors to estimate community-level exposures to coarse fraction particles. According to the commenters, use of central monitoring data generally results in an overestimation of exposure due to the significant spatial variability associated with coarse particle distributions. The commenters claim the high spatial variability, limited transport, and overestimation inherent in the use of central monitors would invalidate any statistical associations found between ambient coarse PM data and adverse health effects. Studies in Detroit and Coachella Valley are specifically cited as providing only limited informational value as a result of this bias.

Response: The Criteria Document and Staff Paper contain detailed analyses of the spatial variability of coarse particle concentrations, as well as other issues that generally result in greater exposure measurement error for coarse particles as compared to fine particles (EPA, 2004, p. 3-52-53, Appendix 3A; EPA, 2005a, pp. 2-36-40, 2-70-73). As noted in the preamble to the final rule, while EPA agrees that coarse particle measurements from central monitors is subject to potentially large measurement error when used to reflect

population exposures in epidemiologic studies, the Agency disagrees with the commenters' assessment of the direction of the resulting bias and with their conclusion that any statistically significant associations between centrally monitored air quality concentrations and adverse health effects measured in these studies are invalid as a result. This issue received substantial attention in the Criteria Document (EPA, 2004, section 8.4.5). The Criteria Document concluded that such measurement errors are more likely to *underestimate* the strength and the significance of any association between coarse particles and any adverse health effects observed in the study, thereby decreasing the likelihood of an association reaching statistical significance and the likelihood of a false identification of an association (EPA, 2004, pp. 5-126, 8-341). While the spatial variation of coarse particle data is larger than for fine particles, the Staff Paper notes that, on a day-to-day basis, coarse particle data from monitor sites within an urban area can be fairly well correlated, even when substantial differences exist in the absolute concentrations between the sites (EPA, 2005a, p. 3-41). The signal that drives statistical associations between ambient concentrations and health effects in time-series studies is the day-to-day changes in concentration, not the absolute daily values. The staff concluded that appropriately located central $PM_{10-2.5}$ monitors can adequately characterize such day-to-day changes (EPA, 2005a, p. 3-41).

Time-series epidemiologic studies (e.g., such as the studies conducted in Detroit and Coachella Valley referenced by the commenter) evaluate associations between day-to-day changes in air pollution and health outcomes. In accord with the principle explained in the previous paragraph, the EPA carefully evaluated the monitor locations and correlations between monitoring sites (where multiple sites were available) in considering the epidemiologic evidence on effects of urban or industrial $PM_{10-2.5}$. As observed in Ross and Langstaff (2005), in the Detroit analysis, the researchers conducted a detailed evaluation of data from numerous sites across the Detroit metropolitan area, including TSP data from 14 monitoring stations (Lippmann et al., 2000). The authors observed "The Windsor sites (y and z) are located within a few miles of the clusters of Detroit sites. Thus, there is no reason to treat the Windsor sites any differently from the Detroit sites on the basis of their locations." (p. 9). In fact, the Windsor sites were closer to downtown Detroit than many suburban sites. Lippmann and colleagues (2000) observe that concentrations at TSP sites could vary by a factor of 2 in magnitude, but the correlations between sites ranged from 0.55 to 0.77 (p. 20). This is similar to the data presented in Ross and Langstaff (2005) for $PM_{10-2.5}$ in this study, which showed that $PM_{10-2.5}$ concentrations were greater in magnitude at the sites nearest the central city area, but that the data were fairly well correlated between sites.

> In reacting to this same issue, the California Air Resources Board stated:
>
> The current scientific consensus suggests that measurement of coarse particles will typically involve greater errors than that of fine particles. However we reject the …. implication that therefore these studies are not reliable. In fact, the larger measurement error, which is likely to be random, would make it more difficult to find an association with mortality. It is well accepted in the epidemiological literature that such measurement error will tend to obscure a relationship between

> an exposure and a given health outcome, assuming that such a relationship exists. Therefore, the measurement error argument cannot be used to nullify an effect that has been observed. If anything, it is likely that the real effects are likely to be larger than those that were estimated (CARB, p. 11).

EPA agrees with this analysis of the issue. Therefore, for the purposes of determining whether public health protection is warranted in light of the available evidence, EPA believes that it has interpreted the evidence from these epidemiologic studies correctly, and that the evidence of statistically significant relationships between exposure to urban or industrial coarse particles and adverse health effects is sufficiently strong to support continued regulation of coarse particles.

(6) *Comment:* The National Stone, Sand, and Gravel Association listed six specific reasons for their recommendation that the current standards be revoked and no new coarse standards be established: (1) the lack of an ambient air reference method that accurately indicates coarse particulate matter concentrations; (2) the lack of adequate estimates of coarse particulate matter concentrations, especially in arid regions in the Western U.S. and rural areas throughout the U.S.; (3) information demonstrating that crustal materials of geologic origin are the dominant constituents in coarse PM; (4) the lack of adequate scientific information in the Criteria Document concerning the speculated role of coarse PM as a carrier for toxic constituents in urban areas; (5) the major regional differences in the levels of crustal material in coarse PM and in the ratios of fine and coarse PM; and (6) the technical difficulty in preparing effective coarse PM control strategies for a pollutant for which the emission inventories are very incomplete and uncertain.

Response: Several of the specific concerns raised by this commenter have been effectively resolved by the Administrator's decision to retain the current 24-hour PM_{10} standard. The EPA notes in response to the commenter's first two concerns that the FRM for PM_{10} has been in place since 1987, and there are two decades of PM_{10} air quality data available from a national network of more than 1200 PM_{10} monitors. Similarly, with regard to the last concern noted by the commenter, EPA notes first of all that those kinds of technical difficulties associated with implementation which are not connected to public health protection are not valid considerations in the Administrator's decisions regarding the NAAQS for PM or any other pollutant. In any case, the decision to retain PM_{10} rendered the concerns raised by the commenters moot because EPA and the States have 19 years of data regarding PM_{10} air quality concentrations, emissions inventories, and the availability and effectiveness of control strategies.

The other concerns raised by the commenter relate to the relative proportion of crustal materials in any ambient mix of $PM_{10-2.5}$, the potential for contamination of $PM_{10-2.5}$ in urban areas, and geographic variations in the composition of PM_{10}. The EPA agrees with the commenter that crustal materials generally dominate $PM_{10-2.5}$ by mass; however, the available evidence suggests that these crustal components become contaminated by other constituents in urban areas, where the toxicity of the ambient mix of $PM_{10-2.5}$ has been clearly demonstrated. Furthermore, the relative toxicity of uncontaminated crustal materials remains unclear: there is largely an absence of evidence regarding the health

effects associated with exposure to these materials. The EPA agrees with the commenter that there are substantial differences in the percentage of crustal materials in $PM_{10-2.5}$ in different regions, and in the ratios of fine and coarse PM. However, EPA notes that existing health studies show significant effects of urban or industrial coarse particles in all of the major regions of North America—including eastern urban (Detroit, Toronto) and industrial (Steubenville) areas, the average across the cities in the Harvard Six Cities study, the Pacific Northwest (Seattle, Anchorage, Spokane, tri cities), and the Southwest and California (Phoenix, Coachella, Tuscon, Reno). This evidence is broad enough to suggest that health effects associated with urban or industrial coarse particles are experienced in all regions, and occur despite the differences in composition and relative $PM_{2.5}$ levels cited by the commenter.

(7) *Comment:* Some commenters criticized EPA's risk assessment. These commenters stated that current short-term epidemiologic data are insufficient to serve as the basis for a scientifically sound quantitative risk assessment. In the absence of an adequate risk assessment "indicating a significant risk that adverse effects will occur at current exposure levels and that the concentration levels chosen by EPA are necessary to alleviate such risk," these commenters believe that EPA lacks sufficient evidence to establish a standard on the basis of the current short-term data (Coarse Particle Coalition, p. 43).

Response: EPA disagrees with these commenters. For reasons outlined in the preamble to the final rule, EPA believes the evidence is more than sufficient to justify retaining a standard to protect against the health effects associated with coarse particles. In addition to the sections of the opinion already cited, see also 283 F. 3d at 373-74 upholding EPA's decision not to use its quantitative risk assessment as a basis for establishing the 24-hour standard for $PM_{2.5}$, and thus upholding the standard in the absence of a quantitative risk assessment. Although the data are weaker than for fine particles and subject to greater measurement error, in several of the studies where comparisons are possible, the normalized relative risk estimates for coarse particles from the new studies in the Criteria Document often fall into a similar range as those for fine particles (EPA, 2004, p. 8-64; EPA, 2005a, pp. 3-13 and 3-20). Furthermore, as summarized above, EPA did produce a risk assessment for thoracic coarse particles, which was reviewed by CASAC and included in the Staff Paper (EPA, 2005a, Chapter 4). While the limited number of cities and the significant uncertainties noted in the risk assessment and the proposal limit their quantitative usefulness, EPA concluded that the risk assessment results for the two cities in the assessment that did not meet the current PM_{10} standards are indicative of risks that can reasonably be judged to be important from a public health perspective.

With respect to the significance of the risk of harm at levels of exposure allowed by the current standards, as explained in section III.D.2 of the preamble and in other comment responses, the level of protection afforded by the current 24-hour PM_{10} standard was chosen as the mortality effects observed in coarse particle epidemiologic studies are generally associated with exposure levels that exceed the current standards, and morbidity effects are generally associated with exposure levels that exceeded the current standards on only a few occasions. The decisions to retain the current level of the PM_{10}

standard was therefore based on conclusions drawn from the studies, as compared to a quantified risk assessment, just as it was in the 1997 NAAQS for $PM_{2.5}$, which was upheld in ATA III. Section III.D.2 also explains why the same PM_{10} level is appropriate for non-urban type ambient mixes of coarse particles.

(8) *Comment:* Some commenters felt the uncertainties in the evidence, including the perceived problems with the risk assessment noted above, were so substantial that they precluded setting a thoracic coarse particles NAAQS at the present time. These commenters stressed that EPA's authority stretches only to setting standards that can be demonstrated to be "requisite to protect the public health"—i.e. neither more nor less stringent than necessary. These commenters argued that while EPA may exercise its judgment about future risks and set standards that are preventive in nature, as long as adequate scientific rationale is presented, the Agency does not have the authority to engage in "crystal ball speculation" in the absence of support in the record considered as a whole. (See e.g., Coarse Particle Coalition, p. 8-9, citing Lead Industries Assoc v. EPA, 647 F. 2d 1130, 1146-7 (D.C. Cir. 1980), NRDC v. EPA, 902 F.2d 962, 968, 971 (D.C. Cir. 1990) and Ethyl Corp. v. EPA, 541 F.2d 1, 13 (D.C. Cir. 1976).) These commenters stated that the NAAQS must address only "significant risk", not any risk, and that EPA has failed to demonstrate that coarse particles pose a significant enough risk to human health to warrant a coarse particle standard.

Response: As noted in the preamble to the final rule, there is no requirement that EPA must demonstrate significant risk before promulgating a NAAQS . See also comment response (9) below. The EPA's reliance on evidence from peer-reviewed scientific studies in this review cannot be considered "crystal ball speculation." See, e.g., Lead Industries Assoc. v. EPA, 647 F.2d at 1155: "the statutes and common sense demand regulatory action to prevent harm, even if the regulator is less than certain that harm is otherwise inevitable."

(9) *Comment:* Following discussion of legislative history, case law, and the Supreme Court's decisions in Whitman and Industrial Union AFL-CIO (Benzene), some commenters concluded that Congress and the courts have required EPA to: 1) limit standards to protection against significant national public health risks; 2) support factual determinations with substantial scientific evidence in the record; and 3) in cases where scientific uncertainty prevents establishment of relevant facts, support policy judgments with reasonable extrapolations based on reliable evidence after considering all of the evidence in the record as a whole.

Response: While EPA agrees with much of the commenters' summary of legislative history and legal precedent involving the NAAQS, the summary fails to include other aspects of section 109 and significant additional case law relevant to the issue raised. For example, section 109 expressly requires that the standards provide an "adequate margin of safety", which requires that the NAAQS "protect against effects which have not yet been uncovered by research and effects whose medical significance is a matter of disagreement." Lead Industries, 647 F. 2d at 1154; see also ATA III, 283 F. 3d at 369.

One commenter inferred from the Benzene case that "EPA must set concentration limits based on scientific data and analyses adequate to ensure that the potential public health risk can 'be quantified sufficiently to enable [EPA] to characterize it as significant in an understandable way.'" This is at odds with the D.C. Circuit's post-Whitman opinion, ATA III. The court held repeatedly that EPA is not required to quantify levels of risk or harm in establishing NAAQS. See, e.g. 283 F. 3d at 369, 378.

Section 109 requires that the Administrator set a standard that is requisite to protect public health with an adequate margin of safety. In determining what standard is requisite, the Administrator does take into account the significance of the risks to public health. Based on his evaluation, he determines what standard is requisite to protect public health with an adequate margin of safety in light of these risks. However, the Administrator is not required to follow any single approach such as that suggested by commenters.

In this case, the Administrator has explained his judgment of the significance of the public health risk presented by exposure to coarse particles. As discussed in Section III.B and III.C.2 of the preamble to the final rule, the degree of health evidence and resulting public health concern vary for different kinds of ambient mixes of coarse particles.

The EPA has set out elsewhere the reasons for providing protection from exposure to ambient mixes dominated by the types of thoracic coarse particles found in urban or industrial areas. The evidence indicates that it is appropriate to target protection from thoracic coarse particles principally towards those types of coarse particles that have been demonstrated to be associated with significant adverse health effects, specifically urban and industrial ambient mixes of coarse particles. With respect to other ambient mixes, some commenters have argued that the scientific evidence, including epidemiologic, dosimetric, toxicologic, and occupational studies, demonstrates that non-urban mixes of thoracic coarse particles are harmful, and therefore that EPA should maintain an unqualified indicator. Other commenters argue that the evidence demonstrates that non-urban mixes of thoracic coarse particles are benign and therefore EPA should retain a qualified indicator. The EPA disagrees with both of these views regarding the strength of the evidence. The existing evidence is inconclusive with regard to whether or not community-level exposures to thoracic coarse particles are associated with adverse health effects in non-urban areas. In light of this uncertainty and the need for caution in considering the evidence, and recognizing the large population groups potentially exposed to non-urban thoracic coarse particles and the nature and degree of the health effects at issue, it is the judgment of the Administrator that the proper response to this body of evidence is to provide some protection from thoracic coarse particles in all areas. Congress "specifically directed the Administrator to allow an adequate margin of safety to protect against effects which have not yet been uncovered by research and effects whose medical significance is a matter of disagreement….Congress' directive to the Administrator to allow an 'adequate margin of safety' alone plainly refutes any suggestion that the Administrator is only authorized to set primary air quality standards which are designed to protect against health effects that are known to be clearly harmful." Lead Industries v. EPA, 647 F.2d at 1154-55; see also American Petroleum Inst. v.

Costle, 665 F.2d at 1186 ("in setting margins of safety the Administrator need not regulate only the known dangers to health").

The EPA agrees with the commenters that the Administrator's conclusions "must be supported by the record, and he may not engage in sheer guesswork." API v. Costle, 665 F. 2d at 369. The criteria for judicial review, however, are spelled out in section 307(d) of the CAA. In this case, Section III of the preamble explains in some detail EPA's scientific and technical basis for the final decisions on coarse particle primary standards. In this proceeding, the Administrator has taken an approach for coarse particles consistent with the "preventative and precautionary nature of the Act," American Lung Ass'n, 134 F. 3d at 389, in adopting an unqualified indicator for coarse particles although the strength of the evidence as to coarse particle effects differs considerably with respect to different types. See section III.C.2 of the preamble to the final rule.

This decision is not based on "sheer guesswork." The preamble sets out the variety of evidence EPA has considered, covering dosimetry, toxicology, and epidemiology studies, as well as other scientific information. The preamble (see especially section III.B) discusses how this body of evidence provides the basis for providing protection from exposure to ambient mixes found typical of urban or industrial areas. With respect to other ambient mixes, some commenters have argued that the scientific evidence, including epidemiologic, dosimetric, toxicologic, and occupational studies, demonstrates that non-urban mixes of thoracic coarse particles are harmful, and therefore that EPA should maintain an unqualified indicator. Other commenters argued that the evidence demonstrates that non-urban mixes of thoracic coarse particles are benign and therefore EPA should retain a qualified indicator. The EPA disagrees with both of these views of the strength of the evidence. The existing evidence is inconclusive with regard to whether or not community-level exposures to thoracic coarse particles are associated with adverse health effects in non-urban areas. In light of this uncertainty and the need for caution in considering the evidence, and recognizing both the large population groups potentially exposed to non-urban thoracic coarse particles and the nature and degree of the health effects at issue, it is the judgment of the Administrator that the proper response to this body of evidence is to provide some protection from thoracic coarse particles in all areas, in keeping with requirements of the Clean Air Act.

As summarized in the preamble to the final rule, EPA believes that in light of the entire body of evidence concerning thoracic coarse particles, and given the potentially serious nature of the health risks posed by at least some thoracic coarse particles and the potential size of the population exposed, it is appropriate to provide some protection for all types of thoracic coarse particles, consistent with the requirement of the Act to allow an adequate margin of safety. See section II.B.2.b below for a detailed discussion of the scientific issues surround the coarse particle indicator.

(10) *Comment:* One commenter stated that in adopting ambient standards, EPA must demonstrate that they are necessary to address a nationwide public health problem and are capable of uniform national application. The commenter argued that Congress did

not intend for EPA to adopt national standards to address local or site-specific concerns, which were expressly left to the states (Coarse Particle Coalition).

Response: As noted above, the decision to retain the national PM_{10} standard is premised in part on the view that across the nation, all ambient mixes of coarse particles warrant some degree of protection. Exposure to coarse particles occurs all across the nation, and is not a local or site-specific concern. While the degree of concern clearly varies across the nation, it is an issue of nationwide scope. In the case of coarse particles, providing the appropriate variable level of allowable concentrations is best accomplished through the use of the PM_{10} indicator which, as explained in section III.C.3.b of the preamble to the final rule, appropriately targets protection at urban areas where the evidence of effects from exposure to coarse particles is strongest and still affords protection in rural and non-urban areas.

b. Indicator

Many commenters expressed views on the type of indicator that would be most appropriate to protect against the effects of thoracic coarse particles. Most commenters did not disagree with EPA's proposal to shift from a PM_{10} indicator to an indicator focused specifically on coarse fraction particles, i.e. $PM_{10-2.5}$. However, many commenters expressed views on whether it was appropriate to qualify the $PM_{10-2.5}$ indicator to focus on particles from particular sources or typical of certain areas. Some commenters opposed EPA's proposal to qualify the proposed $PM_{10-2.5}$ indicator to include any ambient mix of $PM_{10-2.5}$ that is dominated by resuspended contaminated dust from high-density traffic on paved roads and PM generated by industrial sources and construction sources, and to exclude any ambient mix of $PM_{10-2.5}$ that is dominated by rural windblown dust and soils and PM generated by agriculture and mining sources. These commenters advanced both scientific and legal/practical arguments against a qualified indicator. Other commenters supported the proposed qualifications, again on both scientific and legal grounds. A few commenters supported retaining the PM_{10} indicator, in some cases with adjustment to subtract $PM_{2.5}$ to avoid double regulating the fine fraction, to satisfy a concern voiced by the D.C. Circuit in ATA I.

The preamble to the final rule presents the Agency's response to these views (see section III.C), discussing in detail: 1) the appropriateness of shifting to a $PM_{10-2.5}$ indicator at this time; 2) the strengths and limitations of the scientific evidence on differences between thoracic coarse particles derived from different sources and the health effects associated with different particle mixes; 3) the advice of CASAC on the appropriate indicator to adopt given the state of scientific knowledge at this time; and 4) other policy and legal considerations connected to the indicator for thoracic coarse particles. More detailed responses to the full range of significant issues raised in these comments are presented below.

i. Scientific arguments against a qualified coarse particle indicator

Numerous commenters advanced scientific arguments against adopting a qualified indicator for thoracic coarse particles as proposed. In the view of these commenters, EPA either lacked sufficient evidence to rule out health effects from coarse particles outside of urban areas,

or had ignored evidence suggesting that non-urban coarse particles are harmful. Because the Administrator has decided to retain the current unqualified PM_{10} indicator, rather than adopting a qualified $PM_{10-2.5}$ indicator as proposed, many of the concerns raised by these commenters are now moot, although in many cases these same concerns support EPA's reasons for retaining the unqualified PM_{10} indicator. The EPA has addressed these issues in section III.C.3 of the preamble, and here provides more detailed responses to the following specific points raised by commenters:

(1) *Comment:* Some commenters expressed the view that the scientific evidence does not support drawing a distinction between "urban" and "rural" particles with respect to composition, toxicity, or associated adverse public health effects. Regarding the nature of the evidence on urban and rural particles, commenters made the following points:

- The EPA misinterpreted several key studies, such as Gordian et al. (1996), Choudhury et al. (1997), Ostro et al. (2003), Smith et al. (2000) and Mar et al. (2003), which linked thoracic coarse particles to adverse health effects in environments where crustal components formed a significant part of the ambient mix of $PM_{10-2.5}$. Regarding the results of their study of Anchorage, Gordian et al. (1996) actually state "This study is one of the few which shows that silicaceous or earth crustal coarse particulate pollution may have an acute, adverse health effect on respiratory health even at relatively low ambient concentrations." Furthermore, the study conducted by Ostro et al. (2003) in Coachella Valley, which found statistically significant associations between exposure to coarse particles and mortality, provides direct evidence of harm from exposure to rural particles, which dominate the mix in this area.
- The lack of statistically significant mortality results in results of Schwartz et al. (1999) is attributable to avoidance behavior (i.e., people may stay inside during dust storms) and the study might have drawn different conclusions if morbidity endpoints had been considered. The EPA's conclusion, based on this single study, that "mortality and possibly other health effects are not associated with thoracic coarse particles from dust storms or other such wind related events" was too sweeping and too definitive. Other studies which used respiratory morbidity as an endpoint (Gordian et al., 1996; Choudhury et al., 1997) found associations between medical visits and PM_{10} in Anchorage, Alaska, where PM_{10} is primarily crustal dust. Furthermore, Hefflin (1994), which examined hospitalizations for bronchitis and sinusitis during dust storms in Southeast Washington in 1991, did find a small increase in these impacts. This study directly contradicts the conclusions drawn from Schwartz et al. (1999). Commenters note several instances where a lack of response to episodic high fine or coarse particles is consistent with avoidance behavior (Ostro et al. 1999, which found lower effects for high wind dust days, citing both Gordian et al. 1996; and Hefflin et al. 1994 as support, and anecdotal evidence from Alaska concerning no increase of mortality or morbidity after a fire induced fine episode
- The EPA has failed to explain why the evidence from occupational studies, which was used to justify the need for a standard as upheld in ATA I[5], is no longer relevant.

[5] Commenters cited a statement in the proposal that "in the 1987 review, EPA found that occupational and toxicological studies provided ample cause for concern related to higher levels of thoracic coarse particles" (71 FR 2654).

The American Lung Association claims that the likelihood of overlap between occupational and community exposures is especially high for the agricultural and mining sectors and note that, as proposed, the $PM_{10-2.5}$ NAAQS would prohibit control of emissions from those sectors to meet the NAAQS even if air quality concentrations reached occupational levels (American Lung Association et al., p. 103-108, and the Center on Race, Poverty and the Environment, citing ten studies or reviews of occupational exposures for agriculture and mining).

- With regard to volcanic ash, EPA relied too heavily on a few animal and in vitro studies of Mt. St. Helens ash that found the ash had little toxicity. There are epidemiologic studies that contradict these, including studies of people who worked in the Mt. St. Helens' forests after the eruption that found respiratory problems associated with exposure to ash (Bernstein at al., 1986, Buist et al. 1986).
- Furthermore, EPA should not equate exposure to volcanic ash to exposure to coarse particles emitted from agricultural and mining industries. Volcanic ash lacks many of the organic components typical of rural coarse PM, including pesticides and PAHs. Agricultural or mining activities produce a variety of coarse particle components, including endotoxins, pesticides, and metals, that are associated with adverse health effects. In fact, effects noted in epidemiologic studies of thoracic coarse particles, such as Mar et al. (2003), occurred in areas dominated by agricultural or mining dusts.
- In general, coarse particles in rural and other non-urban areas are not generally "uncontaminated materials of geologic origin" or "uncontaminated natural crustal dusts." The coarse PM found in rural areas is commonly contaminated with the same toxic components as particles found in urban areas, as well as additional toxic contaminants such as molds, fungi, endotoxins, pesticides, and carbonaceous compounds including polycyclic aromatic hydrocarbons (PAHs), all of which are associated with rural sources and have been shown to produce toxic effects (citing Monn and Becker, 1999; Soukup and Becker, 2001; Horvath et al., 1996; Offenberg and Baker, 2000; Eleftheriadis and Colbeck, 2001).
- Studies of the composition of coarse particles in particular locations, such as Owens and Mono Lakes in California, clearly show the dangerous nature of rural particles. Coarse particles from these areas are contaminated by heavy metals, arsenic, and other toxic contaminants, but would be excluded from the proposed qualified indicator.

Response: The EPA's position on the relative health risk of urban and rural coarse particles is informed by the weight of the evidence, and in particular by the epidemiological studies, all of which were conducted in urban or industrial areas. The EPA does not agree with these commenters that several epidemiologic studies conducted in urban areas subject to high proportions of crustal materials (e.g. Coachella Valley, Phoenix, Anchorage, Tri-cities Washington) provide direct evidence of harm from non-urban or rural crustal material. While EPA acknowledges that crustal particles may have dominated the ambient mix in some of the locations in which these studies were done, it is also the case that these areas are all urban, so the crustal materials in the ambient mix typically would be contaminated by metals, tire and break wear, and other combustion byproducts. At the same time, EPA notes that CASAC cited the studies by Ostro et al.

(2000, 2003) as suggestive of health effects associated with exposure to rural crustal materials: "Little is known about the potential toxicity of rural dusts, although the 2000 and 2003 Coachella Valley, CA studies from Ostro et al. showed significant adverse health effects, primarily involving exposures to coarse-mode particles arising from crustal sources" (Henderson, 2005a, p. 4). Thus while EPA does not agree with these commenters that these particular epidemiologic studies demonstrate that non-urban or rural crustal particles are harmful, at the same time EPA believes the studies do suggest the need to be cautious in interpreting the epidemiologic and other evidence.

The EPA agrees with these commenters that the several published studies cited above find reduced effects estimates on very high concentration days, suggesting that it is possible that the lack of mortality effects on dust storm days observed in Schwartz et al. (1999) may be due to avoidance behavior. As noted in the proposal (71 FR 2666), there is a possibility that people may reduce their exposure to ambient particles on the most dusty days. This argues for caution in interpreting the results of Schwartz et al. (1999) on this issue.

The EPA continues to find it inappropriate to assume that effects observed in occupational studies should be considered representative of effects that would occur at community exposure levels. Cf. Lead Industries, 647 F. 2d at 1166-67 (EPA properly disregarded comments that certain lead particles are insoluble, or non-respirable because of size when only limited evidence was presented that these particles are insoluble and non-respirable and that evidence came from occupational studies and therefore was of little relevance in setting standards for the entire population). However, EPA agrees with commenters that the number of occupational exposure studies demonstrating adverse effects lends further support to a cautious approach in considering revisions to the standards affording protection from thoracic coarse particles.

The EPA agrees that particles in non-urban locations can contain varying amounts of potentially toxic materials cited by commenters. The EPA's assessment of the available information on the composition of urban and rural particles found generally higher levels of contaminants from combustion, industrial processes, traffic, and in some cases, biological materials ground up by traffic (EPA, 2005a, pp. 2-44 to 46), activities more typically associated with urban areas. However, the relative contribution of the higher levels of these specific contaminants (as opposed to other coarse components) to the effects observed in urban and industrial community epidemiological studies has not been established. Even less is known about the relative toxicity of coarse contaminants in rural areas and how it may vary in different locations around the U.S. This also argues for the approach taken by the Administrator on the standards.

The EPA also agrees with commenters that thoracic coarse particles in non-urban areas can deposit in the regions of the lung of most concern and may become contaminated with a wide variety of toxic materials (EPA, 2004, p. 8-344). With regard to the toxicity of particles in particular non-urban locations, EPA agrees with the commenters that the scientific evidence clearly shows that crustal material associated with some locations, such as the dry lakebeds of Owens and Mono Lakes, can be highly contaminated with

metals, salts, and other toxic constituents. The EPA agrees with commenters that the potential toxicity of these components is well recognized. However, EPA also notes that such locations tend to be isolated and not representative of other locations. Cf. ATA III, 283 F. 3d at 374-75 (form of NAAQS need not be directed at unusual extreme events); S. Rep. No. 91-1196, 91st Cong. , 2d Sess. 10 (1970) (NAAQS is not intended to protect most sensitive person in a vulnerable subpopulation).

(2) *Comment:* Several commenters objected to the proposed regulatory definition for the qualified $PM_{10-2.5}$ indicator, stating that the Agency failed to establish what chemical or physical component or components of coarse particulate matter are responsible for "alleged" health effects. According to the Alliance of Automobile Manufacturers (p. 9), "by proposing to establish an urban coarse standard NAAQS that cannot be identified or measured in terms of any physical, chemical, toxicological, or other such properties, the NPRM does not answer the hard, but necessary and legally required, predicate questions," in particular questions of causality.

Response: As noted in the preamble to the final rule, EPA has concluded that the limited available information is not sufficient to define an indicator for thoracic coarse particles solely in terms of metrics other than size-differentiated mass, such as specific chemical components. In evaluating relevant information from atmospheric sciences, toxicology, and epidemiology related to thoracic coarse particles, the Staff Paper noted that there appear to be clear distinctions between (1) the character of the ambient mix of particles generally found in urban areas as compared to that found in non-urban and, more specifically, rural areas, and (2) the nature of the evidence concerning health effects associated with thoracic coarse particles generally found in urban versus rural areas. Based on such information, and on specific initial advice from CASAC (Henderson, 2005a), the Staff Paper considered, and EPA proposed, a more narrowly defined indicator for thoracic coarse particles that would focus on the mix of such particles that is characteristic of that generally found in urban areas where thoracic coarse particles are strongly influenced by traffic-related or industrial sources. However, for the reasons outlined in section III.C. of the preamble to the final rule, the Administrator ultimately decided not to revise the current PM_{10} indicator. Given the Administrator's final decision to retain the PM_{10} indicator, the concerns raised by these commenters are moot, although they do support EPA's decision to retain the unqualified PM_{10} indicator.

(3) *Comment:* A number of commenters referenced "new" epidemiologic studies which were not included in the Criteria Document in support of their arguments in favor of an unqualified $PM_{10-2.5}$ indicator. Specifically, the commenters pointed to recent epidemiologic studies showing statistically significant adverse health effects from exposure to coarse particles of varying composition, such as one study that found an association between exposure to volcanic ash and wheeze and exercise-induced bronchoconstriction (Forbes et al., 2003). In addition, commenters cited several "new" studies of health effects associated with exposure to coarse particles during Asian dust storms (Derbyshire, 2003; Chen Y-S et al., 2004; Chen and Yang, 2005; Yang C-Y et al., 2005; Chang et al., 2006).

Response: The EPA has already noted that it is basing the final decisions in this review on the studies and related information included in the PM air quality criteria that have undergone CASAC and public review, and will consider the newly published studies for purposes of decision making in the next PM NAAQS review. For further discussion of this issue, see section I.C. of the preamble. In provisionally considering the results of these studies, however, EPA observes most of the publications are reporting increases in various health outcomes in the city of Taipei, Taiwan on days following Asian dust storms. While the pattern of associations was generally positive, most reported associations in this group of studies were not, in fact, statistically significant. The average levels on days without dust storms suggest the area is well above levels allowed by the U.S. PM_{10} standards. More importantly for the issue raised by commenters, without a more complete assessment, it is difficult to determine the extent to which the increased dust was or was not contaminated by urban sources in a city with a population of several million people.

Forbes et al. (2003) reports a significant association between children reporting having wheezed in the past 12 months with reported exposure to volcanic ash in Montserrat. The authors do not report data on air pollutant concentrations, but observe that during ashfall, PM_{10} concentrations could reach 150 mg/m^3 (a value 1000 times the PM_{10} level allowed in this rule), "when visibility was temporarily lost" (Forbes et al., 2003, p. 207).

In provisionally considering the results of these studies based on an initial incomplete assessment, it appears that any health effects associations they reveal for contaminated or uncontaminated coarse particles are occurring at concentrations considerably above the level EPA has chosen in this standard decision.

(4) *Comment:* Commenters also pointed to "new" toxicologic studies such as Horwell et al. (2003), Schins et al. (2004), Veranth et al. (2004, 2006), Becker et al. (2005), Labban et al. (2004, 2006), and Steerenberg et al. (2006), arguing that toxicological studies do not show consistent differences between urban and rural dusts. Veranth, in discussing his own work and other recent studies, stated that laboratory toxicology studies have identified both anthropogenic-urban and agricultural-mining-rural particles that are potent for inducing inflammatory responses in airway tissues and cells. In the commenters' view, the distinction between regulated and exempt sources of coarse PM is not supported by toxicology, and all coarse PM sources should be included in the indicator.

Response: The EPA has already noted that it is basing its final decisions in this review on the studies and related information included in the PM air quality criteria that have undergone CASAC and public review, and will consider the newly published studies for purposes of decision making in the next PM NAAQS review. However, in provisionally evaluating commenters' arguments, EPA notes that the EPA Provisional Assessment of new studies found that some of these studies, including two *in vitro* studies noted above (Veranth et al., 2004; Veranth et al., 2006) provide evidence that both urban and rural particles can both induce cellular responses. In provisionally considering the potential implications of such studies, EPA also notes that while these new results are of interest, such toxicologic tests do not permit definitive conclusions regarding the potential effects

of such materials on human populations at current ambient levels found in rural areas of the U.S.

ii. Scientific arguments supporting a qualified coarse particle indicator

Some commenters expressed conditional support for a qualified indicator. Most of these commenters primarily argued that there is insufficient scientific evidence to warrant retaining any standard for thoracic coarse particles at this time. However, the commenters stated that if EPA were to adopt any standard for coarse particles, they believed the coarse particle indicator should be qualified to include certain types of sources and to exclude other types of sources. In support of this position, commenters advanced the following specific arguments:

(1) *Comment:* Some commenters cited differences in the composition of the mix of particles in urban areas versus the mix of particles in non-urban areas, noting that though the coarse particle mix in urban areas also contains significant crustal materials, it is contaminated by a wide variety of industrial and combustion-related byproducts, such as metals and organic materials (tire and break wear, vehicle exhaust, industrial emissions, residential fuel combustion). These commenters noted that studies conducted in urban areas have linked health effects specifically to these urban-industrial contaminants. For example, the American Farm Bureau Federation cited the distinction between studies that found health effects related to traffic emissions in urban areas.

Response: The EPA agrees that the strongest available evidence relates to the toxicity of the ambient mix of coarse particles found in urban environments. The limited evidence available from epidemiologic and toxicologic studies indicates exposure to ambient thoracic coarse particulate in urban areas is associated with health effects, and the health evidence more strongly implicates coarse particles from urban types of sources such as resuspended contaminated dust from high-density traffic on paved roads and PM generated by industrial sources and construction sources than coarse particles from uncontaminated soil or geologic sources. In addition, EPA recognizes that urban sources may significantly alter both the relative quantity and character of crustal and natural biological materials in ambient mixes in urban areas. Metals and other contaminants such as elemental carbon tend to appear in higher concentrations in the urban $PM_{10-2.5}$ mix, and vegetative materials are ground and resuspended by traffic-related activities into forms not common outside urban areas.

(2) *Comment:* Some commenters argued that EPA should focus regulatory efforts on the sources known to be associated with toxic coarse particles, especially traffic. Several commenters stated that while the Staff Paper and CASAC letters specifically referred to the need to regulate urban road dust, they were vague with respect to the "industrial" or "construction" emissions that would also be included in the proposed qualified indicator, and had failed to provide an adequate scientific rationale for including these sources. Some of these commenters also argued that EPA failed to indicate how it would distinguish coarse particle emissions from construction sites that are of crustal geologic origin from other sources of windblown dust or why differential treatment of emissions in the former category was appropriate. The commenters concluded that EPA should

explain and justify which industrial or construction emissions would be regulated, or should limit applicability of the standard to urban road dust.

Response: As noted in the preamble to the final rule, the strongest available evidence regarding health effects of thoracic coarse particles points to the toxicity of the ambient mix of coarse particles found in urban environments. Though limited, the evidence available from epidemiologic and toxicologic studies indicates exposure to the total ambient mix of thoracic coarse particles in urban areas is associated with health effects, which includes not just urban road dust but also emissions from industrial and construction sources, and the crustal components of the ambient mix which may come from outside urban areas but become contaminated. Furthermore, in the CASAC request for reconsideration letter to the Administrator, the Committee noted, "The CASAC neither foresaw nor endorsed a standard that specifically exempts all agricultural and mining sources" (Henderson, 2006, p. 4). The EPA believes that given the limitations on the evidence regarding health effects associated with coarse particles from different sources or of differing composition, and given the potentially serious nature of the health risks posed by at least some thoracic coarse particles and the potential size of the population exposed, it is appropriate to provide some protection for all types of thoracic coarse particles, consistent with the requirement of the Clean Air Act to provide an adequate margin of safety.

(3) *Comment:* Some commenters cited new studies completed after the close of the Criteria Document as providing additional evidence of associations between traffic-related emissions and adverse health effects (e.g. Kim et al., 2004; Ryan et al., 2005; Garshick et al., 2003; McDonald et al., 2004; and Ostro et al., 2006).

Response: The EPA has already noted that it is basing the final decisions in this review on the studies and related information included in the PM air quality criteria that have undergone CASAC and public review, and will consider the newly published studies for purposes of decision making in the next PM NAAQS review. For further discussion of this issue, see section I.C. of the preamble. In provisionally considering these studies, however, EPA notes that a number of new studies indicate traffic related exposures are associated with morbidity and mortality. However, documentation of health effects would not in any way negate findings for other pollutants and sources. Because roadways are a significant source of coarse as well as fine particles and some gases, it is difficult to discern the relative contribution of various pollutants, or to exclude the possible role of urban road dust emissions in contributing to such effects.

(4) *Comment:* Some commenters expressed the view that EPA should exclude non-urban wind-blown dust and soil, including fugitive dust from agricultural and mining operations, from the $PM_{10-2.5}$ indicator, claiming that such particles have been shown to be nontoxic, and that the scientific studies show that they are not associated with adverse health effects.

Response: As noted in section III.C.2 of the preamble to the final rule and in the previous subsection of this Response to Comments document, EPA disagrees that there is

sufficient evidence to demonstrate that there are no adverse health effects from community-level exposure to coarse particles in non-urban areas. Rather, the existing evidence is inconclusive with regard to whether or not community-level exposures to thoracic coarse particles are associated with adverse health effects in non-urban areas. Although there is some evidence that coarse particles of natural geologic origin are relatively non-toxic in their uncontaminated form, the Criteria Document notes that thoracic coarse particles in non-urban areas may become contaminated with a wide variety of toxic materials (EPA, 2004, p. 8-344).

(5) *Comment:* Some commenters recommend excluding crustal materials from the coarse particle indicator based on studies that have found a lack of effects associated with exposure to natural crustal materials in general. These commenters cite Schwartz et al. (1999), and the 6-city study by Laden et al. (2000) as showing that crustal materials, in both the fine and coarse fractions, are not associated with increased mortality. Similarly, the commenters state that Mar et al. (2000) found a strong association between cardiovascular mortality and motor vehicle exhaust components, but a negative association between soil and total mortality. Thus, these commenters argued that there is sufficient evidence to show that crustal particulate matter is essentially benign and therefore should be excluded from the coarse particle indicator.

Response: The summary of the results of Mar et al. (2000) misses some important elements of the study results. A major finding of the original study as well as the reanalysis (Mar et al., 2003) was an association between $PM_{10-2.5}$ particles and mortality. The analyses in this work that examined sources and components examined contributions to the effects of $PM_{2.5}$, not to $PM_{10-2.5}$. In the opinion of the authors, the factor that the commenters called 'motor vehicle exhaust' "probably represents the influence of motor vehicle exhaust and resuspended road dust" (Mar et al., 2000, p. 351). The negative association for 'soil' in the fine fraction cited by the commenter was apparently related to problems in the $PM_{2.5}$ measurement. When the data were assessed for a period with an improved sampler, the authors report that the association between soil and mortality was "positive and significant at 0 days lag" (ibid., p. 352).

The Laden et al. (2000) study cited by commenters was reanalyzed in Schwartz (2003), with qualitatively similar findings. As in Mar et al. (2000, 2003), this study examined the associations of crustal materials in the fine particle fraction, in which they make up such a small fraction of fine mass that one of the six cities had to be excluded from the analysis (Laden et al. 2000, p. 945). While this result does not provide any support for associations between coarse crustal materials and mortality, given the lower concentrations of coarse particles in five of the six cities and the lack of examination of coarse particle composition, the results are inconclusive with respect to the potential effects of higher concentrations of coarse particles. Based on assessment of all the available evidence, therefore, in EPA's view it is inappropriate to exclude crustal materials from the coarse particle indicator.

(6) *Comment:* Some commenters argued that coarse mode particles, especially crustal coarse mode particles, are unlikely to serve as carriers of urban-area contaminants because they

have less surface area per unit mass than fine particles, do not adsorb contaminants easily, have short atmospheric residence times, and are removed from the respiratory tract more efficiently than fine particles.

Response: The commenters' fundamental rationale is flawed and inconsistent with observations of the composition of urban coarse particles, which demonstrates coarse particles are contaminated by a number of potentially toxic components, including a number of metals, asbestos, endotoxins, organic products of incomplete combustions and secondary materials such as nitrates (EPA, 2005a, p 244 to 46). Studies of the composition of urban road dust, in particular, list a large number of inorganic and organic materials (EPA, 2004, p. 3D-1 to 3D-5). In describing the physico-chemical properties of such resuspended materials, the 1996 Criteria Document notes:

> "[T]he deposited particles probably lose their individual identity by becoming attached to host (soil) particles. When the pollutant particle is transported downwind, it is usually attached (aggregated) to this host particle" (Sehmel, 1973). Furthermore the host particle is most likely an aggregate itself. Studies of the cross section of particles, mineralogy, and scanning electron microscope analysis of dust samples show that particles suspended from the soil are aggregated (EPA, 1996, p. 3-36 to 37).

The aggregation of irregular shaped smaller materials mean that the surface area per unit mass of such course particles can be substantially larger than that displayed in surface area distributions that assume all particles have a spherical shape. The elevated coarse nitrate levels often seen in western areas (e.g. Sardar et al., 2005) is evidence that this fraction has enough surface area to take up significant quantities of nitric acid vapor. This interaction is enhanced when the fine particles concentrations are low or are acidic (EPA, 1996, p. 3-17).

The shorter residence times alluded to mean that some urban coarse particles can settle out within the urban boundary only to be further contaminated and resuspended. Whatever the transport distance,[6] it is clear from the measurement of urban coarse particles and road dust that the urban coarse mix is contaminated by a number of components of potential concern.

Thus, EPA believes that these commenters are in error: available information on composition, transport, and particle dosimetry all are consistent with the notion that urban coarse particles can be causally linked to significant health effects.

iii. Legal and practical considerations

(1) *Comment:* Some commenters stated that the proposal to exclude coarse PM from agricultural and mining sources from the $PM_{10-2.5}$ indicator was consistent with the longstanding determinations of EPA, Congress and the courts. Several of these commenters cited Alabama Power Co. v. Costle, 636 F.2d 323 (D.C. Circuit 1979),

[6] Other comments and responses in this document address the extent of coarse particle transport in more detail.

where the Court stated that "EPA has the discretion to define the pollutant termed 'particulate matter' to exclude particles of a size or composition determined not to present substantial public health or welfare concerns" by removing them from the section 108(a) list of criteria pollutants, based on a finding that such "excluded particulates" would no longer cause or contribute to air pollution which may reasonably be anticipated to endanger public health or welfare (369-70, fn 134). Further, these commenters pointed to EPA's practice of excluding fugitive dust emissions from agricultural and mining sources in making attainment determinations and for purposes of PSD determinations.

Response: For the reasons discussed in section III.C. of the preamble to the final rule and other comment responses, EPA has decided to adopt an unqualified indicator for thoracic coarse particles. In that context, the *dictum* from Alabama Power is not relevant.

(2) *Comment*: The American Farm Bureau Federation expressed strong support for the proposed exclusion of agricultural sources from the indicator for coarse particles. Given the agency's conclusion at proposal that "this [proposed exclusion] is designed to make clear that there is no need nor basis to control these sources to obtain the public health benefits intended by the proposed indicator," this commenter stated that an indicator which includes coarse particles from agricultural sources would not be requisite to protect the public health because it would be more stringent than necessary, taking into account the latest scientific knowledge of the nature and severity of health risks involved, the size of the sensitive populations at risk, the relative degrees of exposure and risk to sensitive populations, and the kind of degrees of uncertainties involved.

Response: The statement cited from the proposal refers to the health benefits intended by the proposed qualified indicator, and the relationship between the regulatory exclusion for agricultural, mining and other similar sources and achievement of the health benefits from a qualified indicator. However, EPA has decided to adopt an unqualified indicator to obtain broader health protection than proposed. Therefore commenter's argument about the "requisite" degree of protection fails because the predicate of a qualified indicator is no longer the case. As discussed in section III.C.2 of the preamble to the final rule, there are many reasons that the qualified indicator and related source exclusions are now considered inappropriate. For example, comments made it clear that even with a qualified indicator the source exclusions had a significant flaw, in that emissions from the excluded sources could become part of the ambient mix covered by the qualified indicator, could contribute to the health risks presented by that ambient mix through contamination, and the exclusions could limit the state's choices and practical ability to achieve attainment (see, e.g. Maricopa County Air Quality Department, pp. 4-6).

The preamble also explains in detail the Administrator's decision to adopt an unqualified indicator for thoracic coarse particles. The decision to include all coarse particles in the indicator is premised on a decision to provide broader but still targeted protection than that provided by a qualified indicator. Given the decision to provide broader protection extending to all coarse particles, and in light of the current state of the science, it would be inconsistent to exclude any sources from the scope of the NAAQS. As explained in

section III.C. 2 of the preamble and in other comment responses, EPA concludes that the record justifies control of all thoracic coarse particles at ambient levels in order to provide an adequate margin of safety to the exposed public.

At the same time, as also described in section III.C.2, EPA believes that there is a significant difference in the amount of evidence available regarding adverse health effects associated with those ambient mixes of coarse particles typically found in urban and industrial areas versus those typically found in rural and non-urban areas such that it is appropriate for a standard to target protection at coarse particle mixes in urban and industrial areas. After careful consideration, it is the view of the Administrator that the PM_{10} indicator will in fact provide the type of targeted protection from thoracic coarse particles which is justified by the emerging body of scientific evidence, that it will do so more effectively and more appropriately than all other indicators evaluated by EPA during the course of this review. See section III.C.3 of the preamble to the final rule, explaining why PM_{10} is the best indicator for this purpose.

(3) *Comment:* The American Farm Bureau stated that by proposing to exclude agricultural sources from the PM coarse NAAQS, EPA has considered the "variable factors" (CAA section 108(a)(2)(A)) that alter the effects of PM coarse on public health and has proposed to define the PM coarse NAAQS in a way that is "not lower or higher than is necessary" (Whitman) to protect public health. The commenter believes that in effect, EPA has proposed to exclude the sources of PM that cannot "reasonably be anticipated to endanger public health of welfare" (section 108(a)(1)).

Response: The EPA agrees with the commenter that the varying strength of evidence regarding toxicity of coarse particles of different origin may appropriately be considered in setting the NAAQS for coarse particles, and agrees that this is a "variable factor" reflected in the air quality criteria under section 108(a)(2) on which the standard is based. The PM_{10} indicator for coarse particles does appropriately reflect the varying strength of the evidence by targeting protection at those areas where the evidence of effects is strongest. See preamble section III.C.b.3. However, EPA does not agree with the commenter's ultimate conclusion that an exclusion of agricultural sources is necessary in order for the standard to be requisite to protect public health, as explained in the previous responses. In addition, EPA does not agree with the commenter that the proposal was a de facto delisting of a pollutant under section 108(a)(1)(A). That provision deals with classes of pollutants, not emitting sources.

As noted above, EPA has decided to include all coarse particles in the indicator, using an indicator that appropriately varies the allowable concentration of coarse particles to reflect the varying evidence of risk and public health concern. For this reason, it would be inconsistent to exclude any sources from the NAAQS.

(4) *Comment*: Some commenters argued that the proposed $PM_{10-2.5}$ indicator, as qualified, is consistent with the D.C. Circuit's analysis in ATA I. These commenters stated that the proposed indicator directly reflects the lack of evidence of adverse health effects from

non-urban sources of $PM_{10-2.5}$. In the view of these commenters, this targeted approach is the logical and appropriate response to the ATA I court's analysis.

Response: Since EPA is not adopting the proposed qualified indicator, the comment is moot. However, EPA notes that the ATA I case addressed the issue of using PM_{10} as the indicator for coarse particles, and did not address the issue of using a qualified indicator. In addition, as explained in section III.C.3.b of the preamble to the final rule, there are sound reasons for adopting a PM_{10} indicator, and EPA believes that these reasons satisfy the concerns raised by the court in ATA I. Use of a PM_{10} indicator is likewise consistent with the relative strength of the evidence regarding adverse health effects associated with urban vs. non-urban ambient mixes of coarse PM, and so addresses the commenter's other concern.

(5) *Comment*: Some commenters stated that while EPA has considerable authority under the "adequate margin of safety" requirement of the Act to act in the face of evidence that shows potential threats to public health, the Agency must have some evidence. The commenters stated that in this case, the "available" and "reliable" evidence demonstrates that non-urban $PM_{10-2.5}$ and $PM_{2.5}$ both generally result from wind-blown crustal materials, which have been shown to be nontoxic. The commenters stated that including these pollutants within the NAAQS would be impermissible guesswork.

Response: Currently available studies do not provide a sufficient basis for supplementing mass-based fine particle standards with standards for any specific fine particle component or subset of fine particles, or for eliminating any individual component or subset of components from fine particle mass standards. See section II.C to the preamble to the final rule, as well as other comment responses, summarizing ample evidence in the Criteria Document supporting this conclusion. The CASAC likewise endorsed an unqualified $PM_{2.5}$ indicator (Henderson, 2005a, p. 6).

With respect to non-urban $PM_{10-2.5}$, the Administrator has taken an approach for coarse particles consistent with the Clean Air Act (CAA). Specifically, in this final decision EPA is retaining an unqualified indicator for coarse particles despite differences in the strength of the evidence regarding health effects associated with different ambient mixes of coarse particles. See section III.C.2 of the preamble to the final rule, as well as responses to comments in this document. This decision is not based on "sheer guesswork," but rather on a careful consideration of the scientific evidence as described in the preamble to the final rule.

(6) *Comment*: According to the National Mining Association, fugitive dust from mining operations remaining after implementation of Best Management Practice fugitive dust controls has never been shown to have adverse impacts on public health. Therefore, EPA has not historically included such dusts when making determinations of compliance with ambient standards. The commenter cites as examples a) the 30-year history of specific exclusion of fugitive dust from attainment demonstrations for the PM NAAQS, plus various "natural events" policies; b) the "fugitive dust exemption" in the Prevention of Significant Deterioration (PSD) program; and c) the "rural fugitive dust policy." Specific

documents and actions cited are 43 FR 26395 (June 19, 1978) (exclusion of fugitive dusts from application of the PM NAAQS and increments ambient air quality impact analyses under the PSD program), 45 FR 78122 (Nov. 25, 1980); 56 FR 37564 (August 8, 1991)(classification of what would otherwise be PM nonattainment areas as attainment areas through application of the "fugitive dust policy"); and 54 FR 48870 (Nov. 28, 1989) (exclusion of mine fugitive dust emissions and consequent non-listing of surface mine as major stationary sources under the PSD program). The commenter also cites legislative history from the 1977 amendments, stating that Congress decided not to enact a statutory exclusion of fugitive dusts from the PSD program, but expected EPA to exercise "administrative good sense" in administering the program to avoid undue regulation of such dusts. S. Rep. No. 95-127, 95th Cong., 1st Sess. 98 (1977). The commenter argues that EPA's proposal to exclude coarse PM from agricultural, mining, and similar sources is in keeping with all of these past determinations.

Response: As discussed in detail in section III.C of the preamble to the final rule, EPA has decided to retain the unqualified PM_{10} indicator for thoracic coarse particles. This indicator will include all thoracic coarse particles, including those emitted by agricultural and mining sources, but will effectively target protection toward ambient mixes of coarse particles typical of urban and industrial areas, for which there is the greater evidence of public health concern, as compared to ambient mixes of coarse particles typical of non-urban areas, such as dusts in areas characterized by mining or agricultural operations. The evidence EPA is relying on for this decision is in this rulemaking record, and the evidence has been subject to in-depth review and assessment by EPA, CASAC, and the public. Given EPA's decision to establish an unqualified indicator, which includes all coarse particles, an exclusion of agricultural and mining sources is not warranted.

The EPA also does not necessarily agree with the commenter's characterization of prior EPA actions. The prior agency actions cited by the commenter do not require or justify a different final decision by EPA, and are consistent with the adoption of an unqualified indicator for coarse particles.

At the same time, the decision not to exclude particular sources from control under the coarse particle standard does not itself address many of the implementation issues referred to by commenter. The EPA anticipates that its existing policies, including those mentioned by the commenter, will continue to be implemented under the PM_{10} standard. Section VII of the preamble briefly addresses a number of implementation-related issues related to the treatment of fugitive dust emissions and the contribution of anthropogenic sources, such as agricultural and mining sources, to NAAQS exceedances associated with exceptional events.

(7) *Comment:* One commenter stated that fugitive dust is controlled under a panoply of federal and state laws even if it were not controlled under the PM NAAQS (National Mining Association).

Response: Though the EPA agrees with commenters that fugitive dust emissions from agricultural and mining sources may be controlled by numerous other federal and State

laws, EPA disagrees that this warrants the adoption under section 109 of a qualified indicator for coarse PM or excluding these sources from control under the coarse particle NAAQS. Section III of the preamble to the final rule explains in detail EPA's reasons for deciding that all coarse particles should be included in the indicator. This decision is based on the scientific evidence, and the degree of current control exercised under other laws or regulations does not change this evidence or its implications. Of course, emissions levels of emitting sources and the existing regulatory or voluntary controls on such sources are of great relevance in the actual process of implementing a NAAQS. The EPA assumes that States would consider the successes of such pre-existing programs in developing control strategies to attain and maintain the PM_{10} NAAQS.

(8) *Comment:* Many commenters advanced detailed arguments against the proposed qualified indicator on legal and/or practical grounds. These arguments were numerous, and included the following positions:

- The proposal's provision that "agricultural sources, mining sources, and other similar sources of crustal materials shall not be subject to control in meeting this standard" (71 FR 2699) is flatly illegal (Commonwealth of Virginia v. EPA, 108 F.3d 1397, 1407-8 (D.C. Cir. 1997), Bethlehem Steel Corp. v. Gorsuch 742 F.2d 1028, 1036-7 (7^{th} Cir. 1984)). The proposed source exclusion violates Congress' clear intention, expressed in CAA section 101(a)(3), to preserve for the States the decision of which sources to control to meet the NAAQS. Train v. NRDC, 421 U.S. 60, 76 (1975): "The Act gives the Agency no authority to question the wisdom of States' choices of emission limitations if they are part of a plan which satisfies the standards of §110(a)(2)." (e.g. American Lung Association et al., p. 89-91)
- In its March 21, 2006 request for reconsideration, CASAC stated that it "neither foresaw nor endorsed a standard that specifically exempts all agricultural and mining sources, and offers no protection against episodes of urban-industrial $PM_{10-2.5}$ in areas of populations less than 100,000." CASAC recommended the "expansion of our knowledge of the toxicity of rural dusts rather than exempting specific industries (e.g. mining, agriculture)" from control under the standard.
- The EPA failed to demonstrate that its proposed qualified indicator would protect public health with an adequate margin of safety. The EPA must demonstrate affirmatively that the coarse particle standards will ensure an absence of adverse effects on sensitive individuals, and will protect against effects that have not yet been uncovered by research (American Lung Association, p. 82, citing Lead Industries Ass'n v. EPA, 647 F.2d 1130, 1153-54 (D.C. Cir. 1980) and American Lung Ass'n v. EPA, 134 F.3d 388, 389 (D.C. Cir. 1998)). In the absence of evidence, or in the face of significant uncertainty, the CAA requirement to provide an adequate margin of safety obligates EPA to regulate all coarse particles equally (Lead Industries Ass'n v. EPA, 647 F.2d 1154-55). The D.C. Circuit Court instructed in ATA III that "[t]he Act requires EPA to promulgate protective primary NAAQS even where… the pollutant's risks cannot be quantified or 'precisely identified as to nature or degree'" (ATA III, 283 F.3d 355, 369 (quoting PM NAAQS, 62 FR 28653)).
- Under the CAA, EPA is charged with setting ambient standards that are national in scope and application, and the proposed qualified indicator fails this test (Whitman,

531 U.S. at 473). The proposed qualified indicator is a thinly veiled attempt to establish a coarse particle standard that only applies to urban areas, and that it denies citizens in non-urban areas adequate health protection (NRDC v. NRC, 666 F.2d 595 (D.C. Cir. 1981): an agency may not do "indirectly" what "it is forbidden by statute from doing directly").

- The qualified indicator, by virtue of depriving non-urban populations of protection from coarse particles, violates principles of environmental justice and the government's Trust Responsibility to Tribes.
- The proposed qualified indicator inadequately describes the substance(s) being regulated. The EPA is attempting to establish a composition-based indicator without being able to define adequately which particular chemical or physical components are associated with adverse health effects. The proposed indicator is defined in large part through an implementation strategy—i.e. via the placement of monitors—rather than in scientific terms. The result would be that two sources of coarse particulate matter with similar composition that presumably produce similar health impacts would be "given different regulatory treatment based merely on the non-scientific qualifiers established in EPA's indicator" (Alliance of Automobile Manufacturers, p. 9).
- There is a logical paradox inherent in the proposed $PM_{10-2.5}$ indicator, which is defined to include any ambient mix "dominated by" particles from particular types of sources. The same concentration of "harmful" coarse particles—i.e. particles from high-density traffic, industrial sources and construction sources—may be regulated differently in different locations depending on what percentage of the ambient mix it constitutes relative to "crustal" particles. The coarse particle standard must provide a consistent level of protection from particles of concern, and use of a 50 percent domination threshold would result in a variable level of protection from particles of concern.
- The EPA failed to specify which source types were included in the broad source category descriptions listed in the indicator. The EPA must define what can be considered an "agricultural source," a "mining source," or "other similar sources of crustal material" (i.e. those sources that would be excluded from control under the proposed standard), and which "industrial" and "construction" sources are included in the indicator. The EPA must clarify how sources that are neither explicitly included in nor excluded from the proposed indicator, such as residential and commercial sources, would be treated. In addition, it is impossible to determine which set of sources is "dominant," given the scarcity of knowledge about coarse particle emissions and air quality concentrations, and the lack of suitable source attribution techniques.
- ATA I established that surrogates for a pollutant must be properly matched. The proposed monitoring site-suitability criteria are not suitably matched to the effects for which they purport to be surrogates.
- As written, the proposed five-part test for siting NAAQS-comparable monitors would arbitrarily prohibit monitoring and regulation of coarse particles outside urbanized areas of 100,000 population, regardless of the presence of large or numerous sources of the types of coarse particles of concern or the nature of the ambient mix. The monitor siting criteria, by virtue of their highly prescriptive role in defining where the pollutant can and cannot be measured, in essence define the indicator itself, and

artificially narrow its scope such that in many instances, coarse particles of concern would not be covered by the indicator. By failing to provide protection from coarse particles of concern in non-urban areas even though the composition of those particles may be identical to that of coarse particles found in large urban areas, the qualified indicator, as EPA proposed to implement it, would be under inclusive.

- The proposed monitor siting criteria have serious environmental justice implications and violate EPA's Trust Responsibility toward Tribes, because Tribal lands would be virtually excluded from coverage, regardless of the mix of particles present.
- The monitor siting criteria undermine the proposed standard on a practical level because they would be impossible to implement. This is especially true of the fifth part of the monitor-site suitability test, which as proposed would require an affirmative demonstration that the ambient mix at the site was dominated by sources of concern, even if all of the other four monitor site-suitability criteria were met. Such a demonstration would be impossible to execute due to the lack of suitable data and techniques, undermining the siting of any NAAQS-comparable $PM_{10-2.5}$ monitors.

Response: After evaluating the large number of adverse comments received on the proposed qualified indicator, EPA agrees that the proposed indicator is beset by numerous problems and it is not appropriate to adopt such an indicator at the present time. Specifically, EPA recognizes the difficulties inherent in attempting to effectively and precisely identify the ambient mixes of concern, caused by: 1) the artificial constraints on the reach of the indicator resulting from the application of quantitative monitor site-suitability criteria such as the requirement that NAAQS-comparable monitors be sited in urbanized areas with minimum 100,000 population; and 2) the difficulties associated with attempting to determine with any precision which sources "dominate" the ambient mix of coarse particles in different locations.

As acknowledged in the preamble, the quantitative constraints in the monitor site-suitability criteria result in an under-inclusive indicator that fails to include all ambient mixes of concern. Smaller urban and/or industrial areas, for example, would not meet the proposed monitor siting criteria, but might have an ambient mix of concern. Moreover, EPA also acknowledges in the preamble that, as a general matter, the use of a qualified indicator without such objective monitor site-suitability criteria would still present serious problems because it is currently impossible to determine with any precision which sources "dominate" the ambient mix in many different locations.

The EPA is also aware that the legal concerns raised by commenters with regard to the exemption of agricultural and mining sources from control under the standard, and the specific sections of the Clean Air Act that speak to this issue, would require careful consideration if the proposed qualified indicator were to be adopted.

Further discussion can be found in the preamble.

(9) *Comment:* A few commenters suggested that EPA should fix specific problematic aspects of the proposal (e.g. restructure the monitor site suitability criteria, or clarify the definition of included vs. excluded industries).

Response: The EPA has considered several options to modify the quantitative criteria, including those discussed in the proposal (see Weinstock, 2006). For example, EPA evaluated different possible minimum population thresholds (e.g., 25,000 or 50,000 instead of 100,000) for areas eligible to site NAAQS-comparable monitors, and/or the possibility of adding additional criteria to include areas that do not meet a quantitative population threshold but are dominated by industrial or traffic-oriented sources. Each of these options, however, was found too inflexible to capture all relevant areas and too difficult to implement in practice. Thus, EPA believes that even a more complex set of quantitative criteria would fail to resolve the basic problem inherent in precisely identifying those ambient mixes to include and those to exclude. There still remains a clear risk of failing to capture all ambient mixes of concern, or of capturing ambient mixes that are intended to be excluded from the qualified indicator based on the data available to us in this review. The EPA now agrees with commenters that the proposed qualified indicator is fundamentally flawed, because it cannot effectively and precisely identify the ambient mixes of concern and because modifications to the indicator that could rectify this and other problems highlighted by the commenters have not been identified. At the present time, therefore, EPA believes that there is an inherent risk that a qualified indicator would not include all of the ambient mixes of concern which the indicator is intended to capture.

(10) *Comment*: Some commenters supporting adoption of an unqualified $PM_{10-2.5}$ indicator recommended that EPA utilize the Exceptional Events Rule, proposed on March 10, 2006 (71 FR 12592-12610), to exclude violations caused by rural windblown dust. According to these commenters, this would be consistent with historical practice, because in the past the Natural Events Policy has been applied in many instances to exclude data associated with dust storms and other events from consideration under the PM_{10} standard.

Response: As described in section VII of the preamble to the final rule, EPA does intend to utilize the Exceptional Events Rule to exclude air quality violations caused by exceptional or natural events. Consistent with historical practice, this will include violations associated with rural windblown dust, assuming those violations meet the requirements of the final Exceptional Events Rule.

iv. Alternative approaches: PM_{10}

In the preamble to the proposed rule, EPA requested comment on a number of alternatives with regard to the indicator for thoracic coarse particles. Most commenters expressing an opinion on indicator commented either in favor of, or in opposition to, the qualified $PM_{10-2.5}$ indicator, as described in the previous section. Whether directly or by assumption, most of these commenters appeared to support revising the PM_{10} indicator to focus on the coarse fraction ($PM_{10-2.5}$). However, some commenters recommended that EPA not adopt a coarse fraction indicator, but rather retain the current PM_{10} indicator. In this section, EPA replies to the specific points made by these commenters.

(1) *Comment:* Some commenters stated that, given the limitations on the scientific evidence, and in light of some of the other problems identified with the proposed qualified indicator, EPA should consider retaining the current PM_{10} standards. For example, the American Lung Association et al. stated:

> We strongly support the need for a coarse PM standard…. However, the coarse particle standard proposed by EPA is an egregious step backwards in protection of human health and welfare compared to the status quo…. If EPA feels it lacks adequate data to undertake the change in the coarse PM indicator to a $PM_{10-2.5}$ standard, without reducing current protections…then the Agency must retain the existing PM_{10} NAAQS (American Lung Association et al., p. 81).

Response: As explained fully in section III.C.3 of the preamble to the final rule, EPA has determined that it is indeed appropriate to retain the 24-hour PM_{10} standard, for many of the reasons noted by these commenters and described earlier in this Response to Comments document.

(2) *Comment:* Some commenters stated that the D.C. Circuit Court's opinion in ATA I bars use of PM_{10} as an indicator for coarse particles because PM_{10} is confounded by the presence of $PM_{2.5}$. The commenters stressed the court's statement that "[i]t is the very presence of a separate $PM_{2.5}$ standard that makes retention of the PM_{10} indicator arbitrary and capricious." 175 F.3d at 1054.

Response: As explained in detail in section III.C.3.b to the preamble to the final rule, the decision to retain PM_{10} as the indicator is not inconsistent with the ATA I decision. The EPA believes there are reasonable justifications for use of a PM_{10} indicator for coarse particles which speak directly to the court's concerns.

One of the related issues EPA has considered in the decision to use PM_{10} as the indicator for thoracic coarse particles was the potential impact of the revised 24-hour $PM_{2.5}$ standard on the level of protection afforded by the PM_{10} standard. As described in the preamble, with a PM_{10} indicator, the "headroom" allowed for thoracic coarse particles (i.e. the allowable PM_{10} level minus the corresponding $PM_{2.5}$ concentration) will vary with $PM_{2.5}$ concentrations. Theoretically, it might appear that the reduction in the level of the fine particle standard from 65 $\mu g/m^3$ to 35 $\mu g/m^3$ would serve to increase the allowable "head room" for thoracic coarse particles by 30 ug/m^3. In practice, however, only two areas in the US actually violate the 65 μg/m3 standard. Most other areas have substantially cleaner air quality. Air quality analyses suggest that in the eastern US and in many California cities, attainment of the current annual standard will also result in attainment of the new daily standard. Therefore, for the majority of US cities that either currently meet the new 35 $\mu g/m^3$ standard or will meet it upon attainment of the annual $PM_{2.5}$ standard, the "headroom" ultimately allowed for thoracic coarse particles under the current PM_{10} 24-hour standard will be unchanged by the revision to the fine particle standard. As noted in the preamble, the new standard would serve to cause those remaining areas that meet the annual $PM_{2.5}$ standard, but have high 24-hour $PM_{2.5}$ concentrations, to adopt additional controls. While this would result in an increase in the

allowable thoracic coarse particle level in such areas, it would also make the "headroom" more similar to other areas that already or will soon meet both the annual and 24-hour fine particle standards. EPA believes this is a desirable result because it reduces the variability in allowable thoracic coarse particles among cities, providing for more uniform protection.

(3) *Comment:* One commenter stated that EPA has suggested that as a result of the ruling in ATA I, the 1987 PM_{10} standard "springs back." According to this commenter, for the very same reasons that the court vacated the 1997 standard, the 1987 PM_{10} standard would be invalid because it is just as confounded by inclusion of $PM_{2.5}$ as the 1997 standard. The commenter believes EPA itself understands this since it requests comment on whether to retain the current PM_{10} standard in the proposal, while noting that retaining the standard would also include modifying "the standard to exclude the double-counted $PM_{2.5}$ contribution." (National Mining Association).

Response: The commenter is mistaken about the applicability of ATA I to the 1987 PM_{10} standard, because in that review, PM_{10} did not serve solely as the indicator for coarse particles; it served as the indicator for both fine and coarse particles. The issue addressed in this comment and in ATA I at 175 F. 3d at 1054-1055 is thus not presented by the 1987 standard.

In any case that issue is moot, because in this review EPA is deciding whether to revise the 1987 standards based on the current evidence, not the evidence as it was in 1987. The final decisions in this review to retain the daily standard and revoke the annual PM_{10} standard, are explained and supported by the evidence in this rulemaking, and as discussed elsewhere, are fully consistent with ATA I.

(4) *Comment:* A few of the commenters advocating the retention of the PM_{10} standards suggested that measurements of PM_{10} could be adjusted by subtracting out $PM_{2.5}$ to avoid double regulating the fine fraction, to satisfy a concern voiced by the D.C. Circuit in ATA I (e.g., Alliance of Automobile Manufacturers, p. 22).

Response: The EPA has considered and rejected this alternative. As noted in the preamble to the final rule, this alternative, like an unadjusted PM_{10} indicator, would allow variable ambient concentrations of coarse particles. The net result, however, would be that $PM_{10-2.5}$ levels would be allowed to increase relative to the current PM_{10} standard when $PM_{2.5}$ levels are highest. As explained in section III.C.3.c of the preamble to the final rule, this is the opposite result from that desired from a public health perspective. There should be less coarse particulate matter allowed as $PM_{2.5}$ levels increase because these are the conditions under which $PM_{10-2.5}$ tends to become more contaminated and therefore more harmful. Furthermore, this approach would essentially relax the level of protection afforded by the current 24-hour PM_{10} standard because it would allow higher total PM_{10} levels on days with high $PM_{2.5}$ levels. As explained in section III.D.2 of the preamble to the final rule, EPA believes it is important to maintain the current level of protection from health effects associated with exposure to thoracic coarse particles. For both of these reasons, EPA rejected this approach.

c. Averaging Time

(1) *Comment:* Some commenters agreed with EPA's proposal not to retain an annual standard for thoracic coarse particles. One such commenter argued that there is no legal basis for adopting an annual standard for coarse particles. According to this commenter, although the statutory adequate margin of safety requirement allows EPA to guard against standards that future research may reveal, this does not authorize EPA to issue a standard when there is substantial evidence in the record to support a fact, in this case, that there is a current absence of adverse effects from long term exposure to coarse PM. The commenter stated that the margin of safety requirement cannot be used to bootstrap support for a standard where none exists, and has no application in cases such as this where there is no evidence of adverse effects (Coarse Particle Coalition).

Response: As explained in section III.D.2 of the preamble to the final rule and in other comment responses, EPA agrees that the evidence in the record justifies the Administrator's decision not to adopt an annual standard for coarse particles. The CASAC Panel agreed unanimously with this conclusion (Henderson, 2005b, p. 5). The EPA also notes that the short-term standard for coarse particles, which is generally controlling, has and will continue, as a practical matter, to limit long-term exposures to coarse particles. Thus the 24-hour standard will, in effect, also provide protection against any as yet unidentified potential effects of long-term exposure at ambient levels (see Schmidt, 2006).

(2) *Comment:* Some commenters urged EPA to retain an annual standard as well as a 24-hour standard. The American Lung Association et al., in particular, stated that EPA had inappropriately focused on the absence of reported long-term mortality effects and had ignored evidence of long-term morbidity effects in several studies, including Gauderman et al. (2000, 2002) and Avol et al. (2001), and had also ignored substantial evidence from European studies as well as the recommendations for an annual PM_{10} standard made by a WHO working group. These commenters argued that an annual standard was requisite to protect public health with an adequate margin of safety.

Response: The EPA disagrees that it ignored the evidence that is relevant to evaluating the health effects associated with long-term exposure to thoracic coarse particles. The EPA's assessment, both in this review and the previous review, placed greatest weight on studies that measured $PM_{10-2.5}$ or on studies conducted in areas where it is reasonable to expect the PM_{10} measurements to be dominated by coarse particles (EPA, 2005a). By contrast, these commenters have placed inappropriate reliance on studies that measured PM_{10}, and were conducted in Southern California cities (Gauderman et al., 2000, 2002) or in European cities where it is not reasonable to assume that PM_{10} associations are dominated by coarse particles. The only one of these studies (Gauderman et al., 2000) to include measurements of coarse particles found an association between lung function growth for PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, NO_2, and acids. The authors were unable to cite any single pollutant as responsible for these results, but they chose not to include measures for coarse particles in their follow-up study (Gauderman et al., 2002). As noted in the

1996 PM Staff Paper, the other major study of lung function and long-term air pollution in children found no associations with coarse particles (EPA, 1996, p. 5-67a).

Given that coarse particles were unlikely to have dominated the ambient mix of PM_{10} in the studies cite by commenters, it is difficult to draw meaningful conclusions about the relative role of coarse as opposed to fine particles. The WHO panel recommendations for PM_{10} limits cited by commenters also do not provide any independent scientific justification regarding the need for a separate long-term standard for coarse particles. The WHO panel essentially developed their recommendations for PM_{10} standards by deriving a ratio of fine particles to PM_{10} and adjusting their recommended levels for $PM_{2.5}$ to derive an equivalent PM_{10} metric, for areas that do not yet have access to $PM_{2.5}$ monitors (WHO, 2005, p. 8).

The long-term exposure studies of mortality and morbidity that permit comparisons of fine and coarse particles continue to suggest that, at current ambient levels in the U.S., fine particles are associated with health effects and coarse particles are not. See EPA, 2004, pp. 8-306 to 307 ("no statistically significant associations have been reported between long-term exposure to coarse fraction particles and cause-specific mortality"); pp. 8-313 to 314 ("[t]he recent studies suggest that long-term exposure to fine particles is associated with development of chronic respiratory disease and reduced lung function growth; little evidence is available on potential effects of exposure to coarse fraction particles"). The EPA believes that the revised $PM_{2.5}$ standards will address the major risk suggested in the PM_{10} studies cited by commenters.

To the extent that additional concerns may exist with regard to long-term exposures to coarse particles that have not been fully identified by scientific research, the Staff Paper notes that the short-term standard for coarse particles, which is generally controlling, has and will continue, as a practical matter, to limit such long-term exposures. The Staff Paper analysis of PM_{10} air quality data indicates that the current 24-hour PM_{10} standard is 'controlling' in virtually every area in the US; that is, virtually all areas that violate the PM_{10} standards violate the 24-hour PM_{10} standard. Some of them may violate the annual PM_{10} standard as well, but (depending on the year) few, if any, areas violate the annual PM_{10} without violating the 24-hour PM_{10} standard (EPA, 2005a, p. 2-31 to 32). As demonstrated in Schmidt (2006), based on an analysis of air quality data for 2003-2005, all of the areas that would violate the annual PM_{10} standard also violate the 24-hour standard. Thus EPA believes that the short-term PM_{10} standard will in effect also provide protection against any as yet unidentified potential effects of long-term exposure at ambient levels.

d. Level and Form

Most commenters expressing views on the appropriate level and form of a standard for thoracic coarse particles focused on two questions: 1) whether the proposed level of 70 $\mu g/m^3$ for a 24-hour $PM_{10-2.5}$ standard would make that standard generally "equivalent" to the current 24-hour PM_{10} standard of 150 $\mu g/m^3$; and 2) whether the proposed level of 70 $\mu g/m^3$ was overly stringent, or not stringent enough given the health effects evidence. The EPA notes that the

Administrator's decision to retain the current 24-hour PM_{10} standard effectively resolves all comments about equivalence, since the level of protection provided by that standard will remain unchanged. However, EPA notes that commenters voiced the following concerns about the proposed equivalence determination:

(1) *Comment:* Some commenters stated that seeking "equivalence" to the PM_{10} standard was fundamentally flawed because, in their view: 1) the level of the current PM_{10} standard was not based on coarse particle studies; 2) the proposed standard is more stringent than, and therefore not equivalent to, the PM_{10} standard; 3) the Court in ATA I had already declared any standard based directly or indirectly on PM_{10} to be invalid; and 4) EPA has not adequately considered, either in this review or in the 1997 review, whether the 150 $\mu g/m^3$ concentration level is requisite (neither higher nor lower than necessary). Thus, according to the National Mining Association, the current PM_{10} standards cannot serve as the foundation for any coarse particle standard, and furthermore "equivalence to 150 $\mu g/m^3$ of PM_{10} would be a logical basis for a coarse standard only if the 150 $\mu g/m^3$ level were rooted in coarse particle evidence" (National Mining Association, p. 23-5).

Response: As noted in the preamble to the final rule, EPA agrees that the 1987 PM_{10} standards were designed to protect against the health effects of both fine and coarse particles, and based in part on epidemiological studies that variously measured particles both smaller and larger than PM_{10}. However, the arguments regarding the origin of the 1987 standards as well as commenters' claims about the basis for the PM_{10} standards promulgated in 1997[7] are not relevant to the current review. In determining whether to revise the standards in this review, EPA has examined the degree of protection provided by the current 24-hour PM_{10} standard in light of the quantitative evidence from the expanded epidemiological data base that includes studies using direct $PM_{10-2.5}$ measurements as well as studies using PM_{10} measurements in areas where coarse particles dominate the distribution.

Because the Administrator has decided that it is appropriate to retain PM_{10} as the indicator for thoracic coarse particles, there can be no uncertainty as to whether the final standard is equivalent to the current standard, making the commenters' second point above moot. With regard to their third point, for reasons outlined in section III.C.3 of the preamble to the final rule, EPA believes that it has addressed the concerns raised by the Court regarding PM_{10} as an indicator, and in any case, the D.C. Circuit did not address the issue of the level of protection afforded by the 1997 or 1987 24-hour PM_{10} standard. As explained in detail in section III.C.3.b of the preamble to the final rule, EPA believes that the decision to retain PM_{10} as the indicator is consistent with the Court's decision in ATA I.

[7] Some commenters also suggested that, in promulgating revised PM_{10} standards in 1997, EPA did not consider whether the level of the PM_{10} standards it promulgated was lower than necessary and did not base the levels on coarse particle health effects data. While EPA disagrees with both of these claims – for example, EPA relied on two PM_{10} studies done in areas dominated by coarse particle in selecting the level (62 FR 38679) – this argument is not relevant to this review.

(2) *Comment*: According to some commenters, using "equivalence" to the current (1987) PM_{10} standard as a basis for determining the level of a standard for thoracic coarse particles is legally flawed since it rests on the level of a discredited standard (the 1987 PM_{10} standard) which was not primarily a standard for coarse particles. This approach is at odds with EPA's obligation under section 109 (b) to base the standards on established air quality criteria which reflect the latest scientific knowledge (National Mining Association/National Cattlemen's Beef Association).

Response: The historic basis for the level of the 1987 and the 1997 standards for PM_{10} is not relevant to EPA's decision here that standards for thoracic coarse particles, measured using a PM_{10} indicator, should provide protection equivalent to that afforded by the existing standard. This is because EPA's determination is based on the expanded epidemiological database, which includes studies using direct $PM_{10-2.5}$ measurements, as well as studies using PM_{10} measurements in areas where coarse particles dominate the distribution. These are the studies included in the Criteria Document for this review. While the specific levels reported in studies are not used to determine the numerical level of the standard, an expanded examination of the air quality data in the study cities indicates that potential mortality effects have been associated with air quality levels above the current 24-hour standard, but not with air quality levels that would generally meet that standard, and that morbidity effects have been associated with air quality levels that exceeded the current 24-hour standard only a few times. The information gained from this evaluation of the PM_{10} attainment status of the areas in which the studies were conducted is relevant for the purpose of determining the appropriate standard level in this review, irrespective of the scientific basis when the current standards were adopted or the purposes of the standards when they were adopted. The CASAC reviewed and concurred with EPA's approach of developing a range for the level of the coarse particle standard that was based in part on equivalency to the current PM_{10} standard (Henderson, 2005b, p. 6). The EPA believes that this approach fully satisfies its obligations under section 109(b) of the Act to base standards on criteria reflecting the latest scientific knowledge.

(3) *Comment:* Some commenters criticized EPA's proposed level of 70 $\mu g/m^3$ on the grounds that, due to the highly variable nature of PMc concentrations around the country, this standard would be significantly more stringent in some locations as compared to the current standard than in others. According to these commenters, the broad nationwide variation in the relative proportions of $PM_{10-2.5}$ and $PM_{2.5}$ in the PM_{10} mix renders uniform national regulation "equivalent to" the protection provided by the current 24-hour PM_{10} standard of 150 $\mu g/m^3$ extremely difficult. Other commenters argued that EPA's approach to determining an equivalent level resulted in a proposed level for the 24-hour $PM_{10-2.5}$ standard that would be less protective than the current standard, even in urban areas.

Response: In general, all of these commenters misunderstood EPA's approach to providing an equivalent level of protection in the proposal. The level of 70 $\mu g/m^3$ was based on an analysis showing that a 98^{th} percentile standard set at this level would result in approximately the same number of non-attainment counties as the current PM_{10} standard of 150 $\mu g/m^3$, one-expected-exceedance form, rather than some equivalent

"average" level of air quality. Further details of EPA's approach are described in the proposal preamble (71 FR 2670-71).

Again EPA notes, however, that because the Administrator has decided to continue the use of PM_{10} as the indicator for coarse particles, these commenters' concerns about whether the proposed levels for $PM_{10-2.5}$ are as protective as current standards are now moot.

In addition to their comments on equivalence, commenters also expressed the following concerns about whether the current standards were appropriately health protective:

(4) *Comment:* Some commenters pointed to exposure error in epidemiologic studies in support of arguments that EPA has failed to establish a reasonable scientific justification for determining that a level of 150 $\mu g/m^3$ for the 24-hour PM_{10} standard, or an equivalent level of 70 $\mu g/m^3$ for a 24-hour $PM_{10-2.5}$ standard, is requisite. The commenters express concern about the spatial locations of the monitors used to describe the exposures of study populations, the use of the difference method rather than dichotomous samplers to determine coarse particle levels, and the estimation of coarse particle levels in areas where they are derived from PM_{10} measurements (Borak pp. 5-9). According to these commenters, EPA lacks any basis for quantifying or deriving the concentration term of a PM coarse standard, and given the uncertainty about level it is not appropriate to establish any coarse particle standard at this time.

Response: As discussed in section III.B.2 of the preamble to the final rule, and in section II.B.2.a of this Response to Comments, EPA disagrees with commenters regarding the extent to which exposure error has affected the results of key epidemiologic studies. As discussed previously, EPA carefully evaluated the data used in U.S. and Canadian epidemiologic studies, and found that the concentrations at one monitoring site could be generally higher or generally lower than concentrations at another, but that the data from different monitors used in epidemiologic studies were generally well correlated with one another and thus appropriately characterized the day-to-day changes in thoracic coarse particle concentrations. Furthermore, in considering the results of these key studies in establishing the appropriate level and form for the 24-hour PM_{10} standard, EPA carefully analyzed and considered the implications of monitor locations and measurements for the exposure metrics presented in the studies (see section III.E of the preamble to the final rule; Langstaff and Ross, 2005; EPA, 2005a, p 5-64 to 5-66). In reaching the final decision, greater reliance was placed on the most representative monitoring results from the regulatory network in the respective localities.

EPA also disagrees with the assumption that studies using available dichotomous samplers are inherently superior to those using a difference method for measuring thoracic coarse particles. The CASAC transmitting their monitoring subcommittee review of EPA's approach to developing a coarse particle Federal reference method (FRM), noted: "A majority of the Subcommittee members expressed the opinion that the demonstrated data quality of the $PM_{10-2.5}$ difference method and its documented value in correlations with health effects data support its being proposed as the PM coarse FRM"

(Henderson, 2005c). While existing dichotomous samplers have some advantages, they also have limitations (72 FR 2688-2689). The EPA observes that all of the studies discussed in the proposal notice that obtained $PM_{10-2.5}$ data by subtraction of $PM_{2.5}$ from PM_{10} measurements used PM data from co-located monitors (e.g., Mar et al., 2003; Ostro et al., 2003; Sheppard et al., 2004). Numerous studies also used data from dichotomous samplers, including all Canadian studies, the Harvard Six Cities study, Fairley (2003), and Ito (2003).

The EPA also does not agree that the results from studies using imputation or regression methods to fill missing PM data are invalid. The EPA acknowledges that directly measured data are preferable. A number of research groups have used methods for filling missing PM data; these studies have included validation analyses to test the predicted values against available measured data. The commenters refer in particular to a study conducted in Coachella Valley. Ostro et al. (2000) obtained 2 ½ years of measured data on $PM_{10-2.5}$ and $PM_{2.5}$ and 10 years of measured data for PM_{10}, and used regression methods to fill in the missing data for $PM_{10-2.5}$. The authors found that estimated $PM_{10-2.5}$ data were very highly correlated with measured $PM_{10-2.5}$ data in a validation analysis of the estimation technique (r=0.97), and used the 10-year data set in analyses. The researchers observed that their estimation methods were not as good for predicting $PM_{2.5}$ data and thus used only the $PM_{2.5}$ measured data in analyses. It is of note that PM_{10} concentrations, which were not imputed, and $PM_{10-2.5}$ concentrations were both significantly associated with daily mortality in this study. The EPA believes that the use of estimated data increases exposure measurement uncertainty, but does not agree that this type of analysis is invalid, particularly for this study, where a high degree of correlation exists for PM_{10} and $PM_{10-2.5}$, and the results are significant for $PM_{10,}$ the indicator that is used for the coarse standard. The EPA also notes that CASAC referred positively to Ostro et al. (2000) and Ostro (2003) as part of its unanimous recommendation that there is a need for a thoracic coarse standard (Henderson, 2005b, p. 2), indicating that CASAC regarded this study as reliable.

Finally, as discussed in section III.D of the preamble to the final rule, EPA did not use the measured air quality values from the studies to determine the appropriate level, recognizing the uncertainty in projecting exposure from the measured values at the monitors. Instead, EPA compared the study areas to their PM_{10} attainment status, and based on that determined the appropriate level for the PM_{10} standard.

(5) *Comment:* In questioning the basis for the level of the proposed coarse standard, a consultant for the National Mining Association and National Cattlemen's Beef Association states that the only two studies cited by EPA in support of its coarse PM_{10} standard in 1997 (Hefflin, 1994; Gordian 1996) were at concentrations well above 1,000 $\mu g/m^3$, while several studies have shown no effects from exposure to concentrations well above 10,000 $\mu g/m^3$ (Borak, p.12).

Response: The EPA observes that the PM_{10} levels in the studies by Hefflin et al. (1994) and Gordian et al. (1996) were generally well below 1000 $\mu g/m^3$. In the Anchorage study, the mean and maximum PM_{10} concentrations were 45.5 $\mu g/m^3$ and 565 $\mu g/m^3$,

respectively (Gordian et al., 1996). Hefflin et al. (1994) reported peak PM_{10} concentrations of nearly 1700 $\mu g/m^3$, but with a mean of 40 $\mu g/m^3$; the authors also concluded that the high concentration days had a minimal impact on the association reported between respiratory emergency department visits and PM_{10}. This indicates that the highest concentration days did not drive the association between PM_{10} and respiratory morbidity, not that there are no effects associated with high concentrations of PM_{10}.

(6) *Comment*: Some commenters argued that exposure measurement error should prompt EPA to adopt a more stringent level for the coarse particle standard. According to these commenters, EPA's choice of level for the proposed standard contradicts the principle that EPA must adopt protective primary NAAQS even where the pollutant's risks cannot be quantified or precisely identified by nature or degree, quoting ATA III, 283 F. 3d at 369. These commenters stated that the uncertainties regarding measurement error in the relevant epidemiologic studies cut in both directions, and the proper protective course is to establish levels based on those in the epidemiologic studies with an adequate margin of safety.

Response: The approach of setting a standard which provides protection equivalent to that provided by the current 24-hour PM_{10} standard, was considered scientifically acceptable by CASAC. See also section III.D.2 of the preamble to the final rule and other comment responses regarding the reasonableness of EPA's approach. See ATA III, 283 F. 3d at 370, 377, 378-79, 380 (standards found reasonable based in part or in whole on CASAC support for them). Commenters' characterization of EPA's decision as insufficiently precautionary and thus at odds with a basic statutory purpose reflects their basic disagreement with the public health judgment made by the Administrator in deciding what level is requisite—neither higher nor lower than necessary—to provide protection. While EPA respects the commenter's opinion, it is at core a difference in judgment regarding how to apply the applicable law in light of an uncertain body of evidence, and not a difference in interpretation of the legal framework in which NAAQS decisions must be made.

(7) *Comment:* Some commenters stated that the scientific record does not support the proposed level of 70 $\mu g/m^3$, which they argue is based in large part on the short-term mortality studies which the Criteria Documents found to be the most uncertain of the coarse PM studies. The commenters note that both the CASAC and EPA staff recommended against reliance on the mortality studies as a basis for coarse PM standards, but that "[R]emarkably, the mortality studies judged … to be an insufficient basis for standards are used to shore up the deficiencies of the morbidity studies" for purposes of setting level (Coarse Particle Coalition, p. 42).

Response: These commenters misstate EPA staff and CASAC's conclusions on the relevance and use of mortality studies in standard setting. Moreover, they appear to ignore the substantial reliance placed on the morbidity studies in developing the proposal as well as in the final decision.

While overall, as noted in the Staff Paper and Criteria Document, the evidence from mortality effects is not as strong for coarse particles as for fine particles, both the serious nature of the effect as well as the pattern of results from studies conducted in locations with relatively high coarse particle levels and comparatively lower fine particle levels make it important to give careful consideration to this effect in this standard review. In particular, as discussed in section III.B of the preamble, the more robust, statistically significant results for coarse particles and cardiovascular mortality as compared to fine particles in the three Phoenix studies (Mar et al., 2003; Clyde et al., 2000; Smith et al., 2000) and in Coachella Valley (Ostro et al., 2003) are suggestive of a significant mortality risk. By contrast, the six cities study reanalyses find no coarse particle effect on total mortality, except for Steubenville, an industrial location with the highest levels of coarse particles (50 $\mu g/m^3$) of the six. In this location, the positive coarse particle effect (significant in Schwartz, 2003) is notably larger than that for fine particles, which is not significant in either reanalysis (Schwartz, 2003; Klemm and Mason, 2003). Given these results and the greater measurement error for coarse as compared to fine particles, the lack of mortality effects for single or two pollutant models in a number of locations with lower coarse particle concentrations cannot be used to rule out a potential causal link between coarse particles and mortality.

The pattern of association at higher levels with no effects at lower levels as well as the problem of assigning appropriate concentration levels limited the utility of the mortality study results in the cities selected for the coarse particle risk assessment, which looked at a range of alternative standard levels well below those permitted by the current standards. Given the mixed results, staff chose not to use these studies in the risk assessment (EPA, 2005a, chapter 4). In developing recommendations for alternative standard levels, however, EPA staff placed substantial reliance on the mortality studies in establishing the upper bound of the recommended range (70 $\mu g/m^3$) (e.g. EPA, 2005a, p. 5-67). Recognizing the exposure measurement issues for coarse particles, staff did additional assessments examining the monitoring data used in the studies and then examining the PM_{10} levels reported for regulatory networks in the same locations as a check (Ross and Langstaff, 2005). The CASAC consensus endorsed the assessment in the staff paper and a majority accepted the range for the standard levels as appropriate.

The EPA also notes that the Staff Paper, the proposal, and the final decision on the level and form of the 24-hour coarse particle standard all also place substantial weight on the results of the morbidity studies (see section III.D.2 of the preamble to the final rule).

(8) *Comment:* Some commenters argued the scientific evidence mandates a lower level to protect against adverse health effects. These commenters cited studies reviewed in the Staff Paper which they claimed showed significant associations between health effects and $PM_{10-2.5}$ concentrations at levels between 30-40 $\mu g/m^3$, and recent decisions by the European Union and the State of California to adopt 24-hour PM_{10} standards of 50 $\mu g/m^3$. These commenters argued that, even considering EPA's analyses of the uncertainties in the relevant ambient concentration measurements, these studies, particularly those in Atlanta, Seattle, and Toronto and the six-cities study of respiratory symptoms in children (Schwartz and Neas, 2000), demonstrate the need for a more stringent level of protection

than that provided by the current standards. In addition, these commenters pointed to the study review conducted by Brunekreef and Forsberg (2005) and numerous "new" studies published too recently for inclusion in the Criteria Document such as Mar et al. (2004), Chen Y et al. (2005), and Lin et al. (2005), as supportive of lower levels.

Response: The EPA has conducted a careful assessment of the studies cited by commenters from the Staff Paper assessment but reaches substantially different conclusions about their implications for the level of a 24-hour standard for thoracic coarse particles. The EPA had various reasons for not placing primary reliance on the reported air quality results in these studies for selecting a standard level. The Atlanta study (Tolbert et al, 2000), found a significant effect for PM_{10}, but not for coarse particles. Both the Six Cities children's diary study (Schwartz and Neas, 2000) and the Toronto hospital admissions study (Burnett et al., 1997) were conducted for a periods of less than one year, making it difficult to determine what peak value across all seasons in a year might represent exposures of concern.

Based on a careful assessment of available studies, EPA staff recommended consideration of a range of levels for a 24-hour $PM_{10-2.5}$ standard extending from a level equivalent to the current PM_{10} standard down to a level of 50 $\mu g/m^3$, which is clearly above that suggested by these commenters. The CASAC found general agreement that the "staff had presented a reasonable justification" for this range of levels. While EPA strongly agrees that the available scientific evidence supports and requires maintaining the level of protection provided by the current 24-hour PM_{10} standard, the limited extent of epidemiological evidence as well as the unusually large uncertainties in measuring exposures to thoracic coarse particles, particularly at lower levels, argue for the more restrained interpretation advocated by EPA staff and CASAC.

As stated above in section II.B.2.c on Averaging Time, EPA does not believe that standards adopted by the State of California or, by extension, the European Union, which operates under a different legal and policy structure, provide a relevant guide for establishing U.S. National Ambient Air Quality Standards.[8] While EPA agrees that the assessment of Brunekreef and Forsberg (2005) supports separate regulation of fine and coarse particles, these authors make no recommendations with respect to appropriate levels of protection.

To the extent that commenters cited "new" studies in support of their argument for a more stringent standard to protect against health effects associated with exposure to coarse particles, EPA notes that as in past NAAQS reviews, EPA is basing the final decisions in this review on the studies and related information included in the PM air quality criteria that have undergone CASAC and public review, and will consider the newly published studies for purposes of decision making in the next PM NAAQS review. While a provisional evaluation of these newer studies, taken at face value, may suggest mortality and morbidity effects occur at levels comparable or lower than those considered

[8] See California Health and Safety Code section 39606 (d) (1) (which lacks any requirement that ambient standards be "requisite" to protect public health, and (a) (2) (public health standard may take into account effects on the economy).

in the current review, it would be inappropriate to draw that conclusion, as commenters do, without the kind of assessment and analysis provided by the formal criteria and standards review process. As evidenced by the uncertainties found in the detailed assessment of key coarse particle studies in the Staff Paper, such analyses are particularly crucial for coarse particle studies that may be relevant to selecting the level of the standard.

(9) *Comment:* In the view of some commenters, the proposed standards for coarse particles are not requisite to protect human health, because EPA has not made any showing that the standard is "sufficient" to protect against the absence of adverse effects. Moreover, limited data is not an excuse for failing to establish the level at which there is an absence of adverse effect. To the contrary, data limitations are relevant to ensuring that there is an adequate margin of safety beyond the level established as creating no adverse effects (citing Lead Industries, 647 F. 2d at 1154-55).

*Response***:** Notwithstanding the significant difference in evidence regarding which types of thoracic coarse particles may be associated with adverse health effects, EPA is adopting a standard applicable to all such particles, in large part to provide an adequate margin of safety from effects which have not yet been uncovered. See section III.C. 2 of the preamble to the final rule, citing to (among other authorities) the same part of Lead Industries cited in this comment. The EPA thus agrees with the comment that limited data in and of itself does not automatically justify a qualified indicator for thoracic coarse particles. The commenters appear to argue that in setting a NAAQS, EPA must affirmatively demonstrate that exposure at the level of NAAQS has been demonstrated to not be harmful, i.e. to demonstrate that there is an absence of risk of harm at the level of the NAAQS. As discussed in more detail in section E of this Response to Comments, that conclusion is not supported by Lead Industries or other applicable case law.

(10) *Comment:* Some commenters expressed support for the proposed 98th percentile form for the proposed $PM_{10-2.5}$ standard, largely because the 98th percentile would provide a more stable statistical basis for making nonattainment determinations.

Response: While EPA generally favors the concentration-based form for short-term standards, EPA also notes that adopting such a form in this review without changing the level would result in a standard that would not provide the same protection as the current standard, and the level of the standard would have to be adjusted downward to achieve the desired protection. Given the overall decision to provide the same protection as the current standards, the Administrator has concluded it is best to retain both the form and the level of the current primary 24-hour PM_{10} standard.

(11) *Comment:* Some commenters opposed the proposed 98th percentile form for the proposed $PM_{10-2.5}$ standard because they felt it was inappropriate to allow as many as 21 days over the level of the standard over the course of a three-year period. These commenters argued for a more restrictive form (generally 99th percentile) to ensure the protection of public health with an adequate margin of safety.

Response: The EPA notes that the current one-expected-exceedance form of the 24-hour PM_{10} standard allows only three days above the standard over a three-year period, satisfying the concerns of these commenters.

3. Specific Comments on Interpreting the Scientific Evidence

(1) *Comment:* Some commenters disagreed with EPA's interpretation of five key epidemiologic studies conducted in urban areas (Ito, 2003; Burnett et al., 1997; Sheppard et al., 2003; Mar et al., 2003; Ostro et al., 2003) that found statistically significant relationships between coarse particles and health effects based on single pollutant models. These commenters placed significant weight on the alternative interpretations of these studies that EPA described in the proposal to encourage additional public comment (71 FR 2671-72). In particular, the commenters argued that when $PM_{2.5}$ or gaseous co-pollutants were added to the underlying models, the effects associated with $PM_{10-2.5}$ lost statistical significance. In the view of these commenters, by relying on single-pollutant models within these studies, even when multiple-pollutant models are available, EPA has deliberately selected the least rigorous evidence, and has systematically overstated the apparent effects of coarse particle pollution. The National Mining Association and National Cattlemen's Beef Association submitted an analysis conducted by a consultant who pointed, as an example, to EPA's reliance on the single pollutant model from Burnett et al. (1997) in the proposal, despite the fact that positive associations noted in a single-pollutant model disappeared after adjustment for O_3, NO_2, and SO_2.

Response: The EPA does not agree that the results of thoracic coarse particle health studies have been "systematically overstated". The potential for confounding between PM and other air pollutants has been extensively evaluated in the 2004 Criteria Document and in previous Criteria Documents. As discussed in Section 8.4.3 of the 2004 Criteria Document, EPA has long recognized that the determination of the extent to which associations with health outcomes can be attributed to PM acting alone or in combination with other pollutants is complex. The concentrations of many air pollutants may be closely correlated due to emissions by common sources and dispersion by common meteorological factors. There may also be biological interactions between pollutants for some health responses.

Single-pollutant models have the potential to overestimate the effect of that pollutant, to the extent that other co-varying pollutants that are not included in the analysis also contribute to the health outcome. However, multi-pollutant models can produce misleading results for several reasons. As discussed in Section 8.4.3 of the Criteria Document, including several highly correlated pollutants in a statistical model can yield unstable results that do not provide reliable estimates of effect for any of the pollutants. Including variables that are unrelated to the effect (model "over-fitting") but correlated with the pollutant can result in increasing the standard error of the effect. Omitting a predictive variable (model "mis-fitting") can result in bias of the effect size; a common example of mis-fitting is using the same lag period for effect of each pollutant when different lag structures may be appropriate for different pollutants.

One key factor that can influence the results of multi-pollutant models is measurement or exposure error. As discussed above in section II.B.2.a.ii, measurement error is likely to be greater for thoracic coarse particles than for fine particles or the gaseous criteria pollutants. Exposure error is also likely to be increased for $PM_{10-2.5}$, based on observations that thoracic coarse particle concentrations are more spatially variable than fine particles and some gaseous pollutants, and concentrations of ambient thoracic coarse particles attenuated inside buildings. As discussed in Section 8.4.5 of the 2004 PM Criteria Document, "transfer of causality" can occur when pollutants are highly correlated with one another, when the "truly causal" variable is measured imprecisely and the potentially confounding variable is measured precisely. For complete transfer of causality to occur, the correlation between variables must be high, and the difference in precision of measurements large. However, EPA reported that it is likely that the coefficient size for $PM_{10-2.5}$ is underestimated in models that include co-pollutants with somewhat greater precision in measurement. This is likely to be the case in models including $PM_{10-2.5}$ and either $PM_{2.5}$ or the gaseous pollutants, all of which are generally measured with less error than $PM_{10-2.5}$.

Thus, EPA has recognized that there are uncertainties inherent in the results of both single and multipollutant model results, and has presented results of both in the Criteria Document and in the risk assessment. As shown in Figures 8-16 through 8-19 of the Criteria Document, in many cases the PM effect estimates are, in fact, robust to inclusion of gaseous co-pollutants in the models. The EPA concluded "It is also the case that the most consistent findings from amidst the diversity of multipollutant model evaluation results for different sites is that the PM signal comes through most clearly" (EPA, 2004, p. 8-254). In particular, Figures 8-16 through 8-18 show results for associations with $PM_{10-2.5}$ in single- and multi-pollutant model from studies conducted in Detroit (Ito, 2003), Coachella Valley (Ostro et al., 2003), Pittsburgh (Chock et al., 2000), and Toronto (Burnett et al., 1997).

Looking at each of these Figures in greater detail:

- In Figure 8-16, the associations between $PM_{10-2.5}$ and total mortality in single-pollutant models were not statistically significant, though the effect estimates were positive and of the same magnitude as those for $PM_{2.5}$ (Chock et al., 2000; Ito, 2003). Chock and colleagues (2000) report results of multi-pollutant models that include all four gaseous copollutants, and it can be seen that the effect estimates for $PM_{10-2.5}$ are nearly identical, even slightly larger, to the single-pollutant model results. Ito (2003) reports results for two-pollutant models that include each of the four gaseous copollutants, and again the effect estimates are only very slightly smaller or larger than that reported in the single-pollutant model. Overall, none of the associations with $PM_{10-2.5}$ was changed substantially in co-pollutant models.

- Figure 8-17 includes results for associations with cardiovascular mortality or hospitalization. Ostro et al. (2003) report a significant association between PM_{10-}

$_{2.5}$ and cardiovascular mortality in a single-pollutant model, and the association remains statistically significant and little changed in size in two-pollutant models with O_3 or NO_2. Ito (2003) reports an association between $PM_{10-2.5}$ and circulatory mortality that is positive but not statistically significant. In two-pollutant models, the association is slightly increased in size with O_3 or SO_2, and slightly decreased in size with NO_2 or CO (remains not statistically significant). Ito (2003) reports an association between $PM_{10-2.5}$ and hospital admissions for ischemic heart disease that is positive and statistically significant in a single-pollutant model. This association remains statistically significant in two-pollutant models with O_3 or NO_2, and it reduced slightly and of borderline significance in models that include SO_2 or CO. Ito (2003) also reports a positive, but not statistically significant association between $PM_{10-2.5}$ and hospitalization for heart failure. In two-pollutant models, the effect estimate shows a small increase in size with O_3, remains about the same with NO_2 or SO_2, and shows a small decrease with CO. Finally, Burnett et al. (1997) report a positive, statistically significant association between $PM_{10-2.5}$ and hospitalization for cardiovascular diseases in a single-pollutant model. This association remains statistically significant in two-pollutant models that include O_3, SO_2 or CO, though the effect estimate size is reduced somewhat in the model with SO_2; the effect estimate size is reduced and the association loses statistical significance in a two-pollutant model and a model that includes all four gaseous pollutants. Overall, $PM_{10-2.5}$ associations are not substantially changed with adjustment for co-pollutants for three of four associations, and is reduced in size with NO_2 (and all four gases together) in one.

- Figure 8-18 includes results for associations with respiratory mortality or morbidity. Ito (2003) reports a positive, but not statistically significant association between $PM_{10-2.5}$ and respiratory mortality in a single pollutant model that remains unchanged in two-pollutant models with NO_2, SO_2 or CO, but is reduced to nearly zero in a two-pollutant model with O_3. Similarly, a positive but not statistically significant association is reported with hospitalization for COPD that remains nearly unchanged in two-pollutant models with NO_2, SO_2 or CO, but is reduced to nearly zero in a two-pollutant model with O_3. In contrast, Ito (2003) reports a statistically significant association between $PM_{10-2.5}$ and hospital admissions for pneumonia that remains nearly unchanged in two-pollutant models with NO_2, SO_2 or CO, but is increased in size in a two-pollutant model with O_3. Finally, Burnett et al. (1997) report a positive, statistically significant association between $PM_{10-2.5}$ and hospitalization for respiratory diseases in a single-pollutant model. This association remains statistically significant in two-pollutant models that include O_3, SO_2 or CO; the effect estimate size is reduced and the association loses statistical significance in a two-pollutant model and a model that includes all four gaseous pollutants. Overall, $PM_{10-2.5}$ associations with respiratory mortality and COPD hospitalization are reduced in size with adjustment for O_3 (but not NO_2) in Ito (2003) and reduced in size with NO_2 (and all four gases together) in Burnett et al. (1997); note that the $PM_{10-2.5}$ association with pneumonia hospitalization increased in size with adjustment for ozone in Ito (2003).

These results clearly indicate that associations between mortality or morbidity and $PM_{10-2.5}$ are, in almost all cases, little changed with adjustment for gaseous co-pollutants. In some models, the effect estimates were reduced in multi-pollutant models; for example, with O_3 (but not NO_2) in associations for respiratory mortality or COPD hospitalization in Detroit (Ito, 2003) or with NO_2 (but not O_3) or all four gaseous pollutants and respiratory hospitalization in Toronto (Burnett et al., 1997). The results provide no indication that any of the gaseous pollutants is consistently and systematically more strongly associated with a particular health endpoint than is $PM_{10-2.5}$.

The commenters' consultant refers to the Toronto study (Burnett et al., 1997) as an example of co-pollutant confounding for thoracic coarse particle associations, and includes two quotes from the authors – that the PM results "disappeared after adjustment for O_3, NO_2 and SO_2" and that PM associations "could be completely explained by NO_2, a risk factor not as widely considered in North American locales as the other criteria pollutants" (p. 3). Taken in context, it can be seen that the authors are not discounting the associations reported with PM (the authors are not specifically discussing $PM_{10-2.5}$, but rather all PM mass indicators), but rather emphasizing the need to consider health benefits resulting from the reduction of *both* particles and gaseous pollutants.

The EPA observes that, while these authors recommend including all air pollutants simultaneously in statistical models, there is no consensus that such models are in fact optimal. Where gaseous and particulate air pollutant concentrations are correlated on a day-to-day basis, as is the case in many studies, including those in Detroit and Toronto, the collinearity between the various pollutants can be expected to inflate the variance or standard error of the coefficients, as discussed in Section 8.4.3 of the Criteria Document, and this effect would only be magnified with multiple collinear pollutants.

The Criteria Document also discussed alternative approaches to simple reliance on multipollutant modeling to evaluate more fully the likelihood that exposures to gaseous co-pollutants can account for the ambient PM-health effects associations now having been reported in numerous published epidemiology studies. One such approach is the use of principal component or factor analysis to determine which combinations of gaseous criteria pollutants and PM size fractions or chemical constituents together cannot be easily disentangled, and which pollutants are substantially independent of the linear combinations of the others. For example, the source-oriented factor analysis study of Mar et al. (2000) produced evidence suggesting independent effects of regional sulfate, motor vehicle-related particles, particles from vegetative burning, and $PM_{10-2.5}$ for cardiovascular mortality in Phoenix (as discussed in Section 8.2.2.4.3).

The EPA also notes that three different studies used essentially the same air quality data set to examine coarse and fine particles in Phoenix (Mar et al., 2000, 2003; Clyde, 2000; Smith et al., 2000). All three studies found significant associations between mortality and $PM_{10-2.5}$, but only one found a significant association for $PM_{2.5}$ (EPA, 2004, p. 8-57 to 66). Ito (2003) found a significant association between hospital admissions for ischemic heart disease and exposure to coarse particles, but not fine particles. While all

of these studies have limitations, it is difficult to ignore the fact that, despite the differential measurement error associated with coarse particles, a number of these studies find statistically significant associations for coarse particles, but not for fine particles. For these reasons, EPA believes that it would be inappropriate to presume that all of the effects associated with coarse particles in single pollutant models are actually the result of confounding by fine particles or gaseous pollutants.

(2) *Comment:* The consultant for the National Mining Association and the National Cattlemen's Beef Association also stated that in several key studies, "the use of two-pollutant models including both $PM_{2.5}$ and $PM_{10-2.5}$ reduced or eliminated the effects" of coarse particles (citing Schwartz and Neas, 2000; Lippman et al., 2000; Ito, 2003; Moolgavkar, 2000; and Burnett et al., 2000) (Borak, p. 4).

Response: The EPA agrees with the observation that fewer studies have considered potential confounding between fine and thoracic coarse particles. However, EPA does not agree that these studies show no associations with $PM_{10-2.5}$. First, EPA observes that the author is not correct in footnote 2 that describes the presentation of these studies in the preamble. The author observes that the Los Angeles and eight Canadian cities results are excluded from Figure 2, and postulates that this is because they used generalized additive models (GAM) and were not reanalyzed. In fact, eight Canadian cities study results were reanalyzed to address GAM issues, and the single-pollutant models results are included in Figure 2 (Burnett and Goldberg, 2003); however, the multi-pollutant model results presented in the initial report were not reanalyzed. For Los Angeles, the results of analyses using PM_{10} or $PM_{2.5}$ were reanalyzed, but not those for $PM_{10-2.5}$, and thus are not included in Figure 2.

Considering each of the four studies cited by the consultant:

- Eight Canadian cities studies: In the reanalysis report, the association between $PM_{10-2.5}$ and mortality was borderline significant or did not reach statistical significance in most models (Burnett and Goldberg, 2003); the association was not statistically significant in the original analysis (Burnett et al., 2000). In the original study, Burnett et al. (2000) present results for two multipollutant models; note that these results were not reanalyzed. Model I includes $PM_{2.5}$ and $PM_{10-2.5}$ as well as O_3, NO_2, SO_2 and CO. Model II includes the four gaseous pollutants and four fine particle components (sulfate, Zn, Ni and Fe). In the first model, the effect estimate for the relationship between $PM_{10-2.5}$ and mortality was 0.6 with a t-statistic of 1.6 (a t-statistic of 1.96 or greater indicates statistical significance); in a single-pollutant model, the effect estimate was 0.9 with a t-statistic of 1.4. Thus, the effect estimate was reduced by about one-third. However, the effect estimates for $PM_{2.5}$, O_3, NO_2, SO_2 and CO were reduced to a greater extent, from 1.6 to 1.0 for $PM_{2.5}$, from 3.4 to 1.6 for O_3, from 3.9 to 1.1 for NO_2, from 1.1 to 0.7 for SO_2 and from 2.1 to 0.7 for CO; the associations for all five pollutants were statistically significant in the multi-pollutant model (Burnett et al., 2000, p. 31). Thus, it can be said that the effect estimate for the association between

mortality and $PM_{10-2.5}$ was not as substantially changed in the multi-pollutant model as were effect estimates for $PM_{2.5}$ and the gaseous pollutants, though the association did not reach statistical significance in either the single- or multi-pollutant model. $PM_{10-2.5}$ and $PM_{2.5}$ were moderately correlated (r=0.37) in this study.

- Los Angeles: Moolgavkar (2000) included only limited evaluation of thoracic coarse particle effects, stating only "Because I had monitoring data on both PM_{10} and $PM_{2.5}$ in Los Angeles, I could investigate the association between coarse particles (defined as the difference between PM_{10} and $PM_{2.5}$) and COPD admissions. The results for the three age groups are presented in Table 5" (Moolgavkar, 2000, p. 79). In single pollutant models, there were associations between $PM_{10-2.5}$ and COPD hospital admissions for age groups 0-19 and 20-64 that were statistically significant on lag days 0, 2 and 3 for both age groups; smaller associations are reported for those aged >64 years. Two-pollutant model results are presented for the two younger age groups. At the 0-day lag, the size of the effect estimate remained unchanged for the 0-19 year group (4% change, t-statistics of 2.8 and 2.3 in single-pollutant and two-pollutant models, respectively), and was slightly increased, though the t-statistic was reduced, in the 20-64 year age group (from 2.2% with a t-statistic of 2.1 to 2.4% with a t-statistic of 1.9). In the younger age group, the effect estimates for $PM_{10-2.5}$ were generally unchanged, or reduced to a small extent, for the other lag days; larger reductions in $PM_{10-2.5}$ effect estimate size are seen in the two-pollutant models for the 20-64 year age group, such as a change from 3.5% (t-statistic of 3.0) to 2.2% (t-statistic of 1.7) at a 2-day lag. However, the effect estimates for $PM_{2.5}$ were sometimes more substantially changed in these two-pollutant models. At lag day 0, for example, where there was practically no change in the results for $PM_{10-2.5}$, effect estimates decreased from 1.7% (t-statistic of 1.9) to 0.6% (t-statistic of 0.5) for the 0-19 year age group, and from 1.7% (t-statistic of 2.5) to 1.0% (t-statistic of 1.3) in the 20-64 year age group. It is important to note that these results were not reanalyzed to address GAM issues; however, they provide no indication that $PM_{10-2.5}$ is especially sensitive to adjustment for effects of $PM_{2.5}$.

- Detroit: Ito (2003) presents results of two-pollutant models for $PM_{10-2.5}$ and $PM_{2.5}$ in the reanalysis report, observing that "the pattern found in the original analysis was essentially unchanged" (p. 146). In single-pollutant models, statistically significant associations were reported between $PM_{10-2.5}$ and hospital admissions for ischemic heart disease and pneumonia, and a borderline significant association with circulatory mortality; positive but not significant associations were reported with the other health outcomes under study. In two-pollutant models, the relative risk (RR) for $PM_{10-2.5}$ and circulatory mortality decreased from 1.075 to about 1.04 (based on Figure 7), and the association goes from borderline significant to not significant; the results for $PM_{10-2.5}$ show a similar pattern, decreasing from an RR of 1.046 to about 1.03, and were not significant in either model. For pneumonia hospital

admissions, the decline in RR for $PM_{10-2.5}$ is more dramatic, going from 1.114 to about 1.025 and losing significance; associations with $PM_{2.5}$ were also reduced from 1.185 to about 1.10, also losing statistical significance. Results for hospital admissions for ischemic heart disease for $PM_{10-2.5}$ changed from RR of 1.101 to 1.04, losing statistical significance, while the RR's for $PM_{10-2.5}$ changed from 1.063 to 1.05 (not significant in either model). $PM_{10-2.5}$ and $PM_{2.5}$ were moderately correlated (r=0.42) in this study.

- Six U.S. Cities: Schwartz and Neas (2000) report that cough was the only response with which there was a statistically significant association with thoracic coarse particles. The correlation between $PM_{10-2.5}$ and $PM_{2.5}$ was moderate (0.41). In two-pollutant models, the association between $PM_{10-2.5}$ and cough remained statistically significant (Odds Ratios of 1.20 and 1.18 in one- and two-pollutant models, respectively), while the association with $PM_{2.5}$ lost significance. Thoracic coarse particles was not significantly associated with lower respiratory symptoms, and in two pollutant models [look up].reduced (Odds Ratios of 1.16 and 1.07 in one- and two-pollutant models, respectively). For lower respiratory symptoms, there was a nonsignificant association with $PM_{10-2.5}$ that was reduced in two pollutant models (Odds Ratios of 1.14 and 1.05 in one- and in two-pollutant models, respectively), whereas associations with $PM_{2.5}$ were statistically significant in both one- and two-pollutant models (Odds Ratios of 1.33 and 1.29 in one- and two-pollutant models, respectively).

Additional support for independence of effects for fine and thoracic coarse particles can be provided in results from studies where the associations appear to have different lag periods. Some insight into this concern may be obtained by looking at one study in Phoenix (Mar et al., 2000, 2004) that found statistically significant results for $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}. Results are shown in Table 1. β is the increase in relative risk for a 1 μg increase in PM in the log (effect), linear (cause) model used in community, time-series epidemiology. The relative risk for an increase in PM of x μg is given by $\text{Exp}(\beta \bullet x)$ and the % increase in risk per x μg increase in PM is given by $((\text{Exp}(\beta \bullet x))-1)*100$. Note that on lag day zero, $PM_{10-2.5}$ is significant but $PM_{2.5}$ is not. However, on lag day one, $PM_{2.5}$ is significant but $PM_{10-2.5}$ is not. Thus, $PM_{10-2.5}$ has its effect on lag day zero and $PM_{2.5}$ has its effect on lag day one. This indicates that $PM_{2.5}$ and $PM_{10-2.5}$ have independent effects on cardiovascular mortality.

Table 1. Data taken from Mar et al. (2003)

	Mar et al. (2003)					% Increase in Risk for an increase in PM of	
Pollutant	IQR	Lag	B	SE	T	10 μg/m3	IQR
$PM_{10-2.5}$	18.39	0	0.00242	0.00108	**2.24**	2.45	4.55
		1	0.00166	0.00106	1.57	1.67	3.10

$PM_{2.5}$	8.52	0	0.00397	0.00283	1.40	4.05	3.44
		1	0.00698	0.00278	**2.51**	7.23	6.13

(3) *Comment*: A consultant for the Engine Manufacturers Association noted that in the review of studies conducted by Brunekreef and Forsberg (2005), the authors concluded that the evidence of mortality effects is stronger for fine particles than for coarse particles. The authors found that for mortality studies that analyzed $PM_{2.5}$ and $PM_{10-2.5}$ jointly, the effects of $PM_{10-2.5}$ were reduced to non-significance after adjustment for $PM_{2.5}$, but adjustment in the reverse order did not reduce $PM_{2.5}$ effects to non-significance (Gradient, p. 11).

Response: The EPA notes that the conclusions drawn by Brunekreef and Forsberg (2005) review of the health evidence with respect to coarse particle effects on mortality and morbidity are generally consistent with those drawn in EPA's evaluation of the evidence. For mortality, Brunekreef and Forsberg (2005) conclude that there is "some evidence" of effects, although they observe that the associations between $PM_{10-2.5}$ and mortality are reduced in two-pollutant models with $PM_{10-2.5}$, while the associations with $PM_{2.5}$ are not. For morbidity, the authors conclude: "In studies of COPD, asthma and respiratory admissions coarse PM has a stronger or as strong short-term effect as fine PM" (Brunekreef and Forsberg, 2005, p. 315). In the few studies that reported two-pollutant models for $PM_{10-2.5}$ and $PM_{2.5}$, the authors report that $PM_{10-2.5}$ is more robust for some health outcomes while $PM_{2.5}$ is more robust in two-pollutant models for others; the authors state that the evidence isn't sufficient to draw conclusions about the relative importance of one fraction over another. These conclusions are entirely consistent with those drawn in EPA's review of the evidence. Based on their assessment of the evidence, these authors also conclude that "the coarse particle fraction is also of importance in the regulatory process as well as for control measures" (Brunekreef and Forsberg, 2005, p. 316).

While overall the evidence from mortality effects is not as strong for coarse particles as for fine particles, both the serious nature of the effect as well as the pattern of results from studies conducted in locations with relatively high coarse particle levels and comparatively lower fine particle levels make it important to give careful consideration to this effect in this standard review. In particular, as discussed in section III.B of the preamble, the more robust, statistically significant results for coarse as compared to fine particles in the three Phoenix studies (Mar et al., 2003; Clyde et al., 2000; Smith et al. 2000) and in Coachella Valley (Ostro et al. 2003) are suggestive of a significant mortality risk. By contrast, the Six Cities study reanalyses find no coarse particle effect, except for Steubenville, an industrial location with the highest levels of coarse particles (50 $\mu g/m^3$) of the six. In this location, the positive coarse particle effect (significant in Schwartz, 2003) is notably larger than that for fine particles, which is not significant in either reanalysis (Schwartz, 2003; Klemm and Mason, 2003). Given these results and the greater measurement error for coarse as compared to fine particles, the lack of mortality effects for two pollutant models in a number of locations with lower concentrations cannot be used to rule out a potential causal link between coarse particles and mortality.

(4) *Comment*: One commenter claimed that EPA has over-emphasized results from some studies (e.g., Ito et al., 2003) while ignoring weak or negative results from other studies (e.g., Cifuentes et al., 2000). Furthermore, the commenter believed EPA has failed to account for results seen in studies such as Lipfert et al. (2000) (negative associations between mortality and $PM_{10-2.5}$ in Philadelphia) and Schwartz and Neas (2000) (negative associations between PEF measurements in children and $PM_{10-2.5}$ exposure) (Engine Manufacturers Association).

Response: The EPA does not agree that results of one group of studies were selectively emphasized over another. Cifuentes et al. (2000) is a study conducted in Santiago, Chile, and the results of this study have been included in EPA's assessment of the epidemiologic evidence; the results are presented along with other studies in Table 8-2 and Figure 8-5 of the Criteria Document. As shown in Figure 8-5, statistically significant associations were reported between mortality and both $PM_{10-2.5}$ and $PM_{2.5,}$ but the authors report that associations with $PM_{10-2.5}$ were more sensitive to adjustment for co-pollutants than were associations with $PM_{2.5}$; associations with $PM_{10-2.5}$ were reduced in two-pollutant models with $PM_{2.5}$ (correlation of 0.52 between the two PM indices) (Cifuentes et al., 2000). As stated in the Staff Paper and the preamble to the proposed rule, EPA placed emphasis on the results of U.S. and Canadian studies in the policy assessment, due to the potential for differences in air quality mixtures and demographics in other countries; however, EPA observes that this study's findings were included in the basis for EPA's conclusion the evidence is suggestive for associations between short-term exposure to $PM_{10-2.5}$ and mortality. The EPA also presents the results of Lipfert et al. (2000) in Figure 8-5 of the Criteria Document, where it can be seen that associations between $PM_{10-2.5}$ and $PM_{2.5}$ are generally of the same magnitude, but the association for $PM_{10-2.5}$ is not statistically significant. The commenters refer to negative associations between mortality and $PM_{10-2.5}$ in Philadelphia, but a review of the numerous results presented in Tables 3, 4, 5 and 7 reveals that a negative association is reported only with respiratory mortality using mortality data from Philadelphia and suburban Pennsylvania counties (Lipfert et al., 2000, p. 1506). In all other model results, the associations between mortality and $PM_{10-2.5}$ are positive, with larger associations for cardiovascular mortality. These results are consistent with EPA's conclusions about the relationship between $PM_{10-2.5}$ and mortality. Finally, EPA included the pulmonary function results from Schwartz and Neas (2000) in its assessment of evidence, and from the results of this study two European studies, concluded that in non-asthmatic subjects "Coarse fraction particles had little association with evening peak flow" (EPA, 2004, p. 8-312). The EPA did not downplay these results, but rather recognized that the few available studies did not indicate an association between $PM_{10-2.5}$ and lung function in non-asthmatic subjects.

(5) *Comment:* A consultant for the National Mining Association and the National Cattelemen's Beef Association objected to the absence of a well-defined criterion for determining whether health effects data from time-series epidemiological studies were sufficiently precise to be used in quantitative estimates of exposure-response relationships. Noting that EPA had used such a criterion—based on length of the study period and number of deaths per day—in the final PM Staff paper (EPA, 2005a), the

commenter stated that this was appropriate because it demonstrated "that some studies are better than others (because of their size or for other reasons) and that studies of lesser quality should not be relied upon as one might rely on studies of higher quality." (Borak p. 4) The commenter believes that in departing from this approach in the proposed rule, EPA "has deleted its Staff's criterion for objectively distinguishing between individual studies." The result, according to the commenter, is that EPA has inappropriately placed great reliance on the results of the Coachella Valley studies and the Six Cities results from Steubenville, even though "EPA Staff had objectively determined that both data were too imprecise to be used for quantitative assessments and thus their conclusions should be viewed with caution." The commenter is concerned that the approach taken in the proposal serves to conceal the limitations of those studies, and to avoid the exclusion of positive findings that derive mainly from weaker studies (Borak, p. 5, 9).

Response: The EPA does not agree that these studies would not meet this criterion for use in quantitative risk assessment. Based on the number of days with $PM_{10-2.5}$ data, and the average number of deaths/day (total nonaccidental mortality), the log of mortality-days in the Coachella Valley study was 9.8 (Ostro et al., 2003) and in the Steubenville study was 8.6 (Klemm et al., 2003).

The EPA also notes that this criterion was not used as a characterization of the quality of studies, but rather as an indicator of statistical power of the study, or likelihood that the study was of sufficient size to be able to detect an association if it was present. Lower levels of study precision would likely result in increased standard error values for an association, but low statistical power does not cast doubt on statistically significant associations that are found despite the lower level of precision in the study.

(6) *Comment:* Some commenters stated that EPA failed to consider and give appropriate weight to a significant number of studies which relied on larger and more powerful data sets, were of longer duration, and assessed $PM_{10-2.5}$ using multi-pollutant models, but did not find any statistically significant associations, including Schwartz et al. (1996), Thurston et al. (1994), Sheppard (2003), Fairley (2003), and Lipfert et al. (2000).

Response: The EPA considered the results of all of the studies noted by these commenters, as evidenced by the inclusion of all of them in Figure 2 of the proposal.[9] The EPA's responses to other comments in this section and in earlier sections of this document address the approach EPA used in an integrated assessment of the epidemiological data, which includes these studies.

(7) *Comment:* In support of arguments against any coarse particle standard, and particularly one qualified to focus on urban-type particles, the Engine Manufacturers Association submitted an analysis done by a consultant stating that foreign studies, several of which reported results directly contrary to the risks attributed to coarse PM in the proposal, challenged the idea that urban coarse particles have been shown to be toxic. In particular, the commenter pointed to a study done in the urban-industrial region of Birmingham, UK

[9] Figure 2 of the proposal displayed the results of the updated reanalysis of the Schwartz et al. (1996) data by Klemm and Mason (2003).

(Anderson et al., 2001). The commenter noted that the study results indicated that urban coarse particles were negatively associated with respiratory mortality (results statistically significant) and with all-cause and cardiovascular mortality (results not statistically significant). The commenter stated that "it is difficult to reconcile the proposed toxic nature of urban PM-coarse with these 'healthy' results for a population of 2.3 million." (Gradient, p. 10)

Response: The reason for placing greater weight on epidemiological studies conducted in the U.S. and Canada, particularly for quantitative risk assessment and decisions on the level and form of the standards, is discussed elsewhere in this document. In considering the implications of the study, however, it is of note that however large the population, the PM levels in this area are generally low. With a maximum PM_{10} level of 102 $\mu g/m^3$, and an annual average $PM_{2.5}$ level of 14.5, the area would comply with all current U.S. standards. Given these relatively low levels, it is not surprising that the authors concluded that it was "difficult to discern clear effects on mortality and hospital admissions except in certain age or diagnostic subgroups and seasonal analyses" (Anderson et al., 2001, p. 504). The authors found clearest evidence for fine particle components from motor vehicles and secondary particles. Despite the very low annual and daily levels of thoracic coarse particles, however, the authors concluded that "effects of the coarse fraction cannot be excluded" (Anderson et al., 2001, p. 504). This is apparently based on their observation of positive and nearly significant associations between 'warm season' $PM_{10-2.5}$ and both all cause (Figure 1), and respiratory disease related mortality (Figure 2) (Anderson et al., 2001, p. 507). It is difficult to see why commenters offer this British study as evidence of a lack of coherence with North American studies with respect to the effects of urban coarse particles.

(8) *Comment:* A consultant for the National Mining Association and the National Cattlemen's Beef Association offered a detailed critique of EPA's treatment of the evidence regarding the association between asthma and exposure to coarse particles, concluding that "there is no sound basis for concluding that coarse particulates aggravate asthma or provokes [sic] asthma symptoms, even at exposure levels considerably higher than those considered in the Proposed Coarse PM NAAQS" (Borak, pp. 10-14)

Response: The EPA observes that the consultant quotes from the proposal notice on the link between thoracic coarse particles and asthma are drawn from a brief summary of statements made in the preamble[10] to the PM NAAQS decision in 1997 and authors' conclusions about their own study results. The summary of the relevant evidence from health studies in the January 2006 proposal makes it clear that it is EPA's view that exposure to thoracic coarse particles is linked with a range of health effects, especially respiratory morbidity effects, of which asthma is an important effect. The EPA disagrees

[10] In referencing the brief summary of studies used in the 1997 decision, the consultant for National Mining Association/National Cattlemen's Beef Association apparently misreads EPA's statement to suggest that both studies cited by reference to that decision (Gordian et al., 1997 and Hefflin et al., 1994) found significant associations between PM_{10} and aggravation of asthma. As is made clear in the 1997 preamble, EPA recognizes that one study found an asthma association and the other found associations with respiratory infections and symptoms.

with a number of points in the consultant's overview of the health evidence regarding the link between $PM_{10-2.5}$ and asthma (and other respiratory morbidity effects).

The consultant raises a series of issues regarding two PM_{10} studies done in Anchorage by Gordian et al. (1996) and Choudbury et al. (1997). The consultant criticizes the health outcomes used in the study, and questions the pattern of results for asthma and upper respiratory infections (URI). He also states that studies of outpatient visits may have overestimated effect sizes based on the possibility that repeated visits were made by the same individual.

As discussed elsewhere, EPA believes these studies are relevant to evaluating the health effects of coarse particles, because the authors provide evidence that PM_{10} is dominated by coarse particles, mainly of crustal and volcanic origin. Gordian et al. (1996) and the related study (Choudbury et al., 1997) report associations between outpatient visits for asthma and PM_{10} that are significant at both the 0-day and 1-day lag, and a significant association with outpatient visits for URI at a 0-day lag. There is no reason to believe that these associations should be temporally linked as the consultant claims. The authors have not evaluated potential associations with both initial aggravation of asthma followed by development of URI in the same individuals. In fact, both are associations between daily changes in PM_{10} and the number of daily outpatient visits for asthma or URI. The association links pollution changes with acute changes in health outcome, and does not necessarily indicate that PM_{10} exposure on a given day caused a person to develop a URI; rather the PM_{10} exposure likely aggravated the URI condition such that the patients sought medical assistance. With regard to the potential for repeated outpatient visits, the authors employed a commonly used statistical technique, a weighted moving average filter, to remove autocorrelation in the pollution and outpatient visit series (Gordian et al., 1996, p. 291). The authors observe that the data set may have included repeat visits to a doctor by the same individuals, but their statistical methods should serve to control for effects of autocorrelation in the outpatient visit data. Thus, EPA disagrees that this study's results should be dismissed as was done by this consultant.

The consultant also questions the results of the two Anchorage studies as well as other studies by Schwartz et al. (1997) because, in these studies, the outcome measures were not associated with the highest levels of exposure. The EPA does not agree that this observation calls into question the results of the studies. It is clearly stated in the studies that the purpose was to test for the presence of an association when the days with the highest concentrations were removed. In all cases, it was found that the associations remained statistically significant, indicating that they were not driven by just a few high exposure days. Because the peak exposures in some of these studies were very high, on the order of 1000 $\mu g/m^3$ or more, it is not unreasonable to expect that the population could readily perceive the elevated levels, possibly leading more sensitive individuals to curtail outdoor activities to reduce exposure (cf. Hefflin et al., 1994).

EPA also disagrees with the consultant's dismissal of the results reported by Burnett et al. (1997) on the basis of confounding by gaseous co-pollutants, as discussed at some length above.

The consultant also dismisses the study in Detroit (Ito, 2003) as not being new for this review, but in fact the original publication (Lippmann et al., 2000) was one of the more recent studies, meaning that it was published after completion of the previous PM NAAQS review. The EPA disagrees that the HEI Review Committee summarily dismissed the results of this study as "inconclusive." Reflecting on the investigators' originally stated hypothesis that acidic particles, sulfates and fine particles would have the strongest associations with health outcomes, the HEI review committee observes:

> In the 1992-1994 analysis, $PM_{10-2.5}$ effect-size estimates were similar to those for $PM_{2.5}$, and sometimes even higher – for example, for ischemic heart disease and stroke. Because $PM_{10-2.5}$ and $PM_{2.5}$ were not highly correlated in correlation coefficient and factor analyses, it is possible that the observed associations between coarse particles and health outcomes were not confounded by smaller particles. This result suggests that there may still be a rationale to consider the health effects of the coarse thoracic fraction as well as the fine fraction of PM (HEI, 2000, p. 81).

Similarly, the consultant dismisses the results of a study of asthma hospitalization in Seattle (Sheppard et al., 1999; reanalyzed 2003), criticizing the air quality data used in the studies and stating that wood burning and motor vehicle exhaust were the two major contributors to PM in this area. The EPA notes that imputation methods were used to replace missing data for both $PM_{2.5}$ and $PM_{10-2.5}$ in this study, thus it is not clear why the consultant finds that the study provides more support for $PM_{2.5}$-related effects than thoracic coarse particle effects on the basis of data quality.

The EPA believes that the specific issues raised by the consultant with individual studies do not support dismissal of this body of literature. The recently published studies, along with evidence available in the previous PM NAAQS review, support the finding that exposure to thoracic coarse particles is associated with respiratory morbidity, including exacerbation of asthma.

(9) *Comment:* One commenter criticized EPA's reliance on Kleinman, et al. (1995) and Steerenberg et al. (2003) regarding the effects of road dust. The commenter stated that "because neither study differentiated between fine and coarse particulate matter, it is difficult to see how either study is relevant to setting a $PM_{10-2.5}$ standard (Alliance of Automobile Manufacturers, p. 12)

Response: Kleiman et al. (1995) exposed rodents to both laboratory-generated fine particles (ammonium sulfate and ammonium nitrate) and resuspended road dust, finding effects (decrements in macrophage-dependent lung defense function) with both fractions. In order to make it possible for rodents to inhale the urban coarse particulate material, it was necessary to use particles in a size range of (< 1 μm): unlike the human upper respiratory system, these animals' upper respiratory system generally exclude particles larger than about 1 μm There is little doubt that this material is representative of the

composition of resuspended urban road dust, and whatever the particle size, the study is clearly of direct relevance to an examination of the toxicity of this material.

Steerenberg et al. (2003) examined the combined effect of coarse and fine road tunnel dust collected with a high-capacity particle size classifier; the adjuvant capacity of the road tunnel dust was the greatest compared to other particle types following ovalbumin sensitization. Over 60% of the mass of the road dust came from traffic-derived particles, although endotoxin was also identified. The mix of fine and coarse origin particles makes this more representative of the composition of resuspended urban road dust that has been significantly enriched by traffic emissions. As with the work of Kleinman et al., (1995) this composition of particles in this studies is of relevance to an examination of the toxicity of resuspended urban coarse particles.

(10) *Comment:* Some commenters noted that several epidemiological studies that examined seasonal effects (e.g. Smith et al., 2000 as well several studies summarized by Brunekreef and Forsberg, 2005), found that some effects varied with season in a way that is suggestive of an influence of bioaerosols in $PM_{10-2.5}$ and not necessarily of "urban" emissions.

Response: The EPA agrees that some of these studies do show stronger effects in spring and summer. The Criteria observed that the higher significance levels for thoracic coarse particles in spring and summer in Smith et al. 2000 occurs when the crustal elements are highest and anthopogenic elements are the lowest. These seasons are usually higher for biological actitivity as well. However, other factors such as changes in activity patterns that increase outdoor exposures or a higher range of coarse concentrations in warmer seasons (e.g. snow cover in cooler regions reduces coarse particle emissions) may also play a role. At present, there are not enough studies documenting consistent seasonal relationships nor enough data on coarse particle composition to draw firm conclusions. Furthermore, urban or industrial emissions contaminated coarse particles in all seasons to some extent.

(11) *Comment:* Some commenters stated that any contention that exposure to natural coarse particles is not associated with adverse health effects directly contradicts previous research. The Colorado Dept. of Public Health and the Environment, for example, stated that existing studies indicate that even chemically non-reactive PM is damaging to lung tissue. The commenter states that inhalation of inert "natural" sand particles (silica) has long been associated with silicosis (Hardy et al., 1994), and even short-term exposure to high levels of natural particles results in lung inflammation, shortness of breath, and low blood oxygen levels. The commenter also states that long-term exposures to even low levels of silica dust provoke the formation of nodules of chronic inflammation and scarring in the lungs and lymph nodes.

Response: The EPA evaluated the potential risk associated with typical levels of naturally occurring silica in crustal materials in the previous review, concluding that the available data do not provide evidence for a significant risk of silicosis at levels allowed by the PM_{10} standards (62 FR 38678). Further, the 1987 and 1997 evaluation of the

concerns related to lesser effects, including simple silicate pneumoconiosis revealed clear basis for establishing quantitative risks at ambient levels (EPA, 1996). In any event because the final decision maintains the protection afforded by the PM_{10} standards, EPA believes it has addressed these commenters' concerns.

(12) *Comment:* Some Tribal commenters submitted health statistics obtained from Kotzebue Hospital which in the commenters' view demonstrated that there is an association between high PM days and the hospital admissions for respiratory complaints. Though acknowledging the data to be rudimentary, the commenter states that the data show that road dust does have effects on public health, and that rural coarse particles should not be excluded from the coarse particle indicator (Bolen on behalf of 12 Tribes).

Response: The EPA appreciates the effort of these commenters to collect evidence regarding potential health effects from PM in tribal locations. While EPA cannot rely on such short-term, anecdotal information, the information will be useful in planning future monitoring and research efforts targeted at identifying and addressing such potential effects. The EPA also believes that the Administrator's final decision to retain the 24-hour PM_{10} standard nationwide is responsive to these commenters' concerns.

(13) *Comment:* Some commenters stated that, by considering only U.S. and Canadian studies, EPA had disregarded useful studies from other countries. Some commenters pointed to foreign studies as demonstrating that adverse health effects are associated with exposure to naturally occurring coarse particles. For example, the State of Alaska Department of Environmental Conservation cited Baris et al. (1987), which examined health effects associated with exposure to erionite fibers (an asbestiform fiber) in the Cappadocian region of Turkey and found an association with malignant mesotheliomas, and Norboo et al. (1991), which found that high levels of silicosis were associated with high dust levels. The American Lung Association et al. stated that EPA's decision to place great weight on U.S. and Canadian epidemiologic studies had "no rational basis," especially with regard to discounting European studies, and pointed to a recent WHO report (WHO, 2005) which reported consistent health impacts in multiple cities around the world. In the view of the commenter, "the evidence suggests that the health effects are independent of national demographic or air pollution characteristics" (American Lung Association et al., p. 92).

Response: The EPA has not discounted studies conducted in other countries. All policy relevant studies were evaluated in the development of the Criteria Document. Specific criteria used by EPA to identify toxicologic and epidemiologic studies for inclusion in the Criteria Document were presented in sections 7.1.1 and 8.1.1 (EPA, 2004, pp. 7-2 to 7-6 and pp. 8.2 to 8.5). In addition, the CASAC and public reviews of various draft versions of the Criteria Document provided multiple opportunities for the additional relevant studies to be identified to EPA.

The Criteria Document included an integrative synthesis of the entire body of evidence of associations between exposure to ambient particles and a broad range of health endpoints (EPA, 2004, Chapter 9). The body of evidence considered in the Criteria Document

included hundreds of studies conducted in many countries around the world, using various indicators of fine particles. As discussed in section II.A.1 of the preamble to the final rule, in evaluating the adequacy of the existing standards for protection of public health and the environment, or for quantitative risk assessment, EPA believes it is appropriate to focus on the quantitative results available from studies conducted in the U.S. and Canada. For these purposes, EPA used the concentration-response functions and air quality data from these studies to quantify health risks in U.S. locations, or to evaluate the adequacy of the NAAQS. While recognizing the value of studies conducted in locations outside the U.S. and Canada for the overall evaluation of evidence, EPA also recognizes that there may be demographic or air quality differences in other countries that make it advisable to rely on U.S. and Canadian studies for the more focused policy assessments.

The rationale for placing quantitative reliance on foreign studies advanced by American Lung Association et al. is not well founded with respect to the assessment of the health effects of coarse particles. In assessing coarse particle effects, EPA has relied in part on U.S. PM_{10} studies conducted in areas where available information indicates that the particle mass is dominated by coarse particles. While the recent WHO report finds similar effects estimates for PM_{10} in a number of different countries, in many, if not most of the study locations sited, it is likely that fine particles compose half or more of the PM_{10} mass. Indeed, in determining an appropriate PM_{10} level, WHO assumes that the typical fine to PM_{10} ratio is 0.5 (WHO, 2005). In such cases, EPA does not believe it is appropriate to ascribe the effects estimates associated with PM_{10} primarily to coarse particles.

The studies cited by the State of Alaska Department of Environmental Conservation do suggest that in some locations, unusually high concentrations of silica or asbestisform fibers in sources of coarse particles can present health risks of concern. But such conditions are rare in most non-urban locations outside of certain occupational settings. EPA evaluated the potential risk associated with typical levels of naturally occurring silica in crustal materials in the previous review, concluding that the available data do not provide evidence for such effects at levels allowed by the PM_{10} standards (62 FR 38678). The EPA does not agree that the foreign studies such as those suggested by the commenter provide any basis for changing this more quantitative assessment. In any event, by maintaining the national protection afforded by the current PM_{10} standard, any concerns raised by these commenters regarding revocation of this standard have been addressed.

(14) *Comment*: Some commenters stated that coarse particles can travel long distances and that EPA had improperly characterized transport distances in the proposal. NESCAUM, for example, disputed EPA's statement that "coarse particles generally deposit rapidly on the ground or other surfaces and are not readily transported across urban or broader areas," noting that this was a distortion of a passage in the Criteria Document referring to particles larger than 10 μm in diameter. The commenter quotes the Criteria Document (p. IV-7) as saying that $PM_{10-2.5}$ "may have lifetimes on the order of days and travel distances of up to 100 km or more," and also notes that long-range transport, such as an

intercontinental dust storm originating in the Gobi desert where the size distribution peak was 2-3 μm, can occur (NESCAUM, Attachment B, p. 2).

Response: The EPA agrees relative transport distance of coarse mode particles is significantly affected by particle size. While it is correct that much of coarse mode mass does deposit rapidly on the ground near sources, this is far more pronounced for larger size ranges than for thoracic coarse particles, which are smaller than a nominal 10 um in aerodynamic diameter. The commenters are also correct that some coarse mode particles may, under certain conditions, transport over more substantial distances, and in special cases desert storms may result in coarse particle transport for thousands of miles across oceans.

(15) *Comment*: A consultant for the National Mining Association and the National Cattlemen's Beef Association submitted a modeling analysis in support of their position that single ambient monitors cannot be used to provide adequate population exposure data for epidemiological studies. According to this analysis, coarse particle sources have a very limited spatial influence: less than 1/3 of a mile for ground-level sources, and not more than 2/3 mile for elevated sources (Hoffnagle, p. 6-7).

Response: The analysis used the ISCST3 model to estimate the impacts of two hypothetical sources emitting 10, 5, and 2.5 μm particles at ground level and at 10 m elevation. Graphical results show an exponential decrease in concentration with distance from the source for both particles sizes, with the implication that levels approach zero at distances of about 1 km from the source. The consultant suggests that this decline would be typical for coarse particle sources and, for this reason, single monitors in urban areas cannot represent population exposures to coarse particles beyond such distances. As discussed below, EPA believes that this limited analysis cannot be used to support such a broad conclusion. Furthermore, the conclusion is inconsistent with real world measurements.

During a presentation on these results by a TRC modeling consultant on behalf of the National Mining Association and National Cattlemen's Beef Association, EPA staff requested results for at least one smaller particle size to help determine the extent to which the graphical results are unique to faster removal of coarse particles, or are more dominated by dispersion of any primary emitted materials. The EPA has not yet received such results from the consultant. Furthermore, because no documentation was provided with the TRC comments regarding the specific source parameters (other than particle size and release height) and meteorological conditions used to generate the results presented in Figures 1 and 2 of the comments, EPA could not assess how reasonable or representative these results may be.

The EPA therefore undertook its own modeling analysis, which is detailed in a brief report appended to this document (Brode, 2006—Appendix B). This analysis compared results for hypothetical emissions of five particle sizes representative of both fine and coarse particles (0.1, 1, 2.5, 5, and 10 μm aerodynamic diameter). These results show, as EPA expected, that coarse particles do "deposit out" more than fine particles under some,

but not all conditions, and there is a noticeable dependence of this effect on meteorology. More specifically, under several assumed conditions, the differences in fine and coarse particle concentrations are insignificant at distances of 1 to 3 km. Overall, these results do not support the assertion that the "area of influence" of coarse PM sources is limited to 1,000 m (or less than 500 m for particles greater than 5 μm). Most of the drop-off of concentration with distance is due to dispersion of the plume rather than deposition of the particles.

Although, as EPA modeling has shown, the results vary markedly with assumed meteorological conditions, these commenters provided results for only one unidentified condition. As the response to NESCAUM comments notes above, the Criteria Document cites conditions under which coarse particles may travel substantial distances. Such conditions, for example, high winds, are likely to produce higher emissions of coarse particles from fugitive sources and cause them to reach higher altitudes than assumed in the consultant's analysis. While both coarse (and primary fine) particle concentrations do generally decrease rapidly from lower level point sources, coarse particle sources such as roadways, construction activities, and disturbed land are ubiquitous in urban areas. The amount of transport from such sources at different distances varies, but the concentrations arriving at a given monitor is the cumulative result from all of them. This serves to provide a more uniform distribution than implied by single source modeling.

A real world illustration is provided in a study of PM_{10} in Las Vegas (Chow, et al., 1999). This area contained strong dust sources as well as general urban activities in an arid city where fugitive dust contributed 80 to 90% of the PM_{10}. The study found that "most of the sampling sites in residential and commercial areas yielded equivalent PM_{10} concentrations in the neighborhood region, even though they were more distant from each other than they were from the nearby construction sources" (Chow, et al., 1999, p. 641). By contrast, the estimated zone of maximum influence around individual strong emitters was 0.75 to 1.5 km (Chow, et al., 1999, p. 653).

As discussed in section III.B of the preamble, EPA recognizes that correlations between measurements at coarse monitors are generally smaller than those for fine particles. As noted in the Criteria Document, some of this smaller correlation may be due to measurement error, while some is due to the greater spatial uniformity in fine particles that is created by secondary formation processes (EPA, 2004, p. 3-52). Nevertheless, the Criteria Document shows spatial correlation between multiple coarse monitor pairs in three cities is frequently on the order of 0.5 to 0.8 (Table 3-5). The Criteria Document also notes instances where the correlation between sites for $PM_{10-2.5}$ is higher than that for$PM_{2.5.}$

Despite the larger exposure measurement errors for coarse particles that should serve to increase uncertainties in effects estimates, a number of epidemiological studies suggest a pattern of positive associations, with some achieving statistical significance. While the greater spatial variability of coarse particles means such studies must be carefully evaluated for quantitative purposes, EPA does not agree that such variability is at all

likely to create false positive, much less statistically significant results in epidemiology studies.

(16) *Comment:* A number of commenters stressed the need for additional research to address the uncertainties in the current body of evidence regarding coarse particles and health effects. In addition, a variety of commenters urged EPA to deploy additional $PM_{10-2.5}$ monitors in both urban and rural areas, consistent with the advice of CASAC, to provide a more robust and complete body of evidence regarding coarse particle effects.

Response: The EPA agrees with these commenters that additional research is needed to reduce some of the other uncertainties regarding the health effects associated with coarse particles. As discussed in the preamble to the final rule, EPA is, in fact, expanding both its research and monitoring programs to collect additional evidence on the differences between coarse particles typically found in urban areas and those typically found in rural areas. Specifically, EPA notes that the Agency's National Center for Environmental Research recently issued a Request for Proposals on "Sources, Composition, and Health Effects of Coarse Particulate Matter" which is designed to (1) improve understanding of the type and severity of health outcomes associated with exposure to $PM_{10-2.5}$; (2) improve understanding of subpopulations that may be especially sensitive to $PM_{10-2.5}$ exposures including minority populations, highly exposed groups, and other susceptible groups; (3) characterize and compare the influence of mass, composition, source characteristics and exposure estimates in different locations and differences in health outcomes, including comparisons in rural and urban areas; and (4) characterize the composition and variability of $PM_{10-2.5}$ in towns, cities or metropolitan areas, including comparisons of rural and urban areas. In addition, as described in the final monitoring rule published elsewhere in today's Federal Register, EPA and the States will require measurement of $PM_{10-2.5}$ at 75 new multi-pollutant monitoring sites around the country. These sites will provide continuous measurements of mass as well as chemical speciation. The EPA will locate 55 of these sites in urban areas and 20 in rural areas in order to gather information on the composition and transport of coarse particles in urban and rural areas. In addition, these monitors will employ the latest in speciation technology to advance the science so that future regulation will provide more targeted protection against the effects only of those coarse particles and related source emissions that prove to be of concern to public health. It is EPA's goal that its new research and speciated monitoring program will produce data to determine what effect differences in particle composition may have on health outcomes. Such results have the potential to provide the kind of certainty and specificity required for making future decisions on indicators for thoracic coarse particles that might incorporate qualifications, such as the proposed qualified indicator related to coarse particles from agriculture and mining.

4. Comments on Transition from PM_{10} to $PM_{10-2.5}$ standards

(1) *Comment:* Many commenters addressing the issue of transition between the current PM_{10} standards and any new $PM_{10-2.5}$ standards urged EPA to ensure continued protection

against the effects of thoracic coarse particles during any transition period. In addition, commenters expressed the following specific views:

- The proposed approach is too hasty in dismantling existing PM_{10} protections. The absence of control in the interim period between the issuance of the final PM NAAQS rule (which as proposed would include the revocation of existing PM_{10} standards in almost all locations) and the completion of designations under a new $PM_{10-2.5}$ standard (which would require deployment of a new monitoring network followed by 3 years of data collection) could potentially have major public health implications. The long delays experienced in the implementation timeline for the 1997 $PM_{2.5}$ standards due to litigation, such that designations were not completed for eight years after promulgation of the final rule, suggest that the 24-hour PM_{10} standard should remain in place everywhere until designations are complete under any 24-hour $PM_{10-2.5}$ standard, or even until $PM_{10-2.5}$ SIPs have been submitted by States.
- The PM_{10} standard should be retained permanently in all areas where the $PM_{10-2.5}$ standard did not apply by virtue of the monitoring requirements, which limited NAAQS-comparable monitors to sites that met the five-point site suitability test outlined in the monitoring rule.
- The EPA has no authority to revoke the PM_{10} standards or the specific pollution controls mandated in Title I Subpart 4 for PM_{10} nonattainment areas.
- States and local areas have invested considerable resources and effort in instituting controls on PM_{10} over the last 20 years, and EPA must issue an anti-backsliding rule to ensure that current levels of public health protection are maintained.

Response: As noted in section VII of the preamble to the final rule, the Administrator's decision to retain the current 24-hour PM_{10} standard alleviates these concerns. Because the 24-hour PM_{10} standard is generally controlling, as described in section III.D of the preamble to the final rule and in section II.B.2.c of this Response to Comments, retention of this standard ensures the continuation of existing public health protections.

(2) *Comment***:** Some commenters contend that EPA does not have authority to revoke the PM_{10} standards or the controls mandated in Subpart 4 for PM_{10} nonattainment areas. The commenters suggest that the Court in Whitman held that Congress codified the 1-hour ozone NAAQS and argue that Congress similarly codified the annual and 24-hour PM_{10} standards, the associated designations and classifications for those standards, and the detailed control requirements and deadlines for attaining the PM_{10} standards. Specifically, the commenters cite to the designation provisions in CAA §107(d) and the provisions of Subpart 4. First, the commenters point out that CAA §107(d)(4) designated PM_{10} nonattainment areas "[b]y operation of law" and further provided that those designations would remain in effect until the area is redesignated pursuant to section 107(d)(3). For areas designated nonattainment section 107(d)(3) only provides for redesignation to "attainment" and only once the area has actually attained the PM_{10} standards and has met all pollution control obligations applicable to PM_{10} nonattainment areas (including those under Subpart 4). Section 107(d)(3) makes no provision for revocation and thus there is no authority to redesignate from "nonattainment" to "standard revoked" for the PM_{10} standards. The commenters also cite to Subpart 4, which classifies

PM_{10} nonattainment areas "by operation of law" and sets forth detailed planning and control requirements for progress toward, and attainment of the PM_{10} standards and deadlines for attainment. The commenters note that the Subpart 4 provisions apply to areas designated nonattainment any time after 1990, *See, e.g.*, CAA §§ 188(a), (c), 189 (a)(1)(C), (a)(2)(B), and that Congress intended these requirements to apply to PM_{10} nonattainment areas (or to continue as contingency measures) even after an area attained the PM_{10} standards. CAA §175A(d).

The commenters contend that "revocation" of the PM_{10} standards would render the above-cited provisions inoperative as to PM_{10} and would conflict directly with the Supreme Court's holding in Whitman that EPA cannot render the Act's detailed anti-pollution regimes "abruptly obsolete." Whitman v. American Trucking Assns., 531 U.S. 457, 476, 481-85 (2001).

*Response***:** This comment is moot with regard to the 24-hour PM_{10} standard because EPA is retaining the standard. With regard to the annual standard, the statutory implementation provisions in CAA §107(d)(4) and in Subpart 4 apply where there is a NAAQS in place that EPA has determined is necessary to protect public health. They do not preclude or limit EPA's authority under sections 108 and 109 to revise or revoke a NAAQS that is no longer necessary to protect public health. Neither section 107 nor section 181 of the CAA explicitly prohibit EPA from determining that one (or both) of the PM_{10} standards in existence at the time of the 1990 Amendments to the CAA is no longer needed to protect public health. Nor should they be read as a revocation of the authority established in sections 108 and 109. To do so would significantly restrict EPA's authority to revise the NAAQS in place in 1990, and there is nothing that indicates that Congress intended such a limitation on the express authority in sections 108 and 109 to review and revise standards.

The designations provisions cited by the commenters apply where there is a NAAQS in place necessary to protect the public health. For example, section 107(d)(3)(E) of the Act applies for purposes of redesignating an area for purposes of a specific NAAQS. Thus, if an area that was designated nonattainment for the PM_{10} standard were now meeting that standard, it could be redesignated to attainment for the that standard if it met the other specified criteria in section 107(d)(3)(E). There is nothing express or implied in this provision that indicates it limits EPA's authority to revise or revoke an existing NAAQS and the associated designations. Similarly, the provisions in Subpart 4 apply to areas designated nonattainment for a specific NAAQS. There is nothing in these provisions that indicate that they must continue to apply once EPA has determined the NAAQS for which an area was designated nonattainment is no longer needed to protect the public health. Furthermore, the fact that the initial PM_{10} designations and classifications were "by operation of law" in 1990 should not be read as Congressional intent to "codify" the PM_{10} standard and the associated designations. Rather, these provisions were for the purpose of immediately applying the CAA Amendments to the then-existing PM_{10} standard and to the areas that were violating that standard at the time of enactment of the 1990 Amendments.

The EPA disagrees with the suggestion that the Court in Whitman held that Congress codified the 1-hour ozone NAAQS (and thus by implication the similar PM_{10} NAAQS) when it promulgated the 1990 CAA Amendments and that the Court held, therefore, that EPA was precluded from revoking that standard. In challenging the 8-hour ozone NAAQS, several litigants argued before the Court of Appeals that EPA had no authority to revise the 1-hour NAAQS because Congress had codified that standard. These litigants relied on the subpart 2 provisions for ozone that are similar to the subpart 4 provisions for PM_{10} relied on by the present commenters. The Court rejected that argument, concluding that these implementation provisions did not alter the Agency's obligation to review and revise the NAAQS as appropriate every five years. ATA I, 175 F.3d at 1047. The Court of Appeals then went on to review EPA's statements regarding implementation of the new 8-hour ozone standard and concluded that the CAA mandated the revised (i.e., 8-hour) ozone standard be implemented under subpart 2. The issue of whether Congress codified the 1-hour ozone standard (and therefore it must be retained) was not raised to the Supreme Court and nothing in its opinion speaks to that issue. Rather, the sole focus of the cited portions of the Court's opinion was on whether the 8-hour ozone standard must be implemented under subpart 2 and, if not, whether EPA's interpretation that it would be implemented under subpart 1 was reasonable.

The commenters also cite language from Whitman to argue that by revoking a NAAQS, EPA is making the provisions that applied to an area for that NAAQS (in this case the provisions of subpart 4) abruptly obsolete. The commenters' argument is misguided. In Whitman, the Supreme Court was considering EPA's interpretation that subpart 2 of the Act (the provisions specifically applicable to ozone nonattainment areas) did not apply for purposes of implementing the 8-hour ozone NAAQS. The Court was troubled that EPA's interpretation might render subpart 2 prematurely obsolete because those provisions would not be used to implement the revised health-based ozone standard. Importantly, if EPA had been precluded from revising or revoking the 1-hour NAAQS, then there would have been no concern that those provisions would be made abruptly obsolete because subpart 2 would have remained in place indefinitely for purposes of continuing to implement the 1-hour standard. Thus, the underlying assumption of the implementation portion of the Court's decision was that the 1-hour standard had been replaced and because subpart 2 had no role under EPA's implementation for the 8-hour standard, it would have been abruptly obsolete.

(3) *Comment***:** Some commenters also state that even if the statute does not preclude revocation of the PM_{10} standards, EPA cannot allow for relaxation of control and planning requirements mandated by Congress in Subpart 4 and thus EPA cannot revoke the PM_{10} standards without addressing anti-backsliding protections.

Response: The EPA's final decision to revoke the annual PM_{10} standard but retain the 24-hour PM_{10} standard effectively resolves this concern. As EPA recognizes in section III.D.2 of the preamble to the final rule, the 24-hour PM_{10} standard is the controlling standard (see also Schmidt, 2006—Appendix C). Thus, the final PM NAAQS rule does not affect current nonattainment designations for PM_{10} and areas designated nonattainment must continue to comply with the nonattainment provisions of the Act,

including the requirements of Subpart 4, and with their approved SIP unless and until EPA takes further action to change the existing status (see section VII of the preamble to the final rule for further discussion of these issues). If and when EPA takes action in the future, the commenter can raise any concerns at that time and EPA would consider and respond to those concerns before taking final action.

(4) *Comment*: The Pinal County Air Quality Control District cited numerous statutory provisions, claiming these provisions demonstrate Congress' intent to "affirm the Administrator's adoption of PM_{10} as an indicator for particle pollution." Specifically, the commenter cited the following provisions of the Clean Air Act:

- The definition of PM_{10} in section 302(t)
- The PM_{10} specific designation provisions under section 107(d)(4)(B)
- Research provisions in section 103(g)(1)
- Local planning efforts provided for under section 174(a)
- Relief under section 179b(d) for PM_{10} areas affected by emissions from outside the United States
- The requirements under section 183(b)(4) to issue control technique guidelines for certain sources that aggravate ambient PM_{10} levels
- The provisions of Subpart 4
- The substitution of PM_{10} increments for total suspended particulate (TSP) increments under section 166(f)
- The requirement to control particulate matter (total and fine) for new sources under section 129(a)(5)
- The requirement to study coal-mine particulate emissions in section 234 of the CAA Amendments of 1990

Response: For the reasons provided above, the designation and provisions in section 107 and the implementation provisions in Subpart 4 do not explicitly or implicitly override the Administrator's authority (in fact, obligation) under sections 108 and 109 to review and revise the NAAQS as appropriate at five year intervals. The provisions in sections 166(f), 174(a), 179b(d) and 183(b)(4) are likewise implementation provisions that simply address the NAAQS pollutant that was in existence at the time those provisions were written. The fact that Congress expressly addressed implementation of the then-existing NAAQS should not be read as an implied limitation of the Administrator's NAAQS revision authority. Nor, for the same reasons, do the other provisions cited by the commenter override that authority. Additionally, we note that section 302(t) simply defines PM_{10} but establishes no regulatory authority and evidences no Congressional intent as to how EPA should regulate that pollutant. Similarly, research provisions such as those in section 103 of the CAA and section 234 of Public Law 101-549, are even less of an indication that Congress intended regulation of PM_{10} as a NAAQS to continue regardless of a determination that a PM_{10} NAAQS is unnecessary to protect against particulate pollution. The provisions in section 129(a)(5) are unaffected by EPA's determination as to whether to retain PM_{10} NAAQS. As is evident by that provision, it applies more broadly to the enumerated air pollutants (many of which are not criteria pollutants, but rather are hazardous air pollutants).

(5) *Comment:* Other commenters stated that EPA is legally required to revoke both the annual and 24-hour PM_{10} standards immediately. These commenters argued that continued application of any PM_{10} standard would not withstand judicial scrutiny. Citing the Court's decision in American Trucking Assn's v. EPA, 175 F.3d 1027, 1054-55 (D.C. Cir. 1999), these commenters noted that the Court found that "PM_{10} is inherently confounded by the presence of $PM_{2.5}$ particles, meaning that any regulation of PM_{10} pollution will include both coarse and fine particles… Far from working in conjunction to regulate coarse particles, PM_{10} and $PM_{2.5}$ indicators, when used together, lead to 'double regulation' of the $PM_{2.5}$ component of PM_{10}." These commenters stated that retaining the 1987 24-hour PM_{10} standard would contradict the Court's vacature of the 1997 PM_{10} standards, because the D.C. Circuit held that "It is the very presence of a separate $PM_{2.5}$ standard that makes retention of the PM_{10} indicator arbitrary and capricious."

Response: As discussed in section III.C.3.b of the preamble to the final rule and in other comment responses, the EPA disagrees that the ATA I decision precludes use of a PM_{10} indicator. The Court did not hold that it was unlawful *per se* to use PM_{10} as an indicator for thoracic coarse particles. Instead, the Court noted two particular problems—the variable level of allowable concentrations of $PM_{10-2.5}$ and double regulation of $PM_{2.5}$—and found that EPA either failed to address these issues, or provided explanations that were inconsistent and unsupported. As discussed in the preamble, far from being arbitrary and capricious, inclusion of $PM_{2.5}$ serves two important functions. First, it is the mechanism that provides for the variation in allowable $PM_{10-2.5}$ concentrations, targeting lower allowable levels in areas where there is greater public health concern. Second, to the extent that there is "double regulation" of $PM_{2.5}$ by virtue of its inclusion in the PM_{10} indicator (175 F.3d at 1054), regulation of $PM_{2.5}$ via this indicator serves valid, non-duplicative purposes in providing requisite protection from thoracic coarse particles.

The EPA notes further that the commenter's statement that ATA I requires repeal of the 1987 standards is not correct. The 1987 standards were not being reviewed in ATA I, and in any case PM_{10} was not used as an indicator for coarse particles in the 1987 standard so the reasoning in ATA I does not apply.

(6) *Comment:* One commenter stated that EPA should not retain the 1987 PM_{10} standard for any purpose, and thus should immediately revoke the 1987 PM_{10} standard in all areas. According to this commenter, use of the 1987 PM_{10} standard for transition purposes will not withstand judicial scrutiny under ATA I. The commenter argued that retention of the standard in any area appeared to be based on the type of administrative convenience rationale rejected in that case (American Farm Bureau Federation).

Response: Most of this comment is moot because it addresses retention of the 1987 PM_{10} standard as a transition to the proposed $PM_{10-2.5}$ standard EPA is instead retaining PM_{10} as the indicator for coarse particles, and retaining the existing 24-hour standard for PM_{10}. The EPA thus is not retaining that standard for transient purposes. As discussed in the preamble and elsewhere in response to comments, retaining PM_{10} as the indicator for coarse particles is fully consistent with ATA I. The EPA is not retaining PM_{10} as the

indicator for reasons of administrative convenience, but rather for the reasons set out in section III.B.3.b of the preamble to the final rule.

C. Secondary PM Standards

A number of comments on the proposed secondary standards for PM were very general in nature, basically expressing one of three substantively different views: (1) support for secondary standards that are distinct from the primary standards; (2) support for setting the secondary PM standards identical to the primary PM standards; or (3) opposition for any secondary standard for coarse particles. Many of these commenters simply expressed their views without stating any rationale, while others gave general reasons for their views but without reference to the factual evidence or rationale presented in the proposal notice as a basis for the Agency's proposed decision.

Some commenters expressed concern that there was little discussion in the preamble of welfare effects associated with $PM_{10-2.5}$, such as visibility effects, materials damage, or soiling. These commenters expressed concern that an urban-focused standard would ignore the substantial welfare effects that arise from rural dusts. Furthermore, many commenters stated that there was no basis for assuming that welfare effects would depend on the source of the particle or its toxicity to human health, and recommended establishing a separate secondary standard based purely on particle size. These commenters called upon EPA to establish a uniform national secondary standard to be applied in both rural and urban areas without source exemptions, noting that dusts that may not affect health can still affect visibility and ecosystems. Several of these commenters pointed to CASAC's request for reconsideration, which recommended that "a secondary $PM_{10-2.5}$ standard be set at the same level as the primary $PM_{10-2.5}$ standard to protect against the various irritant, soiling, and nuisance welfare or environmental effects of coarse particles. Since these effects are not uniquely related to urban sources or receptors, the standard should not be limited to urban areas" (Henderson, 2006).

Incorporating responses contained in Section IV of the preamble to the final rule, EPA provides the following responses to specific issues related to the secondary PM standards. This section addresses comments on visibility effects distinct from comments on other welfare effects.

1. Visibility

The majority of commenters who expressed an opinion on the secondary PM standards, including NESCAUM, STAPPA/ALAPCO, a number of individual States, Tribal associations, and local organizations, and combined comments from various environmental groups argued that the secondary $PM_{2.5}$ standards should be revised to increase protection against visibility impairment. Many of these public commenters supported the more specific EPA staff and CASAC recommendations and urged EPA to adopt a sub-daily (4- to 8-hour averaging time) $PM_{2.5}$ standard to address visibility impairment, within the range of 20 to 30 $\mu g/m^3$ and with a form within the range of the 92^{nd} to 98^{th} percentile. In general, these commenters based their recommendations on the same studies, analyses, and considerations presented in the Staff Paper and outlined section IV.A of the preamble to the final rule.

Some of the commenters who opposed any revisions to the primary $PM_{2.5}$ standards, including UARG, American Public Power Association, and American Electric Power also stated their opposition to a revision to strengthen the secondary $PM_{2.5}$ standards at this time.

Incorporating responses contained in Section IV.A of the preamble to the final rule, EPA provides the following responses to specific issues related to PM-related visibility impairment.

(1) *Comment:* The NESCAUM noted that, though monitors in the northeast region do not exceed the current secondary $PM_{2.5}$ standards, the CAMNET regional haze camera network routinely documents extremely hazy days obscuring city skylines and views. The NESCAUM stated that "this shows that virtually all of $PM_{2.5}$ effects on visibility in the Northeast are occurring below the present secondary standard, justifying EPA's proposal to revise the existing standard to a more stringent level adequately protective of public welfare" (NESCAUM, attachment C, p. C-1).

Response: In general, EPA agrees with these commenters that the more recent information on visibility values, photographic evidence, and air quality/visibility relationships supports the need to revise the current secondary $PM_{2.5}$ standards.

(2) *Comment:* The American Lung Association and other groups submitted comments that disagreed with the Administrator's view that the secondary standards should be focused primarily on providing protection in urban areas, with protection of Class I areas provided by the Regional Haze Rule. These commenters suggested that EPA should not rely on the regional haze program and must set national standards to protect all areas.

Response: The EPA believes that this issue was settled in *ATA I* (See 175F. 3d at 1056-1057). See also comment response (4) below.

(3) *Comment:* The UARG questioned the usefulness of the photographic images and urban studies of acceptable visibility highlighted in the proposal for determining appropriate levels of urban visibility. These commenters further argued that, for most areas, the annual $PM_{2.5}$ standard would prevent any exceedances of 65 $\mu g/m^3$.

Response: While, as summarized in section V.A of the preamble to the proposed rule, the key optical aspects of the relationship between fine particles and visibility have been established for a long time, EPA strongly disagrees that the more recent visibility-related evidence and analyses presented in the Criteria Document and Staff Paper provide no basis for considering more protective $PM_{2.5}$ standards.

As discussed in the Staff Paper, one of the key issues in the last review was whether the differences in humidity between East and West complicated the establishment of a nationally uniform $PM_{2.5}$ secondary standard, even for urban areas (EPA, 2005, p 7-3). With the substantial addition to the air quality and visibility data made possible by the national urban $PM_{2.5}$ monitoring networks, an analysis conducted for this review found that, in urban areas, visibility levels show far less difference between eastern and western regions on a 24-hour or shorter time basis than implied by the largely non-urban data

available in the 1997 review (EPA, 2005, p 7-5). Of equal importance, more recent studies of visibility values conducted for several urbanized areas have found results generally consistent with an earlier study done for the city of Denver. While such studies are still limited in number and subject to uncertainty, EPA believes they suggest a remarkable consistency in public reaction to urban visibility impairment caused by fine particles (EPA 2005, p 6-18 to 23).

Furthermore, staff and CASAC agreed on the utility of photographic evidence in characterizing the nature of particle-induced haze. Moreover, at the level of the current 24-hour $PM_{2.5}$ standard, the potential subtleties associated with alternative photographic views alluded to by UARG would be obscured by the density of the accompanying haze, which would restrict the distance of the farthest discernable dark objects to only 6 miles and greatly reduce the contrast for objects at significantly shorter distances. Although, as suggested by commenters, the annual standard serves to limit such excursions, particularly in eastern urban areas, continuation of the current 24-hr $PM_{2.5}$ standard would permit a large number of exceedances of this level especially in some western urban areas, even when the standard is just attained.

In summary, contrary to the views of this set of commenters, EPA believes that the combination of new insights from air quality analyses, the standards and studies developed to address urban visibility in several areas, as well as an evaluation of the photographic evidence supports the need to revise the current secondary $PM_{2.5}$ standards.

(4) *Comment:* The Clean Air Act requires EPA to adopt secondary NAAQS requisite to protect public welfare throughout the nation from any known or anticipated adverse effects from PM fine pollution (citing section 109 (b) (2) of the Act). EPA therefore cannot lawfully or rationally adopt a secondary PM2.5 standard that fails to protect major parts of the nation from known and anticipated adverse visibility impacts associated with $PM_{2.5}$.

Response: Section IV.A of the preamble to the final rule, as well as other comment responses, explain why the secondary standards for PM are requisite to protect against the adverse welfare effect of impaired visibility. The commenter is incorrect in stating that the secondary NAAQS must protect against all adverse visibility effects. See ATA I, 175 F. 3d at 1056-57 ("Environmental petitioners argue that section 109 (b) (2) … requires the EPA to set secondary NAAQS at a level sufficient to eliminate all adverse visibility effects and that it leaves the EPA no discretion to decide that some visibility impairment is better remedied through another program. This must be wrong….[W]e conclude that the Congress did not intend the secondary NAAQS to eliminate all adverse visibility effects and, therefore, that the EPA acted within the scope of its authority in deciding to rely upon the regional haze program to mitigate some of the adverse visibility effects caused by $PM_{2.5}$."). In this review, EPA is likewise relying in part on the regional haze program as a means of achieving appropriate levels of protection against PM-related visibility effects in urban, non-urban, and Class I areas across the country. See section IV.A to the preamble to the final rule.

(5) *Comment*: Some commenters stated that EPA has ignored the adverse effects of coarse particles on visibility in proposing to set the secondary standard for coarse particles equal to the primary standard. These commenters argued that though fine particles are more potent in reducing visibility on a per-unit-mass basis, coarse particles contribute significantly to visibility impairment, particular in Western areas, and that EPA has presented no rational basis for concluding that exempted sources or types of coarse particles have no adverse effects on visibility. The commenters stated that the proposed coarse particle standard would undermine the regional haze program by reducing controls on sources of coarse particles that states must control to make progress under the Regional Haze Rule. Some of these commenters, including many Tribes, included comments about particular Class I areas that would be negatively affected if EPA were to finalize its proposed approach of setting the secondary coarse particle standard equal to the primary standard, with rural dust excluded from consideration.

Response: As summarized in the proposal, EPA did a thorough examination of the effects of the effects of particulate matter on visibility. That review concluded that fine particles are a dominant cause of impairment, but that high levels of coarse particles over broad expanses, as in windstorms, can also produce episodic impairment (EPA 2005, Chapter 6). Coarse particles can also be of some significance in Class I areas of the West where fine particle levels are often very low. In both the last review and in the present one, EPA has relied on the Regional Haze Rule to provide protection of visibility in Class I areas. The staff and CASAC recommendations for visibility were, however, based largely on the issue of visibility impairment in urban areas. In such areas, coarse particles generally do not dominate impairment, making fine particles the most appropriate indicator for visibility protection. This action has no implications for the relative focus of control in Class I areas under the regional haze programs. To the extent such programs find significant contribution to visibility impairment in Class I areas from coarse particles, EPA believes that the States have mechanisms and authorities to address such impairment under the Regional Haze and related visibility programs.

1. Other Welfare Effects

Only limited public comments were received on issues related to non-visibility PM-related welfare effects. In general, these comments focused on issues related to the current secondary PM_{10} standards. Most of these commenters, including the groups who objected to the use of a qualified indicator for the primary thoracic coarse particle standard, argued that current levels of PM dust contribute or potentially contribute to nuisance, soiling, and irritant impacts on personal comfort and well being, especially in non-urban areas (e.g., Arizona Department of Environmental Quality, Pinal County Air Quality Control District). These commenters representing state and local air pollution control agencies agreed with CASAC that, in the absence of a demonstration to the contrary, EPA is not justified in eliminating or reducing the level of protection to rural areas that is provided by the current suite of secondary standards (e.g., Nevada Department of Conservation and Natural Resources). Most of these commenters recommended that EPA either retain the current PM_{10} secondary standard or replace it with a

$PM_{10-2.5}$ standard set identical to the proposed primary standard without the proposed qualifications that limited application of the standard to urban areas.

A limited number of commenters, including some of those who objected to continuation of a primary coarse particle standard, argued against retaining any secondary standard for coarse particles (e.g., Coarse Particle Coalition). Many of these same commenters argued that if EPA did set a secondary $PM_{10-2.5}$ standard, it should be set equal to the primary $PM_{10-2.5}$ standard because there was insufficient evidence to support adoption of a distinct secondary standard for $PM_{10-2.5}$ at this time. Furthermore, these commenters noted that in the proposal, EPA had correctly excluded from both primary and secondary standards "any ambient mix of $PM_{10-2.5}$ that is dominated by rural windblown dust and soils and PM generated by agricultural and mining sources" because these particles are nontoxic and generally settle quickly. Consistent with the assessment of the evidence in the Staff Paper and the CASAC recommendations, the Administrator disagrees with these commenters who suggested that no secondary standard is needed to protect against the welfare effects associated with coarse particles.

Some commenters suggested that if EPA finalized a qualified $PM_{10-2.5}$ primary standard, it should retain the existing 24-hour PM_{10} standard as a secondary standard to provide protection against welfare effects in rural areas. As discussed in section III of the preamble to the final rule, EPA has decided to retain the current 24-hour PM_{10} primary and secondary standards, therefore, this comment is no longer relevant.

D. Federal Reference Methods

The EPA received very few comments related to the new proposed Federal reference method (FRM) for measuring mass concentrations of coarse particles ($PM_{10-2.5}$) as well as the proposed minor technical changes to the FRM for $PM_{2.5}$. Incorporating responses contained in section VI of the preamble for the final rule, EPA provides the following responses to specific issues related to FRMs.

1. Specific comments related to revisions to FRM for $PM_{2.5}$

(1) *Comment:* One commenter included a report as Attachment 3 to provide evidence of the extent of contamination on field blanks from ambient $PM_{2.5}$ monitoring networks (UARG). The commenter argued that the results reported indicated that the $PM_{2.5}$ contamination of filter blanks varied by about a factor of two among the networks considered even when the same FRM and sampling protocols were used. The commenter noted that EPA's proposal to require the submission of data from $PM_{2.5}$ field blanks is a move in the right direction. The commenter asserted that EPA should go further and require, or at least permit, correction of ambient air measurements for the contamination found on field blanks. The commenter argued that this requirement should be applicable, on a network-by-network basis, to data from chemical speciation monitor networks and from $PM_{10-2.5}$ networks, as well as to $PM_{2.5}$ networks.

Response: While subtraction of field blank values from compliance measurements might seem warranted, EPA believes that the practice would result in lower compliance values and thus might discourage development and implementation of effective procedures to limit blank values. Part 50 Appendix O and Appendix L refer to QA Guidance Document 2.12 for guidance in such QA matters. Document 2.12 says... "Measurements for sampled filters should not be corrected to account for [field] blank measurements. High blank values should not cause the automatic invalidation of sampled filters that were measured during the same weighing session. Instead, high blank values should trigger troubleshooting and corrective action to reduce blank values to acceptable levels." (EPA, 1998).

(2) *Comment:* One commenter asserted that a more realistic approach would be to allow two years from development of Data Quality Objectives and the approval of more than one vendor's FEM before commencement of monitoring. The commenter recognized that this approach might require an initial designation of areas as unclassifiable or require legislative relief in relaxing the designation scheduled as discussed in the Advance Notice or Proposed Rulemaking (71 FR 6723-6725). The commenter noted that monitoring data proposed to be used for designation in the 2009-2011 time frame would then have to be moved to a more reasonable time from (2010-2013) (Central States Air Resource Agencies Association).

Response: The EPA will only require monitoring for $PM_{10-2.5}$ at multipollutant NCore sites for scientific purposes. These sites, which are expected to number approximately 75, are required to be implemented by January 1, 2011. Given this schedule, there should be adequate time for development and approval of candidate $PM_{10-2.5}$ continuous FEM monitors.

(3) *Comment:* One commenter stated that researchers at Texas A&M, U.C. Davis, and USDA-ARS have determined that $PM_{2.5}$ and PM_{10} concentrations measured with FRM samplers are inaccurate when sampling PM with mass median diameters that exceed the sampling range of the respective samplers. This commenter referred to work by Dr. Michael Buser (USDA-ARS) that has determined errors up to 20:1 when using Federal Reference Method (FRM) $PM_{2.5}$ samplers to measure $PM_{2.5}$ emissions. The commenter argued that this can result in gross over-reporting of particulate mass concentrations in agricultural settings (Avant).

Response: The Agency has reviewed the source material represented by this commenter and does not necessarily concur with assumptions upon which the conclusions were based. In particular, the stated research does not accurately represent EPA's development, promulgation, and compliance testing of the FRM for $PM_{2.5.}$ As a result, the Agency does not concur with the commenter's bias estimates when considering use of the $PM_{2.5}$ FRM in agricultural settings.

1. Specific comments related to new FRM for $PM_{10-2.5}$

(1) *Comment:* One commenter representing several northeast state air pollution control agencies asserted that the EPA's proposed coarse particle FRM of low-volume samplers that is based on the existing $PM_{2.5}$ FRM (see 71 FR 2687) is useful only for determining performance of Federal Equivalent Method (FEM) candidates of any class. This commenter agreed with EPA that the difference method for coarse PM is the most defendable approach for a reference measurement method (NESCAUM, Attachment B, p.3). With respect to the proposed FRM, the commenter expressed concerns about the degradation of coarse particle data precision in areas where $PM_{2.5}$ concentrations are substantially greater than coarse particle concentrations. Specifically, they commented, "This includes much of the eastern U.S., especially in the context of National Core Monitoring Network (NCore) spatial scale siting (neighborhood to urban scale, away from mid- and micro-scale PM-coarse sources). While we realize that EPA does not intend the FRM to be widely used for routine monitoring, the proposed regulations require that it will be used for audit purposes." The commenter does not think this is appropriate and provided recommendations for an alternative approach. (NESCAUM, Attachment B pp. 3 to 4).

Response: Because the proposed FRM for $PM_{10-2.5}$ uses numerical subtraction to calculate the coarse fraction of PM_{10}, the Agency recognizes that precision may degrade somewhat in areas where $PM_{2.5}$ is substantially greater than the $PM_{10-2.5}$ concentration. However, the Agency's own field tests under these sampling conditions revealed that an

acceptable level of precision can be achieved using this method. Moreover, the Agency's review of difference method precision obtained by a routine operating network (Jefferson County, AL where $PM_{2.5}/PM_{10}$ ratios were 0.73), indicated that a mean $PM_{10-2.5}$ precision of 8.1% CV was achieved during 48 weekly sampling events in 2004. During 2005, when the mean $PM_{2.5}/PM_{10}$ ratio was 0.64, a mean $PM_{10-2.5}$ precision of 6.3% was achieved during 48 weekly sampling events. These precision values are substantially better than those estimated using the technique provided in Attachment B by the commenter. Acceptable precision levels, therefore, can be expected under carefully controlled conditions such as those expected during an independent performance audit.

(2) *Comment:* One commenter noted that even though EPA is proposing a new $PM_{10-2.5}$ standard, there is no FRM for measuring $PM_{10-2.5}$ or a nationwide monitoring network in rural areas. The EPA proposed a calculation method for determining $PM_{10-2.5}$ concentrations by subtracting $PM_{2.5}$ concentrations from PM_{10} concentrations. The commenter argued that for the coarse fraction agricultural particulate, the "difference" method of measuring $PM_{10-2.5}$ may not be accurate. Specifically, the commenter concluded that subtracting two measured and potentially inaccurate concentrations (based on FRM sampler errors for particulate exceeding the cut point of the sampler) will not produce accurate $PM_{10-2.5}$ concentrations (Avant).

Response: An FRM was proposed that had been shown by considerable evidence to be adequately accurate. Extensive laboratory and field evaluation of the proposed method has demonstrated that the proposed FRM for $PM_{10-2.5}$ provided adequate measurement accuracy and precision and can be successfully implemented in routine operating networks (EPA, 2005b). The EPA is not persuaded by this commenter to change this conclusion. The method has been formally peer reviewed and endorsed by CASAC's Ambient Air Monitoring and Methods Subcommittee as the best available methodology for measuring the coarse fraction of PM_{10} (Henderson, 2005c).

(3) *Comment:* One commenter supported the development and requirement of an automated continuous hourly method for $PM_{10-2.5}$ (North Carolina Division of Air Quality).

Response: The EPA has developed data quality objectives for $PM_{10-2.5}$ equivalency criteria. These criteria provide achievable performance criteria for instrument manufacturers to develop continuous $PM_{10-2.5}$ monitors. The EPA has been evaluating prototype $PM_{10-2.5}$ continuous monitors in recent field campaigns and will continue to do so, when possible.

(4) *Comment:* One commenter agreed that alternative $PM_{10-2.5}$ Federal Reference Method that would directly measure the coarse fraction of particles should be developed (North Carolina Division of Air Quality).

Response: The Agency recognizes that the proposed FRM relies on the use of two collocated measurement methods and thus does not provide a direct measurement of $PM_{10-2.5}$ within a single instrument, such as would be provided by a sampler equipped with a virtual impactor. However, the Agency encourages development of such an

instrument and the proposed revisions to the NAAQS regulations enable introduction of an approved equivalent monitor of this type into compliance networks. The EPA is also actively investigating the possibility that a dichotomous-based method might ultimately provide a more direct means of measuring the coarse fraction of PM_{10} than does the proposed FRM for $PM_{10-2.5}$.

(5) *Comment:* One commenter agreed with the proposed 3 $\mu g/m^3$ lower concentration limit for the $PM_{10-2.5}$ (North Carolina Division of Air Quality)

Response: The comment in support of the proposal is acknowledged.

(6) *Comment:* One commenter supported EPA's efforts to encourage the development of FEM and ARM methods for monitoring $PM_{2.5}$ and PMcoarse, particularly the development of continuous monitoring methods, but expressed concerns about the quality and comparability of data produced by these methods. In addition, temporal and/or geographic variations in aerosol composition can produce variable comparability between monitoring methods. The commenter therefore, encouraged EPA to define performance criteria that avoids any increase in data bias or imprecision compared to the FRM, and requires sufficient collocation with FRM monitoring to evaluate site specific performance (Delaware Department of Natural Resources & Environmental Control).

Response: The performance requirements for Class I and II FEMs are similar to those for the FRM. However, it is recognized that $PM_{10-2.5}$ instruments which provide near-real time response (Class III FEMs) may not provide the same degree of accuracy (i.e. agreement with the FRM) and precision provided by the proposed FRM for $PM_{10-2.5}$. Because of the statistical advantage of their higher sampling frequency, continuous instruments, even with their inherent reduction in accuracy and precision, still provide similar decision making quality to that of the $PM_{10-2.5}$ FRM. Given the multiple monitoring objectives that continuous monitors can help satisfy, the Agency considers their potential reduced accuracy and precision to be acceptable. However, due to concerns regarding use of PM continuous methods in relatively clean areas, EPA has strengthened the additive bias (intercept) requirements for both $PM_{2.5}$ class III and $PM_{10-2.5}$ class II and III methods to ensure the they continue to appropriately match the FRM even when used in areas that are well below the NAAQS.

(7) *Comment:* One commenter noted that an issue that appears to be subject to legal challenge is that in the SAFETEA-LU Act of 2005 there was a specific provision that indicated that US EPA could not utilize the subtraction method as the standard reference method for the measurement of coarse PM. The EPA's proposal indicated that "Section 6012 of the SAFETEA-LU in part requires the Administrator, within two years, to "develop a Federal reference method to measure directly particles that are larger than 2 .5 micrometers in diameter without reliance on subtracting from coarse particle measurements those particles that are equal to or smaller than 2.5 micrometers in diameter." But at the same time, the preamble indicated that EPA was proposing a difference method for the FRM for the coarse $PM_{10-2.5}$. The commenter argued that EPA's justification that this action would actively promote the use of non-difference

methods through the part 53 equivalency designation process seemed to be in conflict with the track record of the technical problems which are invariably encountered in the development of instrumentation and its initial deployment in the field. Further, the commenter asserted that this will result in designations based on an FRM subject to legal challenges, and which in any event will need to be revised within a few years to comply with SAFETEA requirements. Though the commenter recognized that there will be numerous litigations associated with the promulgation of any new regulations, the commenter noted that it is particularly disconcerting when such legal challenges are clearly identified in the proposed regulation per se (Vermont Department of Environmental Conservation).

Response: As the Agency stated at proposal (71 FR at 2690), EPA believes that the proposed FRM is responsive to and consistent with the SAFETEA-LU Act of 2005 and therefore does not conflict with either its specific language or intent. Since the Act does not require that the Agency promulgate a non-difference method as either the sole or an alternative FRM (as specifically defined in Part 53), our action is consistent with the literal language of the statute. Moreover, , the additions to Part 53 that allow designation of equivalent methods for monitoring $PM_{10-2.5}$ will provide a strong incentive to stimulate the further commercial development and refinement of new or existing methods for $PM_{10-2.5}$, most of which will not rely on subtraction of fine mode particle measurements from coarse mode particle measurements. Further, EPA is actively investigating the possibility that a dichotomous-based method might ultimately provide a more direct means of measuring the coarse fraction of PM_{10}. Any one of such methods that is shown to achieve an adequate level of performance may be identified and utilized as a "reference method" as defined in Part 53. Until such new, more direct methods are demonstrated to be suitable and adequate and become commercially available, the proposed difference-based FRM provides a reliable, proven measurement method which can be successfully implemented immediately. Moreover, CASAC expressly agrees with this technical assessment (71 FR at 2689).

(8) *Comment:* The proposed Federal Reference Method specified that ambient $PM_{10-2.5}$ concentrations are to be measured by the "difference method," which separately measures $PM_{2.5}$ and PM_{10} at co-located monitors, and identifies the difference as $PM_{10-2.5}$. Some commenters argued that this method is not an accurate way to measure $PM_{10-2.5}$ (National Mining Association, National Cattlemen's Beef Association).

Response: The commenter provided data from Salt Lake County, Utah which indicated that the difference method produces negative values and is thus inherently inaccurate. However, inspection of the data reveals that only 14 of the 3,714 data points from Salt Lake County were negative, which represents a rate of only 0.4%. Given the uncertainty associated with any air quality measurement, this degree of measurement uncertainty is neither unexpected nor unacceptable. For the other three Utah counties represented in the report submitted by the commenter, no negative $PM_{10-2.5}$ concentrations were reported during 3,554 discrete sampling events. The EPA contends, therefore, that the data do not support the commenter's contention that the proposed FRM for $PM_{10-2.5}$ is inherently inaccurate.

III. RESPONSES TO LEGAL, ADMINISTRATIVE, PROCEDURAL, OR MISPLACED COMMENTS

A number of comments were received that addressed a wide range of issues including legal, administrative, and procedural issues. Many legal issues are addressed generally throughout the preamble to the final rule. Specific legal issues are more fully addressed below in section III.A as well as in section II. Comments related to Statutory and Executive Orders are addressed generally in section VIII of the preamble to the final rule and discussed more fully below in section III.B below. In addition, a number of comments were submitted related to issues that are not germane to the review of the NAAQS, including implementation issues. Implementation issues are addressed generally in section VII of the preamble to the final rule. Comments on implementation and other issues that have been categorized as "misplaced" comments are included in section III.C below.

A. Legal Issues

A number of commenters submitted comments addressing specific legal issues. These issues are generally addressed throughout the preamble to the final rule and more specifically below. A number of legal issues specifically addressing comments related to coarse particles are addressed in section II.B above. In general, these comments are grouped according to the commenter(s) that submitted them.

The following comments addressing legal issues were submitted by American Lung Association et al.

(1) *Comment:* These commenters argued that EPA's proposal cavalierly dismisses the relevance of the risk assessment to decision making on the proposed standards, despite the clear statutory requirement for EPA to evaluate health hazards to the public and to establish a standard that will protect the public from adverse health impacts with an adequate margin of safety (American Lung Association et al.).

Response: The Administrator considered the risk assessment for $PM_{2.5}$ carefully as part of weighing the entire body of evidence in his decision to revise the $PM_{2.5}$ standards and his decision on the appropriate level for both the 24-hour and annual standards. The commenter thus mischaracterizes the Administrator's consideration of the risk assessment. With respect to the determination to revise the existing standards, the Administrator stated that the risk assessment should be given less weight than the epidemiologic evidence, especially in light of the absence of a formal uncertainty analysis which makes it more difficult to assess the probability of various risk estimates. Nonetheless, the risk assessment "informs the determination of the public health significance of risks to the extent the evidence is judged to support an effect at a particular level of air quality", and thus further supports revision of the standards (71 FR at 2643). The Administrator likewise explained in detail his reasons for not using the risk assessment to determine what specific quantitative response (such as level of either the

24-hour or the annual standard) is warranted. Notwithstanding that the Assessment rests on a more extensive body of data and is more comprehensive in scope than the 1997 assessment, significant uncertainties continue to underlie the quantified estimates, making it more reasonable in the Administrator's judgment to rely on the epidemiologic evidence as the basis for determining the appropriate levels of the NAAQS. These uncertainties include (among other factors) the shape of the concentration-response functions in the absence of clear information as to the existence or non-existence of thresholds; issues related to selection of appropriate statistical models for the analysis of the epidemiologic data; and the role of potentially confounding and modifying factors in the concentration-response relationships. See 71 FR at 2648 and section II.F of the preamble to the final rule.

To the extent the commenters suggest that EPA is legally bound to base quantitative features of the standards (such as levels) on the results of the risk assessment, or that the standards must be established at a lower level because the risk assessment quantifies morbidity and mortality effects below the levels the Administrator selected, the commenter is mistaken. See ATA III, 283 F. 3d at 373-74 (EPA not obliged to use the numerical results of the risk assessment to establish the 24-hour PM2.5 standard at a lower level when it provided a reasonable basis for not using the assessment).

(2) *Comment:* These commenters argued that EPA may not decide to deal with uncertainty in data or potential health effects by simply ignoring that data or those effects, citing Public Citizen v. FMCSA, 374 F. 3d 1209, 1219 (D.C. Cir. 2004) ("The mere fact that the magnitude of [an effect] is uncertain is no justification for disregarding the effect entirely") (American Lung Association et al.).

Response: The Administrator has not invoked uncertainties to ignore the possibility that various levels of exposure to PM may be associated with adverse health effects, and EPA has not ignored data. Based on all of the available data, the Administrator has weighed the strength and weaknesses of the evidence, and is relying on the direct evidence from the epidemiological studies as the most reliable basis for determining the levels of the NAAQS. This is not ignoring data and potential health effects, but instead is a reasoned way to address the data and respond to the risk of adverse health effects. Public Citizen v. FMCSA does not call for any different approach, and is not on point. Unlike the situation here, the FMCSA, in making a health and safety determination, literally disregarded potential for risk due to uncertainty. The case involved a determination of the permissible number of working hours for surface transport motor vehicle operators. In its cost-benefit analysis, the agency admitted that crash risks increased as operator on-duty driving time increased, yet disregarded this risk in its analysis because of inability to quantify the precise magnitude of increased risk. 374 F. 3d at 1218-19. This risk was therefore not considered in the weighing required under the statute. Understandably, the court found the agency's analysis insufficient to justify its determination. Here, the Administrator has carefully considered relevant uncertainties and explained how they influenced his decisions.

Public Citizen also did not involve a statutory standard similar to the Clean Air Act's requirement that primary standards be requisite to protect the public health, that is "sufficient but not more than necessary" (Whitman, 531 U.S. at 473). This requires the Administrator to exercise his judgment to balance, among other things, the various uncertainties inevitable in making NAAQS determinations. In contrast, the agency in Public Citizen was required to develop rules that achieved various safety outcomes after considering costs and benefits, and ignored a risk solely because it could not be quantified (374 F. 3d at 1212).

Finally, EPA notes that its consideration of uncertainties in this NAAQS review has not been one-sided, as the comment suggests. In all cases the Administrator has considered all of the evidence on an issue, considering the uncertainties, weighed the strengths and weaknesses of the evidence, and made a judgment reflecting the proper balance to draw under section 109(b). These commenters basically object to the results of this judgment, but are inaccurate in claiming that it is one-sided.

(3) *Comment:* These commenters argued that limited data are not an excuse for failing to establish the level at which there is an absence of adverse effect (American Lung Association et al.) To the contrary, as the D.C. Circuit has explained, "Congress' directive to the Administrator to allow an 'adequate margin of safety' alone plainly refutes any suggestion that the Administrator is only authorized to set primary air quality standards which are designed to protect against health effects that are known to be clear harmful", citing Lead Industries, 647 F. 2d at 1154-55. If a pollutant adversely affects the health of vulnerable subpopulations, EPA must strengthen the entire national standard, citing American Lung Ass'n v. EPA, 124 F. 3d at 390 (sic) and Lead Industries, 647 F. 2d at 1153.

Response: The commenters cited these cases to support arguments that the NAAQS are required to provide protection for sensitive sub-populations, and must provide a margin of safety to address among other things uncertainty in whether adverse effects will occur and uncertainty regarding effects that are unknown at this time. EPA agrees with the commenter that protection of sensitive subpopulations and providing an adequate margin of safety are central components of setting the NAAQS. The Administrator's final decisions in this review are based on a careful consideration of these factors, and a full explanation has been provided of how the final decisions protect sensitive subpopulations with an adequate margin of safety. To that extent, EPA does not disagree with the commenter's interpretation. However, to the extent commenters are claiming that EPA must set a NAAQS that will provide an absence of risk of adverse effect, then EPA disagrees. Neither the cases nor the legislative history cited by the commenter support that view.

The commenters cited the D.C. Circuit as stating that "if a pollutant adversely affects the health of these sensitive individuals, EPA must strengthen the entire national standard". American Lung Ass'n, 134 F. 3d at 389 referring to Lead Industries, 647 F. 2d at 1153. These cases refer back to legislative history from the 1970 amendments, stating that "[a]mbient air quality is sufficient to protect the health of such persons whenever there is

an absence of adverse effect on the health of a statistically related sample of persons in sensitive groups from exposure to the ambient air." S. Rep. No. 91-1196, 91st Cong. 2d sess. 10. This legislative history is directed at assuring that the standards protect sensitive subpopulations, not just persons who are unimpaired or less susceptible to the effects of ambient air pollution, and does not purport to be a binding directive regarding the level of a standard. See, e.g., 71 FR at 2622 n. 1. In addition, the cited cases address issues different from those in this NAAQS revision. In the Lead Industries case, the issue was at what point in a continuum the effects associated with blood lead levels should be considered adverse. The nature and degree of the effects varied with blood lead levels, and there was not a clear-cut level at which one could say above this blood lead level is harmful and below this level it is not. Instead, there was a continuum of varying nature and intensity of effects, as compared to a clear effect threshold. In that context EPA concluded and the court agreed that section 109 did not require evidence of clear harm before determining that a certain blood level presented adverse health effects. EPA cited the legislative history noted above as showing that Congress intended the Administrator to exercise judgment and caution in making the decision on when an effect should be considered adverse for purposes of setting a NAAQS, and the Court agreed with EPA's interpretation. 647 F. 2d at 1153-55. In this review, however, there is no real issue of whether the effects attributed to PM exposure should be considered adverse, as mortality and serious morbidity are the effects involved. Instead the focus is more on the degree of uncertainty over whether certain ambient levels will result in such adverse effects, and the proper public health response to that uncertainty.[11] In American Lung Ass'n, the statement by the court refers to situations once the Agency has determined that an adverse effect is occurring. That case addressed the adequacy of EPA's reasoning for not revising the standard once there was a determination that repeated occurrences of a certain exposure were significant from a public health standpoint. That is also not the issue here.

The central issues in this review are different and more difficult. Here there is no doubt that the mortality and serious morbidity effects at issue should be considered adverse, and EPA treats them as such. The primary issues revolve around what the evidence reasonably tells us about the likelihood that a certain ambient level of PM exposure will cause these effects, and the appropriately cautionary public health response in the face of the uncertainty in this evidence. Put another way, EPA is not trying to decide whether an effect is adverse, or decide whether to address an adverse effect we know is occurring. Instead the Administrator is deciding how to address the risk that an adverse effect may occur where the evidence is uncertain as to the levels at which the adverse effects may occur.

[11] It should be noted that PM is a pollutant for which there is no clear no-effects level, but this does not mean that effects can be considered to occur at all levels of exposure. See EPA, 2004, p. 9-44 ("the available evidence does not either support or refute the existence of threshold for the effects of PM on mortality across the range of concentrations in the studies"). Throughout its comments when citing the cases and legislative history discussed here, the commenter seems to assume that effects occur at all levels of PM exposure, which is a mistaken assumption.

Neither the cases nor the legislative history cited support the view that in this situation EPA is required to ensure that there is an absence of risk of adverse effect. To the contrary, the case law is clear that in such a situation the Administrator must exercise his public health judgment, and decide what level is requisite to protect public health with an adequate margin of safety, taking a cautionary approach and considering the effects on sensitive sub-populations. Even where there is no discernable threshold for effects; that is, where the evidence does not show a level at which it can be concluded with confidence that no adverse effects are likely to occur, the D.C. Circuit has repeatedly upheld NAAQS even though there was (necessarily) no guarantee that such standards result in absence of risk of adverse effects. See, e.g. ATA III, 283 F. 3d at 360 (ozone and PM are or may be non-threshold pollutants), 371-72 (upholding annual $PM_{2.5}$ standard) and 379 (upholding ozone standard); see also, API v. Costle, 665 F. 2d at 1187 (EPA is not required to base the level of the standard on either the lowest (or highest) level from any study in the record, but rather must "make an informed judgment based on available evidence"). The D.C. Circuit has also cautioned that American Lung Ass'n is not to be read as requiring that EPA "definitely identify pollutant levels below which risks to public health are negligible". 283 F. 3d at 370. Lead Industries itself upheld a standard that would keep 99.5 percent of children below the EPA-determined maximum safe individual blood level, a standard at which some risk remains to the most susceptible sub-population. Id. at 1155-61.

The statute commands that the Administrator exercise "judgment" and adopt standards which are "requisite" to protect public health with an adequate margin of safety, meaning sufficient but not more than necessary, all indicate that some type of weighing and balancing must occur in the decision process. See also Whitman, 531 U.S. at 494 (Breyer, J., concurring)("the statute, by its express terms, does not compel the elimination of all risk"); Lead Industries, 647 F. 2d at 1152 ("Section 109 (b) does not specify precisely what Congress had in mind when it directed the Administrator to prescribe air quality standards that are 'requisite to protect the public health'"); ATA III, 283 F. 3d at 369 ("the Agency not only recognized, but acted upon, its statutory obligation to set the primary NAAQS at levels no lower than necessary to reduce public health risks")(emphasis added). Likewise, the requirement that standards provide an "adequate margin of safety" affords the Administrator considerable discretion to make public health judgments, requiring a consideration and weighing of such factors as the nature of effects, the size of the exposed population, and the degree of scientific certainty or uncertainty that effects will occur at a given level of exposure. From the inception of the program, EPA has repeatedly rejected claims that the lack of a clear threshold requires the Administrator to set zero-risk standards. See, e.g., 44 FR at 8213 (Feb. 8, 1979)(final decision on ozone NAAQS). Legislative history likewise indicates that the NAAQS are not to be set at levels which eliminate all risk, or all risk caused by the anthropogenic levels of a pollutant. H.R. Rep. No. 95-294, 95th Cong., 1st Sess. 127 (1977) noted approvingly in Lead Industries, 647 F. 2d 1156 n. 51. (EPA views this legislative history as more probative than the various floor statements from 1970 cited in footnote 8 of the comment.) EPA also repeats what should be evident from the record in this case, and many other NAAQS rulemakings: the scientific data are often sufficiently inconclusive that it is difficult to identify with confidence the lowest pollution level at which an

adverse effect will occur. See, e.g. section II.F to the preamble to the final rule. In conclusion, EPA does not accept the commenters' formulation if they mean that EPA must set the NAAQS at a level that ensures the absence of risk of an adverse effect.

(4) *Comment:* These commenters argued that given the scientific evidence documenting the occurrence of adverse effects year after year in numerous populations at levels allowed by both the current NAAQS and EPA's proposal, risks are by definition "significant" enough to require protection under the Act's protective and precautionary approach, citing H.R. Rep No. 95-294 at 43-51 and Ethyl Corp. v. EPA, 541 F. 2d 1, 18 (D.C. Cir. 1976) (American Lung Association et al.).

Response: The legislative and judicial authorities cited by the commenter concern the "may reasonably be anticipated to endanger public health or welfare" standard for listing air pollutants in section 108 (a) (1) (A) and the same standard for regulating motor vehicle fuels and fuel additives in section 211 (c) (1), and therefore are not directly on point. Nonetheless, the Administrator agrees that under section 109(b) an appropriately precautionary approach is one aspect of establishing and revising the NAAQS (see, e.g., section III.C of the preamble to the final rule, explaining the Administrator's choice of an indicator for thoracic coarse particles which applies in all areas notwithstanding considerable difference in **strength of** evidence of health effects of thoracic coarse particles of different origins). The Administrator also agrees that risks posed by exposure to fine particles and thoracic coarse particles is significant and warrants revision of the PM2.5 standards and retention of the 24-hour standard for PM_{10}. See sections II.B and III.B of the preamble to the final rule, among other discussions. The Administrator does not agree, however, with the commenters' characterization that the scientific evidence documents widespread and certain effects occurring in large portions of the population below levels adopted in the final rule, however. See in particular sections II.F and III.D.2 to the preamble to the final rule.

(5) *Comment:* Some commenters argued that EPA has not provided any rational justification for disagreeing with CASAC's recommendations, in violation of the requirements of section 307 (d) (e.g., American Lung Association et al.).

Response: The EPA disagrees with this characterization of its explanation at proposal, and refers also to its detailed response in sections II.F and III.C regarding decisions not to accept CASAC's recommendations regarding the level of the annual standard for $PM_{2.5}$ and use of a qualified indicator for thoracic coarse particles. It should be noted that the same commenters taking EPA to task for not following CASAC's advice regarding the level of the annual standard energetically urge EPA to adopt $PM_{2.5}$ standards more stringent than those recommended by CASAC.

(6) *Comment:* Some commenters asserted that EPA is required by section 307 (d) (3) to provide in the notice of proposed rulemaking an explanation of the reasons the proposal differs in any important respect from CASAC recommendations. The EPA mistakenly stated that the proposed standards based on the qualified $PM_{10-2.5}$ indicator were

consistent with CASAC's recommendation. Because CASAC submitted a further, post-proposal letter to the Administrator explaining that the proposal was inconsistent with those recommendations in important respects, EPA is not only obligated to respond to CASAC, but must reopen the record for public review and comment to do so, since section 307 (d) (3) indicates that all such explanations must be part of the record for the proposed rule (American Lung Association et al.).

Response: The EPA has explained in detail the reasons for the final rule for coarse particles, including how it differs from certain aspects of CASAC recommendations although consistent with the main thrust of that advice. See sections III.C.2 and III.C.3.b of the preamble to the final rule. The EPA disagrees with the commenters that EPA must reopen the rulemaking record for further comment to do so. The premise of the comment is that section 307 (d) (3) commands that all responses to CASAC recommendations must be part of the record for the proposed rule. This is incorrect. The statute only addresses the situation where a CASAC recommendation precedes issuance of a proposed rule. It does not specifically address the situation where CASAC issues further recommendations after a proposal has issued (an occurrence with precedent, contrary to the commenters' view; see 52 FR at 24637 (July 1, 1987)). Nor does it address the situation where a final NAAQS differs from a proposal in a way that requires further response to a CASAC recommendation. This circumstance would appear to fall within the scope of section 307(d)(6), which calls for EPA to include with the final rule a statement of basis and purpose like that referred to in section 307(d)(3). . The EPA believes that responding to further CASAC recommendations in the record to the final rule is a permissible and reasonable means of proceeding here, and fully satisfies section 307(d)(6), given that EPA provided full notice at proposal that it was considering options involving a PM_{10} indicator, see 71 FR at 2672-73, commenters and others had full opportunity to comment on CASAC's pre- and post-proposal advice, and the overarching issue respecting coarse particles was whether to revise the existing PM_{10} standards. In this case, the procedures for response the agency adopted are also the only means which would allow compliance with the deadlines in the Consent Decree schedule for EPA taking final action in this NAAQS review.

(7) *Comment:* The standards must protect these vulnerable populations – including persons with heart disease, hypertension, diabetes, and chronic bronchitis or asthma -- with an adequate margin of safety, the same standards that apply to the general population (American Lung Association, et al.).

Response: The EPA agrees with this comment, and has carefully considered effects on vulnerable subpopulations in considering whether and how to revise the PM NAAQS (See e.g. section II.F and III.B, C.2, and D.2).

(8) *Comment:* Some commenters argued that EPA must adopt a precautionary approach to the standard setting process, and set standards in a manner that deals with uncertainty not by ignoring uncertain effects but rather by protecting against adverse health effects even where those effects may be uncertain. In support of its argument, the American Lung Association et al. specifically cited ATA III, 283 F. 3d at 369 (EPA must promulgate

protective NAAQS even where risks cannot be qualified or precisely identified) and Lead Industries, 647 F. 2d at 1155 (requiring EPA to wait until it can conclusively demonstrate that a particular effect is adverse to human health is inconsistent with the statute's preventative and precautionary orientation).

Response: The EPA agrees generally with this comment, but notes further that a general invocation of precautionary principles does not determine where in the range of reasonable values EPA could establish the level of a standard --in this case, the annual $PM_{2.5}$ standard. Section II.F.2 to the preamble to the final rule explains in detail why it is appropriate to retain 15 $\mu g/m^3$ as the level of the annual standard. The EPA notes further that this choice is consistent with case law in the D.C. Circuit (not cited by the commenter) that the Administrator is to carefully examine all of the relevant studies in the record, but need not base the level of the standard on either the highest or lowest value in these studies. Rather, an informed judgment is called for. API, 665 F. 2d at 1187; NRDC v. EPA, 902 F. 2d 962, 970. Section II.F 2 to the preamble to the final rule states the basis for the Administrator's exercise of informed judgment here, in particular, setting the level of the annual standard well below the long-term average levels of the two premiere long term epidemiologic studies for $PM_{2.5}$ exposure.

Far from "ignoring uncertain effects," the Administrator has focused closely on the issue of "uncertain effects" in determining where the annual level should be set, recognizing the significant uncertainty over whether adverse effects occur from long-term exposure at various ambient levels of $PM_{2.5}$. As discussed above, Lead Industries is not on point as the issue in that case concerned when an effect should be considered adverse, and the authority to determine that an effect was adverse before there was clear evidence that the effect was harmful. Here there is no issue that mortality and serious morbidity are adverse.

(9) *Comment:* The proposed primary standards for coarse particles ignore the Act's precautionary directives which require the Administrator to err on the side of protecting public health (citing both Lead Industries, 647 F. 2d at 1152 and 1155, and ATA III, 283 F. 3d at 378). Among instances cited in the comment as ignoring this principle are the level of the proposed standard, the various qualifications to the proposed standard, and exemption (sic) of agricultural and mining sources from the standard. The comment further maintains that uncertainties cannot be a basis for not setting a standard or not addressing certain types of coarse particles, or for not adhering to the Act's precautionary purpose. The comment cites the level of the proposed 24-hour standard as an example of the backwards approach, maintaining that EPA, in efforts to be (in the agency's own words) "cautious and restrained" ignored its own calculations of a level equivalent to that afforded by the current PM_{10} standard.

Response: The commenters' specific concerns are no longer relevant since EPA is retaining the 24-hour PM_{10} standard.

The following comments addressing legal issues were submitted by the Coarse Particle Coalition.

(10) *Comment:* Some commenters argued that **t**he D.C. Circuit's decision in ATA I requires EPA to repeal the current NAAQS for PM_{10}. The commenter in particular notes the court's stated "conclusion that PM_{10} amounts to an arbitrary indictor for coarse particle pollution" (175 F. 3d at 1075) (Coarse Particle Coalition).

Response: As discussed in section III.C. 3. b of the preamble to the final rule and in other comment responses, the EPA disagrees that the ATA I decision precludes use of a PM_{10} indicator. The Court did not hold that it was unlawful *per se* to use PM_{10} as an indicator for thoracic coarse particles. Instead, the Court noted two particular problems—the variable level of allowable concentrations of $PM_{10-2.5}$ and double regulation of $PM_{2.5}$—and found that EPA either failed to address these issues, or provided explanations that were inconsistent and unsupported. As discussed in the preamble, far from being arbitrary and capricious, inclusion of $PM_{2.5}$ serves two important functions. First, it is the mechanism that provides for the variation in allowable $PM_{10-2.5}$ concentrations, targeting lower allowable levels in areas where there is greater public health concern. Second, to the extent that there is "double regulation" of $PM_{2.5}$ by virtue of its inclusion in the PM_{10} indicator (175 F.3d at 1054), regulation of $PM_{2.5}$ via this indicator serves valid, non-duplicative purposes in providing appropriate protection from thoracic coarse particles.

The EPA notes further that the commenters' statement that ATA I requires repeal of the 1987 standards is not correct. The 1987 standards were not being reviewed in ATA I, and in any case PM10 was not used as an indicator for just coarse particles in the 1987 standard so the reasoning in ATA I does not apply.

The following comments addressing legal issues were raised by the International Truck & Engine Corporation.

(11) *Comment:* CAA section 109 (b) (1) mandates that NAAQS be set at a level "requisite" to protect public health. The Supreme Court has interpreted the provision to require that EPA set NAAQS at a level "sufficient, but not more than necessary" to protect public health and welfare. Given the foregoing, EPA arguably would be acting *ultra vires* if it were to ratchet down a standard that is already adequate to protect public health. In this case, because the annual PM2.5 standard has resulted in greater protection than EPA considered adequate to protect public health with an ample margin of safety, the Agency lacks statutory authority for requiring additional reductions (International Truck & Engine Corporation).

*Response***:** As explained in section II.B to the preamble to the final rule, the premise of this comment is mistaken. It mischaracterizes the use of the quantitative risk assessment in the 1997 rulemaking; it is factually incorrect in its comparison of the quantitative risk estimates between 1997 and the current rulemaking; and it fails to take into account that with similar risks, increased certainty in the risks presented by $PM_{2.5}$ implies greater

certain than in the last review. Cf. Ethyl Corp., 541 F. 2d 1, 18 ("the public health may properly be found endangered … by a lesser risk of a greater harm"). Thus, the agency does not accept that it is legally bound to retain the level of the annual PM2.5 standard based on comparison with quantitative risk estimates in this review cycle and the last. The bases for the Administrator's determination to retain the level of the current annual standard for $PM_{2.5}$ are explained in section II.F. 2 to the preamble to the final rule, and in other comment responses.

The following comments addressing legal issues were submitted by UARG..

(12) *Comment:* The Administrator must review the NAAQS and the **c**riteria on which they are based at least every five years, and at the completion of that review, he may revise the standards only if "appropriate" under section 109 (b). Some commenters argued that because there is "at least a presumption" that an existing rule best carries out the policies committed to an agency by Congress (citing Atchison, Topeka & Santa Fe Ry. Co. v. Wichita Bd. Of Trade, 412 U.S. 800, 808 (1973)), the Administrator must supply a reasoned analysis before changing the NAAQS based on a change of policy or judgment (citing Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto Ins. Co, 463 U.S. 29, 42 (1983)) (UARG, pp. 5 to 6, 12 to 13).

Response: The commenter cites the plurality opinion in Atchison, Topeka & Santa Fe Ry. Co. to support the proposition that there is a presumption that the existing PM NAAQS best carries out the policies of sections 108 and 109. In that case, the Interstate Commerce Commission, in an adjudicative proceeding, issued a rate order which deviated from prior settled adjudicative precedent of the Commission (412 U.S. at 805-06). The Commission had a settled principle (referred to in the opinion as "settled rule**")** addressing the general issue involved in the case, and attempted to distinguish the pending rate determination from that principle. The adequacy of the Commission's explanation for a departure from the settled principle was the basic issue on judicial review.

The Court addressed this issue with an overall focus on the need for an agency to explain its decision, as the fundamental pre-condition for adequate judicial review. An agency needs to explain its reasoning in order for a court to determine if the decision was within Congress' delegation of statutory authority. In that context an adjudicatory agency could, through a course of agency action, establish a settled rule or principle that embodies the agency's informed judgment on the appropriate way to carry out the policies committed to it by Congress. In those circumstances a court reviewing an agency decision should properly presume that the agency's settled principle embodies the agency's view on what will best carry out the policies of Congress, calling for an adequate explanation by the agency if it departs from its own norm. The basic purpose of both the presumption and the need to explain a deviation from the settled norm derives from the obligation that an agency explain how its decision conforms to the policies committed to it by Congress. An agency may establish such a settled norm, and if it does then that norm provides an explanation for agency action in future cases. Once such a norm has been established, however, an agency must explain a deviation from it so the reviewing Court can

determine whether the agency's decision is still consistent with the policies committed to it by Congress.

The EPA does not see that this situation has any relevance to the periodic NAAQS review process. The 1997 review of the PM NAAQS did not establish any "settled rule" embodying EPA's view on the "requisite" level of protection from PM, which must then be taken as a presumed level of protection in future PM NAAQS reviews. The 1997 PM review determined what standard was "requisite" under section 109 given the science as it then existed. It did not establish a "settled rule" on the requisite level of PM protection, and it is not analogous to the adoption of a settled rule through adjudicatory history – like courts establishing precedent through opinions accompanying adjudicated cases -- which was discussed in Atchison, Topeka & Santa Fe Ry. Co.

To the contrary, section 109 mandates a periodic review based on an updated review **of** the science. Prior NAAQS determinations, based on the then current science, do not have status as adjudicative precedent or "settled rule" on what is "requisite" for purposes of the next review on the updated science. The EPA is required to "review" the NAAQS and the air quality criteria. The review of the air quality criteria is to ensure that NAAQS decisions are based on "the latest scientific knowledge" regarding effects of the pollutant in question. The periodic NAAQS review process is **thus** on-going and dynamic, with an obligation to make revisions judged appropriate in light of the latest scientific knowledge, applying the statutory criteria of section 109(b). The legislative history makes clear that this obligation to review and update the air quality criteria and NAAQS grew out of an expectation that revision of the NAAQS would likely be appropriate over time as scientific knowledge advanced. H.R. Rep. No. 95-294, 95th Cong., 1st Sess. 179-183 (1977). For EPA and a Court to apply a presumption that the 1997 PM NAAQS decision as to the "requisite" level of protection, based on the science as it was known then, remains the right decision under the current scientific knowledge is inconsistent with the statutory obligation to periodically review the NAAQS and the underlying scientific knowledge, apply the science as it is now known to the applicable criteria, and determine whether revisions to the NAAQS are appropriate in light of the current scientific knowledge.

Nor does the statement from State Farm that agencies changing an existing rule are "obligated to supply a reasoned analysis beyond that which may be required when an agency does not act in the first instance" (463 U.S. at 42) support the proposition that the level of protection provided by an existing NAAQS is presumptively correct and that there is some special burden over and beyond the requirements of section 109 (b) and (d) necessary to justify a change. The action reviewed in that case was a rescission of an existing rule adopted pursuant to a statutory scheme which required that standards be practicable. This is quite unlike the statutory scheme of the NAAQS, which not only requires periodic reviews, but requires that those reviews be based on air quality criteria reflecting "the latest scientific knowledge" regarding effects of the pollutant in question.

The EPA agrees, of course, that it must fully explain the basis for its decisions in this NAAQS review (including explanations of policies and judgments involved in those

decisions, as the commenter notes, and explanations of how any changes in the science since the last review were evaluated in making a decision). CAA section 307 (d) (3), (d) (6) (A) and (B). EPA has done so in this proceeding. However the need for an explanation of the basis for the final decisions in this review is not burdened by the type of "presumption" described by commenter.

(13) *Comment:* Courts commonly disregard scientific studies that do not report statistically significant results, citing Amer. Home Products v. Johnson & Johnson, 577 F. 2d 160, 169 n. 19 (2d Cir. 1978), Dunn v. Sandoz Pharmaceuticals, 275 F. Supp. 2d at 681 (M.D.N.C. 2003) and Soldo v. Sandoz Pharmaceuticals, 244 F. Supp. 2d at 455 (W.D. Penn. 2003). Even in a rulemaking context, studies that do not find a statistically significant association have been given "diminished importance", citing 59 FR 346 (1994). These citations support the proposition that the statistical significance of PM2.5 health associations is not robust when one or more gaseous pollutants are included, and therefore ostensible associations may be the product of confounding.

Response: The cases the commenter cites have to do with evidentiary proof introduced in trials and so are not on point since burdens of proof and persuasion in civil adjudications do not apply to expert agency determinations such as are involved in the NAAQS standard-setting process. See, e.g., NRDC v. EPA, 902 F. 2d at 968 ("In reviewing the primary standards for particulate matter, and the 'adequacy' of the margin of safety, we are reviewing 'predictions within an agency's area of special expertise, at the frontiers of science.' In such circumstances, we must defer to the agency's interpretation of equivocal evidence, so long as it is reasonable. And where, as here, the statute is 'precautionary' in nature, the evidence 'uncertain or conflicting' and the 'regulations designed to protect the public health', the court will not demand rigorous step-by-step proof of cause and effect" (internal citations omitted).)

The administrative action cited in the comment involved determination made by the Veterans Administration pursuant to a statute requiring it to determine whether there was a "statistical association" between suspect diseases and herbicide exposure. In addition, in determining whether there was credible evidence of an association, the Veterans Administration was required to "take into consideration whether the results are statistically significant". 59 FR at 341-42. There are no such statutory requirements for the NAAQS standard-setting process.

The commenters' reliance on statistical significance ignores such issues as overall weight of evidence, statistical power, and trends in the evidence. See Ethyl Corp, 541 F. 2d 28 n. 58 (court rejects argument that EPA could rely only on studies whose "probability of error, by standard statistical measurement, is less than 5%", holding "agencies are not limited to scientific fact, to 95 % certainties"); id. at 28 ("EPA may reach reasonable conclusions regarding health risks of a substance from "suspected, but not completely substantiated, relationships between facts, from trends among facts, from theoretical projections from imperfect data, from probative preliminary data not yet certifiable as 'fact', and the like"). It also ignores that EPA's reliance on the results of one-pollutant models reflects the discussion of the issue in the Criteria Document (EPA, 2004, section

8.4.3.3) which was peer-reviewed by CASAC. See Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 574, 579 (1993) (recognizing importance of peer review in assessing scientific validity of a particular technique or methodology). In any case, the key epidemiological studies on which the agency is relying in this review contain statistically significant results. The EPA consequently does not accept either the legal analysis of this comment or its implications concerning support for the commenters' expressed view of the evidence. See also responses in section II.A.3 above explaining why the commenters' argument also lacks technical merit.

The following comments address legal issues submitted by ExxonMobil.

(14) *Comment:* In 1997, EPA determined that a daily standard of 65 ug/m3 was requisite to protect public health with an ample margin of safety. Given EPA's data showing that the estimated risks have declined and EPA's analysis of the studies which shows greater, not less uncertainty, in the likelihood that the observed effects are caused by PM2.5, EPA should not lower the standard. As EPA states in the preamble, its task under section 109 is to establish standards that are neither more nor less stringent than necessary for these purposes. Lowering the standard in light of the 1997 determination would result in controls that would be more than necessary to protect the public health.

Response: For the reasons stated in section II.B to the preamble to the final rule, the factual premise to this comment is mistaken; there is a basis for revising the $PM_{2.5}$ 24-hour standard. Section II.F.1 to the preamble explains why the level of the 1997 standard should be revised to 35 $\mu g/m^3$ in order to provide protection requisite to protect the public health with an adequate margin of safety.

(15) *Comment:* In exercising his judgment to revise the existing NAAQS, the Administrator must provide a reasonable analysis for the change. Specifically, EPA must explain why its earlier judgment regarding what is requisite to protect public health or welfare no longer governs. To reverse its position in the face of precedent that is not persuasively distinguished is arbitrary and capricious. State Farm, 463 U.S. at 42 (presumption "against changes in current policy risks that are not justified by the rulemaking record"). Given that EPA's estimate of health risks has declined and our understanding of the uncertainty surrounding the results of the health studies has increased, EPA cannot persuasively say why it must depart from its 1997 decision that the current standard is requisite to protect public health.

Response: See first response to UARG legal issues comments, explaining why the 1997 PM NAAQS decision did not establish any "settled rule" embodying EPA's view on the "requisite" level of protection from PM, which must then be taken as a presumed level of protection in future PM NAAQS reviews , and why the State Farm case does not indicate that there is some special burden over and beyond the requirements of section 109 (b) and (d) necessary to justify a change in a NAAQS. EPA agrees, of course, that it must fully explain the basis for its decision in this NAAQS standard setting process (including explanations of how any changes in the science since the last review were evaluated in making a decision). See CAA section 307 (d) (3), (d) (6) (A) and (B). EPA has done so

in this proceeding. However the need for an explanation of the basis for the final decision in this NAAQS review is not burdened by the type of "presumption" to which the commenter appears to refer.

See sections II.B and II.F of the preamble to the final rule explaining why the commenters' predicate regarding increased uncertainties since 1997 is incorrect. Moreover, an evident reason why it is appropriate to revise the level of the 24-hour standard in order to provide requisite protection to public health is that "effects associations are observed in areas or at times when the levels of the old PM standards are met." ATA III, 283 F. 3d at 370 (upholding EPA's decision to revise the 1987 PM10 standards on this basis), 378 (upholding need to make existing ozone standard more stringent because, as here, "the record [is] replete with reference to studies demonstrating the inadequacies of the old … standard").

(16) *Comment:* In proposing to lower the daily standard to 35 $\mu g/m^3$, EPA has also failed to fully account for the many different model results included in its CD. By selecting only a handful of studies on which to base its decision, and by ignoring other studies which have higher scientific merit due to greater statistical controls for potential confounders [referring especially to weather, co-pollutants, or GAM-bias, Comment p. 27], EPA's proposed decision is not reasonably supported by the administrative record, and thus is arbitrary and capricious. Specifically, by ignoring studies showing an increase in uncertainty since the 1997 review and a decrease in the magnitude of risk estimates, EPA has failed to consider an important aspect of the case (citing State Farm, 463 U.S. at 43).

Response: EPA has not ignored an important aspect of the case. Sections II.B and other comment responses fully address the issues raised by the commenter regarding the time-series PM2.5 epidemiological studies in the record. Moreover, EPA's interpretation of these studies was subject to peer-review by CASAC, which supported EPA's interpretation as applied to the need to make the 24-hour standard more stringent, and the appropriateness of establishing a level in the range of 30-35 ug/m3.[12] ATA III, 283 F. 3d at 378, 379-80 (consistency with recommendations of CASAC and individual CASAC members provided support for EPA's determinations).

The following comments addressing legal issues were submitted by various commenters.

(17) *Comment:* Some commenters very generally asserted that EPA has not conducted a complete and thorough review of the current body of scientific literature regarding fine particles (e.g., Southern Company).

Response: The EPA strongly disagrees with this comment. The final decision reflects a decision based on air quality criteria reflecting ""the latest scientific knowledge" within the meaning of section 108 (a) (2) of the Act. The CASAC reviewed this enormous body

[12] CASAC also maintained that three of the time-series studies supported a reduction in the level of the annual PM2.5 standard (Henderson 2006, pp. 3-4), a point with which the Administrator does not agree. See section II.F.2 of preamble to final rule.

of material and found it a sufficient basis for agency action with respect to review of the standards for fine particles.

(18) *Comment*: Many commenters argued that EPA must heed the advice of CASAC in changing the PM standards (e.g., Jeffords). Some commenters further asserted that the Administrator has substituted his own opinion for the judgment of the scientific experts on CASAC, leading to a decision that is without merit as a matter of either science or law (e.g., ALA).

Response: EPA agrees that the Agency needs to give careful consideration to CASAC's advice and recommendations, and has done so here. EPA is also clearly required to explain the reasons for any significant differences in approach. CAA section 307 (d) (3). EPA has done so here. See, e.g. 71 FR at 2651-52. However under sections 108 and 109 the Administrator is required to make decisions in reviewing the NAAQS using his own "judgment" in determining what standard is "requisite" in light of all of the evidence, and is not required to accept or follow CASAC's recommendations on what revisions are appropriate. The merits of the Administrator's decision is not determined solely based on whether he did or did not agree with CASAC, but based on a review of the record as a whole, including any explanation the Administrator provides for accepting or rejecting a recommendation from CASAC. EPA has provided such explanations here, both where the Administrator adopted CASAC's advice and where in his judgment it was appropriate to not adopt it.

B. Administrative/Procedural Issues

A limited of comments addressed administrative and procedural issues related to the review of the PM NAAQS. Comments are addressed generally in section VIII of the preamble to the final rule and more specifically below,

(1) *Comment:* In the context of the standards for $PM_{2.5}$, the commenter maintains that EPA must specifically evaluate and discuss the implications of its proposal on low income and minority communities, and must establish standards that specifically address the impacts that these communities face. Failure to do so violates the Agency's obligations under applicable law, including the Clean Air Act (which requires that EPA establish standards that protect everyone), title VI of the Civil Rights Act of 1964, Executive Order 12898, and an appropriation restriction added as a rider to EPA's FY 2006 appropriation requiring that EPA not expend appropriated funds in a manner that delays or contravenes that Executive Order.

Response: The NAAQS must afford requisite protection with an adequate margin of safety to vulnerable subpopulations, as well as to the general populace. See, e.g. S. Rep. No. 91-1196, 91st Cong., 2d Sess. 10 (1970). The EPA considered the effects of PM exposure on minorities and low-income populations. See, e.g., 71 FR at 2647 and fn.39. Minority and low-income populations are often such vulnerable subpopulations. The $PM_{2.5}$ NAAQS established in today's final rule are nationally uniform standards which in

the Administrator's judgment are requisite to protect public health with an adequate margin of safety. As discussed in section II of the preamble to the final rule and in other comment responses, the Administrator expressly considered the available information regarding health effects among vulnerable and susceptible populations, such as those with preexisting conditions, in making these determinations.

In addition, in accordance with Executive Order 12898, the Agency has considered whether the standards for $PM_{2.5}$ (as well as the PM_{10} standard) may have disproportionately high and adverse effects on minority or low-income populations. EPA repeats that this rule establishes uniform, national ambient air quality standards for particulate matter, and is not expected to have disproportionate negative impacts on minority or low income populations. With regard to the concern that the proposed $PM_{2.5}$ standards would permit the continuation of disproportionate adverse health effects on minority and low-income populations because those populations are concentrated in urban areas where exposures are higher and are generally more susceptible (given lack of access to health care and prevalence of chronic conditions such as asthma), the EPA believes that the implications of the newly strengthened suite of $PM_{2.5}$ standards will reduce health risks precisely in the areas subject to the highest fine particle concentrations. (This also is true of the PM_{10} standard.) The EPA thus believes that its actions fully comply with the Executive Order and applicable law. Title VI of the Civil Right Act of 1964, however, does not apply to the federal government. Rather, it applies to the programs and activities of recipients of federal financial assistance.

(2) *Comment*: The EPA's failure to grant a requested extension of the comment period denies parties the right to review and comment on the proposed rule, in violation of section 553 of the APA, section 307(d)(3) of the CAA, and the requirements of procedural and substantive due process provided by the Fifth Amendment to the U.S. Constitution (National Mining Association).

Response: The EPA has afforded all participants in the rulemaking opportunities for participation over and above those required by law. These include opportunities for comment on both the draft Criteria Document and Staff Paper throughout the CASAC review process (opportunities vigorously pursued by the commenter), opportunities to comment on all aspects of the rulemaking (of which the commenter also took advantage, submitting hundreds of pages of comments. The commenter also had a number of direct meetings with senior agency officials (documented in the administrative record) to express its views and concerns. Although the commenter specifically complains of lack of opportunity to review and comment on post-Criteria Document science, when EPA issued a Provisional Assessment addressing this "new" science, the commenter chose not to submit any comment (EPA, 2006, July 2006). The EPA also notes that scores of commenters submitted comments addressing the "new science" in their comments to the proposed rule. In any case, EPA is basing the final decisions in this review on the studies and related information included in the PM air quality criteria that have undergone CASAC and public review. The EPA will consider the newly published studies for purposes of decision making in the next periodic review of the PM NAAQS, which will provide the opportunity to fully assess them through a more rigorous review process

involving EPA, CASAC, and the public. See section I. C of the preamble to the final rule. Consequently, the commenter has not suffered any procedural prejudice, and its comment therefore lacks merit.

(3) *Comment:* Some commenters pointed out that the proposed qualified $PM_{10-2.5}$ indicator and the proposed monitor site-suitability requirements, especially the requirement that monitors used for comparison with the NAAQS be located within urbanized areas with a minimum population of 100,000, would virtually exclude Tribes from applying the $PM_{10-2.5}$ standards because very few tribal sites would meet this criterion. These commenters argued the proposed coarse particle standard would violate E.O.13175 by failing to meet EPA's general trust responsibility to ensure tribal air quality is safe. These commenters stated that by removing federal protection from tribal lands, EPA would violate its trust responsibilities to the Tribes. (Cite: *U.S. v. Mason* (1973), *Seminole Nation v. U.S.* (1942), *U.S. v. Mitchell* (1983), *Nance v. EPA* (1981), *Inter Tribal Council of Arizona, Inc v. Babbitt* (1990), *Morongo Band of Mission Indians v. Federal Aviation Administration* (1998), *Pyramid Lake Paiute Tribe v. Morton* (1972).) Furthermore, these commenters stated that the proposed exclusion of "agricultural sources, mining sources, and other similar sources of crustal material" from the proposed $PM_{10-2.5}$ indicator was illegal and violated tribal sovereignty.

Response: The EPA notes that its final decision, for the reasons noted in section III of the preamble to the final rule, to retain the current 24-hour PM_{10} standard without any qualifications to the indicator, any changes to the monitor siting requirements, or any source exclusions, effectively resolves the concerns raised by these commenters.

(4) *Comment:* Some commenters stated that EPA had violated E.O. 13175 and its trust responsibility to Tribes by failing to engage in meaningful consultation with tribal leaders regarding the proposed qualified $PM_{10-2.5}$ indicator and other aspects of the proposed rule. According to these commenters, EPA's statement in the proposal that consultation was not required under E.O. 13175 was incorrect. These commenters stated that EPA has a mandatory duty to consult with Tribes.

Response: The commenters are mistaken in suggesting that EPA did not engage in meaningful and timely two-way communication with Tribes and their leaders on this rule. EPA conducted extensive outreach to ensure tribal input. EPA contacted tribal environmental professionals throughout the rule development process. EPA staff participated in the regularly scheduled Tribal Air call sponsored by the National Tribal Air Association during the summer and fall of 2005 as the proposal was under development, as well as the call in the spring of 2006 during the public comment period on the proposed rule. The EPA sent individual letters to all federally recognized Tribes within the lower 48 states and Alaska to obtain the views of tribal leaders. EPA staff also participated in tribal public meetings, such as the National Tribal Forum meeting in April 2006, where Tribes discussed their concerns regarding the proposed rule. Furthermore, the Administrator discussed the proposed PM NAAQS with members of the National Tribal Caucus and with leaders of individual Tribes during the spring and summer of 2006, in advance of his final decision.

The EPA notes that, for reasons explained more fully in the following response, it was not required to consult with Tribes under E.O. 13175. Nevertheless, as just explained, the Agency made a significant effort to engage in outreach to Tribes, to solicit tribal comment on the proposed rule, and to take tribal concerns into consideration in development of the final rule. EPA also notes that, the rule was revised in ways that address the commenters' concerns.

(5) *Comment:* Some commenters argued that EPA interpreted the applicability of Executive Order 13175 too narrowly. According to these commenters, EPA interprets "substantial direct effects" in an arbitrarily narrow manner and is incorrect in concluding that the E.O. does not apply because Tribes "are not obligated to adopt or implement any NAAQS." .

Response: The EPA has determined that this rule does not have tribal implications. The rule concerns the establishment of PM NAAQS. The Tribal Authority Rule gives Tribes the opportunity to develop and implement CAA programs such as the PM NAAQS, but it leaves to the discretion of the Tribe whether to develop these programs and which programs, or appropriate elements of a program, they will adopt. Thus, the rule does not have substantial direct effects on Tribes, which means it does not have tribal implications and is not subject to EO 13175. Nevertheless, the Agency has, as explained above, worked to obtain timely and meaningful input from Indian Tribes and their leaders.

(6) *Comment:* Some commenters stated that EPA should complete a Statement of Energy Effects on the impacts of the proposed $PM_{10-2.5}$ rule under Executive Order 13211. The commenters argued that EPA is required to do this before implementing a rule which is more stringent than the current PM_{10} NAAQS.

Response: The EPA notes that its final decision to retain the current 24-hour PM_{10} standard effectively resolves the concerns raised by these commenters. Also, as noted in preamble to final rule, the rule does not (and cannot) prescribe specific pollution control strategies by which the PM NAAQS will be met. Such strategies will be developed by States on a case-by-case basis, and EPA cannot predict whether the control options selected by States will include regulations on energy suppliers, distributors, or users.

(7) *Comment:* Some commenters stated that EPA had violated E.O. 12898 due by failing to engage in environmental justice analysis and outreach. These commenters argued that EPA must specifically evaluate and discuss the implications of its proposal on low-income and minority communities and must establish standards that specifically address the impacts that these communities face in order to fulfill the requirements of the Executive Order. Several commenters criticized the lack of Spanish translations of written materials and what they perceived to be the lack of adequate public comment opportunities for non-English-speaking populations.

Response: In accordance with E.O. 12898, EPA has considered whether the decisions promulgated in the final rule may have disproportionate negative impacts on minority or low-income populations. This rule establishes uniform, national ambient air quality

standards for particulate matter, and is not expected to have disproportionate negative impacts on minority or low income populations. Furthermore, EPA engaged in extensive public outreach in an attempt to communicate the proposed decisions broadly, and also advertised opportunities for public comment on the proposed decisions. The EPA notes the commenters' concerns regarding the need to make Spanish language materials widely available and the need to provide an opportunity for non-English speakers to participate in the public hearings, and will take these concerns into consideration in future rulemaking processes.

(8) *Comment:* Some commenters argued that the proposed $PM_{2.5}$ standard violated Executive Order 12898 because the proposed standard would cause disproportionate and adverse health effects on minority and low-income populations. These commenters stated that the populations are disproportionately affected because of increased susceptibility due to factors such as health care inequalities and because of increased exposure due to their urbanized living environments.

Response: The EPA believes that the implications of the newly strengthened suite of $PM_{2.5}$ standards will reduce health risks precisely in the areas subject to the highest fine particle concentrations. Furthermore, the $PM_{2.5}$ NAAQS established in today's final rule are nationally uniform standards which in the Administrator's judgment protect public health with an adequate margin of safety. In making this determination, the Administrator expressly considered the available information regarding health effects among vulnerable and susceptible populations, such as those with preexisting conditions.

C. Misplaced Comments

Some comments received on the proposed PM NAAQS addressed issues that are not relevant for consideration in the review of the NAAQS. These include several comments that address implementation issues. In addition to comments related to implementation of the PM NAAQS that are generally addressed in section VII of the preamble to the final rule, these comments and other "misplaced" comments are discussed more fully below.

(1) *Comment:* Given that the current annual $PM_{2.5}$ NAAQS is sufficient to protect public health and welfare, EPA need not – indeed must not – promulgate a more stringent standard because doing so would not confer any appreciable air quality benefits. International acknowledges the Supreme Court's determination in Whitman that EPA may not consider costs when establishing NAAQS standards that are no lower or higher than necessary. However, once EPA has determined that particular quantified risks provide the requisite protection, the statute does not preclude EPA from contemplating costs for purposes of assessing whether it may ratchet down an already adequate standard and avoid running afoul of the proscription against setting levels that protect "more than necessary". Section 109 (b) (1) precludes imposition of costly, inefficient regulation, citing Whitman, 531 U.S. at 473 (International Truck & Engine Corporation).

Response: This comment is without merit on a number of grounds. The fundamental premise of the comment is that the 1997 PM NAAQS decision on the level of the annual standard rested on a quantified estimate of risk that was determined to be "requisite," and that deviating from that now would run afoul of the 'more stringent than necessary' prong of "requisite". This is wrong. As explained in the preamble, in 1997 EPA did not base the level of the annual standard on any such quantification of "requisite" risk, nor was it required to do so. As the D.C. Circuit pointed out repeatedly in its post-Whitman ATA III decision, EPA is under no obligation "to quantify its decisionmaking, … to identify perfectly safe levels of pollutants, to rely on specific risk estimates, or to specify threshold amounts of scientific information." 283 F. 3d at 369; see also id. at 373-74, 378, 379. Indeed, "the Act requires EPA to promulgate protective primary NAAQS even where, as here, the pollutant's risks cannot be quantified or precisely identified as to nature or degree". 283 F. 3d at 369. Earlier cases likewise make clear that when there is uncertainty about the health effects of concentrations of a particular pollutant within a particular range, EPA may use its discretion to make the policy judgment to set the standards at one point within the relevant range rather than another. NRDC v. EPA, 902 F. 2d at 969; API v. Costle, 665 F. 2d at 1185; Lead Industries, 647 F. 2d at 1161. See also section II.B of the preamble to the final rule, demonstrating why the premise that the levels of the 1997 standards rest on quantified estimates of risk is incorrect.

The commenter is also wrong that EPA may consider costs as part of the NAAQS standard setting process. Whitman and 20 some years of D.C. Circuit precedent have rejected this argument. Nor is there any language in Whitman supporting the commenter's assertion that "section 109 (b) (1) precludes the imposition of costly, inefficient regulation." Thus, this argument lacks any merit. Pages 25-29 and 38-39 of the comment, setting forth estimated costs of potential annual and daily NAAQS, and attainment implications of different potential standards, are without legal relevance, and EPA may not and has not considered these comments in its consideration of whether it is appropriate to revise the existing standards.

(2) *Comment*: Some commenters, in arguing for more protective $PM_{2.5}$ standards, assert that a suite of $PM_{2.5}$ standards set at levels below those proposed would substantially increase the number of people in the U.S. who would be afforded protection from exposure to fine PM (e.g., NESCAUM).

Response: The number of people who reside in nonattainment areas is a consequence of the decisions made in setting a NAAQS, but is not a basis itself for such decision making. Questions of implementation costs or attainability consequences of a NAAQS are legally irrelevant in determining which standards are requisite to protect public health with an adequate margin of safety. API v. Costle, 665 F. 2d at 1185-86. The EPA therefore did not consider this comment in its decision making process.

(3) *Comment*: One commenter asserted that any tightening of the PM standards would result in the increased possibility of federal highway funding being placed at risk, which could delay critically needed improvements to our nation's infrastructure (American Road and Transportation Builders Association).

Response: Questions like this of implementation or attainability consequences of a NAAQS are legally irrelevant in determining which standards are requisite to protect public health with an adequate margin of safety. API v. Costle, 665 F. 2d at 1185-86. The EPA therefore did not consider this comment in its decision making process.

(4) *Comment*: One commenter argued that lowering the level the of the 24-hour $PM_{2.5}$ standard would negatively impact business development in urban areas encouraging suburban sprawl, discouraging brownfield redevelopment efforts, and increasing the loss of existing farmland to development (Toledo Metropolitan Area Council of Governments).

Response: Questions like this of implementation or attainability consequences of a NAAQS are legally irrelevant in determining which standards are requisite to protect public health with an adequate margin of safety. API v. Costle, 665 F. 2d at 1185-86. The EPA therefore did not consider this comment in its decision making process.

(5) *Comment:* One commenter expressed concerns about implementation of the proposed PM NAAQS specifically related to wildfires and prescribed fires. The commenter argued that any revised standards should be implemented in such a way that allows fuel management techniques to be employed in the most environmentally appropriate manner consistent with land management needs" (comment docket number OAR-2001-0017-1609). The commenter strongly encouraged EPA to finalize its Exceptional Events Rule prior to promulgating the PM NAAQS rule.

Response: Issues like this related to implementation of the PM NAAQS are legally irrelevant in determining which standards are requisite to protect public health with an adequate margin of safety. API v. Costle, 665 F. 2d at 1185-86. The EPA therefore did not consider this comment in its decision making process.

The EPA is currently reviewing public comments submitted on the proposed Exceptional Events Rule which includes criteria and procedures for use in determining if air quality monitoring data have been influenced by exceptional events such as unplanned fires or destructive storms. The rule proposed procedures and criteria that would be used to identify, evaluate, interpret and use monitored air quality data for comparison to the National Ambient Air Quality Standards in situations where state, local, and tribal air quality agencies request special treatment because the data have been affected by an exceptional event. The Safe Accountable Flexible Efficient-Transportation Equity Act (SAFE-TEA-LU) requires EPA to finalize this rule by March 1, 2007.

(6) *Comment*: One commenter argued that EPA's proposed standards will make enforcement of California's air quality laws more difficult, leading to a reduction in air quality in California (Feinstein).

Response: Questions like this of implementation or attainability consequences of a NAAQS are legally irrelevant in determining which standards are requisite to protect

public health with an adequate margin of safety. API v. Costle, 665 F. 2d at 1185-86. The EPA therefore did not consider this comment in its decision making process.

(7) *Comment:* One commenter argued that EPA should take more time to assess the impacts of its current control programs and vehicle fleet turnover, which are likely to produce impressive results, before deciding to make any revisions to the current PM standards (e.g., Mercatus Center). Untimely revision of the $PM_{2.5}$ standard could undermine existing control programs such as CAIR that will reduce emissions from power plants in the eastern U.S. (Minnesota Power).

Response: The schedule for conducting the periodic review of the NAAQS is determined by law, and is not discretionary. See section 109 (d) (1) of the Act and the consent decree in American Lung Ass'n v. Whitman (No. 1:03CV00778, D.D.C 2003). Moreover, emission reductions which may be achieved under regulatory programs are not relevant to whether it is appropriate to revise an existing NAAQS. That determination rests solely on whether, after considering revised air quality criteria, those standards are requisite to protect human health with an adequate margin of safety. Consequently, EPA has not considered these comments in making any of the determinations involved in this review.

(8) *Comment:* Some commenters criticized EPA's Interim Regulatory Impact Analysis (RIA), which was issued in January 2006. According to these commenters, the RIA was inadequate because it did not include a national assessment of costs and benefits. The commenters requested the EPA conduct additional analysis for the final RIA.

Response: Because the costs of implementation cannot be considered in setting or revising the NAAQS (see section I.B of the preamble to the final rule), the results of the RIA were not considered in EPA's decisions on the PM standards. For the same reason, comments on the RIA were not considered in the decisions. Comments on the Interim RIA were considered, as appropriate, in developing the RIA for the final rule.

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Appendix A

Provisional Assessment of Recent Studies on Health Effects of Particulate Matter Exposure

I. INTRODUCTION

In the preamble to the proposed rule, EPA recognized there were a number of new scientific studies on the health effects of PM that had been published recently and therefore were not included in the Criteria Document (71 FR 2625). The EPA committed to conduct a review and assessment of any significant "new" studies, including studies submitted during the public comment period. The purpose of this review was to ensure that the Administrator was fully aware of the new science before making a final decision on whether to revise the current PM NAAQS.

The EPA screened and surveyed the recent literature, including studies submitted during the public comment period, and conducted a provisional assessment that places the results of those studies of potentially greatest policy relevance in the context of the findings of the Criteria Document. The criteria used to identify the studies addressed in the provisional assessment focused on (a) epidemiologic studies that used $PM_{2.5}$ or $PM_{10-2.5}$ and were conducted in the U.S. or Canada, and (b) toxicology or epidemiologic studies that compared effects of PM from different sources, PM components, or size fractions. This provisional assessment, entitled *Provisional Assessment of Recent Studies on Health Effects of Particulate Matter Exposure*, is included as an attachment to the response-to-comments document. Given the limited time to review the individual studies, the provisional assessment did not include a critical review of individual studies or provide the integrated assessment that is included in a Criteria Document.

As discussed in Section I.C of the preamble to the final rule, EPA is basing its final decisions in this review on studies and related information that are included in the Criteria Document, which has undergone CASAC and public review. The EPA is planning to begin a new review of the PM NAAQS immediately following the conclusion of this review. The studies included in the provisional assessment, additional scientific studies submitted during the public comment period, public comments received on the provisional assessment, as well as more recent evidence will be evaluated during this next review.

II. RESPONSE TO PUBLIC COMMENTS ON PROVISIONAL ASSESSMENT

The EPA did not formally request public comments on the provisional assessment of "new" science. However, a small number of commenters submitted comments on this document to EPA. These comments are addressed below.

The following comments were submitted by EPRI.

(1) *Comment:* "The document is not comprehensive in its consideration of relevant studies, with some important papers still missing."

Response: The EPA characterized the selection of studies for consideration in the Provisional Assessment in the introduction to the report (EPA, 2006, p. 1):

> For this provisional assessment, emphasis has been placed on those studies most relevant to considerations for the PM NAAQS decision, such as the choice of indicator, level, or averaging time for the standards. This includes (a) epidemiologic studies that used $PM_{2.5}$ or $PM_{10-2.5}$ and were conducted in the U.S. or Canada, and (b) toxicology or epidemiologic studies that compared effects of PM from different sources, PM components, or size fractions. Over 200 studies have been included in this discussion with attached tables that provide further details the studies; in addition, bibliographies have been attached for studies on topics not discussed in detail in this report.

The EPA notes that studies available through May 2006 were included in the report, since peer review and final completion of the report took place in June 2006. The EPRI provided a list of studies that were omitted from the provisional assessment. The majority of these studies were published too late to be considered in the provisional assessment or did not meet the criteria for inclusion in the provisional assessment. The EPA will consider the studies submitted by EPRI and other commenters in the next review of the PM NAAQS.

> Arena et al. (2006): not included - PM_{10} study
> Atkinson et al. (2006): not included - published in September
> Banauch et al. (2006): not included - published in August
> Belanger et al. (2006): not included - study of indoor exposure to NO_2
> Brackbill et al. (2006): not included - World Trade Center study, no PM data
> Brook et al. (2005): not included - review article
> Cakmak et al. (2005): not included - can't find article
> Cakmak et al. (2006): not included - not a PM study
> Dales et al. (2004): not included - can't find journal
> Delfino et al. (2006): included in report at page B-26
> Diez-Roux et al. (2006): not included - published in September
> Dubnov et al. (2006): not included - exposure metric distance to coal-fired power plant
> Erbas et al. (2005): not included - statistical approach
> Filleul et al. (2006): not included - can't find journal
> Forastiere et al. (2005) : not included - PM_{10} study in Italy
> Fung et al. (2005): not included - statistical approach
> Gehring et al. (2006): not included - published in September 2006
> Gordian et al. (2005): not included - Can't find study; Gordian et al. (2006) included in report on p. B-10
> Groneberg-Kr et al. (2006): not included - can't find study
> Harrabi et al. (2006): not included - PM_{10} study in France

Hathout et al. (2006): not included - ** U.S. diabetes incidence study (sulfates)
Highwood et al. (2006): not included - review article
Hwang et al. (2005): not included - PM10 study in Taiwan
Koop et al. (2004): not included - ** Toronto study, statistical approach
Kulkami et al. (2006): not included - can't find study
Lagorio et al. (2006): not included - ** HRV study in Rome
Lem et al. (2006): not included - can't find study
Leone et al. (2006): not included - study of serum Zn, Cu and Mg
Lepeule et al. (2006): not included - Black smoke study in France
Lippmann et al. (2006): included in report on p. B-20
Madsen et al. (2006): not included - published in July
Modig et al. (2006): not included - published in July
Morabito et al. (2004): not included - study of effects of weather
Morabito et al. (2006): not included - study of effects of weather
Morishita et al. (2006): not included - published in July
Moshammer et al. (2006): not included - ** European lung function study
Murakami et al. (2006): not included - SPM study in Japan
Orozco-Levi (2006): not included - wood smoke, self-reported exposure, in Spain
Pattenden et al. (2006): not included - NO_2 study
Peacock et al (2003): not included - PM_{10} study in England
Rich et al. (2006): included in report on p. B-15
Rich et al. (2006): not included - published in September
Riojas-Rodr (2005): not included - can't find study
Roberts et al. (2006): not included - statistical approach
Roberts et al. (2006): not included - statistical approach
Rosenlund et al. (2006): not included - published in July
Samoli et al. (2006): not included - NO_2 study, published in June
Sarnat et al. (2006): not included - available online on June 6, 2006
Schildcrout et al. (2006): not included - published in September
Schlesinger et al. (2006): not included - review article
Schwartz et al. (2005): Included in report on page A-36
Seagrave et al. (2006): not included - published in September; available online in June
Shikowski et al. (2005): not included - ** European traffic study
Strand et al., (2005): not included - exposure estimation study
Sullivan et al. (2005): not included - published in June – HRV study in Seattle
Symons et al. (2006): not included - published in September
Townshend et al. (2005): not included - can't find study
Tsai et al. (2006): not included - published in July
Tsai et al. (2006): not included - PM_{10} study in Taiwan, published in March
Tuchsen et al. (2006): not included - published in July, study of stroke in professional drivers
Vineis et al. (2006): not included - PM_{10} study in Europe
Viswanathan et al. (2006): not included - wildfire study
Wade et al. (2006): not included - atmospheric study
Wong et al. (2006): not included - published in July, study in Asia

Zeka et al. (2006): not included - available online in July
Zhang et al. (2005): not included - can't find study

The EPA has quickly surveyed the studies listed above (that could be located) and concludes that the vast majority were not included in the Provisional Assessment because they were published in June 2006 or later and were thus not available to be included in the assessment, or because they did not meet the criteria established for inclusion (e.g., review articles, studies using PM indices other than $PM_{2.5}$ or $PM_{10-2.5}$); note that several studies in the list were, in fact, included in the document.

Several studies are marked with ** above as studies that could have been included in the assessment, but were not captured in our literature review. The EPA believes that the addition of these few studies would not have altered the conclusions of the provisional assessment. One study (Koop and Tole, 2004) was published in an economics journal not routinely included in health literature searches. This study uses a Bayesian model averaging approach to and between air pollutants (including $PM_{2.5}$ or $PM_{10-2.5}$) and mortality in Toronto. The authors concluded: "The main empirical finding of the paper is that standard deviations for air pollution-mortality impacts become very large when model uncertainty is incorporated into the analysis. Indeed they become so large as to question the plausibility of previously measured links between air pollution and mortality." The results had been discussed in a public CASAC meeting held July 20-21, 2004. The study by Hathout et al. (2006) reports an association between incidence of diabetes and long-term exposure to sulfates and ozone in the U.S., and the remaining studies could have been included in the appendix bibliography on traffic studies (EPA, 2006, p. B-7) or the list of international studies on the PM-morbidity relationship (EPA, 2006, p. A-15). Overall, EPA agrees with the commenters that "the literature is growing rapidly;" however, EPA believes that the provisional assessment was quite comprehensive in its coverage of the relevant literature to be considered for the purposes of the assessment.

(2) *Comment:* In the CAPs toxicology section, "all significant and nonsignificant results are presented. However, for some studies only positive results are presented (see EPA, 2006, pp. 29 to30). For completeness and consistency, either all positive and negative results should be mentioned, or only positive ones."

Response: The EPA consciously decided to include positive and negative results in the provisional assessment, such that representative findings were presented (EPA, 2006, pp. 29 to30). In the toxicology tables in Appendix A, all endpoints measured are listed with the results for each study that is cited in the text of the document.

(3) *Comment:* "The decision to include more detail on CAPs studies, but relegate all other PM toxicology studies to an appendix with little discussion is arbitrary and downplays the importance of the large amount of valuable toxicology research conducted since 2004 that is not CAPs-related."

Response: Emphasis in the provisional assessment was on CAPs studies because the study design permits exposures to atmospheric PM in real-time. Furthermore, there has been increasing interest in CAPs studies, as there were only nine CAPs studies in the Criteria Document and 27 additional CAPs studies have been published in the past two years. The EPA recognized that human toxicology and epidemiologic studies had repeated effects of several PM components or characteristics, such as traffic-related particles, metals, and ultrafine particles. The EPA acknowledges that numerous "new" studies built on the body of evidence by providing bibliographies of these publications in the Appendix. Because of the nature of the provisional assessment, EPA was not able to critically review and incorporate all of the recent PM literature on these subtopics in the main text of the document within the given time frame.

(4) *Comment:* "In general, review papers are not included…"

Response: Review articles were not included in the PM Provisional Assessment because no new science is presented in these types of manuscripts. As stated in the proposed rule for PM (and repeated in the Executive Summary of the PM Provisional Assessment), EPA committed to conducting a review and assessment of numerous *studies* relevant to the health effects of PM. The EPA is aware of the two referenced review papers from Grahame and Schlesinger (2005) and Schlesinger et al. (2006), but chose not to include them in the provisional assessment, as they did not provide original research.

(5) *Comment:* "In some cases, the descriptions of the study results have been summarized in ways that do not accurately, or thoroughly, reflect the results." "Statistical considerations in the draft document are poorly addressed."

Response: The commenter provided a discussion of recent reports from EPRI-funded research (Lipfert et al., 2006a,b; Klemm et al., 2004; Metzger et al., 2004; Sinclair and Tolsma, 2004). The EPA recognized that Lipfert et al. (2006 a, b) reported that the traffic density indicator was more strongly associated with mortality than fine particle mass in the discussion of these papers in the provisional assessment (EPA, 2006, p. 5). The associations reported with specific PM components for these studies, including Sinclair and Tolsma (2004), are included in Table A-15 (EPA, 2006, p. A-68). For the purposes of the provisional assessment, EPA was focusing on characterizing the study results and provisionally evaluating the results in the context of the findings of the Criteria Document. Given the limited time available, EPA did not attempt to critically review individual studies or provide the kind of full integration found in a typical Criteria Document. The EPA does not believe that it was necessary to include the more extensive interpretation of study results suggested by the commenters. With regard to statistical considerations and evaluation of potential co-pollutant confounding, EPA discussed those concepts extensively in the Criteria Document. The EPA did not feel it was necessary to reiterate such discussions in the context of the provisional assessment.

Comments on the provisional assessment were also submitted by Environmental Defense. These comments are addressed below.

(6) *Comment:* Some commenters argued that the provisional assessment supports their arguments to retain and strengthen standards for PM_{10}. These commenters specifically cited four multi-city PM_{10} studies that were included in the provisional assessment (Environmental Defense).

Response: As discussed in section I.C of the preamble to the final rule, EPA is basing its decisions in this review on studies and related information included in the Criteria Document and Staff Paper which have undergone CASAC and public review. The studies included in the provisional assessment, public comments received on the provisional assessment including additional studies that commenters submitted, as well as more recent scientific evidence will be assessed during the next review of the PM NAAQS. Overall, EPA determined that new study results did not materially change the broad scientific conclusions' response would work.

III. ATTACHMENT - *Provisional Assessment of Recent Studies on Health Effects of Particulate Matter Exposure* July 2006

EPA/600/R-06/063
July 2006

Provisional Assessment of Recent Studies on Health Effects of Particulate Matter Exposure

National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

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Principal Authors

Dr. Jee Young Kim—National Center for Environmental Assessment (B243-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Dennis Kotchmar—National Center for Environmental Assessment (B243-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Mary Ross—National Center for Environmental Assessment (B243-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Lori White—National Center for Environmental Assessment (B243-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Lindsay Wichers—National Center for Environmental Assessment (B243-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. William Wilson—National Center for Environmental Assessment (B243-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Contributors and Reviewers

Mr. John Bachmann—Office of Air Quality Planning and Standards (C404-04),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. James Brown—National Center for Environmental Assessment (B243-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Dan Costa—Office of Research and Development (E205-09),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Robert Devlin—National Health and Environmental Effects Research Laboratory
(mail code 58), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Janice Dye—National Health and Environmental Effects Research Laboratory
(B143-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Kevin Dreher—National Health and Environmental Effects Research Laboratory (B143-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Ian Gilmour—National Health and Environmental Effects Research Laboratory (B143-01),
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Contributors and Reviewers
(cont'd)

Dr. Barbara Glenn—National Center for Environmental Research (8723F), Ariel Rios Building, 1200 Pennsylvania Ave N.W., U.S. Environmental Protection Agency, Washington, DC 20460

Dr. Lester Grant—National Center for Environmental Assessment (B243-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Ms. Beth Hassett-Sipple—Office of Air Quality Planning and Standards (C539-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Bryan Hubbell—Office of Air Quality Planning and Standards (C539-02), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Mary Johnson—National Health and Environmental Effects Research Laboratory (mail code 58), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Srikanth Nadadur—National Center for Environmental Assessment (B243-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Lucas Neas—National Health and Environmental Effects Research Laboratory (mail code 58), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. Haluk Ozkaynak—National Exposure Research Laboratory (E205-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Mr. Harvey Richmond—Office of Air Quality Planning and Standards (C539-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. David Svendsgaard—National Center for Environmental Assessment (B243-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Dr. John Vandenberg—National Center for Environmental Assessment (B243-01), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Executive Summary

In the proposed rule on the National Ambient Air Quality Standards for particulate matter (PM), EPA committed to conduct a review and assessment of the numerous studies relevant to assessing the health effects of PM that were published too recently to be included in the 2004 PM Air Quality Criteria Document (AQCD). This report presents the findings of EPA's survey and provisional assessment of such studies. EPA has screened and surveyed the recent literature and developed a provisional assessment that places those studies of potentially greatest relevance in the context of the findings of the 2004 PM AQCD. The focus is on: (a) epidemiologic studies that used $PM_{2.5}$ or $PM_{10-2.5}$ and were conducted in the U.S. or Canada, and (b) toxicology or epidemiologic studies that compared effects of PM from different sources, PM components, or size fractions. Given the limited time available, the provisional assessment presented here does not attempt to critically review individual studies or to provide the kind of full integration found in a typical AQCD.

This survey and assessment finds that that the new studies expand the scientific information and provide important insights on the relationships between PM exposure and health effects of PM. Taken in context, however, the new information and findings do not materially change any of the broad scientific conclusions regarding the health effects of PM exposure made in the 2004 PM AQCD. In brief, this report finds the following:

- Recent epidemiologic studies, most of which are follow-ups or extensions of earlier work, continue to find that *long-term exposure to fine particles* is associated with both mortality and morbidity, as was stated in the 2004 PM AQCD. Notably, a follow-up to the Six Cities study shows that an overall reduction in $PM_{2.5}$ levels results in reduced long-term mortality risk. Both this study and the analysis of the ACS cohort data in Los Angeles suggest that previous studies may have underestimated the magnitude of mortality risks. Some studies provide more mixed results, including the suggestion that higher traffic density may be an important factor. In addition, the California Children's Health Study reported that measures of $PM_{2.5}$ exposure and PM components and gases were associated with reduction in lung function growth in children, increasing the evidence for increased susceptibility early in life, as was suggested in the 2004 PM AQCD. The results of recent epidemiologic and toxicology studies have also reported new evidence linking long-term exposure to fine particles with a measure of atherosclerosis development and, in a cohort of individuals with cystic fibrosis, respiratory exacerbations.

- Recent epidemiologic studies have also continued to report associations between *acute exposure to fine particles* and mortality and morbidity health endpoints. These include three multi-city analyses, the largest of which (in 204 counties) shows a significant association between acute fine PM exposures and hospitalization for cardiovascular and respiratory diseases, and suggestions of differential cardiovascular effects in eastern U.S. as opposed to western U.S. locations. The new studies support previous conclusions that short-term exposure to fine PM is associated with both mortality and morbidity, including a substantial number of studies reporting associations with cardiovascular and respiratory health outcomes such as changes in heart rhythm or increases in exhaled NO.

- New toxicology and epidemiologic studies have continued to link health outcomes with a range of *fine particle sources and components.* Several new epidemiologic analyses and toxicology studies have included source apportionment techniques, and the results indicated that fine PM from numerous sources, including traffic-related pollution, regional sulfate pollution, combustion sources, resuspended soil or road dust, are associated with various health outcomes. Toxicology studies continue to indicate that various components, including metals, sulfates, and elemental and organic carbon, are linked with health outcomes, albeit at generally high concentrations. Recent epidemiologic studies have also linked different fine PM components with a range of health outcomes; new studies indicate effects of the organic and elemental carbon fractions of fine PM that were generally not evaluated in earlier analyses.

- The recent epidemiologic studies greatly expand the more limited literature on health effects of *acute exposure to thoracic coarse particles ($PM_{10-2.5}$)*. The 2004 PM AQCD conclusion that $PM_{10-2.5}$ exposure was associated with respiratory morbidity is substantially strengthened with these new studies; several epidemiologic studies, in fact, report stronger evidence of associations with $PM_{10-2.5}$ than for $PM_{2.5}$. In two new case-crossover studies, associations with thoracic coarse particles are robust to the inclusion of gaseous copollutants. For mortality, many studies do not report statistically significant associations, though one new analysis reports a significant association with cardiovascular mortality in Vancouver, Canada.

- Evidence of associations between *long-term exposure to thoracic coarse particles* and either mortality or morbidity remains limited.

- New toxicology studies have demonstrated that exposure to *thoracic coarse particles*, or PM sources generally representative of this size fraction (e.g., road dust), can result in inflammation and other health responses. Clinical exposure of healthy and asthmatic humans to concentrated ambient air particles comprised mostly of $PM_{10-2.5}$ showed changes in heart rate and heart rate variability measures. The results are still too limited to draw conclusions about specific thoracic coarse particle components and health outcomes, but it appears that endotoxin and metals may play a role in the observed responses. Two studies comparing toxicity of dust from soils and road surfaces found variable toxic responses from both urban and rural locations.

- Significant associations between improvements in health and reductions in PM and other air pollutants have been reported in intervention studies or "found experiments." One new study reported reduced mortality risk with reduced $PM_{2.5}$ concentrations. In addition, several studies, largely outside the U.S., reported reduced respiratory morbidity with lowered air pollutant concentrations, providing further support for the epidemiological evidence that links PM exposure to adverse health effects.

Provisional Assessment of Recent Studies on Health Effects of Particulate Matter Exposure

1. INTRODUCTION AND METHODOLOGY

EPA is currently in the final stages of the review of the national ambient air quality standards (NAAQS) for particulate matter (PM). As described in more detail in the Federal Register Notice of EPA's proposed rule on the PM NAAQS (71 FR 2620), EPA has prepared the *Air Quality Criteria for Particulate Matter* (hereafter 2004 PM AQCD) that reviewed, summarized and integrated the results of studies on PM (EPA, 2004). As noted in the PM proposal[1], EPA is aware that numerous studies potentially relevant to assessing the health effects of ambient PM have been published recently that were not included in the 2004 PM AQCD. The proposal notice also indicates the Agency's intent to conduct a review and assessment of these new studies before a final decision is made on the PM NAAQS. This report presents the findings of EPA's survey and provisional assessment of potentially relevant recent studies on the health effects of PM exposure. As outlined below, EPA has 1) screened the recently available literature to identify potentially relevant studies, 2) surveyed those studies to summarize the key findings, and 3) developed a preliminary assessment that places those of potentially greatest relevance in the context of the findings of the 2004 AQCD. Given the limited time available, the provisional assessment presented here does not attempt to critically review individual studies or to provide the kind of full integration found in a typical AQCD.

The literature search and submissions from public commenters found that hundreds of studies have been published in the last few years on the health effects of particulate matter. In an initial screen of the literature, more than 700 studies were identified as being potentially relevant to this review. In surveying these studies, EPA emphasized studies more likely to be relevant to considerations for the PM NAAQS decision. The specific criteria focused on (a) epidemiologic studies that used $PM_{2.5}$ or $PM_{10-2.5}$ and were conducted in the U.S. or Canada, and (b) toxicology or epidemiologic studies that compared effects of PM from different sources, PM components, or size fractions. These criteria resulted in a list of over 200 studies that are summarized in tables in this report that provide descriptive and quantitative information. The most significant studies are discussed in the assessment, and where feasible, quantitative results are compared to those from the 2004 PM AQCD. Bibliographies have been attached for studies identified as being potentially relevant through the survey effort but not discussed in detail in this report.

[1] As stated in the PM NAAQS proposal notice: "The EPA is aware that a number of new scientific studies on the health effects of PM have been published since the 2002 cutoff date for inclusion in the Criteria Document. As in the last PM NAAQS review, EPA intends to conduct a review and assessment of any significant new studies published since the close of the Criteria Document, including studies submitted during the public comment period in order to ensure that, before making a final decision, the Administrator is fully aware of the new science that has developed since 2002. In this assessment, EPA will examine these new studies in light of the literature evaluated in the Criteria Document. This assessment and a summary of the key conclusions will be placed in the rulemaking docket." (71 FR 2625)

The overview in the main body of this report is organized into three main sections: (1) epidemiologic studies on effects associated with long-term exposure to PM, focusing on U.S. and Canadian studies with measurements of $PM_{2.5}$ or $PM_{10-2.5}$; (2) results from time-series epidemiologic studies, again focusing on U.S. and Canadian studies with measurements of $PM_{2.5}$ or $PM_{10-2.5}$; and (3) results of recent toxicology and epidemiologic studies that have evaluated health effects with exposure to PM from different sources. This last section includes results of studies that assessed the effects of a range of sources or components in the same study. Most studies have focused on components or sources of fine particles, but information related to sources of thoracic coarse particles was also included to the extent available.

2. OVERVIEW OF RECENT HEALTH STUDY RESULTS

2.1 Epidemiologic Studies of Long-Term Exposure

2.1.1 Mortality

An extensive discussion of prospective cohort studies was included in Section 8.2.3 of the 2004 PM AQCD. These discussions emphasized the results of four U.S. prospective cohort studies. The greatest weight was placed on the findings of the American Cancer Society (ACS) and the Harvard Six Cities studies which had undergone extensive, independent reanalysis and were based on cohorts that were broadly representative of the U.S. population. These studies provided strong evidence that long-term exposure to fine particles and sulfates was associated with mortality. In addition, results from the Seventh-Day Adventist (AHSMOG) cohort provided some suggestive but less conclusive evidence for associations, and results from the Veterans Cohort provided inconsistent evidence for associations between long-term exposures to $PM_{2.5}$ and mortality. Overall, the 2004 PM AQCD concluded that there was strong epidemiologic evidence for associations between long-term exposures to $PM_{2.5}$ and mortality (p. 9-46).

In the 2004 PM AQCD, no association was observed between mortality and long-term exposure to $PM_{10-2.5}$ in the ACS study (Pope et al., 2002), and a positive but nonsignificant association was reported in males in the AHSMOG cohort (McDonnell et al., 2000). Thus, the 2004 PM AQCD concluded that there was insufficient evidence for associations between long-term exposure to thoracic coarse particles and mortality.

Fine Particles:

Recent studies include results of new analyses for the ACS and Harvard Six Cities studies; as highlighted below, the new findings strengthen the evidence linking long-term exposure to $PM_{2.5}$ and mortality. Recent reports have also included analyses from the AHSMOG and Veterans study cohorts, as well as a Cystic Fibrosis cohort and a subset of the ACS for California. These results, along with those from studies available in the 2004 PM AQCD, are shown in Figure 1. The risk estimates and PM concentrations reported in the studies are summarized in Table 1, along with results available in the 2004 PM AQCD; further details on the studies are presented in Appendix A, Table A1.

Table 1. Mortality and Morbidity Effect Estimates and PM Concentrations from U.S. and Canadian Studies with Long-Term Exposures to $PM_{2.5}$ and $PM_{10-2.5}$. Adapted from Appendix 3B of the 2005 OAQPS Staff Paper. Shaded rows present results from recent studies that were not available in the 2004 PM Criteria Document.

Study	Indicator	Relative Risk (95% CI)	Study Concentrations ($\mu g/m^3$) *
Increased Total Mortality in Adults			
Six Cities[A]	$PM_{2.5}$	1.13 (1.04, 1.23)	NR (11, 30)
	SO_4^{2-} (15 $\mu g/m^3$)	1.54 (1.15, 2.07)	NR (5, 13)
Six Cities[B]	$PM_{15-2.5}$	1.43 (0.83, 2.48)	
Six Cities Reanalysis[D]	$PM_{2.5}$	1.14 (1.05, 1.23)	NR (11, 30)
Six Cities Follow-up[AA]	$PM_{2.5}$	1.16 (1.07, 1.26)	NR (10.2, 22)
ACS Study[C]	$PM_{2.5}$	1.07 (1.04, 1.10)	18[1] (9, 34)
	SO_4^{2-} (15 $\mu g/m^3$)	1.11 (1.06, 1.16)	11[1] (4, 24)
ACS Study Reanalysis[D]	$PM_{2.5}$	1.07 (1.04, 1.10)	20 (10, 38)
	$PM_{15-2.5}$	1.00 (0.99, 1.02)	7.1 (9, 42)
ACS Study Extended Analyses[E]	$PM_{2.5}$ (1979-83) $PM_{2.5}$ (1999-00) $PM_{2.5}$ (average)	1.04 (1.01, 1.08) 1.06 (1.02, 1.10) 1.06 (1.02, 1.11)	21 (9, 34) 14 (5, 20) 18 (7.5, 30)
ACS Los Angeles[BB]	$PM_{2.5}$	1.17 (1.05, 1.30)	NR (9, 27)
AHSMOG[H]	$PM_{2.5}$	1.09 (0.98, 1.21) (males)	32 (17, 45)
	$PM_{10-2.5}$	1.05 (0.92, 1.21) (males)	27 (4, 44)
Veterans Cohort[G]	$PM_{2.5}$ (1979-81)	0.90 (0.85, 0.95) (males)	24 (6, 42)
Veterans Cohort[CC]	$PM_{2.5}$ (1999-2001)	1.12 (1.04, 1.20) (males)	14.6 (SD 3.1)
Veterans Cohort[CC]	$PM_{10-2.5}$ (1989-96)	1.07 (1.01, 1.12) (males)	16.0 (SD 5.1)
California Cancer Prevention Study[DD]	$PM_{2.5}$ (1979-83)	1.04 (1.01, 1.07) (deaths 1973-1982) 1.00 (0.98, 1.02) (deaths 1983-2002)	23.4 (10.6-42.0)
U.S. Cystic Fibrosis[EE]	$PM_{2.5}$	1.32 (0.91, 1.93)	13.7 (11.8, 15.9)
Increased Cardiopulmonary Mortality in Adults			
Six Cities[A]	$PM_{2.5}$	1.18 (1.06, 1.32)	NR (11, 30)
Six Cities Reanalysis[D]	$PM_{2.5}$	1.19 (1.07, 1.33)	NR (11, 30)

Table 1. Mortality and Morbidity Effect Estimates and PM Concentrations from U.S. and Canadian Studies with Long-Term Exposures to $PM_{2.5}$ and $PM_{10-2.5}$. Adapted from Appendix 3B of the 2005 OAQPS Staff Paper. Shaded rows present results from recent studies that were not available in the 2004 PM Criteria Document.

Study	Indicator	Relative Risk (95% CI)	Study Concentrations ($\mu g/m^3$) *
Six Cities Follow-up[AA]	$PM_{2.5}$	1.28 (1.13-1.44) (Cardiovascular) 1.08 (0.79-1.49) (Respiratory)	NR (10.2, 22)
ACS Study[C]	$PM_{2.5}$	1.12 (1.07, 1.17)	18[1] (9, 34)
ACS Study Reanalysis[D]	$PM_{2.5}$	1.12 (1.07, 1.17)	20 (10, 38)
	$PM_{15-2.5}$	1.00 (0.98, 1.03)	7.1 (9, 42)
ACS Study Extended Analyses[E]	$PM_{2.5}$ (1979-83) $PM_{2.5}$ (1999-00) $PM_{2.5}$ (average)	1.06 (1.02, 1.10) 1.08 (1.02, 1.14) 1.09 (1.03, 1.16)	21 (9, 34) 14 (5, 20) 18 (7.5, 30)
ACS Cause-specific[FF]: All cardiovascular Ischemic heart disease Dysrhythmia, et al. Hypertensive Other atherosclerosis Cerebrovascular disease Diabetes Other cardiovascular All Respiratory COPD Pneumonia Other respiratory	$PM_{2.5}$ (average)	 1.12 (1.08, 1.15) 1.18 (1.14, 1.23) 1.13 (1.05, 1.21) 1.07 (0.90, 1.26) 1.04 (0.89, 1.21) 1.02 (0.95, 1.10) 0.99 (0.86, 1.14) 0.84 (0.71, 0.99) 0.92 (0.86, 0.98) 0.84 (0.77, 0.93) 1.07 (0.95, 1.20) 0.86 (0.73, 1.02)	17.1 (7.5, 30)
ACS Los Angeles:[BB] Ischemic heart disease Cardiopulmonary	$PM_{2.5}$	 1.39 (1.12, 1.73) 1.12 (0.97, 1.30)	NR (9, 27)
AHSMOG[H]	$PM_{2.5}$	1.23 (0.97, 1.55) (males)	32 (17, 45)
	$PM_{10-2.5}$	1.20 (0.87, 1.64) (males)	27 (4, 44)
AHSMOG[GG] Fatal coronary heart disease	$PM_{2.5}$	1.42 (1.06, 1.90) (females) 1.49 (1.17, 1.89) (postmenopausal) 0.90 (0.76, 1.05) (males)	29 (SD 9.8)
	$PM_{10-2.5}$	1.38 (0.97, 1.95) (females) 1.61 (1.12, 2.33) (postmenopausal) 0.92 (0.66, 1.29) (males)	25.4 (SD 8.5)
Increased Lung Cancer Mortality in Adults			
Six Cities[A]	$PM_{2.5}$	1.18 (0.89, 1.57)	NR (11, 30)

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Study	Indicator	Relative Risk (95% CI)	Study Concentrations ($\mu g/m^3$) *
Six Cities Reanalysis[D]	$PM_{2.5}$	1.21 (0.92, 1.60)	NR (11, 30)
Six Cities Follow-up[AA]	$PM_{2.5}$	1.27 (0.96, 1.69)	NR (10.2, 22)
ACS Study[C]	$PM_{2.5}$	1.01 (0.91, 1.12)	18[U] (9, 34)
ACS Study Reanalysis[D]	$PM_{2.5}$	1.01 (0.91, 1.11)	20 (10, 38)
	$PM_{15-2.5}$	0.99 (0.93, 1.05)	7.1 (9, 42)
ACS Study Extended Analyses[E]	$PM_{2.5}$ (1979-83) $PM_{2.5}$ (1999-00) $PM_{2.5}$ (average)	1.08 (1.01, 1.16) 1.13 (1.04, 1.22) 1.14 (1.05, 1.24)	21 (9, 34) 14 (5, 20) 18 (7.5, 30)
ACS Los Angeles[BB]	$PM_{2.5}$	1.44 (0.98, 2.11)	NR (9, 27)
AHSMOG[H]	$PM_{2.5}$	1.39 (0.79, 2.50) (males)	32 (17, 45)
	$M_{10-2.5}$	1.26 (0.62, 2.55) (males)	27 (4, 44)
Increased Bronchitis in Children			
Six Cities[I]	$PM_{2.5}$	1.3 (0.9, 2.0)	NR (12, 37)
24 Cities[J]	SO_4^{2-} (15 $\mu g/m^3$) $PM_{2.1}$	3.02 (1.28, 7.03) 1.31 (0.94, 1.84)	4.7 (0.7, 7.4) 14.5 (5.8, 20.7)
AHSMOG[K]	SO_4^{2-} (15 $\mu g/m^3$)	1.39 (0.99, 1.92)	—
12 Southern California communities[M] (children with asthma)	$PM_{2.5}$	1.3 (0.9, 1.7)	15.3 (6.7, 31.5)
12 Southern California communities[HH] (children with asthma)	$PM_{2.5}$ $PM_{10-2.5}$	1.34 (1.11, 1.63) 1.10 (0.82, 1.49) (between communities)	13.8 (5.5, 28.5) 17.0 (10.2, 35.0)
12 Southern California communities[HH] (children with asthma)	$PM_{2.5}$ $PM_{10-2.5}$	2.37 (1.13, 4.94) 1.21 (0.59, 2.54) (within community change)	13.8 (5.5, 28.5) 17.0 (10.2, 35.0)
Increased Cough in Children			
12 Southern California communities[M] (children with asthma)	$PM_{2.5}$	1.2 (0.8, 1.8)	15.3 (6.7, 31.5)
Increased Pulmonary Exacerbations in Cystic Fibrosis Patients			
U.S. Cystic Fibrosis[EE]	$PM_{2.5}$	1.21 (1.07, 1.33)	13.7 (11.8, 15.9)

Table 1. Mortality and Morbidity Effect Estimates and PM Concentrations from U.S. and Canadian Studies with Long-Term Exposures to $PM_{2.5}$ and $PM_{10-2.5}$. Adapted from Appendix 3B of the 2005 OAQPS Staff Paper. Shaded rows present results from recent studies that were not available in the 2004 PM Criteria Document.

Study	Indicator	Relative Risk (95% CI)	Study Concentrations ($\mu g/m^3$) *
Decreased Lung Function in Children			
24 City[J]	SO_4^{2-} (15 $\mu g/m^3$)	−6.56% (-9.64, -3.43) FVC	4.7 (0.7, 7.4)
	$PM_{2.1}$	−2.15% (-3.34, -0.95) FVC	14.5 (5.8, 20.7)
12 Southern California communities[Q] (4^{th} grade cohort)	$PM_{2.5}$	−0.18 (-0.36, 0.0) FVC % growth	NR (10, 35)[3]
		−0.4 (-0.75, -0.04) MMEF % growth	NR
	$PM_{10-2.5}$	−0.22 (-0.47, 0.02) FVC % growth	
		−0.54 (-1.0, -0.06) MMEF % growth	
12 Southern California communities[Q] (second 4^{th} grade cohort)	$PM_{2.5}$	−0.06 (-0.30, 0.18) FVC % growth	NR (5, 30)[4]
		−0.42 (-0.84, 0.0) MMEF % growth	
		−0.20 (-0.64, 0.25) PEFR % growth	
12 Southern California communities[II] (first 4^{th} grade cohort, 8-yr follow-up)	$PM_{2.5}$	-26.4 (-72.9, 20.1) FVC growth -35.0 (-67.1, -2.8) FEV_1 growth -74.1 (-151.5, 3.4) MMEF growth	NR (5, 28)
Lung Function Changes in Adults			
AHSMOG[T] (% predicted FEV_1, males)	SO_4^{2-} (1.6 $\mu g/m^3$)	−1.5% (-2.9, -0.1) FEV_1	7.3 (2.0, 10.1)

* Note: Effect estimates presented using standardized increments of 10 $\mu g/m^3$ $PM_{2.5}$ and $PM_{10-2.5}$. Concentrations are presented as mean (min, max), or mean (±SD); NS Changes = No significant changes (no quantitative results reported); NR = not reported.

[1] Median
[2] Results only for smoking category subgroups.
[3] Estimated from Figure 1, Gauderman et al. (2000)
[4] Estimated from figures available in online data supplement to Gauderman et al. (2002)

References:

[A] Dockery et al. (1993)
[B] EPA (1996a)
[C] Pope et al. (1995)
[D] Krewski et al. (2000)
[E] Pope et al. (2002)
[F] Abbey et al. (1999)
[G] Lipfert et al. (2000b)
[H] McDonnell et al. (2000)
[I] Dockery et al. (1989)
[J] Dockery et al. (1996)
[K] Abbey et al. (1995a,b,c)
[L] Peters et al. (1999a)
[M] McConnell et al. (1999)
[N] Berglund et al. (1999)
[O] Raizenne et al. (1996)
[P] Peters et al. (1999)
[Q] Gauderman et al. (2000)
[R] Gauderman et al. (2002)
[S] Avol et al. (2001)
[T] Abbey et al. (1998)

Recent studies:

[AA] Laden et al. (2006)
[BB] Jerrett et al. (2005)
[CC] Lipfert et al. (2006)
[DD] Enstrom (2005)
[EE] Goss et al. (2004)
[FF] Pope et al. (2004)
[GG] Chen et al. (2005)
[HH] McConnell et al. (2003)
[II] Gauderman et al. (2004)

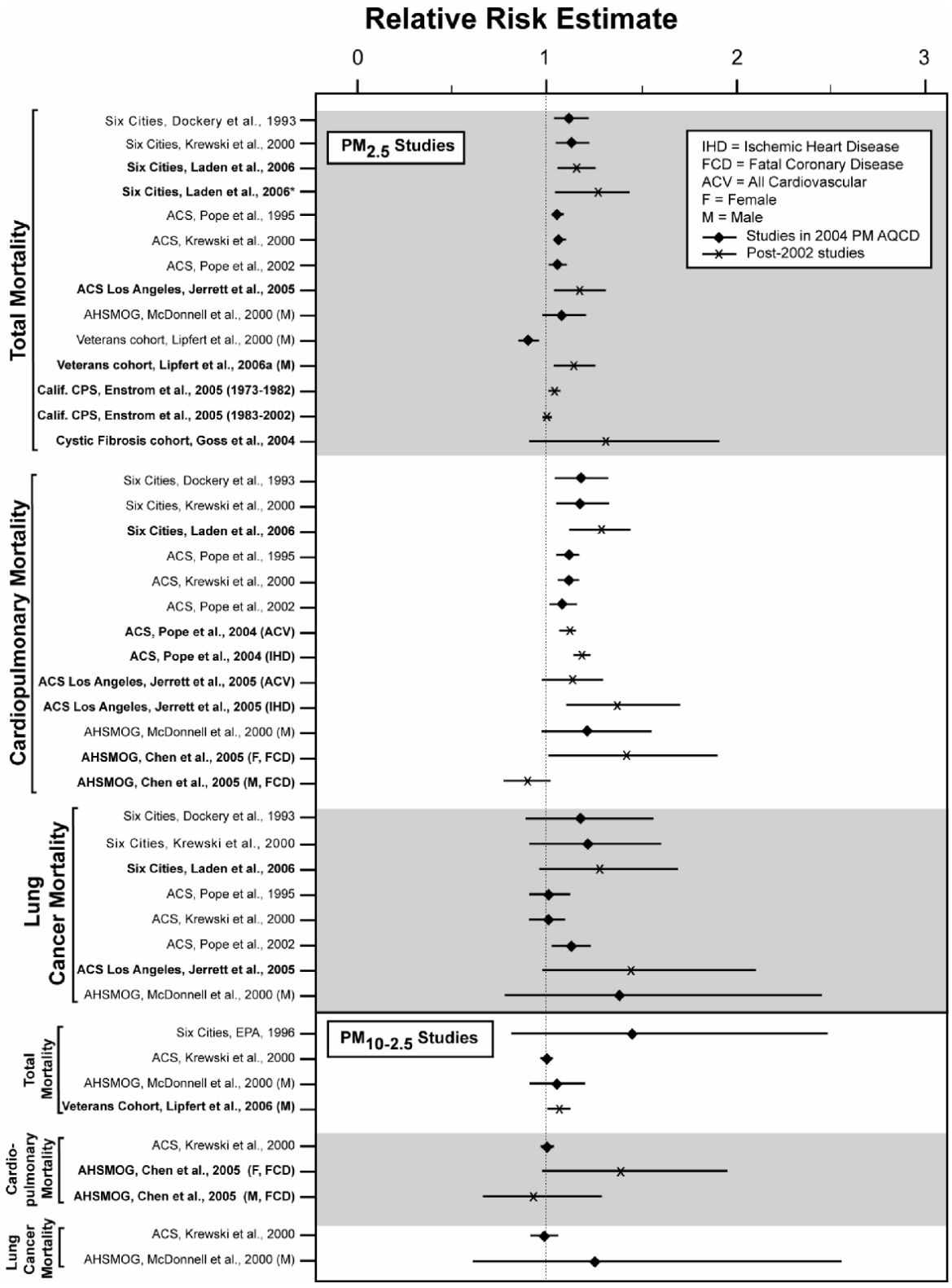

Figure 1. Relative risk estimates (and 95% confidence intervals) for associations between long-term exposure to PM (per 10 $PM_{10-2.5}$) and mortality. *Note: The second result presented for Laden et al. (2006) is for the intervention study results.

Harvard Six Cities: A new study has used updated air pollution and mortality data; an additional 1,368 deaths occurred during the follow-up period (1990-1998) and 1,364 deaths occurred in the original study period (1974-1989). Statistically significant associations are reported between long-term exposure to $PM_{2.5}$ and mortality for data for the two periods (RR = 1.16, 95% CI 1.07-1.26 per 10 $\mu g/m^3$ $PM_{2.5}$). Of note, however, a statistically significant *reduction* in mortality risk is reported with *reduced* long-term fine particle concentrations (RR = 0.73, 95% CI 0.57-0.95 per 10 $\mu g/m^3$ $PM_{2.5}$). This is equivalent to an RR of 1.27 for reduced mortality risk, suggesting a larger effect than in the cross-sectional analysis. This reduced mortality risk was observed for deaths due to cardiovascular and respiratory causes, but not for lung cancer deaths. Mean $PM_{2.5}$ concentrations from the follow-up period range from 10.2 to 22.0 $\mu g/m^3$ in the six cities. The means across the six cities were 18 $\mu g/m^3$ in the first period and 14.8 $\mu g/m^3$ in the follow-up period. The $PM_{2.5}$ concentrations for recent years were estimated from visibility data which introduces uncertainty in interpreting the results of this study (Laden et al., 2006). Coupled with the results of the original analysis (Dockery et al., 1993), this study strongly suggests that reduction in fine PM pollution has yielded positive health benefits.

ACS Extended Analyses: One new analysis further evaluated associations between long-term $PM_{2.5}$ and sulfate exposures in 50 U.S. cities and mortality, adding new information about deaths from specific cardiovascular and respiratory causes. Significant associations were reported with deaths from specific cardiovascular diseases, particularly ischemic heart disease, and a group of cardiac conditions including dysrhythmia, heart failure and cardiac arrest (RR for cardiovascular mortality = 1.12, 95% CI 1.08-1.15 per 10 $\mu g/m^3$ $PM_{2.5}$); no associations were reported with respiratory mortality. The mean $PM_{2.5}$ concentration (1979-1983 and 1999-2000) was 17.1 $\mu g/m^3$ (Pope et al., 2004).

ACS, Los Angeles: Much of the exposure gradient in the national-scale ACS studies was due to city-to-city differences in regional air pollution. A new analysis using ACS data focused on neighborhood-to-neighborhood differences in urban air pollutants, on data from 23 $PM_{2.5}$ monitoring stations in the Los Angeles area and using interpolation methods to assign exposure levels to individuals (Jerrett et al., 2005). This resulted in both improved exposure assessment and an increased focus on local sources of fine particle pollution. Significant associations between $PM_{2.5}$ and mortality from all causes and cardiopulmonary diseases were reported with the magnitude of the relative risks being greater than those reported in previous assessments (after adjustment for potential confounders including traffic, RR for cardiovascular diseases = 1.17, 95% CI 1.05-1.31, per 10 $\mu g/m^3$ $PM_{2.5}$; RR for ischemic heart disease = 1.38, 95% CI 1.11-1.72 per 10 $\mu g/m^3$ $PM_{2.5}$). The authors suggest that reducing exposure error can result in stronger associations between $PM_{2.5}$ and mortality than generally observed in broader studies having less exposure detail.

California cancer prevention study: In a cohort of elderly people in 11 California counties (mean age 73 years in 1983), an association was reported for long-term $PM_{2.5}$ exposure with all-cause deaths in 1973-1982 (RR = 1.04, 95% CI 1.01-1.07 per 10 $\mu g/m^3$ $PM_{2.5}$). No significant associations were reported with deaths in later time periods

(1983-2002) (RR = 1.00, 95% CI 0.98-1.02 per 10 μg/m^3 $PM_{2.5}$) when $PM_{2.5}$ levels had decreased in the most polluted counties. The $PM_{2.5}$ data are from the EPA's Inhalation Particle Network, and represent a subset of data used in the 50-city ACS study (Pope et al., 1995). The use of average values for California counties as exposure surrogates likely leads to significant exposure error as many California counties are large and quite topographically variable. The mean $PM_{2.5}$ concentration (1979-1983) was 23.4 μg/m^3 (Enstrom, 2005).

AHSMOG: In this analysis for the Seventh-Day Adventist cohort in California, positive, statistically significant association with coronary heart disease mortality was reported for 92 deaths among females (RR = 1.42, 95% CI 1.06-1.90 per 10 μg/m^3 $PM_{2.5}$), but not for 53 deaths among males (RR = 0.90, 95% CI 0.76-1.05 per 10 μg/m^3 $PM_{2.5}$). Associations were strongest in the subset of postmenopausal women (80 deaths; RR=1.49, 95% CI 1.17, 1.89 per 10 μg/m^3 $PM_{2.5}$). The authors speculated that females may be more sensitive to air pollution-related effects based on differences between males and females in dosimetry and exposure, along with the generally lower blood cell levels in females. The mean $PM_{2.5}$ concentration averaged over 1973-1998 was 29.0 μg/m^3 (Chen et al., 2005).

Veterans cohort: A recent analysis of the Veterans cohort data focused on exposure to traffic-related air pollution (traffic density based on traffic flow rate data and road segment length) reported a stronger relationship between mortality with long-term exposure to traffic than with $PM_{2.5}$ mass. A significant association was reported between total mortality and $PM_{2.5}$ in single-pollutant models (RR = 1.12, 95% CI 1.04-1.20 per 10 μg/m^3 $PM_{2.5}$); the author observes that this risk estimate is larger than results reported in a previous study (Lipfert et al., 2000). In multi-pollutant models including traffic density, the association with $PM_{2.5}$ was reduced and lost statistical significance. Traffic emissions contribute to $PM_{2.5}$ so it would be expected that the two would be highly correlated, and thus these multi-pollutant model results should viewed with caution. The mean $PM_{2.5}$ level was 14.6 μg/m^3 using data from 1997-2001 (Lipfert et al., 2006a).

In a companion study, Lipfert et al. (2006b, in press) used data from EPA's fine particle speciation network, and reported findings for $PM_{2.5}$ were similar to those reported in the Lipfert et al., 2006a. A positive association was also reported for mortality with sulfates using the more recent data, but was not statistically significant. Using 2002 data from the fine particle speciation network, significant associations were found between mortality and nitrates, EC, Ni and V, as well as traffic density and peak ozone concentrations. In multi-pollutant models, associations with traffic density remained significant, as did nitrates, Ni and V in some models. The mean $PM_{2.5}$ level was 13.2 μg/m^3 using data from 2002 (Lipfert et al., 2006b, in press).

U.S. Cystic Fibrosis cohort: A positive, but not statistically significant, association was reported in this cohort (RR = 1.32, 95% CI 0.91-1.93 per 10 μg/m^3 $PM_{2.5}$) in a study that primarily focused on evidence of exacerbation of respiratory symptoms (as discussed in the following section). Only 200 deaths had occurred in the cohort of over 11,000 people

(average age in cohort was 18.4 years) thus the power of the study to detect associations is limited. The mean $PM_{2.5}$ concentration was 13.7 $\mu g/m^3$ (Goss et al., 2004).

Infant mortality: A new study in California has reported statistically significant associations between mortality from respiratory causes with exposure to $PM_{2.5}$, using $PM_{2.5}$ levels averaged over the time between the infant's birth and death (RR 1.07, 95% CI 0.93-1.24 per 10 $\mu g/m^3$ $PM_{2.5}$ for overall mortality and 2.13, 95% CI 1.12-4.05 for respiratory mortality). The mean $PM_{2.5}$ exposure concentrations ranged from 17.3 to 19.8 $\mu g/m^3$ (Woodruff et al., 2006).

Thoracic coarse particles:

In the original analyses of the Six Cities and ACS cohort studies, no associations were found between long-term exposure to $PM_{10-2.5}$ and mortality; the extended and follow-up analyses that are discussed above for fine particles did not evaluate potential associations with $PM_{10-2.5}$. Two recent reports from the AHSMOG and Veterans study cohorts have provided some limited suggestive evidence for associations between long-term exposure to $PM_{10-2.5}$ and mortality, as summarized below.

AHSMOG: As was found with fine particles, a positive association with coronary heart disease mortality was reported for females (RR = 1.38, 95% CI 0.97-1.95 per 10 $\mu g/m^3$ $PM_{2.5}$), but not for males (RR = 0.92, 95% CI 0.66-1.29 per 10 $\mu g/m^3$ $PM_{2.5}$); associations were strongest in the subset of postmenopausal women (80 deaths). The mean $PM_{10-2.5}$ concentration over 1973-1998 was 25.4 $\mu g/m^3$ (Chen et al., 2005).

Veterans cohort: A significant association was reported between long-term exposure to $PM_{10-2.5}$ and total mortality in a single-pollutant model (RR = 1.07, 95% CI 1.01-1.12 per 10 $\mu g/m^3$ $PM_{2.5}$), but the association became negative and not statistically significant in a model that included traffic density. As it would be expected that traffic would contribute to thoracic coarse particle concentrations, it is difficult to interpret the results of these multi-pollutant analyses. The average $PM_{10-2.5}$ concentration over 1989-1996 was 16.0 $\mu g/m^3$ (Lipfert et al., 2006).

Conclusions

As shown in Figure 1, the pattern of results from the new studies for both fine and thoracic coarse particles is generally similar to those available previously. Overall, the recent evidence supports associations between long-term $PM_{2.5}$ exposure and mortality, with key new evidence from the Six Cities cohort study showing a relatively large risk estimate for reduced mortality risk with decreases in $PM_{2.5}$ (Laden et al., 2006). The results of new analyses from the Six Cities cohort and the ACS study in Los Angeles suggest that previous and current studies may underestimate the magnitude of the association (Jerrett et al., 2005). In addition, exposure to $PM_{2.5}$ was associated with increased respiratory mortality in infants in a new study in California (Woodruff et al., 2006). New evidence from the Veterans cohort study report associations with $PM_{2.5}$ in single-pollutant models, though the authors report that traffic density is a stronger predictor of mortality than $PM_{2.5}$ (Lipfert et al., 2006a). There is also suggestive

evidence for an association with mortality in the analysis of the Cystic Fibrosis cohort data. The new study using Cancer Prevention Study cohort data in Los Angeles, however, indicates no association with $PM_{2.5}$ except when using the first time period in the study (Enstrom et al., 2005).

In the 2004 PM AQCD, results from the ACS and Six Cities study analyses indicated that thoracic coarse particles were not associated with mortality. The new findings from AHSMOG and Veterans cohort studies provide some suggestive evidence of associations between long-term exposure to $PM_{10-2.5}$ and mortality in areas with mean concentrations from 16 to 25 $\mu g/m^3$. The 2004 PM AQCD placed greatest weight on the ACS and Six Cities study findings; further evidence will need to be evaluated in the next review of the PM NAAQS on whether long-term exposure to thoracic coarse particles is associated with mortality.

2.1.2 Morbidity

The 2004 PM AQCD (Section 8.3.3.2) included results from two U.S. and Canadian children's cohort studies that had been available in the 1996 PM AQCD—the Harvard Six Cities and Harvard 24-cities studies—that reported significant associations between respiratory symptoms and decreased lung function with long-term exposure to fine particles and acid aerosols. More recent studies were available, using data from the Children's Health Study in southern California; these studies also indicated that long-term exposure to fine particles was associated with decreased lung function growth[2] in children. The results from analyses of data from the AHSMOG showed suggestive, but inconsistent findings between long-term exposure to PM and respiratory morbidity in adults. Overall, the 2004 PM AQCD concluded that long-term exposure to PM, especially fine particles, was associated with respiratory morbidity (2004 PM AQCD, p. 8-343). Limited and inconsistent evidence was available on associations between long-term exposure to $PM_{10-2.5}$ and respiratory morbidity.

Among the recently published studies are longer follow-up analyses of respiratory morbidity using data from the Children's Health Study, as well as a study based on data from the U.S. Cystic Fibrosis Cohort. The quantitative results of these studies are included in Table 1, and further details presented in Appendix A, Table A1.

Fine particles:

> *Children's Health Study*: Significant associations are reported between long-term exposure to fine particles, as well as acid vapor and NO_2, and reduced lung function growth (Gauderman et al., 2004) and increased risk of bronchitic symptoms, prevalence of chronic cough, or bronchitis (McConnell et al., 2003). These results expand upon the findings available in the 2004 PM AQCD, including assessment of lung function measurements in children over an 8-year follow-up period (Gauderman et al., 2004). In addition, McConnell et al. (2003) measured respiratory symptom prevalence over a

[2] In these studies, lung function measurements were repeated several years apart. Increases in lung function measures over this time period are referred to as lung function growth by the authors, with "decreased lung function growth" indicating smaller increases in lung function measurements for the children with higher air pollution exposure.

4-year period, and reported larger effect estimates with changes in $PM_{2.5}$ concentration over time within the communities than with changes in $PM_{2.5}$ between communities. The mean $PM_{2.5}$ concentration for the 12 California communities in 1994-2000 was 13.8 $\mu g/m^3$ (McConnell et al., 2003; mean concentrations range from 5 to 28 $\mu g/m^3$ in Gauderman et al., 2004). One additional analysis, based on monthly prevalence of respiratory symptoms, reports no significant associations with $PM_{2.5}$ (Millstein et al., 2004).

U.S. Cystic Fibrosis cohort: The risk of experiencing pulmonary exacerbations was significantly increased with long-term exposure to $PM_{2.5}$ (Goss et al., 2004). The mean $PM_{2.5}$ concentration in 2000 was 13.7 $\mu g/m^3$.

Cardiovascular clinical studies: One new study has provided insight into the potential effect of long-term exposure to $PM_{2.5}$ on the development of cardiovascular disease; no such studies were available in the 2004 PM AQCD. Using data from two clinical trials conducted in the Los Angeles area, the authors reported a significant association between long-term exposure to $PM_{2.5}$ and carotid intima-media thickness, a measure of atherosclerosis development. The mean $PM_{2.5}$ concentration was 20.6 $\mu g/m^3$ (Kunzli et al., 2005).

Thoracic coarse particles:

Two reports from the Children's Health Study included results for *thoracic coarse particles*. A significant association was observed between monthly prevalence of wheeze and $PM_{10-2.5}$ during March-August in one new study, but no association was seen in other parts of the year (Millstein et al., 2004). No significant associations were reported between long-term exposure to $PM_{10-2.5}$ and incidence of bronchitic symptoms in another report in which the mean $PM_{10-2.5}$ concentration was 17.0 $\mu g/m^3$ (McConnell et al., 2003).

The recent findings from the southern California Children's Health Study add support to previous conclusions that long-term fine particle exposure is associated with increased incidence of respiratory symptoms and decreased lung function growth in children. The new evidence from the Cystic Fibrosis Cohort provides additional evidence for associations with pulmonary exacerbations, particularly in a cohort of likely more susceptible individuals. These new studies also report associations with fine particle concentrations that are somewhat lower than those from studies available in the 2004 PM AQCD. These recent findings, however, do not show associations between respiratory morbidity and long-term exposure to $PM_{10-2.5}$; in contrast, one earlier analysis from the Children's Health Study in California had suggested such associations.

No studies available in the 2004 PM AQCD had assessed associations between long-term PM exposure and cardiovascular morbidity. A new analysis shows an association between long-term $PM_{2.5}$ exposure and a measure of atherosclerosis development (Kunzli et al., 2005).

2.2 Epidemiologic Short-Term Exposure Study Results

The 2004 PM AQCD included the results of many new epidemiologic studies reporting associations between short-term exposure to PM and a range of health outcomes. The larger body of evidence from studies of PM_{10} and other PM indicators provided strong evidence for associations between short-term PM exposure and both mortality and morbidity (2004 PM AQCD, p. 8-337).

The 2004 PM AQCD concluded that there was strong epidemiological evidence linking short-term exposures to $PM_{2.5}$ with cardiovascular and respiratory mortality and morbidity. Positive, often statistically significant associations were observed between $PM_{2.5}$ and these various health endpoints (2004 PM AQCD, p. 9-46). The epidemiological evidence was found to support likely causal associations between $PM_{2.5}$ and both mortality and morbidity from cardiovascular and respiratory diseases, based on an assessment of strength, robustness, and consistency in results (2004 PM AQCD, p. 9-48).

Fewer studies were available to assess associations between $PM_{10-2.5}$ and health outcomes. The magnitude of the effect estimates for associations between $PM_{10-2.5}$ and mortality and morbidity effects (especially respiratory morbidity) was found to be similar to that for $PM_{2.5}$, but the strength of the evidence for $PM_{10-2.5}$ effects was reduced due to lower precision (AQCD, p. 9-46). Despite the reduced strength, the associations were found to be generally robust to alternative modeling strategies or consideration of potential confounding by co-pollutants. The collective evidence was found to be suggestive of associations for morbidity with short-term changes in $PM_{10-2.5}$ (2004 PM AQCD, p. 9-48).

Sections 2.2.1 and 2.2.2 highlight results from recent time-series epidemiologic studies. Tables A2 through A12 (Appendix A) summarize results of recent epidemiologic studies that evaluated relationships between health effects and short-term exposure to $PM_{2.5}$ and $PM_{10-2.5}$. The discussions below emphasize results of studies conducted in the U.S. and Canada; however, some results are also presented from additional international studies or studies using indicators, such as PM_{10}, that assess key issues or questions highlighted in the 2004 PM AQCD.

The 2004 PM AQCD included a particular focus on results of multicity studies due to their evaluation of a wide range of PM exposures and large numbers of observations, which lead to generally more precise effects estimates than most smaller scale independent studies of single cities. The multicity studies also allowed investigation of homogeneity or heterogeneity of PM-health relationships, evaluation of confounding by co-pollutants across communities with different air pollution mixtures, and assessment of potential effect modifiers. Numerous multicity analyses have been published in recent years. Most of the recent multi-city studies report statistically significant associations between short-term exposure to PM_{10} and mortality or morbidity and these study results are briefly summarized in Section 2.2.3 as being particularly relevant to help address key methodological questions. In addition, 3 new multi-city studies have evaluated associations with $PM_{2.5}$, one of which included $PM_{10-2.5}$, and these studies are highlighted in the following sections.

2.2.1 Mortality

Results from multi- and single-city epidemiologic studies on mortality were presented in Figure 9-4 of the 2004 PM AQCD. Associations were mostly positive and of similar magnitude for both $PM_{2.5}$ and $PM_{10-2.5}$. A number of the associations between mortality and short-term $PM_{2.5}$ exposure were statistically significant, while few associations with $PM_{10-2.5}$ reached statistical significance, possibly due to increased measurement error in estimating $PM_{10-2.5}$ exposure (2004 PM AQCD, p. 9-28). Several recent studies have reported associations between mortality and short-term exposure to $PM_{2.5}$ and $PM_{10-2.5}$. These findings are included with those available from the 2004 PM AQCD in Figure 2, where it can be seen that the new study results are generally quite similar to those previously available. Note that Figure 2 presents results from single-pollutant models for purposes of comparing results across studies that included different mixes of copollutants, as done in the 2004 PM AQCD.

2.2.1.1 Associations Between Acute Exposure to Fine Particles and Mortality

A number of recent studies have evaluated associations between fine particles and mortality, including two multicity studies (Appendix A; Table A2). Evidence for associations between short-term exposure to $PM_{2.5}$ and all-cause, cardiovascular, and respiratory mortality comes from the multi-site study by Ostro et al. (2006) conducted in nine California counties that had mean $PM_{2.5}$ concentrations ranging from 14 to 29 $\mu g/m^3$. Significant associations were reported in single-pollutant models for all-cause, cardiovascular and respiratory mortality for all ages, as well as a significant association with all-cause mortality for those aged >65 years. The authors observed that in multipollutant models, the $PM_{2.5}$ effect estimate was attenuated when highly correlated pollutants (NO_2 and CO) were added to the model, but was not affected by the inclusion of O_3. However, in those aged >65 yr (who generally experienced stronger associations with mortality), adjusting for gaseous pollutants did not affect the $PM_{2.5}$ coefficient.

Burnett et al. (2004) evaluated the relationship between NO_2 and mortality in 12 Canadian cities during the period 1981 to 1999. While the focus of this analysis was on associations with NO_2, the analysis included other pollutants as well. $PM_{2.5}$ data were available only on 12% of days with mortality data, compared to the other gaseous pollutants that had >90% data available, and for most of the study time period, $PM_{2.5}$ was measured every 6th day. In analyses using these data, the association between $PM_{2.5}$ and all-cause mortality was marginally significant (as shown in Figure 2). In two-pollutant models with NO_2, the effect estimate for $PM_{2.5}$ became negative (not significant), while the estimate for NO_2 remained robust. NO_2 concentrations were found to be correlated with $PM_{2.5}$ concentrations ($r = 0.48$).

Burnett and colleagues (2004) also report results from a separate analysis using more recent data with daily $PM_{2.5}$ measurements (1998-2000). The authors state that a positive association was found between mortality and $PM_{2.5}$ in this additional analysis (presumably significant, but confidence intervals were not provided). In this case, the NO_2 association was reduced considerably after adjustment for $PM_{2.5}$, whereas the $PM_{2.5}$ association remained fairly robust with NO_2 adjustment. These findings emphasize the difficulty of working with data collected every 6th day. The mean $PM_{2.5}$ concentration for all 12 cities was 12.8 $\mu g/m^3$ with city-specific means ranging from 8.1 $\mu g/m^3$ in St. John to 16.7 $\mu g/m^3$ in Windsor.

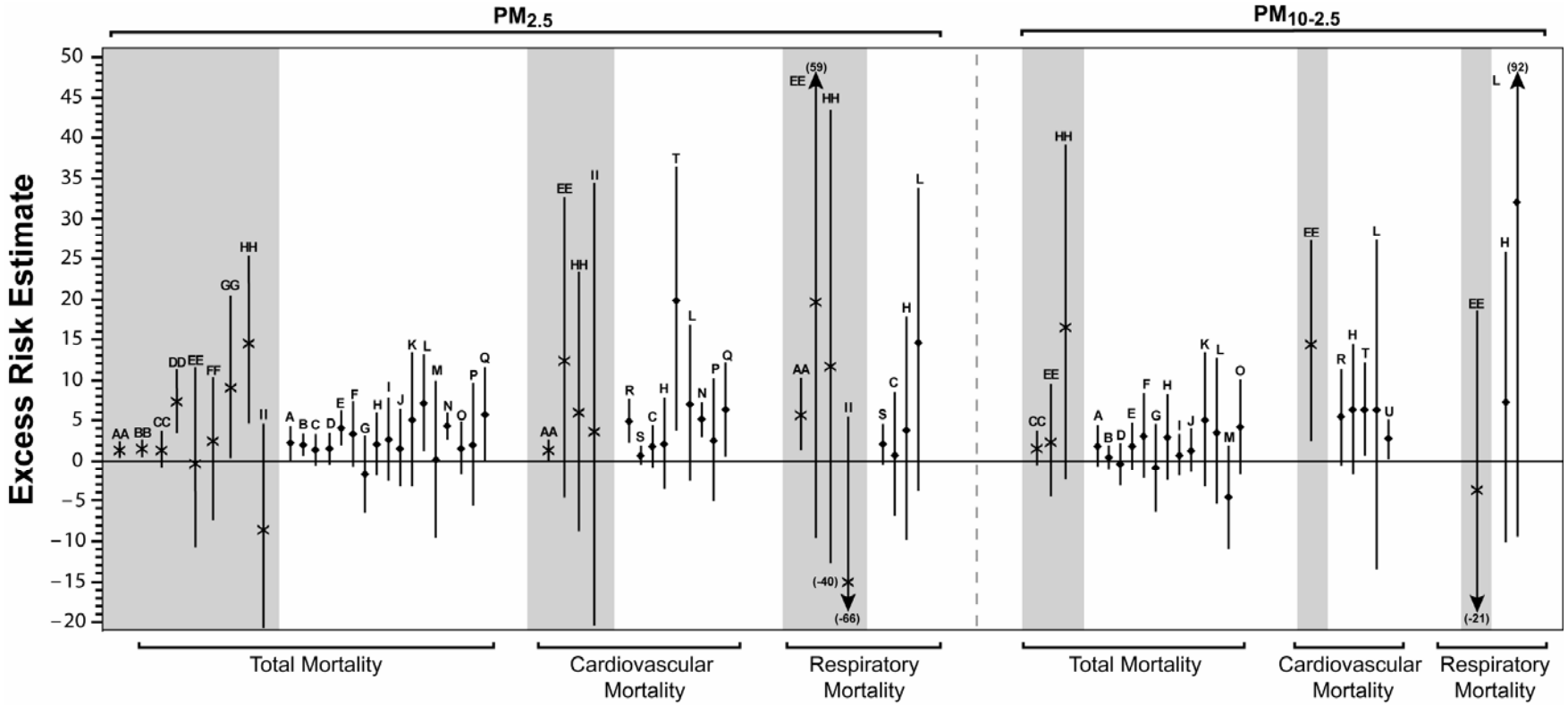

Figure 2. Excess risk estimates for total nonaccidental, cardiovascular, and respiratory mortality in single-pollutant models for U.S. and Canadian studies, including aggregate results from multicity studies (denoted in bold print below). PM increment used for standardization was 25 μg/m^3 for both $PM_{2.5}$ and $PM_{10-2.5}$. Results presented in the 2004 PM AQCD are marked as ♦ in the figure (studies A through T). Results from recent studies are shaded in grey and marked as × in the figure (studies AA through HH).

A. **Burnett and Goldberg (2003), 8 Canadian cities**
B. Klemm and Mason (2003), 6 U.S. cities
C. Moolgavkar (2003), Los Angeles
D. Klemm and Mason (2003), St. Louis
E. Klemm and Mason (2003), Boston
F. Klemm and Mason (2003), Kingston-Harriman
G. Klemm and Mason (2003), Portage
H. Ito (2003), Detroit
I. Chock et al. (2003) Pittsburgh (age <75 yr)
J. Chock et al. (2003) Pittsburgh (age 75+ yr)
K. Klemm and Mason (2000), Atlanta
L. Fairley (2003), Santa Clara County
M. Klemm and Mason (2003), Topeka
N. Tsai et al. (2000), Newark
O. Klemm and Mason (2003), Steubenville
P. Tsai et al. (2000), Elizabeth
Q. Tsai et al (2000), Camden
R. Lipfert et al. (2000), Philadelphia
S. Ostro et al. (1995), Southern California
T. Mar et al. (2003), Phoenix
U. Ostro et al. (2003), Coachella Valley
AA. Ostro et al. (2006), 9 counties in CA
BB. Ostro et al. (2006), 9 counties in CA (age >65 yr)
CC. Burnett et al. (2004), 12 Canadian cities
DD. Ito et al. (in press), Washington, DC
EE. Villeneuve et al. (2003), Vancouver, Canada
FF. Slaughter et al. (2005), Spokane
GG. Goldberg et al. (2006), Montreal, Canada (age 65+ yr)
HH. Klemm et al. (2004), Atlanta (age 65+ yr)
II. Klemm et al. (2004), Atlanta (age <65 yr)

Several single-city studies have also been published. Evidence for associations between fine particles and mortality was seen in studies in Montreal (Goldberg et al., 2006) and Atlanta (Klemm et al., 2004), as well as in studies that focused on source apportionment in Phoenix (Mar et al., 2006) and Washington, DC (Ito et al., 2006). No associations were reported in studies in Vancouver (Villeneuve et al., 2003) and Spokane (Slaughter et al., 2005); these studies reported low $PM_{2.5}$ concentrations. Finally, one new analysis reports no evidence for associations between short-term exposure and death due to sudden infant death syndrome (Dales et al., 2004). The mean $PM_{2.5}$ concentrations in locations where statistically significant associations were reported ranged from about 12 to greater than 20 $\mu g/m^3$.

In Figure 2, the results of the recent time-series studies are presented alongside the findings available in the 2004 PM AQCD. In this figure, it can be seen that the results of the larger multicity studies are quite consistent with those in earlier studies. The studies have been presented in order of decreasing statistical power (based on number of days and number of health events per day) from left to right for each group of studies. Some of the recent studies have fairly low statistical power which is reflected in the large confidence intervals and more variable effect estimate sizes shown in Figure 2. These results, while imprecise, are also generally consistent with earlier study results. Collectively, evidence regarding the $PM_{2.5}$-mortality association from the most recent literature appears to be consistent with that available from the 2004 PM AQCD.

2.2.1.2 Associations Between Acute Exposure to Thoracic Coarse Particles and Mortality

Several new studies examined the association between $PM_{10-2.5}$ and mortality in the U.S. and Canada (Appendix A; Table A3). The multicity study by Burnett et al. (2004), aimed primarily at NO_2, also examined the association between $PM_{10-2.5}$ and all-cause, nonaccidental mortality for lag day 1 (i.e., previous day) using data from 12 Canadian cities. The association with $PM_{10-2.5}$ was positive but not significant; there was a significant association with PM_{10} that lost significance with adjustment for NO_2. However, particle data were available only on 12% of days in this study, as discussed above. The mean $PM_{10-2.5}$ concentration in this study was 11.4 $\mu g/m^3$ (12 city means range from 5.5 to 15.9 $\mu g/m^3$).

Figure 2 includes results from the recent single-pollutant studies and those available in the 2004 PM AQCD. Looking across all studies, it can be seen that associations between $PM_{10-2.5}$ and total and cardiovascular mortality are generally positive and a number are statistically significant, particularly for cardiovascular mortality. As discussed in the 2004 PM AQCD, some studies indicated stronger associations between acute $PM_{10-2.5}$ exposure and cardiovascular mortality than for all-cause mortality. One recent study in Vancouver, Canada, also observed a statistically significant relationship with cardiovascular mortality on lag day 0 (i.e., same day) but not on lag day 1 or 2 or the 3-day average lag periods (i.e., 24-hour average concentrations measured 1-, 2- or 3-days prior) (Villeneuve et al., 2003). No associations were found for all-cause, respiratory, or cancer mortality in this study. The mean $PM_{10-2.5}$ concentration in this study was 6.1 $\mu g/m^3$ (range 0 to 72 $\mu g/m^3$).

Other recent studies did not report statistically significant associations between $PM_{10-2.5}$ and total mortality. Slaughter et al. (2005) did not find a significant relationship for $PM_{10-2.5}$ with all-cause, nonaccidental mortality in Spokane, WA, which likely had higher $PM_{10-2.5}$ concentrations than Vancouver, Canada (data not shown). Neither Slaughter et al. (2005) nor Burnett et al. (2004) investigated the relationship with cardiovascular mortality. A recent PM_{10} study in El Paso (Staniswalis et al., 2005) supports the hypothesis that wind-blown dust coming from non-urban areas during high wind speeds (assumed largely coarse-fraction particles) is less toxic than particles generated within the urban area. Finally, Klemm and colleagues (2004) reported a positive, but not statistically significant association between $PM_{10-2.5}$ and mortality in Atlanta. The mean $PM_{10-2.5}$ concentration in this study was 9.7 $\mu g/m^3$ (range 1.7 to 25.2 $\mu g/m^3$).

2.2.2 Morbidity

Results from epidemiologic studies on hospital admissions were presented in Figure 9-5 of the PM AQCD. Associations were all positive and of similar magnitude for both $PM_{2.5}$ and $PM_{10-2.5}$. Many of the associations with short-term $PM_{2.5}$ exposure were statistically significant, especially for respiratory diseases. Likely due to increased measurement error, some, but not all, of the associations with $PM_{10-2.5}$ reached statistical significance (2004 PM AQCD, p. 9-29). Several recent studies have reported associations between short-term exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and hospitalization or emergency department visits for cardiovascular and respiratory diseases. These findings are included with those available from the 2004 PM AQCD in Figure 3.

2.2.2.1 Associations Between Acute Exposure to Fine Particles and Morbidity

These new studies substantially expand the evidence for associations between $PM_{2.5}$ and effects on the cardiovascular system (Appendix A; Tables A4, A6 and A8). These include a powerful new multi-city study by Dominici et al. (2006) that used data from the Medicare National Claims History Files for 11.5 million people living in 204 urban counties in the U.S.; the average $PM_{2.5}$ concentration for 1999-2000 was 13.4 $\mu g/m^3$. There was only limited consideration of other pollutants in this analysis. Hospital admission rates for cause-specific cardiovascular and respiratory diseases were significantly associated with short-term $PM_{2.5}$ exposure in individuals aged >65 yr. The largest association was reported with heart failure. Significant associations were also found between short-term $PM_{2.5}$ exposure and hospital admissions for cerebrovascular disease, and positive though not statistically significant associations were seen with peripheral vascular disease, ischemic heart disease, and cardiac rhythm. When evaluated on a region-specific basis, positive associations with cardiovascular disease hospitalization were seen in the Midwest, Northeast, and Southern regions; the authors suggest that differences in the sources and composition of fine particles contributes to the geographic differences seen in effect estimates.

One recent study reports significant associations between short-term exposure to $PM_{2.5}$ and emergency department visits for all cardiovascular diseases, congestive heart failure and peripheral vascular and cerebrovascular disease in Atlanta (Metzger et al., 2004). Another study reports no evidence of associations with cardiovascular visits in Spokane, where the $PM_{2.5}$ concentrations were low (authors report that 90% of concentrations ranged between 4.2 and 20.2 $\mu g/m^3$) (Slaughter et al., 2005).

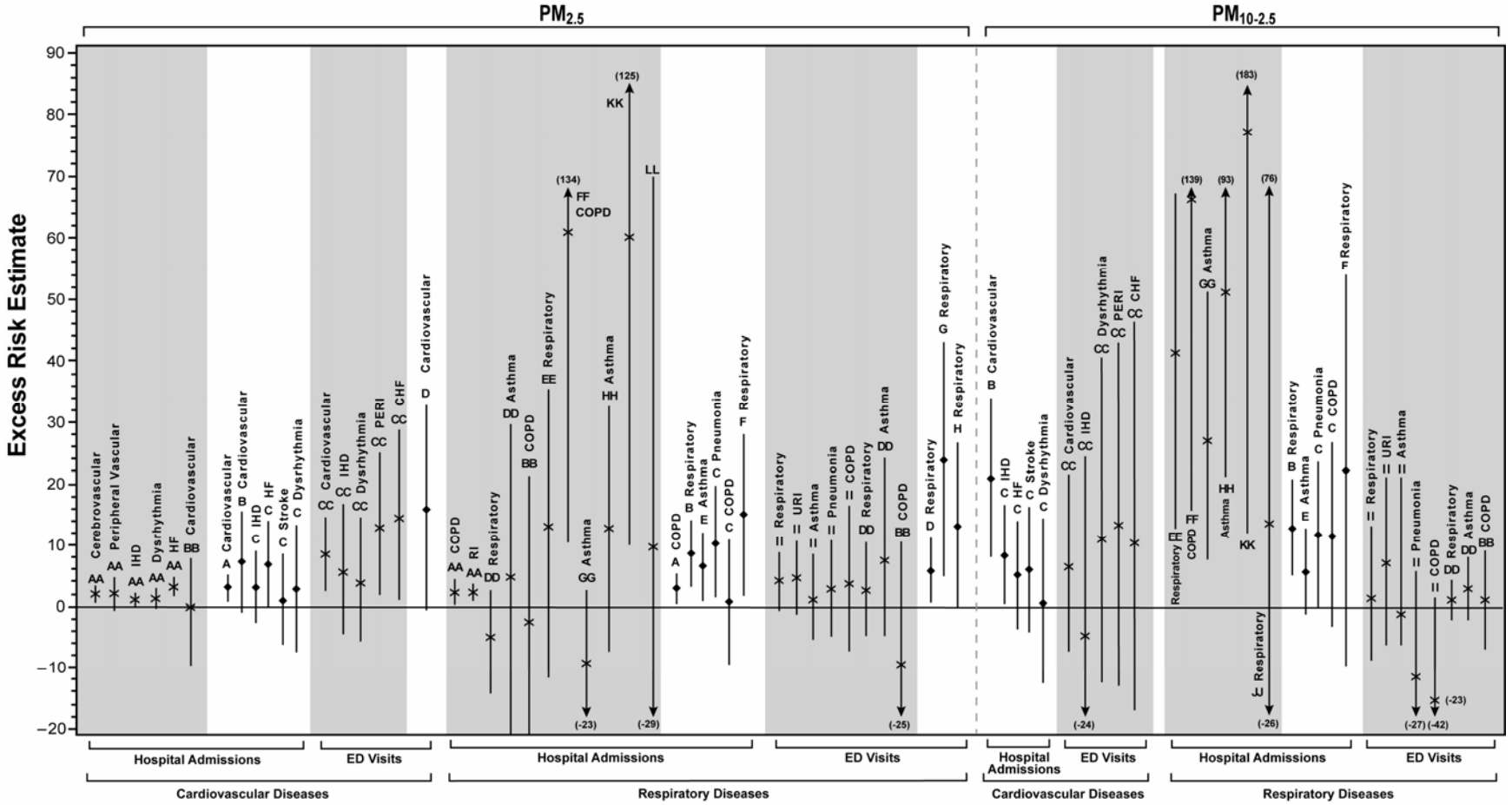

Figure 3. Excess risk estimates for hospital admissions and emergency department visits for cardiovascular and respiratory diseases in single-pollutant models for U.S. and Canadian studies, including aggregate results from a multicity study (denoted in bold print below). PM increment used for standardization was 25 μg/m^3 for both $PM_{2.5}$ and $PM_{10-2.5}$. Results presented in the 2004 PM AQCD are marked as ♦, in the figure (studies A through H). Results from recent studies are shaded in grey and marked as × in the figure (studies AA through JJ). (CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; HF = heart failure; IHD = ischemic heart disease; PERI = peripheral vascular and cerebrovascular disease; RI = respiratory infection; URI = upper respiratory infection).

A. Moolgavkar (2003), Los Angeles
B. Burnett et al. (1997), Toronto
C. Ito (2003), Detroit
D. Stieb et al. (2000), St. John
E. Sheppard (2003), Seattle
F. Thurston et al. (1994), Toronto
G. Delfino et al. (1997), Montreal
H. Delfino et al. (1998), Montreal

AA. Dominici et al. (2006), 204 U.S. counties (age >65 yr)
BB. Slaughter et al. (2005), Spokane (age 15+ yr)
CC. Metzger et al. (2004), Atlanta
DD. Slaughter et al. (2005), Atlanta
EE. Chen et al. (2005), Vancouver, Canada (age 65+ yr)
FF. Chen et al. (2004), Vancouver, Canada (age 65+ yr)

GG. Lin et al. (2002), Toronto, Canada (age 6-12 yr, boys)
HH. Lin et al. (2002), Toronto, Canada (age 6-12 yr, girls)
II. Peel et al. (2005), Atlanta
JJ. Yang et al. (2004), Vancouver, Canada (age >3 yr)
KK. Lin et al. (2005), Toronto, Canada (age <16 yr, boys)
LL. Lin et al. (2005), Toronto, Canada (age <16 yr, boys)

Numerous new studies have reported associations between ambient $PM_{2.5}$ and subtle cardiovascular effects such as changes in cardiac rhythm or heart rate variability (Appendix A; Table A8). In the 2004 PM AQCD, the data base was characterized as having some studies with conflicting results and a note of caution was raised in regard to drawing conclusions relating $PM_{2.5}$ and heart rate variability and other measures of cardiovascular pathophysiological alterations. Of about 10 new studies evaluating associations between acute $PM_{2.5}$ exposure and heart rate variability, most reported statistically significant associations with $PM_{2.5}$. . Two new studies showed associations for $PM_{2.5}$ with ST segment depressions, an indicator of myocardial ischemia (Gold et al., 2005). One new study examined $PM_{2.5}$ effects on bronchial artery reactivity (a marker for cardiovascular disease risk) and reported a significant association (O'Neill et al., 2005). Noting that many of these studies were conducted over shorter time periods, nevertheless, it is reported that mean or median $PM_{2.5}$ concentrations in a number of studies were in the range of 10-11 $\mu g/m^3$, with maximum levels ranging from about 40 to 60 $\mu g/m^3$.

For respiratory effects, Dominici et al. (2006) report significant associations between $PM_{2.5}$ and hospitalization for chronic obstructive pulmonary disease (COPD) and respiratory infection in the study of 204 U.S. counties mentioned above (Appendix A; Table A4). Less regional variation was seen for respiratory hospitalization than for cardiovascular hospital admissions; in contrast with the results for cardiovascular diseases, effect estimates for both COPD and respiratory infections admissions were larger for the western U.S. than the eastern U.S.

There are also several single-city studies that were conducted in Canada that show no associations between hospitalization and acute exposure to $PM_{2.5}$ (Lin et al., 2002; Lin et al., 2005; Yang et al., 2004; Chen et al., 2004; Chen et al., 2005). All were studies of hospitalization for respiratory diseases, though studies differed in age group and respiratory endpoint, and the mean $PM_{2.5}$ concentrations in the studies ranged from 7.7 to 18 $\mu g/m^3$. Another recent study reports positive associations with respiratory emergency department visits, although none are statistically significant (Peel et al., 2005) (mean concentration of 19.2 $\mu g/m^3$). Finally, there was no evidence of associations with respiratory visits in Spokane, where the $PM_{2.5}$ concentrations were low (90^{th} percentile was 20.2 $\mu g/m^3$) (Slaughter et al., 2005).

There are numerous new studies that examined various respiratory outcomes in relation to $PM_{2.5}$ exposure (Appendix A; Table A10), including one new multicity study that reported a significant association between respiratory symptoms and short-term $PM_{2.5}$ exposure (Gent et al., 2003) (mean concentration of 13.1 $\mu g/m^3$); however, the effect estimate is reduced and not statistically significant with adjustment for ozone. Associations have also been reported between acute $PM_{2.5}$ exposure and a new endpoint not previously reported, FE_{NO} (fractional exhaled nitric oxide, a marker of airway inflammation), in three studies conducted in Seattle, WA (Jansen et al., 2005; Koenig et al., 2005; Mar et al., 2005) and one in Steubenville, OH (Adamkiewicz et al., 2004). In addition, a study in Seattle reports statistically significant associations with lower respiratory symptoms in children with asthma (Mar et al., 2004). One study in Atlanta reported no positive associations between $PM_{2.5}$ and medical visits for various respiratory conditions—in fact, some associations were negative in direction—but positive associations were reported for several components of $PM_{2.5}$ (Sinclair and Tolsma, 2004).

2.2.2.2 Associations Between Acute Exposure to Thoracic Coarse Particles and Morbidity

A number of new epidemiologic studies are available for assessing associations between short-term $PM_{10-2.5}$ exposure and various morbidity health outcomes, especially related to respiratory morbidity (Appendix A; Tables A5, A7, A9, and A11). As shown in Figure 3, a number of recent reports have shown significant associations between respiratory hospitalization and acute exposure to $PM_{10-2.5}$. These include associations with hospitalization in Vancouver for respiratory illness in children <3 years of age (Yang et al., 2004), COPD in the elderly, (Chen et al., 2004) and respiratory illness in the elderly (Chen et al., 2005). Associations were also reported with hospitalization for asthma in children (Lin et al., 2002) and respiratory illness in children (Lin et al., 2005) in Toronto. These associations with hospital admissions for respiratory disease were observed for $PM_{10-2.5}$ in both time-series and case-crossover analyses, and the associations remained significant with adjustment for gaseous co-pollutants in four of the five studies (except Chen et al., 2005). The effect estimate increased with longer averaging times up to 4-7 days. Slaughter et al. (2005) did not observe significant associations between $PM_{10-2.5}$ and hospitals admissions or emergency room visits in Spokane, WA for all ages taken together. Overall, these studies provide evidence for associations between acute $PM_{10-2.5}$ exposure and respiratory morbidity in locations where reported mean concentrations range from 5.6 to 12.2 $\mu g/m^3$, and maximum concentrations from 24.6 to 68 $\mu g/m^3$.

One new panel study in Spokane indicated that exposure was associated with several upper respiratory tract symptoms in children with asthma, but no association was reported in adults (Mar et al., 2004). Peel et al. (2005) reported no significant associations between $PM_{10-2.5}$ and respiratory emergency department visits in Atlanta; however in another Atlanta study, significant associations were reported between acute $PM_{10-2.5}$ exposure and outpatient medical visits for several respiratory conditions (Sinclair and Tolsma, 2004).

Little evidence was available on associations between cardiovascular morbidity and $PM_{10-2.5}$ in the 2004 PM AQCD. In Atlanta, no significant associations were found between acute exposure and cardiovascular emergency department visits (Metzger et al., 2004). However, one recent study in Coachella Valley, CA reported significant associations between decreases in heart rate variability with short-term exposure to $PM_{10-2.5}$, but not with $PM_{2.5}$ (Lipsett et al., 2006). In addition, a panel study in Vancouver (Ebelt, et al., 2005) found significant associations between estimates of personal exposure to ambient particles, and to a lesser extent, ambient concentrations with decreased FEV_1 and increases in systolic blood pressure and supraventricular ectopy. However, associations were not significant with measures of heart rate variability. No associations were reported with estimates of personal exposure to nonambient particles. The mean $PM_{10-2.5}$ concentrations in the Coachella Valley and Vancouver studies range from about 10 to over 20 $\mu g/m^3$ At the low end of reported concentrations is Vancouver, where $PM_{10-2.5}$ means were 6-7 $\mu g/m^3$ and maxima were about 25 $\mu g/m^3$. Of note, correlations reported between $PM_{10-2.5}$ and combustion-related gaseous co-pollutants (CO, NO_2, SO_2) are generally higher than those reported between $PM_{2.5}$ and the gases in Vancouver. At the high end is Coachella Valley, where PM_{10} concentrations were quite high, with peak levels exceeding the current PM_{10} standard level.

Taken together, there is a substantial new body of evidence linking acute exposure to $PM_{10-2.5}$ with morbidity, including associations with respiratory hospitalization, respiratory

symptoms, and cardiovascular health outcomes. Of note, several recent studies have reported associations for several indicators of morbidity with $PM_{10-2.5}$, but not with $PM_{2.5}$. In addition, some new studies have used case-crossover methods and reported little evidence for confounding by co-pollutants. A key research question that has been identified during the current PM NAAQS review is to better understand the sources and components of $PM_{10-2.5}$ that may be responsible for different health effects, and these findings continue to support that research need.

2.2.3 Issues for Interpretation of Epidemiologic Study Results

More than 20 new multicity studies have been published in recent years. Three of these studies have included measurements of $PM_{2.5}$ and one included $PM_{10-2.5}$ and these studies are summarized in more detail above (Burnett et al., 2004; Dominici et al., 2006; Ostro et al., 2006). The remaining studies used PM_{10}; the results are summarized briefly in an annotated bibliography (Appendix B). Most of these recent studies continue to report associations between short-term exposure to PM_{10} and mortality or morbidity.

Methodological Issues: The results of the PM_{10} multicity studies are briefly highlighted here due to the importance of multicity studies in being able to evaluate issues that are not readily addressed in single-city analyses. The studies are grouped in Appendix B by the general issues being evaluated in the analyses. These studies address a range of questions and uncertainties that remained in the 2004 PM AQCD, including:

- Several recent multicity studies reported that associations between PM_{10} and mortality are not likely to be confounded by weather or influenza epidemics (Schwartz 2004a; Welty and Zeger, 2005; Analitis et al., 2006; Touloumi et al., 2005). As observed in the 2004 PM AQCD, assessments of copollutant confounding are complicated when the air pollutants are closely correlated, such as pollutants generated from common sources. Results from single-pollutant models may overestimate effects from that pollutant; however, multi-pollutant model results may be misleading when reporting results for correlated pollutants. One new multi-city study used case-crossover design and reported no evidence of confounding between PM_{10} and gaseous co-pollutants in associations with mortality in 14 U.S. cities (Schwartz et al., 2004b). Using more traditional time-series methods, Ostro et al. (2006) reported attenuation of associations between $PM_{2.5}$and mortality with highly-correlated gaseous pollutants in adults <65 years of age, but not in analyses for the elderly. In 12 Canadian studies, $PM_{2.5}$ and $PM_{10-2.5}$ were robust to adjustment for NO_2 in models using only data from the time period when daily PM data were available, but effect estimates were not statistically significant in models using data from the full time period (Burnett et al., 2004). Dominici et al. (2006) report little evidence of effect modification by ozone concentrations in the relationship between $PM_{2.5}$ and hospitalization.

- Daniels et al. (2004) reported that there was no evidence for a threshold level in the PM_{10}-mortality association in analyses of data from the National Morbidity, Mortality and Air Pollution Study.

- The recent multicity studies continue to report somewhat stronger associations with the use of a distributed lag model (Analitis et al., 2006; Zanobetti et al., 2003; Zeka et al., 2005). In addition, one new analysis shows little evidence that the associations are unlikely to represent advancement of death by only a few days (Dominici et al., 2003).

- The recent studies also report findings that are robust to the use of different analytical methods (Roberts and Martin, 2006) and assess the influence of measurement error in underestimation of the PM_{10}-mortality association (Zeka and Schwartz, 2004).

Variation in effects between locations: Numerous new multicity analyses in Europe and the U.S. have studied the variation of PM-health associations between locations, and assessed factors that may influence heterogeneity in PM-related health effects (Dominici et al., 2003; Medina-Ramon et al., 2006; Samoli et al., 2005; Le Tertre et al., 2005; Zeka et al., 2005; Zeka et al., 2006). Consistent with the findings available in the 2004 PM AQCD, the recent studies highlight exposure differences (e.g., air conditioning use) and the influence of traffic as potentially associated with larger effects of PM_{10}. Some recent studies also suggest that variability in climate and a number of preexisting health conditions may modify the effects of PM.

New health outcomes: New multicity analyses have also reported associations between PM_{10} and new health outcomes, including emergency admissions for myocardial infarction (Zanobetti and Schwartz, 2005), readmission to the hospital for cardiac causes (Von Klot et al., 2005) and potential changes in physiological cardiac indicators (Ibald-Mulli et al., 2004; Timonen et al., 2006)Numerous recent single-city studies also expand of the health endpoints that are reported to be associated with PM, generally focusing on $PM_{2.5}$ exposures. These newly reported health endpoints include: (1) indicators of the development of atherosclerosis with long-term PM exposure; (2) indicators of changes in cardiac rhythm, including arrhythmia or ST-segment changes; (3) effects on developing children and infants; (4) markers of inflammation such as exhaled NO; and (5) effects on organ systems outside the cardiopulmonary systems. Numerous new epidemiologic studies have reported associations between PM, primarily using $PM_{2.5}$, and cardiovascular health outcomes such as cardiac arrhythmia, ST segment depression, and decreased heart rate variability. New toxicology reports suggest that the brain may be affected by exposure to PM, including reports of increases in inflammatory biomarkers and neurodegeneration following exposure to CAPs (Campbell et al., 2005; Veronesi et al., 2005).

Potentially susceptible or vulnerable subpopulations: In the 2004 PM AQCD, people with preexisting heart or lung disease, children, and older adults were considered likely to be more susceptible to PM-related effects. Recent studies provide increasing evidence that pre-existing diseases, particularly diabetes, may increase susceptibility to the cardiovascular effects of PM. Goldberg et al. (2006) reported significant associations between $PM_{2.5}$ and diabetes deaths, as well as total mortality in people with previous diagnoses of diabetes. One new toxicology study has suggested mechanistic evidence for diabetes-related susceptibility (Proctor et al., 2006). Additional research utilizing susceptible animal models of vascular conditions (e.g., the Spontaneously Hypertensive rat and the apolipoprotein deficient mouse) have demonstrated that exposure to CAPs or surrogate PM can exacerbate symptoms, compromise function and potentiate disease states.

2.3 Intervention Studies

The 2004 PM AQCD highlighted the results of several new "intervention" studies or "found experiments" that reported associations between reductions in air pollution and improvements in public health (2004 PM AQCD, Sections 8.2.3.4 and 9.2.2.6). While few in number, these studies were found to provide important support to the epidemiologic evidence linking air pollution exposure with adverse health effects.

One new study reported evidence for reduced mortality risk when ambient pollution was decreased (Laden et al., 2006). As discussed briefly above, the authors report a statistically significant reduction in mortality risk with reduced long-term fine particle concentrations (RR 0.73, 95% CI 0.57-0.95, per 10 $\mu g/m^3$ $PM_{2.5}$).

Several recent intervention studies have evaluated changes in respiratory health outcomes associated with decreased pollution levels; the results of these studies are summarized in Table A13 (Appendix A). One U.S. study reported reductions in respiratory medical visits with decreased traffic volume that resulted from closure of the Peace Bridge in Buffalo, NY, following September 11, 2001 (Lwebuga-Mukasa et al., 2003). Studies conducted in Switzerland and East and West Germany have also reported reductions in respiratory symptoms or improved lung function with decreases in ambient PM concentrations measured as TSP or PM_{10} (Bayer-Oglesby et al., 2005; Sugiri et al., 2006; Frye et al., 2003; Heinrich et al., 2002). In addition, Burr et al. (2003) reported associations between reduced respiratory symptoms and reductions in traffic volume. Overall, this group of studies indicates that declining concentrations of PM and other pollutants is associated with reduced mortality risk and improved respiratory health and thus add substantial support to the evidence available in the 2004 PM AQCD.

2.4 Health Effects Related to Sources or Components of PM

The current PM NAAQS have been established using $PM_{2.5}$ and PM_{10} mass as the indicators, as opposed to singling out any particular component or class of particles. This decision was based on evidence from epidemiologic studies that reported significant associations between various PM components or characteristics, evidence that PM was associated with health effects in numerous areas that had differing components or sources of PM, and evidence from animal toxicology and controlled human exposure studies that had reported health effects associations with high concentrations of numerous fine particle components (e.g., sulfates, nitrates, transition metals, organic compounds).

In the 2004 PM AQCD, epidemiologic and toxicology studies provided evidence for effects associated with various fine particle components or size-differentiated subsets of fine particles. Toxicology studies reported effects with exposure to different sources or components of PM (generally at high levels), such as metals, diesel particles, acid aerosols, and bioaerosols (Chapter 7 of the 2004 PM AQCD). The findings of these studies indicated that, for a given health response, some fine particle components were more closely linked with that response than other components. However, the evidence did not suggest that any component could be singled out as potentially the sole contributor to toxicity, or as having no toxic effects.

Chapter 8 of the 2004 PM AQCD included a discussion of three new epidemiologic studies that reported associations between various health outcomes and different PM components. Three new studies that had conducted source-oriented evaluation of PM provided new insights into the relationship between fine particles from different sources and mortality. While few in number and somewhat preliminary in nature, these studies suggested that a number of source types were associated with mortality, including motor vehicle emissions, coal combustion, oil burning, and vegetative burning; no associations were reported with the crustal factor from fine particles (2004 PM AQCD, Section 8.2.2.5).Considered together, the 2004 PM AQCD concluded: "These studies suggest that many different chemical components of fine particles and a variety of different types of source categories are all associated with, and probably contribute to, mortality, either independently or in combinations" (p. 9-31). Conversely, there was no basis to conclude that any individual fine particle component cannot be associated with adverse health effects.

Many new studies have been published in recent years that provide interesting new insights into the effects of different sources or types of PM. For the purposes of this provisional assessment of new literature published since the release of the 2004 PM AQCD, emphasis has been placed on studies that investigated the health effects related to PM sources or comparisons of various PM components. To highlight the scientific content of the recent literature while focusing on key PM study categories, this section focuses on results of studies that evaluated the effects of a range of sources or components. This includes studies that used source apportionment, or that compared effects for a range of PM components. Thus, the discussion includes: (1) recent epidemiologic studies using source apportionment; (2) epidemiologic evidence on effects with PM components; (3) results of new toxicology studies using source apportionment with exposures to concentrated ambient particles (CAPs) to provide insight into potential effects related to PM from different sources, and comparative toxicology studies using fine particle components; and (4) toxicology study results for different surrogates and size fractions of PM, including thoracic coarse PM ($PM_{10-2.5}$). In addition, numerous epidemiologic and/or toxicology studies have reported effects of several sources, components, or characteristics as discussed in the 2004 PM AQCD. Specific findings for these PM characteristics are not discussed in detail; instead, the available new studies are included in reference lists for the following categories:

- ultrafine PM;
- metals (including residual oil fly ash);
- traffic;
- woodsmoke; and
- endotoxin.

2.4.1 Epidemiologic Studies Using Source Apportionment

Some recent epidemiologic studies have employed statistical approaches of source contributions from source apportionment analyses in evaluating associations of health effects with particular source categories of PM. Since source apportionment analysis is based on finding independent groupings of chemical components, the source categories should not confound each other.

A workshop was held in May 2003 during which several groups determined source category contributions (using multiple techniques) using ambient PM chemical concentration data from Washington, D.C. (U.S. Park Service, IMPROVE) and from Phoenix (U.S. EPA). An intercomparison of the source apportionment results was also published (Hopke et al., 2006). The statistical associations of these source category contributions with total (non-accidental) and cardiovascular mortality were then determined by Ito et al. (2006) for Washington and Mar et al. (2006) for Phoenix. The results from different groups varied, in part depending on the participants' experience and expertise with source apportionment and time-series epidemiologic analyses (Appendix A; Table A14). Although several groups separated the traffic source into diesel and gasoline, for the reported analyses, all traffic-related source categories were summed into a "traffic" source category. For Washington, DC, the correlations of daily contributions of source categories across the various investigators/techniques were fair for crustal, secondary sulfate, secondary nitrate, primary residual oil combustion, and incinerator, but poor for traffic, wood burning, and salt (correlation not reported for primary coal combustion). In Phoenix, AZ, the correlations of daily contributions across the various investigators and analysis techniques were high for traffic, secondary sulfate, and sea salt, and low for biomass burning, metals, and primary coal burning.

In Washington, DC, secondary sulfate and primary coal combustion were statistically significant with total mortality on lag day 3. $PM_{2.5}$ had a statistically significant relationship with total mortality on lag day 1 and 3 before controlling for temperature, but only on lag day 3 after controlling for temperature. For cardiovascular mortality, no source categories were statistically significant across all investigators/techniques. However, for one or more analyses, statistically significant results were found for soil (lag 2, 3, and 4), traffic (lag 3), secondary sulfate (lag 0 and 3), residual oil (lag 0), wood smoke (lag 3), and primary coal burning (lag 3). The Washington, DC samples were collected on Saturday and Thursday only; so, each lag has a different set of mortality days which may introduce some uncertainty into the lag structure.

In Phoenix, only sea salt (lag 5) was statistically significant with total mortality for all analyses, while 3/5 data sets gave statistically significant results for Cu smelter (lag 0) and 1/8 for sulfate (lag 0). For cardiovascular mortality, most data sets gave statistically significant (or nearly so) associations for traffic (lag 1, 6/9), secondary sulfate (lag 0, 6/8), sea salt (lag 5, 6/6), and Cu smelter (lag 0, 3/5). Data sets from both cities show secondary sulfate as the source category with the highest statistically significant relative risk (5-95th percentile increments), although the lag days and mortality categories differ by city (lag 0 for cardiovascular mortality in Phoenix, AZ, and lag 3 for total mortality in Washington, DC, with some Washington, DC, data sets reporting lags 0 and 3 for cardiovascular mortality). A generalized traffic source is implicated for cardiovascular mortality at lag 1 in Phoenix, AZ and lag 3 in Washington, DC.

One study used source apportionment techniques to assess relationships between cardiovascular morbidity and acute fine particle exposure in a panel of healthy young male patrol officers in Wake County, NC. Riediker et al. (2004) reported the strongest associations between a "speed change" factor (Cu, S, and aldehydes) and a number of cardiovascular health indicators. There were suggested associations with a gasoline combustion factor, and there was limited evidence for associations with fine particles of crustal origin.

Taken together, the results of these new studies are consistent with previously-available evidence that link health outcomes with fine particles from a range of sources, including motor vehicles and combustion of oil or coal. The use of source categories in community time-series epidemiology shows promise but additional work is needed in characterizing the various sources, understanding the spatial variability of the different source categories, and obtaining daily composition and concentration data for periods of several years in additional cities.

2.4.2 Epidemiologic Studies on Effects of Fine Particle Components

As summarized in Section 8.2.2.5 of the 2004 PM AQCD, epidemiologic studies have reported generally positive, often statistically significant associations between various fine particle components and mortality. Numerous studies have reported associations between short-term sulfate exposures and mortality and morbidity; the effect estimates reported for mortality range from about 1 to 9% increases in mortality per 5 $\mu g/m^3$ increase in ambient sulfate concentration (as shown in Figure 8-6 of the 2004 PM AQCD). Associations have also been reported with other PM components, including carbonaceous components (elemental carbon, organic carbon, and coefficient of haze), nitrates, and metals.

Associations between mortality and long-term exposure to ambient sulfates was reported in prospective cohort studies, with effect estimates reported in the range of 11 to 50% increases in mortality per 15 $\mu g/m^3$ increase in sulfates (2004 PM AQCD, Table 8-15). Prospective cohort studies have also reported associations between long-term exposure to sulfates and respiratory effects, such as prevalence of chronic bronchitis (2004 PM AQCD, section 8.3.3.2).

Several recent epidemiologic studies have evaluated associations between *short-term exposure* to fine particle components and various health outcomes, as shown in Table A15 (Appendix A). Overall, this group of studies reports associations between mortality and morbidity with several fine particle components. A number of studies report associations with sulfates that are generally consistent with those in earlier reports. Several recent studies have also shown associations with the organic carbon and elemental carbon components of fine particles.

- For mortality, significant associations were reported with sulfates in a new study in Montreal (Goldberg et al., 2006), and a positive, borderline significant, association with sulfates was reported in a study of 12 Canadian cities (Burnett et al., 2004). Positive, but not statistically significant, associations between mortality and fine particle sulfates was reported in Vancouver (Villeneuve et al., 2003). A study in Atlanta also evaluated associations with other fine particle components, and reported positive but not significant associations between mortality and sulfates and EC, OC, and not association with nitrates (Klemm et al., 2004).

- For emergency department visits, two reports from the ARIES study in Atlanta evaluated associations between short-term fine particle component exposures and visits for cardiovascular or respiratory diseases (Metzger et al., 2004; Peel et al., 2005). Both studies report no significant associations for short-term exposures to either sulfates or water-soluble metals with visits for cardiovascular or respiratory diseases. Significant

associations were reported between OC and EC and emergency department visits for all cardiovascular diseases and congestive heart disease (Metzger et al., 2004). No significant associations were reported between any component and respiratory visits, except for an association between OC and emergency department visits for pneumonia (Peel et al., 2005).

- For cardiovascular health outcomes, one study that was conducted in Boston, MA reported a significant association between short-term sulfate exposure and percent change in brachial artery diameter, an indicator of vascular reactivity (O'Neill et al., 2005); other components were not evaluated.

- For respiratory health outcomes, medical visits for asthma in children and lower respiratory infections (all ages) were associated with the EC and OC components of fine particles in Atlanta, but no associations were reported with sulfates or acidity (Sinclair and Tolsma, 2004). Metals were positively associated with medical visits for lower respiratory infection, but not for other outcomes. For adult asthma and upper respiratory infections, there were no significant positive associations with any of the fine PM components; however, sulfates were negatively associated with upper respiratory infection visits (Sinclair and Tolsma, 2004). In a panel study of Hispanic children, OC and EC (measured in PM_{10}) were significantly associated with asthma symptoms; other PM components were not included in this study (Delfino et al. 2003).

In addition, one recently published epidemiologic study has also assessed associations between mortality and *long-term exposure* to fine particle components (see Table 1). Mortality was significantly associated with long-term exposure to four fine particle components (EC, nitrates, nickel, and vanadium), and a positive but not statistically significant association was reported with sulfates using the Veterans cohort (Lipfert et al., 2006b, in press).

2.4.3 Toxicology Studies—Source Apportionment and Fine Particle Components

There were nine studies in the 2004 PM AQCD that investigated the effects of fine particle CAPs exposure in humans and laboratory animals (Sections 7.2.2 and 7.3.1). The results of these studies generally showed associations between the CAPs exposure and cardiovascular parameters. Effects on the respiratory system were largely absent for pulmonary function, but were present for markers of inflammation. Source apportionment was largely absent in the previous CAPs studies, although some evidence linked transition metal components in ambient PM with lung injury. Additionally, as CAPs composition varies day-to-day, it is difficult to establish clear relationships between individual components and adverse health effects. The 2004 PM AQCD pointed to a "critical need for the systematic conduct of studies in the potential respiratory effects of major components of PM from different regions of the U.S., in recognition that PM of different composition and from different sources can vary markedly in its potency for producing different respiratory effects" (2004 PM AQCD, p. 7-85).

Toxicological studies employing CAPs offer a relevant surrogate for atmospheric PM. As ambient PM is just one component of a complex mixture that interacts with gases and other aerosols, CAPs systems provide a method of exposing subjects to the particle phase. Gases

(such as O_3 and SO_2) are not concentrated and organic PM components in CAPs likely differ from components in ambient PM, particularly for ultrafine CAPs systems (Su et al., 2006). Similarly, thoracic coarse PM is not enriched (except for the coarse particle concentrator) and only certain systems are capable of concentrating ultrafine PM.

There are three main CAPs exposure systems currently in use. The Harvard Air Particle Concentrator (HAPC) uses virtual impactor technology to concentrate particles from 0.15 to 2.5 μm (Sioutas et al., 1997). The versatile aerosol concentration enrichment system (VACES) is also based on virtual impactor technology and concentrates ultrafine particles, as well as those in the fine particle range (Sioutas et al., 1999). It is important to note that both ultrafine systems (HAPC and VACES) do not uniformly concentrate particles across all size fractions and that the enrichment factor has been shown to decrease for PM sized <75 nm (Su et al., 2006). The centrifugal concentrator most efficiently concentrates particles in the 0.5–2.5 μm size range (Gordon et al., 1998). For the purposes of this provisional assessment, CAPs studies have been grouped into those that conducted source apportionment analyses or those that linked PM components to health outcomes. Additional CAPs studies that reported linkages between mass and toxicity are presented in a subsequent section.

Among the recent toxicology studies are 27 new studies reporting effects of CAPs exposure. These include several reports from a large study of subchronic exposure to CAPs that was carried out using three different mice strains. Four of the acute and one subchronic study (with an additional *in vitro* study) performed complex source apportionment or factor analyses. Eight (three human and five animal studies) used regression approaches to estimate the relationship between health effects and the concentration of individual PM constituents. Additional exposure details, endpoints, and results for all of the CAPs studies are provided in Appendix A (Tables A16–A18); the tables present only those findings that were positive in the "Results" column.

Source Apportionment Studies

Table 2 shows those endpoints which were associated with various source categories from humans exposed to Chapel Hill, NC, CAPs (Huang et al., 2003b) and mice exposed subchronically to Tuxedo, NY, CAPs (Lippman et al., 2005b). Increases in blood fibrinogen levels in healthy humans were correlated with a Cu-Zn-V factor (stated by the authors to be linked to combustion, including oil combustion) in the acute exposure study (Huang *et al.*, 2003b). In addition, elevated polymorphonuclear leukocytes in bronchoalveolar lavage fluid (BALF) were observed with CAPs, and this increase was associated with a Fe-Se-sulfate factor; the authors considered this factor to represent sulfurous smog and photochemical air pollution. There were no other identifiable CAPs factors that were linked to any health outcome.

Using mouse models, Lippmann et al. (2005b) reported post-exposure decreases in heart rate variability (HRV) parameters in subchronic exposures to CAPs for three factors—secondary sulfate, residual oil, and motor vehicles—but an increase in HRV parameters with a CAPs factor representing resuspended soil. Similar findings were reported for heart rate, with slight increases and decreases being observed for different source categories at one interval or another.

Table 2. CAPs Sources and Associated Endpoints: Acute and Subchronic Exposures

Source Category	Endpoint Affected	Time	Species	Reference
Zn-Cu-V	↑ blood fibrinogen	18 hr post-exposure	Human	Huang, Y-C.T (2003)
Fe-Se-sulfate	↑ BALF PMN	18 hr post-exposure	Human	Huang, Y-C.T (2003)
Secondary sulfate (S, Si, OC)	↓ HR ↓ SDNN, ↓ RMSSD	Afternoon post-exposure Night post-exposure	$ApoE^{-/-}$ mouse	Lippmann et al. (2005b)
Resuspended soil (Ca, Fe, Al, Si)	↓ HR ↑ HR ↑ SDNN, ↑ RMSSD	During exposure Afternoon post-exposure Night post-exposure	$ApoE^{-/-}$ mouse	Lippmann et al. (2005b)
Residual oil (V, Ni, Se)	↓ SDNN, ↓ RMSSD	Afternoon post-exposure	$ApoE^{-/-}$ mouse	Lippmann et al. (2005b)
Motor vehicle/other	↓ RMSSD	Afternoon post-exposure	C57 mouse	Lippmann et al. (2005b)

As shown in Table 2, not all source categories were linked to HR or HRV parameters at any given time during or after exposure.

One *in vivo* study employed rats and mice (Steerenberg et al., 2006) which were exposed to one of five PM types collected from Europe. The traffic, industry/combustion/incinerator, and wood smoke source clusters were associated with the adjuvant activity for respiratory allergy, whereas the secondary inorganic/long range cluster correlated with systemic allergy (Steerenberg et al., 2006). The crustal material and sea spray sources were linked to acute inflammation, although the endotoxin content also correlated with some of these biomarkers (Steerenberg et al., 2006).

In the remaining CAPs studies that included source apportionment, Batalha et al. (2002) reported changes in lumen/wall ratio, an indicator of vasoconstriction, with sulfate and Si (suggested to be an indicator of road dust) in normal rats and with OC in chronic bronchitic rats. Wellenius et al. (2003) also linked a cardiovascular response, ST-segment elevation, with Si and other crustal elements derived from Boston CAPs. In the latter study, there were a number of tracer elements that were not associated with any electrocardiogram measure, including Ni, S, and carbon black.

Studies of fine particle components in CAPs

In addition, six CAPs studies have reported associations between observed cardiovascular or respiratory endpoints and specific PM constituents. Table 3 presents more specific results, and the overall findings are briefly summarized below:

Table 3. CAPs Components and Associated Endpoints for Acute Studies

Component	Endpoint Affected	Species	Reference
Al	lipid peroxidation oxidative stress (heart)	rat rat	Rhoden et al. (2004) Gurgueira et al. (2002)
Si	lipid peroxidation oxidative stress (heart) lumen/wall ratio ST-segment elevation	rat rat rat dog	Rhoden et al. (2004) Gurgueira et al. (2002) Batalha et al. (2002) Wellenius et al. (2003)
Fe	lipid peroxidation oxidative stress (lung) oxidative stress (heart)	rat rat rat	Rhoden et al. (2004) Gurgueira et al. (2002) Gurgueira et al. (2002)
Zn	oxidative stress (lung) plasma fibrinogen	rat rat	Gurgueira et al. (2002) Kodavanti et al. (2005)
Mn	oxidative stress (lung)	rat	Gurgueira et al. (2002)
Cu	oxidative stress (lung)	rat	Gurgueira et al. (2002)
Ti	oxidative stress (heart)	rat	Gurgueira et al. (2002)
Sulfate	FEV_1 decrements FVC decrements lumen/wall ratio	human ($+NO_2$) human ($+NO_2$) rat	Gong et al. (2005) Gong et al. (2005) Batalha et al. (2002)
OC	brachial arterial diameter diastolic blood pressure lumen/wall ratio	human human rat	Urch et al. (2004) Urch et al. (2005) Batalha et al. (2002)
EC	brachial arterial diameter lumen/wall ratio	human rat	Urch et al. (2004) Batalha et al. (2002)
Pb	lumen/wall ratio	rat	Batalha et al. (2002)

- Si—oxidative stress and cardiovascular endpoints;
- Fe—oxidative stress;
- OC and EC—cardiovascular effects;
- Zn—oxidative stress and fibrinogen; and
- Sulfate—pulmonary and cardiovascular effects.

Fine Particle CAPs Studies Without Source Apportionment or Identified Components

Effects on the cardiovascular system have been reported in a number of human studies. Markers of cardiovascular function, such as brachial arterial diameter and blood pressure, have been shown to decrease with CAPs exposure (Urch et al., 2004, 2005). Increased occurrence of ectopic and abnormal beats has also been reported in healthy and COPD subjects with exposure to CAPs (Devlin et al., 2003). Similar to studies cited in the 2004 PM AQCD, elevated blood fibrinogen levels were observed in volunteers exposed for two hours to Chapel Hill, NC CAPs

(Ghio et al., 2003). Hematological alterations, including increased peripheral basophils (Gong et al., 2004a) and decreased white blood cell counts (Ghio et al., 2003), have also been reported. Two recent studies measuring heart rate (HR) and heart rate variability (HRV) have demonstrated that a single two-hour exposure to CAPs from Los Angeles, CA, or Chapel Hill, NC, can result in decreased HRV in human volunteers (Devlin et al., 2003; Gong et al., 2004a). Interestingly, in the Los Angeles studies, healthy subjects were reported to have greater decreases in HRV compared to compromised individuals with COPD (Gong et al., 2004a).

In addition, a few studies have reported some associations with respiratory health endpoints. Arterial oxygen saturation decreased in healthy and COPD patients exposed for two hours to $PM_{2.5}$ Los Angeles CAPs (Gong et al., 2005). Elevated polymorphonuclear leukocytes in bronchioalveolar lavage fluid were observed in healthy volunteers at 18-hr post-exposure to Chapel Hill, NC, CAPs (Ghio et al., 2003). Of the two recent fine CAPs studies that measured pulmonary function, only one showed decreased maximal mid-expiratory flow, forced expiratory volume and forced vital capacity and the latter two responses were only observed with co-exposure to NO_2 (Gong et al., 2005); the other study did not report any changes in spirometry or respiratory symptoms (Gong et al., 2004a).

To date, the CAPs animal studies reported in the scientific literature have been of relatively short duration (i.e., four weeks or less). There is one large subchronic PM inhalation study in the recent literature on toxicological effects of repeated exposures to ambient particles in mice exposed to Tuxedo, NY, CAPs for five or six months during the spring and summer of 2003 (Lippmann et al., 2005a; Sun et al., 2005). Following CAPs exposure, mice models of aortic and/or coronary atherosclerosis had altered HR and HRV (Chen and Hwang, 2005; Hwang et al., 2005; Lippmann et al., 2005b), advanced plaque deposits and lesions in the aorta and heart (Chen and Nadziejko, 2005), and changes in vasomotor tone (Sun et al., 2005). Additional molecular and biochemical analyses demonstrated altered gene expression post-exposure, including those genes involved in the regulation of circadian rhythm, heat shock, inflammation, and signal transduction (Gunnison and Chen, 2005). CAPs exposure also induced neurodegeneration in the substantia nigra nucleus compacta of $ApoE^{-/-}$ mice (Veronesi et al., 2005). Interestingly, subchronic CAPs-exposure did not appear to cause pulmonary effects in any mouse strain.

Finally, three reports do not specifically link PM components to health endpoints, but two draw inferences that relate the effects seen with a heavy industrial source located near the study site (Dvonch et al. 2004; Morishita et al., 2004). One additional study of mice exposed to fine CAPs in Los Angeles, downwind of heavily trafficked highways, demonstrated effects on biomarkers of inflammation in the brain (Campbell et al., 2005). Additionally, in the one *in vitro* study that applied factor analysis to CAPs for cytokine release, the oil-fired power plant emission source (comprised of V, Ni, and Se) was linked to the response, but not the regional secondary sulfate or resuspended soil factors (Maciejczyk and Chen, 2005). Considered as a group, these new studies suggest that many fine particle components can adversely affect health, and that PM-associated cardiovascular and respiratory effects may be linked to resuspended soil, regionally transported air pollution, and combustion or industrial sources.

2.4.4 Toxicology Studies—Thoracic Coarse Particles

Few studies examined the effects of thoracic coarse PM on cellular responses prior to the release of the 2004 PM AQCD. When considered together, the four *in vitro* studies discussed in Chapter 7 of the 2004 PM AQCD document provided some evidence that exposure to thoracic coarse PM may result in proinflammatory effects, as well as cytotoxicity and oxidant generation (Section 7.4.2). However, as little data was available at that time on thoracic coarse PM toxicity, a very limited evaluation of the literature was conducted. Recent publications include sixteen new studies (one human, six *in vivo*, and nine *in vitro*) that have specifically focused on the thoracic coarse fraction of PM, with the majority of these providing direct comparisons with smaller size fractions (i.e., fine and ultrafine).

In one important new study, healthy and asthmatic humans were exposed to CAPs via a high concentration efficiency coarse particle concentrator, in which 80% of the PM mass was comprised of the thoracic coarse fraction (Gong et al., 2004b). Exposure to thoracic coarse CAPs from Los Angeles also caused lowered HR and HRV. Asthmatics exposed to thoracic coarse Los Angeles CAPs had no changes in arterial oxygen saturation (Gong et al., 2004b). Healthy subjects were reported to have greater decreases in HRV compared to compromised individuals with COPD (Gong et al., 2004b).

Two *in vitro* studies evaluated cytokine release and cell viability following exposure to $PM_{2.5}$ soil dusts from a variety of southwestern U.S. locations (Veranth et al., 2004, 2006). The responses were quite variable and did not appear to be attributable to sample location category (e.g., urban/rural, road surface/open land, military/civilian) or endotoxin content. A multivariate analysis of the findings demonstrated a handful of correlations with soil dust constituents (Veranth et al., 2006).

The *in vivo* rodent studies provide evidence that the observed effects from exposure (via non-inhalation routes) to thoracic coarse or fine PM are related to the endotoxin or allergen levels, which were often associated with sampling location. These effects included elevated cytokine release (Nygaard et al., 2005; Schins et al., 2004) and adjuvant activity (Steerenberg et al., 2005). Schins et al. (2004) reported differences between thoracic coarse PM from rural and urban areas in The Netherlands, with greater responses for elevated neutrophils and tumor necrosis factor-α in BALF from rural PM, but greater induction of macrophage inflammatory protein-2 *in vitro* from urban PM (both PM types contained relatively high levels of endotoxin). Otherwise, the thoracic coarse fraction tended to induce similar toxic responses as that observed with the fine fraction. In the one study that employed coal fly ash, no differences in effects were reported for the thoracic coarse fraction compared to saline control animals (Gilmour et al., 2004).

Similar to the *in vivo* research with surrogate and size-fractionated PM, *in vitro* studies have also shown associations between the induction of inflammatory mediators and PM endotoxin content (Huang et al., 2003a; Pozzi et al., 2003), whereas others have found seasonal relationships with thoracic coarse PM effects (Becker et al., 2005b; Hetland et al., 2005; Li et al., 2002). The latter finding could be partially attributable to microbial products or their interactions with metals (Hetland et al., 2005). Becker et al. (2005b) further examined possible associations between cellular responses and PM components using principal component analysis

and reported a Cr/Al/Si/Ti/Fe/Cu factor correlating with IL-6 and IL-8 release. Examination of IL-6 induction in alveolar macrophages and IL-8 release in normal human bronchial epithelial cells following thoracic coarse PM exposure showed associations with Toll-like receptor (TLR) 4 and TLR2 gene expression, respectively (Becker et al., 2005a). Generation of hydroxyl radicals has also been recently observed with thoracic coarse PM (Shi et al., 2003). In contrast, some studies have also demonstrated greater effects with the fine or ultrafine size fraction compared to thoracic coarse PM (Li et al., 2002; Li et al., 2003; Gilmour et al., 2004).

2.4.5 Toxicology Studies—Comparison of Ambient PM

There were numerous studies included in the 2004 PM AQCD that employed ambient particles collected on filters. These included extracts of collected or stored PM and the majority of studies utilized Ottawa (EHC-93) or Provo, Utah PM_{10}. Generally, animals exposed to these particles had elevated biomarkers of pulmonary injury and inflammation, as well as systemic and cardiovascular responses (Chapter 7). The 2004 PM AQCD stated that studies using collected urban PM "have provided evidence indicating that the chemical composition of ambient particles can have a major influence on toxicity" (Section 7.10.2.1, pg 7-127). The results of research published since 2002 have largely supported and expanded the findings of previous studies cited in the 2004 PM AQCD. Five studies are highlighted which evaluated the toxicity of urban PM or that collected on filters (one human, two *in vivo*, and two *in vitro*). Further details on these studies are included in Table A19 (Appendix A).

Two recent studies investigated the effects of urban (Hettstedt) and rural (Zerbst) particles ($PM_{2.5}$) on lung inflammation and pulmonary function in humans and rodents (Gavett et al., 2003; Schaumann et al., 2004). In healthy human volunteers, instillation of either PM induced airway inflammation, whereas Hettstedt PM resulted in greater influxes of BALF monocytes and increased oxidant radical generation compared Zerbst PM (Schaumann et al., 2004). In allergic mice, exposure to either PM type induced lung injury and proinflammatory cytokines (Gavett et al., 2003). However, aspiration of Hettstedt PM caused heightened airway responsiveness and elevated lung inflammatory cells in sensitized mice exposed before allergen challenge (Gavett et al., 2003). The endotoxin content was below 0.32 EU/mg in both PM samples.

Two other *in vivo* toxicology studies examined the cardiovascular and cytogenetic effects of urban PM exposure (Rhoden et al., 2005; Soares et al., 2003). Rhoden et al. (2005) compared autonomic nervous system (ANS) effects between Boston CAPs (via inhalation) and SRM 1649 (via intratracheal instillation). Both particles altered ANS function and these changes preceded and were required for increased cardiac reactive oxygen species generation (Rhoden et al., 2005). Soares et al. (2003) measured micronuclei (MN) in peripheral erythrocytes of mice exposed to urban air of Sao Paulo or Atibaia, Brazil (with the latter being a rural location) and reported that there were significant increases in MN frequency for mice exposed to the Sao Paulo atmosphere.

The results of recent studies assessing effects of different components from different particle samples or size classes are summarized in Table 4, along with other studies that attempted to link *in vitro* effects with PM components (discussed in the preceding section).

Table 4. PM Components, Size Fractions, and Associated *In Vitro* Toxicity

Component	Endpoint Affected	Size Fraction	Cell Type	Reference
Br	IL-8	Fine	BEAS-2B	Veranth et al. (2006)
Cr	IL-8 IL-8 TNF-α	Fine, ultrafine Fine Ultrafine	NHBE BEAS-2B RAW 264.7	Becker et al. (2005b) Huang et al. (2003a) Huang et al. (2003a)
Cu	Hydroxyl radical 8-OHdG formation	Coarse Coarse	A549 A549	Shi et al. (2003) Shi et al. (2003)
Si	IL-6	Coarse	Human AM	Becker et al. (2005b)
Fe	IL-6 TNF-α	Coarse, fine Ultrafine	Human AM RAW 264.7	Becker et al. (2005b) Huang et al. (2003a)
Mn	IL-8 Cell viability	Fine Fine	BEAS-2B BEAS-2B	Huang et al. (2003a) Veranth et al. (2006)
Ni	IL-6	Fine	BEAS-2B	Veranth et al. (2006)
OC	Lipid peroxidation IL-6 Hydroxyl radical	Fine Fine Ultrafine	BEAS-2B BEAS-2B BEAS-2B	Huang et al. (2003a) Veranth et al. (2006) Li et al. (2003)
EC	Lipid peroxidation IL-6	Fine Fine	BEAS-2B BEAS-2B	Huang et al. (2003a) Veranth et al. (2006)

These recent studies continue to show that exposure to different types of surrogate fine PM is associated with a range of health outcomes, particularly those related to the cardiovascular system. These findings also expand upon the body of evidence related to the effects of thoracic coarse particles and PM composition. Exposure to thoracic coarse particles has been linked with a number of effects, including inflammatory mediator release and reactive oxygen species generation. The results are still too limited to draw conclusions about specific thoracic coarse particle components and health outcomes, but it appears that endotoxin and metals potentially play roles in the observed responses. While these studies provide interesting new insight into potential links between different types of particles and observed effects, it is much too early to distinguish any PM components as being primarily responsible for any specific effect or conversely, as not involved in any toxicological response.

2.4.6 Studies of Specific Fine Particle Components or Characteristics

Toxicological evidence on the effects of different types of particles or particle components was discussed in Section 7.10.2 of the 2004 PM AQCD. The particle characteristics or sources discussed included acid aerosols, metals, diesel exhaust particles, organic components, ultrafine particles and bioaerosols. In addition to the discussions above, EPA observes that numerous recent individual toxicology studies have investigated the effects of exposure to these particle components or characteristics. For this provisional assessment, EPA has not critically reviewed the large number of studies that have assessed effects of

individual components, but will highlight below the general nature of the new findings. Bibliographies for these groups of particle types or characteristics are included in Attachment B.

The main overarching conclusion from these groups of studies is that the recent studies generally substantiate and support conclusions drawn from earlier work. For example, numerous studies had suggested that metals (e.g., transition metals such as V or Ni) contributed to the toxic effects observed with PM exposures (albeit at generally high exposure levels). Recently-published studies provide more evidence that metal constituents of particles may play important roles in PM-related toxicity.

Ultrafine Particles: The 2004 PM AQCD had an extensive discussion of the physical and chemical properties and behavior of ultrafine particles (diameter <0.1 μm). A growing body of evidence from toxicology studies indicated that ultrafine particles were linked with a number of health outcomes; however, there was very limited information on the health effects of ultrafine particles from epidemiologic studies. The 2004 PM AQCD observed that acute exposures to ultrafine particles were associated with slight increases in blood viscosity and with respiratory symptoms or decreased lung function, and one study had reported associations with mortality. Toxicological studies used various types of ultrafine model particles (e.g., carbon black), and reported greater inflammatory responses when compared at the same mass of fine particles of the same chemical composition at similar mass doses (2004 PM AQCD, p. 7-221). Hence, in the ambient environment where fine particle mass greatly exceeds ultrafine mass, it remains to be determined whether this relative difference in potency is reflected in real world exposures.

Since April 2002, about 60 recent studies have evaluated effects of ultrafine particles, and over 150 have assessed effects associated with diesel exhaust or traffic-related PM (see Attachment B). Diesel and other forms of traffic are considered to be major sources of atmospheric ultrafine PM. Recent toxicology studies continue to indicate that ultrafine particles have effects and many toxicology studies indicate that, on a mass basis, ultrafine particles are more toxic than fine particles. Ultrafine particles have been observed to translocate from the olfactory mucosa to the brain and from the lungs to the liver and the systemic circulation. However, a number of uncertainties remain regarding the extent of ultrafine particle extrapulmonary translocation, including clearance rates and routes (e.g., lymphatic system or gastrointestinal tract). Ultrafine particles appear to enter cells and cause mitochondrial damage, based on evidence from *in vitro* studies. Most studies using laboratory-generated carbon particles do not demonstrate lung inflammation, but report cardiac and vascular effects. Additionally, exposure to ambient ultrafine PM causes lung inflammation that is associated with organic carbon carried by the ultrafine particles. A few epidemiologic studies have associated health effects with particle number, particle surface area, or active surface area, all variables that are thought to be associated more with ultrafine than fine particles. As was true in the 2004 PM AQCD, the epidemiologic studies generally do not indicate that ultrafine PM is more strongly associated with health effects than fine PM. In general, studies report associations between both fine and ultrafine particles, and in a number of cases the associations are reported to be stronger for fine than for ultrafine PM. Thus, further evaluation is needed on effects of ultrafine particles in the next review of the PM NAAQS.

Sulfates and Acid Aerosols: As stated in the 2004 PM AQCD, there is "little new information on the effects of acid aerosols." There was a much more extensive discussion on the toxicity of sulfates in Section 11.2 of the previous PM AQCD (U.S. EPA 1996), which concluded that human and animal toxicology studies indicated that acid aerosols are associated with small changes in pulmonary function, but generally at concentrations greater than those measured in ambient air. The results of four recent acid aerosol toxicological studies generally agree with conclusions in the 2004 PM AQCD. Three of these studies involve controlled human and animal exposures to acid aerosols with or without gaseous co-pollutants such as ozone (O_3). One study employed *in vitro* techniques to assess the toxic effects of sulfate on different cell types, including alveolar macrophages and blood polymorphonuclear leukocytes. As shown in Table A20 the recent studies reported limited evidence for effects with exposure to sulfuric acid or sulfate aerosols. One study found that there was some suggestion for interactive effects with ozone (Kleinman et al., 2003). There were no new toxicological studies published in the last four years that utilized nitrate aerosols (i.e., ammonium nitrate or nitric acid) to examine health outcomes.

Diesel exhaust particles: This source of particles has been the subject of numerous studies; the 2004 PM AQCD highlighted findings from the Diesel Health Assessment Document along with some additional studies. There are a number of new studies which have investigated the toxicity of diesel exhaust by eliminating the particle or gas portion of the exposure atmosphere or by separating the organic constituents from the carbonaceous core. Some studies have suggested that the gases, organic particle compounds, or particle core are responsible for the observed effects, and it is likely that all exhaust components contribute to toxicity. Comparison of these results across laboratories or studies is difficult, as the composition of diesel exhaust is highly dependent upon the generation method.

Traffic-related particles: A large body of literature is accumulating on a range of health effects that may be associated with exposure to traffic. These exposures include both particulate and gaseous pollutants and the reported findings include cardiovascular responses, inflammatory changes, allergenic effects, and mutagenicity. Toxicology studies and a partially annotated bibliography of epidemiologic studies are included in Attachment B.

Organic compounds: Little evidence was available on effects of particulate organic compounds in the 2004 PM AQCD (Section 7.10.2.5). A number of the recently published studies have used fine particle speciation data, along with factor analysis methods, to assess potential effects of the organic component of fine PM. Previous studies indicated that PM organic compounds (e.g., PAHs) can be mutagenic. However, few studies had provided information on potential associations with other health endpoints. Recent study results suggest that organic constituents of ambient PM can be linked to a number of biomarker and physiological responses, such as lipid peroxidation and oxidative stress generation, cytokine release, elevated plasma fibrinogen, and decreased diastolic blood pressure and vessel diameter.

Metals: As stated in Section 7.10.2.3 in the 2004 PM AQCD, the effects of metals leached from ambient filter extracts or residual oil fly ash have been shown to consistently result in cell injury and inflammation (albeit often at high concentrations). A number of new studies have reported that exposure to metals results in detectable health effects (see Attachment B).

These recent studies highlight findings for several metals which may be involved in PM toxicological effects, including Fe, Zn, V, and Ni. Furthermore, the activation of select pro-inflammatory pathways with metal exposure has been linked to particular cell surface receptors. Other research suggests a role for metal-containing PM (including those derived from oil or coal combustion sources) in altering cardiovascular parameters, which is consistent with the epidemiological findings.

Conclusions

Recent analyses continue to indicate that particles related to traffic, residual oil combustion, wood smoke, and regional sulfate pollution and primary coal burning are associated with increased mortality. A number of new studies continue to indicate that traffic-related PM exposures are associated with mortality and morbidity. Recent epidemiologic observations continue to support associations between various fine PM components and both mortality and morbidity effects.

3. SUMMARY AND CONCLUSIONS

The new study results support and expand upon findings in the 2004 PM AQCD and provide interesting new insights into relationships between ambient particles and health effects. The essential conclusions of this provisional assessment are that the science supporting evaluation of the potential health impacts of PM on human health continues to expand and hence provides a larger knowledge base for better characterizing the relationships between fine and thoracic coarse particles and health effects. The new studies provide important insights on the health effects of PM exposure, but the results do not dramatically diverge from previous findings. We find that: (a) the new studies generally strengthen the evidence that acute and chronic exposures to fine particles and acute exposure to thoracic coarse particles are associated with health effects, (b) some of the new epidemiologic studies report effects in areas with lower concentrations of $PM_{2.5}$ or $PM_{10-2.5}$ than earlier reports; (c) new toxicology and epidemiologic studies link various health outcomes with a range of fine particle sources and components, in particular from traffic-related pollution; and (d) new toxicology studies report effects of thoracic coarse particles, but do not provide evidence to support distinguishing effects from exposure to urban and rural particles. This survey and provisional assessment of new studies does not materially change any of the broad scientific conclusions regarding the health effects of PM exposure made in the 2004 PM AQCD.

In brief, this provisional assessment found:

- Recent epidemiologic studies, most of which are follow-ups or extensions of earlier work, continue to find that *long-term exposure to fine particles* is associated with both mortality and morbidity, as was stated in the 2004 PM AQCD. Notably, a follow-up to the Six Cities study shows that an overall reduction in $PM_{2.5}$ levels results in reduced long-term mortality risk. Both this study and an analysis of the ACS cohort data in Los Angeles suggest that previous studies may have underestimated the magnitude of mortality risks. Some studies provide more mixed results, including the suggestion that

higher traffic density may be an important factor. In addition, the California Children's Health study reported measures of $PM_{2.5}$ exposure and PM components and gases were associated with reduction in lung function growth in children, increasing the evidence for increased susceptibility early in life, as was suggested in the 2004 AQCD. In addition, one study reported increased infant mortality from respiratory causes with exposure to $PM_{2.5}$. The results of recent epidemiologic and toxicology studies have also reported new evidence linking long-term exposure to fine particles with a measure of atherosclerosis development and, in a cohort of individuals with cystic fibrosis, respiratory exacerbations.

- Recent epidemiologic studies have also continued to report associations between *acute exposure to fine particles* and mortality and morbidity health endpoints. These include three multi-city analyses, the largest of which (in 204 counties) shows a significant association between acute fine PM exposures and hospitalization for cardiovascular and respiratory diseases, and suggestions of differential effects in eastern U.S. as opposed to western U.S. locations. The new studies support previous conclusions that short-term exposure to fine PM is associated with both mortality and morbidity, including a substantial number of studies reporting associations with cardiovascular and respiratory health outcomes such as changes in heart rhythm or increases in exhaled NO. The fine PM concentrations reported in these studies are in some cases lower than in the previously-published studies.

- New toxicology and epidemiologic studies have continued to link health outcomes with a range of *fine particle sources and components*. Source apportionment epidemiologic analyses were conducted by teams of analysts for two cities, and the results indicate that fine PM from several sources, including regional sulfate and several combustion sources, are associated with mortality. Additionally, a number of new studies indicate that traffic-related PM exposures are associated with mortality and morbidity. A few new toxicology studies have used source apportionment techniques to assess effects related to PM from different emission categories. While limited in number and preliminary in nature, the findings suggest that several PM sources may contribute to toxicity, including combustion-related sources and regional sulfate pollution, as suggested in epidemiologic studies. Several studies have also indicated that particles from resuspended soils, such as road dust, may be associated with health effects. Toxicology studies indicate that various components, including metals, sulfates, and elemental carbon and organic carbon, are linked with health outcomes, albeit at generally high concentrations. Recent epidemiologic studies also report associations between sulfates and mortality and morbidity, and provide new evidence that organic or elemental carbon may be linked with health effects.

- The recent epidemiologic studies greatly expand the evidence on health effects of *acute exposure to thoracic coarse particles*. The 2004 PM AQCD conclusion that $PM_{10-2.5}$ exposure was associated with respiratory morbidity is substantially strengthened with these new studies; several epidemiologic studies, in fact, report stronger evidence of associations for hospital admissions with thoracic coarse particles than for fine particles. Some of the recent morbidity studies were also located in cities with low $PM_{10-2.5}$

concentrations. For example, significant associations have been reported with respiratory hospital admissions in several Canadian studies, where the reported mean and maximum $PM_{10-2.5}$ concentrations ranged from about 6 to 12 $\mu g/m^3$ and 25 to 70 $\mu g/m^3$, respectively. For mortality, many studies do not report statistically significant associations, though one new analysis reports a significant association with cardiovascular mortality in Vancouver, Canada.

- New toxicology studies have demonstrated that exposure to *thoracic coarse particles*, or PM sources generally representative of this size fraction (e.g., road dust), can result in inflammation and other health responses. Clinical exposure of healthy and asthmatic humans to concentrated ambient air particles comprised mostly of $PM_{10-2.5}$ showed changes in heart rate and heart rate variability measures. The results are still too limited to draw conclusions about specific thoracic coarse particle components and health outcomes, but it appears that endotoxin and metals may play a role in the observed responses. Two studies comparing toxicity of dust from soils and road surfaces found variable toxic responses from both rural and urban locations.

- Evidence of associations between *long-term exposure to thoracic coarse particles* and either mortality or morbidity remains limited.

- Significant associations between improvements in health and reductions in PM and other air pollutants have been reported in intervention studies or "found experiments." One new study reported reduced mortality risk with reduced $PM_{2.5}$ concentrations. In addition, several studies, largely outside the U.S., reported reduced respiratory morbidity with lowered air pollutant concentrations, providing further support for the epidemiological evidence that links PM exposure to adverse health effects.

PM PROVISIONAL ASSESSMENT—ABBREVIATIONS AND ACRONYMS

A549	human alveolar basal epithelial cell line
AA	arachidonic acid
ACE	angiotensin converting enzyme
ACS	American Cancer Society
ADMA	asymmetric dimethylarginine
AHSMOG	Adventist Health and Smog
ARIES	Aerosol Research and Inhalation and Epidemiology Study
ALP	alkaline phosphatase
AM	alveolar macrophage
$ApoE^{-/-}$	apolipoprotein deficient (mouse model of atherosclerosis)
AQS	Air Quality System
β-gluc	β-glucuronide
BAD	brachial artery diameter
BALF	bronchoalveolar lavage fluid
BC	black carbon
BEAS-2B	human bronchial epithelial cell line
BN	Brown Norway (rat)
BP	blood pressure
BrdU	bromodeoxyuridine
BS	black smoke
CAPs	concentrated ambient particles
CARB	California Air Resources Board
CB	chronic bronchitis
CBC	complete blood count
CC16	clara-cell 16 protein
CD11b	cell surface receptor
CI	confidence interval
CL	chemiluminescence
CO	carbon monoxide
CO	carbon dioxide
CoH	Coefficient of Haze
CPC	coarse particle concentrator
CRP	C-reactive protein

COPD	chronic obstructive pulmonary disease
CVD	cardiovascular disease
DBP	diastolic blood pressure
DD	desert dust
DK	double knockout mouse strain (for ApoE and LDL)
DNA	deoxyribonucleic acid
EC	elemental carbon
ECG	electrocardiogram
eNO	exhaled nitric oxide
eNOS	endothelial nitric oxide synthase
ER	emergency room
ERK	extracellular signal-regulated kinase
ET	endothelein
f	breathing frequency
F344	Fischer 344 (rat)
FA	filtered air
FE_{NO}	fractional exhaled nitric oxide
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
GAM	general additive model
GEE	generalized estimating equations
GGT	γ-glutamyl transferase
GLM	Generalized Linear Model
SD	geometric standard deviation
GSH	reduced glutathione
GSH/GSSG	reduced glutathione/glutathione disulfide (ratio)
GSSG	glutathione disulfide
H&E	hematoxylin and eosin
HAPC	Harvard ambient fine particle concentrator
Hb	hemoglobin
Hct	hematocrit
5-HETE	5-hydroxy-eicosatetraenoic acid
HF	high frequency of heart rate variability
12-HHT	12-hydroxyheptadecatrienoic acid
HO-1	heme oxygenase

HR	heart rate
HRV	heart rate variability
H_2SO_4	sulfuric acid
ICAM	intercellular adhesion molecules
ICD	Implantable cardioverter defibrillator
ICP-MS	inductively coupled plasma mass spectrometry
Ig	immunoglobulin (e.g., IgA, IgE, IgG, IgM)
IHD	ischemic heart disease
IL	interleukin (e.g., IL-5, IL-6, IL-8, IL-13)
IMPROVE	Interagency Monitoring of Protected Visual Environments (network)
iNOS	inducible nitric oxide synthase
IPN	Inhalable Particle Network
IQR	interquartile range
IT	Intratracheal instillation
JNK	Jun kinase
LBW	low birth weight
LDH	lactate dehydrogenase
LF	low frequency component of heart rate variability
$LDL^{-/-}$	low-density lipoprotein receptor deficient
LPS	lipopolysaccharide
LRI	lower respiratory infection
LT	leukotriene (e.g., LTB_4)
L/W	lumen to wall (ratio)
MAP	mean arterial pressure
MCh	methacholine
MCT	monocrotaline
MCV	Mean cell volume
MI	myocardial infarction
MIP	macrophage inflammatory protein (e.g., MIP-1α, MIP-2)
MLRA	multiple linear regression analysis
MMD	mass median diameter
MMEF	maximal mid-expiratory flow
MN	micronuclei
mm Hg	millimeters of mercury
MPO	myeloperoxidase

MV	minute ventilation
n	number of observations
NAC	*N*-acetyl cysteine
NAG	*N*-acetyl-β-D-glucosaminidase
NHAPS	National Human Activity Pattern Survey
NHBE	normal human bronchial epithelial (cells)
NF-κB	nuclear transcription factor-κB
NN	normal-to-normal (R-R) interval of electrocardiogram
NO	nitric oxide
NO_2	nitrogen dioxide
NO_3	nitrate
NOI	nose-only inhalation
NR	not reported
O_3	ozone
OC	organic carbon
OHC	oxygenated hydrocarbons
8-OHdG	8-hydroxy-2'-deoxyguanosine
OR	odds ratio
OVA	ovalbumin
p	probability value
PAF	platelet activating factor
PAH	polycyclic aromatic hydrocarbon
PAU	pause
PE	post-exposure
PEF	peak expiratory flow
PIF	peak inspiratory flow
Penh	enhanced pause
PG	prostaglandin (e.g., PGE_2)
PLA_2	phospholipase-A2
PLN	popliteal lymph node
PM	particulate matter
$PM_{2.5}$	fine particulate matter (mass median aerodynamic diameter ≤2.5 μm)
PM_{10}	combination of coarse and fine particulate matter
$PM_{10\text{-}2.5}$	Thoracic coarse particulate matter (mass median aerodynamic diameter between 10 and 2.5 μm)

PMN	polymorphonuclear leukocyte
PMR	proportionate mortality ratio
PNC	particle number concentration
PNN50	percentage of NN intervals >50 msec (measure of heart rate variability)
ppb	parts per billion
ppm	parts per million
QAI	QA-interval
R4	range 40
RAW 264.7	mouse macrophage cell line
R_{aw}	airway resistance
RBC	red blood cell
RMSSD	root mean square of successive differences of adjacent normal-to-normal intervals
RO	residual oil
ROFA	residual oil fly ash
ROI	reactive oxygen intermediates
ROS	reactive oxygen species
RR	risk ratio
RS	resuspended oil
RTD	road tunnel dust
SaO_2	arterial oxygen saturation
SD	Sprague-Dawley (rat)
SDNN	standard deviation of normal-to-normal intervals
SES	socioeconomic status
SH	spontaneously hypertensive
SIDS	sudden infant death syndrome
SMPS	scanning mobility particle sizer
SO_2	sulfur dioxide
SO_4^{2-}	sulfate
SOD	superoxide dismutase
SRM	Standard Reference Material
SpO_2	arterial oxygen saturation
SS	secondary sulfate
TBARS	thiobarbituric acid-reactive species
TEOM	tapered element oscillating microbalance

THP-1	human monocytic leukemia cell line
TLC	total lung capacity
TLR4	toll-like receptor-4
TNF	tumor necrosis factor (e.g., TNF-α)
TRPV1	transient receptor potential vanilloid
TSP	total suspended particulates
TWA	time-weighted average
TX	tromboxane (e.g., TXB_2)
UA	uric acid
UCPC	ultrafine condensation particle counter
UF	ultrafine
URI	upper respiratory infection
USC	University of Southern California
V_T	tidal volume
VACES	versatile aerosol concentration enrichment system
WB	whole blood
WBC	white blood cell
WBI	whole body inhalation
WKY	Wistar-Kyoto (rat)

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APPENDIX A

Summary Information from Recent Studies on the Health Effects of Particulate Matter

Table A1: Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Mortality Studies:				
Harvard Six Cities follow-up Laden et al. (2006)	Initial Harvard impactor data for 1974-1989 (period I). Period II data (1990-1998) based on additional $PM_{2.5}$ data (a) estimated from visibility and PM_{10} measurements and (b) measured at AQS monitors w/in 50 miles; r = 0.93 between estimated and measured $PM_{2.5}$. $PM_{2.5}$ decreases ranged from <1 $\mu g/m^3$/decade in Topeka to 7 $\mu g/m^3$/decade in Steubenville. Recent $PM_{2.5}$ means range from 10.2 to 22 $\mu g/m^3$	8096 white participants, 25+ yr, death records through 1998.	RR (total mortality) for $PM_{2.5}$ (per 10 $\mu g/m^3$): entire study period: 1.16 (1.07-1.26) period I: 1.17 (1.08-1.26) period II: 1.13 (1.01-1.27) RR with $PM_{2.5}$ in year of death: 1.14 (1.06-1.22) RR for reduced mortality risk with reduction in $PM_{2.5}$: 0.73 (0.57-0.95). Similar results presented for cardiovascular and respiratory deaths. Positive, nonsignificant associations reported for lung cancer deaths in different periods, but no significant association for reduced risk.	Lower risk ratios in second period suggests that "$PM_{2.5}$ associated mortality in this 25 year follow-up was at least in part reversible".

Table A1 (cont'd): Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Mortality Studies (cont'd)**:**				
AHSMOG Chen et al., 2005	1973-1998 CARB data for PM_{10} and gases; $PM_{2.5}$ estimated from visibility; no discussion of $PM_{10-2.5}$ determination. Monthly estimates (1973-1998) of PM for each individual. $PM_{2.5}$ mean = 29.0 μg/m^3 $PM_{10-2.5}$ mean = 25.4 μg/m^3	3239 Adventist adults, fatal coronary heart disease (ICD 410-414) (92 cases)	Significant associations in females, not males; stronger and statistically significant associations in subset of postmenopausal females (80 of 92 cases). Females: $PM_{2.5}$ RR = 1.42 (1.06-1.90) and remains significant in 2-pollutant models (increased size with O_3 and SO_2, no change with NO_2) $PM_{10-2.5}$ RR = 1.38 (0.97-1.95) and increases, becomes significant with O_3 and NO_2 in 2-pollutant models, little change with SO_2. Males: $PM_{2.5}$ RR = 0.90 (0.76-1.05) $PM_{10-2.5}$ RR = 0.92 (0.66-1.29) (both little change with co-pollutants) (all per 10 μg/m^3)	Authors note consistency with results of Kunzli et al. (2005); "suggests that health effects of air pollution are different in males and females." Also observe "we cannot rule out the possibility" that there is differential measurement error since males were more likely to work >5 miles from home. Note: susceptible groups (e.g., CHD, stroke, diabetes) excluded)
ACS, Los Angeles Jerrett et al., 2005	$PM_{2.5}$ from 23 stations in LA basin (and 42 ozone monitors) for year 2000. Kriging and interpolation methods used to assign exposure levels. Also traffic buffers of 500 and 100 m from freeway based on zip code centroids $PM_{2.5}$ mean = NR, range 9-27 μg/m^3	22,905 subjects in 267 zip code areas; death records 1982-2000	Significant associations between $PM_{2.5}$ and deaths from all causes (RR 1.24, 1.11-1.37 per 10 μg/m^3), IHD, cardiopulmonary diseases, lung cancer, endocrine disease, digestive disease. No significant associations with digestive and other cancers, diabetes, accidents and other causes. Associations generally decreased with addition of ecologic covariates. After adjustment for 44 covariates and freeways w/in 500 m, significant associations with death from all causes (RR 1.17, 1.05-1.31) and IHD (RR 1.38, 1.11-1.72).	"Generally, our results agree with recent evidence suggesting that intraurban exposure gradients may be associated with even larger health effects than reported in interurban studies."

Table A1 (cont'd): Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Mortality Studies (cont'd)**:**				
ACS, cause-specific deaths Pope et al. (2004)	Results reported for average $PM_{2.5}$ exposure levels, using IPN data from 1979-1983 (mean 21.1 $\mu g/m^3$) and AQS data from 1999-2000 (mean 14.0 $\mu g/m^3$). 3-digit zip codes at residence used for exposure estimates. $PM_{2.5}$ mean 17.1 $\mu g/m^3$ (averaged data)	ACS cohort, 16-year follow-up, ~300,000 subjects	Significant associations between average $PM_{2.5}$ and all CV diseases (RR 1.12, 1.08-1.15), IHD (RR 1.18, 1.14-1.23) and dysrhythmias/heart failure/cardiac arrest (RR 1.13, 1.05-1.21). Positive nonsignificant associations with some other CV diseases. Negative association with COPD (RR 0.84, 0.77-0.93) and no associations with diabetes, pneumonia and other respiratory diseases.	When stratified by smoking status, significant associations reported between $PM_{2.5}$ and mortality from all CV diseases and IHD for all three categories (never, former and current smokers). For dysrhythmia and hypertension, significant associations in the current smokers group.

Table A1 (cont'd): Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Mortality Studies (cont'd)**:**				
Veterans cohort Lipfert et al. (2006)	Traffic density estimated [vehicle-km traveled/county land area] using data from 1985, 1990 and 1997. $PM_{2.5}$ data restricted to 1999-2001, averaged across period. $PM_{2.5}$ mean of 14.6 μg/m^3 for 1997-2001; sulfate mean 10.7 μg/m^3 for 1976-1981; $PM_{10-2.5}$ mean 16.0 μg/m^3 for 1989-1996.	Veterans cohort, deaths through 2001, ~25,000 subjects	For cohort members dying in 1989-1996 who originally lived in counties with AQ data: significant associations with: traffic density (RR 1.176, 1.100-1.258 per 2.6 10^6 vehicles km^2 in 1999 data) $PM_{2.5}$ (RR 1.118, 1.038-1.203 per 8 μg/m^3 1999 data) $PM_{10-2.5}$ (RR 1.072, 1.013-1.124 per 12 μg/m^3 1999 data) nonsulfate $PM_{2.5}$ (RR 1.091, 1.025-1.161) but not sulfates. In 3-poll models, traffic density is little changed, $PM_{2.5}$ effect reduced and nonsignificant (RR 1.032) and $PM_{10-2.5}$ effect negative, nonsignificant. Significant associations between mortality and traffic density in all time periods (RR's range from 1.019-1.036). Also significant associations with peak O_3 (95^{th} percentile of daily max values).	"...modest changes in traffic-related mortality risks over time, from 1976-2001, despite the decline in regulated tailpipe emissions per vehicle since the mid-1970s. This suggests that other environmental effects may be involved, such as particles from brake, tire and road wear, traffic noise, psychological stress, and spatial gradients in socioeconomic status."

Table A1 (cont'd): Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Mortality Studies (cont'd)**:**				
Veterans cohort Lipfert et al. (in press)	Traffic density and historic air pollution data used as Lipfert et al., 2006, also fine particle speciation data from 2002. Gravimetric $PM_{2.5}$ mean of 13.2 $\mu g/m^3$ for 2002	Veterans cohort, deaths through 2001	In single-pollutant models for 1997-2001 mortality and 1999-2001 AQ data and 2002 speciation data, significant associations reported between mortality and traffic density, EC, nitrate, V and Ni. In two- or three-pollutant models, traffic density associations remain significant. Associations with nitrates, V and Ni also remain significant in some multi-pollutant models. Peak ozone concentration also significantly associated with mortality. $PM_{2.5}$ and sulfates also positively associated with mortality, but not statistically significant.	"Traffic density is also consistently the most important environmental predictor in multiple-pollutant models . . . it is not possible to discern which aspects of traffic (pollution, noise, stress) may be the most relevant to public health or whether an area-based predictor such as traffic density may have an inherent advantage over localized measures of ambient air quality. It is also possible that traffic density could be a marker for unmeasured pollutants or for geographic gradients *per se*."

Table A1 (cont'd): Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Mortality Studies (cont'd)**:**				
CA cancer prevention study Enstrom et al. (2005)	1979-1983 IPN data for 11 CA counties, average over time and across stations for each county. overall $PM_{2.5}$ mean 23.4 $\mu g/m^3$ (10.6-42.0 range)	35,789 elderly people in 11 CA counties with $PM_{2.5}$ data (28,441 deaths by 2002)	Many results presented. RR's presented for each county relative to Los Angeles ($PM_{2.5}$ mean 28.2 $\mu g/m^3$) and none are significant, many negative. RR's by decade of death-significant associations for 1973-1982, not for 1983-92 or 1993-2002. For 1973-1982 period, RR reduced somewhat but remains significant with addition of individual potential confounders (e.g., age, sex); for 1973-2002 and 1983-2002 more marked reduction in RR size and loss of significance with addition of covariates.	"These epidemiologic results do not support a current relationship between fine particulate pollution and total mortality in elderly Californians, but they do not rule out a small effect, particularly before 1983." Note: use of California county-level average levels as an exposure surrogate likely leads to significant exposure error.
U.S. cystic fibrosis cohort Goss et al. (2004)	AQS data for 2000, annual average, subject assigned data from population-oriented monitor closest to zip code centroid. 713 monitors for $PM_{2.5}$ PM_{10} mean 24.9 (20.3-28.9) $\mu g/m^3$ $PM_{2.5}$ mean 13.7 (11.8-15.9) $\mu g/m^3$	11,484 adults and children >5 yr, enrolled in Cystic Fibrosis Foundation National Patient Registry in 1999-2000.	Main reported results are respiratory symptoms (below). Also evaluated associations with mortality from 22,303 patients in initial cohort (fewer than 200 deaths in cohort). Positive nonsignificant association reported for $PM_{2.5}$ (RR 1.32, 0.91-1.93), no associations with PM_{10}, O_3, NO_2, SO_2 or CO.	

Table A1 (cont'd): Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Mortality Studies (cont'd)**:**				
California Woodruff et al. (2006)	CARB air monitoring data obtained. Birth record data linked to data from monitor w/in 5 miles of mother's residence; data averaged over time period between birth and death. $PM_{2.5}$ means ranged from 17.3 to 19.8 $\mu g/m^3$ for different groups	Birth records for infants born in California 1999-2000 (n = 788 infant deaths)	Median concentrations of $PM_{2.5}$ were somewhat higher for infant deaths from all causes or respiratory causes than concentrations for matched survivors; not for SIDS or external causes. OR for all-cause deaths (adjusted for maternal characteristics) 1.07 (0.93-1.24) , and for respiratory deaths 2.13 (1.12-4.05) per 10 $\mu g/m^3$ $PM_{2.5}$	
Morbidity studies:				
2 atheroschlerosis clinical trials, Los Angeles CA, Kunzli et al. (2005)	Using data from 23 monitoring sites in 2000, modeling used to assign exposure at zip code level. Mean $PM_{2.5}$ exposure level at 20.6 $\mu g/m^3$, range 5.2-26.9 $\mu g/m^3$.	798 adults in 2 studies in LA basin.	Outcome measure = CIMT (carotid intima-media thickness), a measure of atherosclerosis. Significant associations of 5.9% (1-11%) increase in CIMT per 20 $\mu g/m^3$ $PM_{2.5}$ for total study population. Effects significant in women, not in men; strongest association for women >60 yr	
CA Children's Health Study Gauderman et al. (2004)	Means of annual averages (1994-2000) of measurements from stations in 12 communities, included PM_{10} (hourly) and $PM_{2.5}$ (2-week integrated filter), acid vapor, ED and OC. Mean $PM_{2.5}$ ranges from 5 to 28 $\mu g/m^3$ from figure.	Recruited 1759 4^{th} grade children	Significant decreases in FEV_1 growth with $PM_{2.5}$, acid vapor, ED and NO_2. Decreases also for FVC and MMEF growth but less often statistically significant.	"...current levels of air pollution have chronic, adverse effects on lung development in children from the age of 10 to 18 years, leading to clinically significant deficits in attained FEV_1 as children reach adulthood."

Table A1 (cont'd): Associations Between Long-Term Exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and Mortality and Morbidity

Cohort, Location Study	PM Data, Concentrations	Cohort Description	Quantitative Results	Comments and Author Conclusions
Morbidity studies (cont'd)**:**				
CA Children's Health Study Millstein et al. (2004)	Monthly means of pollutant data (data presented in figures only).	2034 4th grade children, questionnaire in 1995.	Monthly prevalence of asthma medication use associated with monthly average O_3, HNO_3, and acetic acid levels, not with $PM_{2.5}$, PM_{10} or $PM_{10-2.5}$. Prevalence of wheeze associated with $PM_{10-2.5}$ during spring and summer months.	
CA Children's Health Study McConnell et al. (2003)	4-year means of pollutants for 1996-1999 (same sites from Gauderman et al. (2004); $PM_{10-2.5}$ determined by subtraction of $PM_{2.5}$ from PM_{10} (2-wk integrated). Means across communities of 13.8 µg/m^3 $PM_{2.5}$, 17.0 µg/m^3 $PM_{10-2.5}$	475 children with asthma, questionnaire 1996-1999	Bronchitic symptoms associated with yearly variability of $PM_{2.5}$ (per µg/m^3), OR 1.09 (1.01-1.17), with OC, OR 1.41 (1.12-1.78), NO_2 and O_3. No significant associations with $PM_{10-2.5}$. Larger OR's with within-community yearly variability than between-community (per µg/m^3 $PM_{2.5}$ OR = 1.03, 1.01-1.05). OC and NO_2 effects strongest in 2-pollutant models	
U.S. cystic fibrosis cohort Goss et al. (2004)	AQS data for 2000, annual average, subject assigned data from population-oriented monitor closest to zip code centroid. 713 monitors for $PM_{2.5}$ PM_{10} mean 24.9 (20.3-28.9); $PM_{2.5}$ mean 13.7 (11.8-15.9)	11,484 adults and children >5 yr, enrolled in Cystic Fibrosis Foundation National Patient Registry in 1999-2000.	Increased odds of having 2 or more pulmonary exacerbations per 10 µg/m^3 $PM_{2.5}$ (21%, 7-33%) and $PM_{2.5}$ (8%, 2-15%) as well as ozone. No associations with NO_2, SO_2, or CO. Negative associations with lung function in cross-sectional analysis. Decreased FEV_1 with $PM_{2.5}$ and PM_{10}; no clear associations with gaseous pollutants.	"In conclusion, exposure to ambient PM_{10}, $PM_{2.5}$, and ozone may increase the risk for pulmonary exacerbations and increase the rate of change in lung function in the CF population."

Other studies using PM_{10} or other PM indicators:

Mortality:

Evans and Smith (2005) used data from U.S. Health and Retirement Study, a national panel survey of birth cohorts 1931-1941 with follow-up in 1992-2004. Long-term (1990-2000) PM_{10} exposure associated with a new heart condition (reported between 1994 and 1996) (coefficient = 0.004, t = 1.74) and significantly associated with shortness of breath (coefficient = 0.017, t = 2.25) but not with new lung conditions. Recent (1994-6) PM_{10} exposure associated with new heart condition (coeff = 0.0004, t = 1.74); also association with shortness of breath, but not with new lung condition. Long-term O_3 exposure also associated with new lung condition and shortness of breath

Filleul et al. (2005) used data from a respiratory disease survey data of 14,000+ adults in 24 areas in 7 cities. For 24 areas no association was reported between particles (BS) and mortality (RR 0.99, 0.98-1.01). Further analyses excluded data from 6 areas where monitors were in an area "heavily influenced by the local traffic and, so, non-representative of the mean exposure of the population of the entire area" based on NO/NO_2 ratio. For these 18 areas, RR with BS of 1.07 (1.03-1.10) for total mortality; nonsignificant RR's of 1.03 and 1.05 for lung cancer and cardiopulmonary diseases. Significant associations also with TSP for total and cardiopulmonary diseases. Significant associations also with NO, NO_2, but not SO_2. No consistent modifying effect of gender or education level. BS means ranged from 21 to 152 $\mu g/m^3$; "heavy traffic" BS means of 46, 105, 141, 111, and 91 $\mu g/m^3$.

Morbidity:

Tager et al. (2005) used data from UC Berkeley students—255 never-smoking students from LA and San Francisco areas—and reported consistent inverse associations between O_3, PM_{10} and NO_2 and FEF_{75}, FEF_{25-75} in both men and women. O_3 associations were more robust in co-pollutant models than PM_{10} or NO_2. Mean lifetime PM_{10} exposure was 48 $\mu g/m^3$ for men and 45 $\mu g/m^3$ for women.

Salam et al. (2005) used birth certificate information obtained for California-born children participating in the Children's Health Study (n = 3901) to test for associations between air pollution exposure and birth weight. Air pollution estimates assigned using zip code of maternal residence at birth, with spatial interpolation based on data from up to the three nearest stations within 50 km of zip code. Exposure estimates calculated as monthly average of 24 hr measurements, computed for trimesters and full pregnancy. A nonsignificant association was reported between higher PM_{10} exposures during the third trimester and decreased birth weight. Significant associations were reported with first-trimester CO exposure and third-trimester O_3 exposure.

Penard-Morand et al. (2005) uses questionnaire data for 6672 children in six French cities with air pollution data collected at children's schools from 1998-2000. The PM_{10} mean in high and low cities was 23.8 and 18.0 $\mu g/m^3$, respectively; the overall mean was approximately 21 $\mu g/m^3$ (from figure). Significant associations were reported with PM_{10} and asthma, atopic dermatitis, exercise-induced bronchial reactivity and allergic rhinitis.

Pierse et al. (2006) reported an association between PM_{10} and symptoms in children surveyed in 1998 and 2001 in Leicester UK. The OR for prevalence of cough without cold in 1998 and 2001 was 1.21 (1.07-1.38) and 1.56 (1.32-1.84), respectively, PM_{10} was also associated with the incidence of wheeze.

Zhang et al. (2002) used questionnaire data for 7621 children in four Chinese cities and 1995-1996 air pollution data. Grand means were $PM_{2.5}$ = 92 $\mu g/m^3$ (not a typo) and $PM_{10-2.5}$ = 59 $\mu g/m^3$. Significant associations were observed between $PM_{10-2.5}$ and incidence of bronchitis (2.20, 1.14-4.26), persistent cough (1.46, 1.12-1.90) and persistent phlegm (2.83, 1.93-4.16); positive nonsignificant association with incidence of asthma, wheeze, and ever-hospitalization for respiratory disease. For all six endpoints positive but nonsignificant associations were reported with $PM_{2.5}$. No significant associations (some nonsignificant negative) were observed with SO_2 and NO_x.

Bayer-Oglesby et al., (2005) used data from a study of 9591 school-children in nine Swiss communities with a respiratory questionnaire administered in 1992-2001. A decrease in PM_{10} (per 10 $\mu g/m^3$) was associated with a decrease in prevalence of chronic cough (OR 0.65, 0.54-0.79), bronchitis (OR 0.66, 0.55-0.80), common cold (OR 0.78, 0.6800.89), nocturnal dry cough (OR 0.70, 0.60-0.83) and conjunctivitis symptoms. No significant associations were reported with wheeze, asthma, sneezing, or hay fever. PM_{10} decreased 9.8 $\mu g/m^3$ between 1993 and 2000; the decreases in PM_{10} concentration were three times greater in urban than rural communities and ranged from 10-34 $\mu g/m^3$ in 2000.

Table A2. Associations of Acute $PM_{2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{2.5}$						
Ostro et al. (2006) 9 counties in California Jan 1999-Dec 2002	All nonaccidental, cardiovascular, and respiratory causes, as well as deaths from ischemic heart disease and diabetes; all ages and age >65 yr	24-h avg $PM_{2.5}$: Range of means across counties: 14 (Contra Costa and Sacramento) to 29 (Riverside) Range of daily concentrations across counties 0-160	NO_2, CO, O_3	2-d lag and 0-1 d avg lag	Time-series study. Poisson regression using penalized and natural spline models. Default model used penalized spine regression. County-specific results pooled based on meta-analysis using random-effects model. At least one monitor collected daily $PM_{2.5}$ data in each county. A substantial number of days were missing data, which varied by county and appeared to be generally random.	% excess risk per 10 $\mu g/m^3$: <u>All causes</u>: All ages: Lag 0-1: 0.6% (0.2, 1.0) Age >65 yr: Lag 0-1: 0.7% (0.2, 1.1) <u>Cardiovascular</u>: All ages: Lag 0-1: 0.6% (0.0, 1.1) <u>Respiratory</u>: All ages: Lag 0-1: 2.2% (0.6, 3.9) In multipollutant models, $PM_{2.5}$ effect estimate was attenuated when highly correlated pollutants (NO_2 and CO) were added to the model, but was not affected by the inclusion of O_3. However, in those aged >65 yr, adjusting for gaseous pollutants did not affect the $PM_{2.5}$ coefficient. Analysis of different mortality categories and subpopulations indicated somewhat stronger associations of daily $PM_{2.5}$ with mortality for age >65yr, diabetics, females, white, and non-high school graduates.

Table A2 (cont'd). Associations of Acute $PM_{2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{2.5}$ (cont'd)						
Burnett et al. (2004) 12 Canadian cities Jan 1981-Dec 1999	All nonaccidental, cardiovascular, and respiratory causes	24-h avg $PM_{2.5}$: All 12 cities: 12.8 SD not provided. Range of means across cities: 8.1 (St. John) to 16.7 (Windsor)	$PM_{10-2.5}$, PM_{10}, SO_4^{2}, NO_2, SO_2, CO, O_3	0-, 1-, or 2-d lag	Time-series study. Natural spline functions used to model nonlinear associations. $PM_{2.5}$ data collected every 6th day. $PM_{2.5}$ data available on 12% of days with mortality data. In 11 of 12 cities, daily $PM_{2.5}$ data collected from Jan 1998 to Dec 2000.	% excess risk per 12.8 $\mu g/m^3$: <u>All causes</u>: Using all available data: Single-pollutant model: Lag 1: 0.77% (0.04, 1.58) Two-pollutant model with NO_2: Lag 1: -0.13% (-1.10, 0.85) Significant associations observed for NO_2 in two-pollutant model. Similar results observed for $PM_{10-2.5}$. Significant associations observed with PM_{10}, which also became nonsignificant after adjusting for NO_2. Only using data from period when daily $PM_{2.5}$ levels available (1998-2000): Single-pollutant model: Lag 1: 1.13% (95% CI not presented) Two-pollutant model with NO_2: Lag 1: 0.98% (0.16, 2.13) When restricting analysis to only days when daily $PM_{2.5}$ data were available, the NO_2 association was reduced considerably after adjustment for $PM_{2.5}$, whereas $PM_{2.5}$ effect remained fairly robust to NO_2 adjustment.

Table A2 (cont'd). Associations of Acute $PM_{2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{2.5}$ (cont'd)						
Dales et al. (2004) 12 Canadian cities Jan 1984-Dec 1999	SIDS; age <1 yr	24-h avg $PM_{2.5}$: All 12 cities: 12.27 IQR 8.98 Range of means across cities: 8.07 (St. John) to 16.67 (Windsor)	$PM_{10-2.5}$, PM_{10}, NO_2, SO_2, CO, O_3	0-, 1-, 2-, 3-, 4-, or 5-d lag; multiday lags of 2 to 6 d	Time-series study. Nonlinear random-effects regression model used. $PM_{2.5}$ data collected every 6th day.	No association observed between incidence of SIDS and $PM_{2.5}$ (no effect estimates presented). Similar results observed for $PM_{10-2.5}$ and PM_{10}. Significant associations observed for NO_2, SO_2, and CO.
Slaughter et al. (2005) Spokane, WA Jan 1995-Jun 2001	All nonaccidental causes	24-h avg $PM_{2.5}$: 10th%-90th% 4.2-20.2	PM_1, $PM_{10-2.5}$, PM_{10}, CO	0-, 1-, 2-, 3-d lag	Time-series study. Poisson GLM with natural splines. Hourly $PM_{2.5}$ data available. Daily averages calculated.	RR per 10 $\mu g/m^3$: Lag 1: 1.01 (0.97, 1.04) No associations observed between nonaccidental mortality and $PM_{2.5}$. Similar results observed for $PM_{10-2.5}$ and PM_{10}.

Table A2 (cont'd). Associations of Acute $PM_{2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{2.5}$ (cont'd)						
Mar et al. (in press) Phoenix, AZ Feb 1995-Dec 1997	All nonaccidental and cardiovascular causes; age 65 yr	24-h avg $PM_{2.5}$: Gravimetric sampler: 12.0 SD 6.6 Range 2-39 TEOM sampler: 13.0 SD 7.2 Range 0-42	Various $PM_{2.5}$ sources, including soil, traffic, secondary SO_4^{2}, biomass/wood combustion, sea salt, and copper smelter	0-, 1-, 2-, 3-, 4-d, or 5- lag	Time-series study. Poisson GLM with natural splines. Daily $PM_{2.5}$ data collected using both gravimetric and TEOM samplers. Focus of study was to assess variability of different methods/ investigators in estimating source apportioned $PM_{2.5}$ health effects.	% excess risk per 5th% to 95th% increment (using TEOM sampler): <u>Cardiovascular</u>: Lag 1: 15.0% (1.5, 30.3) Magnitude and lag structure of the association between $PM_{2.5}$ and cardiovascular mortality were similar to those for the combined traffic factor.

Table A2 (cont'd). Associations of Acute $PM_{2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{2.5}$ (cont'd)						
Ito et al. (in press) Washington, DC Aug1988-Dec 1997	All nonaccidental, cardiovascular, and cardiorespiratory causes	24-h avg $PM_{2.5}$: 17.8 SD 8.7 5th%-95th% 28.7	Various $PM_{2.5}$ sources, including soil, traffic, secondary SO_4^{2-}, NO_3^-, residual oil, wood smoke, sea salt, incinerator, and primary coal	0-, 1-, 2-, 3-, or 4-d lag	Time-series study. Poisson GLM with natural splines. $PM_{2.5}$ data collected every Wednesday and Saturday. Focus of study was to assess variability of different methods/ investigators in estimating source apportioned $PM_{2.5}$ health effects.	% excess risk per 28.7 $\mu g/m^3$: All causes: Lag 3: 8.3% (3.7, 13.1) Significant association between all cause mortality and $PM_{2.5}$ only observed at lag 3 d.
Klemm et al. (2004) Atlanta, GA Aug 1998-July 2000	All nonaccidental, circulatory, respiratory, cancer, and other causes; age <65 yr and 65 yr	24-h avg $PM_{2.5}$: 19.62 SD 8.32 IQR 11.62 Range 5.29-48.01	$PM_{10-2.5}$, SO_4^{2-}, EC, OC, NO_2, NO_3^-, SO_2, CO, O_3, ultrafines, hydrocarbons, acid	Multiday lag of 0-1 d	Time-series study. Poisson GLM using natural cubic splines with quarterly, monthly, or biweekly knots. Default model used monthly knots. Daily $PM_{2.5}$ data collected.	% excess risk per 19.62 $\mu g/m^3$: All causes: Age 65 yr: Lag 0-1: 11.3% (3.7, 19.4) Results differ across model specifications (i.e., choice of lag and number of knots). Weaker associations observed with $PM_{10-2.5}$. No significant associations observed in those aged <65 yr.

Table A2 (cont'd). Associations of Acute $PM_{2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{2.5}$ (cont'd)						
Villeneuve et al. (2003) Vancouver, British Columbia, Canada Jan 1986-Dec 1998	All nonaccidental, cardiovascular, respiratory, and cancer causes; SES status	24-h avg $PM_{2.5}$: Daily data from 1995-1998: 7.9 10th%-90th% 4.0-13.0 Range 2.0-32.0 Every 6th day data from 1986-1998: 11.6 10th%-90th% 4.7-20.4 Range 1.8-43.0	$PM_{10-2.5}$, PM_{10}, TSP, coefficient of haze, SO_4^2, SO_2, NO_2, CO, O_3	0-, 1-, or 2-d lag; multiday lag of 0-2 d	Time-series study. Poisson regression using natural spline functions. Daily $PM_{2.5}$ data collected from 1995 to 1998 using TEOM; $PM_{2.5}$ data collected every 6th day from 1986 to 1998 using a dichotomized sampler.	% excess risk per 9.0 $\mu g/m^3$: Results using daily $PM_{2.5}$ data: <u>All causes</u>: Lag 0:. 0.1% (-4.1, 4.1) <u>Cardiovascular</u>: Lag 0: 4.3% (-1.7, 10.7) <u>Respiratory</u>: Lag 0: 6.7% (-3.7, 18.3) <u>Cancer</u>: Lag 0:. 4.5% (-11.2, 2.8) Collectively, results suggest no association between $PM_{2.5}$ and mortality. There is some suggestive evidence of a modest increase in the risk of cardiovascular mortality among individuals of low SES status. Significant associations with cardiovascular mortality were observed for daily $PM_{10-2.5}$ and PM_{10} data.

Table A2 (cont'd). Associations of Acute $PM_{2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{2.5}$ (cont'd)						
Goldberg et al. (2006) Montreal, Canada 1986-1993	Diabetes, and nonaccidental mortality in subgroups with diabetes diagnosed at least 1 year before death in adults >65 yr. Also considered subgroups with cardiovascular diagnoses.	24-h avg $PM_{2.5}$: 17.4 SD 11.4 24-h avg predicted $PM_{2.5}$: 17.6 SD 8.8	PM_{10}, TSP, coefficient of haze, SO_4^2, predicted SO_4^2, SO_2, NO_2, CO, O_3	0-, 1-, and average of 0- to 2-day lags ("3-day mean")	Time-series study. Poisson regression using natural spline functions. Report results for predicted $PM_{2.5}$; used statistical model to estimate mass when measurements were not available; measured data available on 636 days and predicted data for 3653 days.	% excess risk per 9.5 $\mu g/m^3$: (all 3-day mean lag) mortality from diabetes: 8.37% (1.80, 15.37) nonaccidental mortality in subjects with diabetes: 3.64% (0.07, 7.33) Greater effects seen generally in the warm season. No significant association for nonaccidental mortality in subjects with diabetes, but without cancer, cardiovascular disease or airways disease. Associations reported for nonaccidental mortality in subjects with diabetes who also had any cardiovascular disease, chronic coronary disease and atheroschlerosis.

Table A3. Associations of Acute $PM_{10-2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{10-2.5}$						
Burnett et al. (2004) 12 Canadian cities Jan 1981-Dec 1999	All nonaccidental, cardiovascular, and respiratory causes	24-h avg $PM_{10-2.5}$: All 12 cities: 11.4 SD not provided. Range of means across cities: 5.5 (Vancouver) to 15.9 (Winnipeg)	$PM_{2.5}$, PM_{10}, SO_4^{2}, NO_2, SO_2, CO, O_3	0-, 1-, or 2-d lag	Time-series study. Natural spline functions used to model nonlinear associations. $PM_{10-2.5}$ data collected every 6th day. $PM_{10-2.5}$ data available on 12% of days with mortality data.	% excess risk per 11.3 $\mu g/m^3$: All causes: Single-pollutant model: Lag 1: 0.74% (-0.12, 1.61) Two-pollutant model with NO_2: Lag 1: 0.35% (-0.55, 1.26) No significant associations observed for NO_2 in two-pollutant model.
Dales et al. (2004) 12 Canadian cities Jan 1984-Dec 1999	SIDS; age <1 yr	24-h avg $PM_{10-2.5}$: All 12 cities: 11.28 IQR 8.76 Range of means across cities: 5.46 (St. John) to 15.88 (Winnipeg)	$PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, O_3	0-, 1-, 2-, 3-, 4-, or 5-d lag; multiday lags of 2 to 6 d	Time-series study. Nonlinear random-effects regression model used. $PM_{10-2.5}$ data determined by difference. $PM_{2.5}$ and PM_{10} data collected every 6th day.	No association observed between incidence of SIDS and $PM_{10-2.5}$ (no effect estimates presented). Significant associations observed for NO_2, SO_2, and CO.

Table A3 (cont'd). Associations of Acute $PM_{10-2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{10-2.5}$						
Klemm et al. (2004) Atlanta, GA Aug 1998-July 2000	All nonaccidental, circulatory, respiratory, cancer, and other causes; age <65 yr and ≥65 yr	24-h avg $PM_{10-2.5}$: 9.69 SD 3.94 IQR 5.25 Range 1.71-25.17	$PM_{2.5}$, SO_4^{2-}, EC, OC, NO_2, NO_3^-, SO_2, CO, O_3, ultrafines, hydrocarbons, acid	Multiday lag of 0-1 d	Time-series study. Poisson GLM using natural cubic splines with quarterly, monthly, or biweekly knots. Default model used monthly knots. Daily $PM_{10-2.5}$ data collected.	% excess risk per 9.69 $\mu g/m^3$: <u>All causes</u>: Age ≥65 yr: Lag 0-1: 6.2% (-0.9, 13.7) Results differ across model specifications (i.e., choice of lag and number of knots). No significant associations observed in those aged <65 yr.

Table A3 (cont'd). Associations of Acute $PM_{10-2.5}$ Exposure with Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
$PM_{10-2.5}$ (cont'd)						
Slaughter et al. (2005) Spokane, WA Jan 1995-Jun 2001	All nonaccidental causes	24-h avg $PM_{10-2.5}$: Not reported.	PM_1, $PM_{2.5}$, PM_{10}, CO	0-, 1-, 2-, 3-d lag	Time-series study. Poisson GLM with natural splines. $PM_{10-2.5}$ calculated as difference between PM_{10} and $PM_{2.5}$ measurements. Hourly $PM_{2.5}$ and PM_{10} data available. Daily average values calculated.	No associations observed between nonaccidental mortality and $PM_{10-2.5}$. Quantitative results not provided.
Villeneuve et al. (2003) Vancouver, British Columbia, Canada Jan 1986-Dec 1998	All nonaccidental, cardiovascular, respiratory, and cancer causes; SES status	24-h avg $PM_{10-2.5}$: Daily data from 1995-1998: 6.1 10th%-90th% 2.0-13.0 Range 0.0-72.0 Every 6th day data from 1986-1998: 8.3 10th%-90th% 3.1-15.0 Range 0.7-35.0	$PM_{2.5}$, PM_{10}, TSP, coefficient of haze, SO_4^2, SO_2, NO_2, CO, O_3	0-, 1-, or 2-d lag; multiday lag of 0-2 d	Time-series study. Poisson regression using natural spline functions. Daily $PM_{10-2.5}$ data collected from 1995 to 1998 using TEOM; $PM_{10-2.5}$ data collected every 6th day from 1986 to 1998 using a dichotomized sampler.	% excess risk per 11.0 $\mu g/m^3$: Results using daily $PM_{10-2.5}$ data: All causes: Lag 0: 1.0% (-1.9, 4.0) Cardiovascular: Lag 0: 5.9% (1.1, 10.8) Respiratory: Lag 0: 1.5% (-9.4, 7.1) Cancer: Lag 0: 3.1% (-2.9, 9.4) Significant associations with cardiovascular mortality were observed for daily $PM_{10-2.5}$ and PM_{10} data.

Additional U.S. and Canadian PM-Mortality Studies:

Staniswalis et al. (2005): This study shows that the effects of airborne PM on daily mortality can be underestimated when using daily averages to summarize hourly profiles, because the daily average does not capture information about very acute exposures, that is, large exposures occurring over very short periods of time. A principal component data analysis is shown to be useful for characterizing hourly measurements of air pollution constituents. In addition, it is shown that in El Paso, the risk of PM-induced mortality is higher during still-air inversions (i.e., at low wind speeds) than it is during sandstorms (i.e., at high wind speeds). These results suggest that coarse and fine PM from resuspended fugitive dust is less toxic than fine PM of urban type.

De Leon et al. (2003): The effects of PM_{10} on circulatory and cancer mortality with and without contributing respiratory causes were examined in this study conducted in New York City. Among those aged ≥ 75 yr, effect estimates were greater for circulatory mortality with contributing respiratory causes (6.6% [95% CI: 2.7, 10.6] per 18.16 $\mu g/m^3$ increase in PM_{10}) at a 0- to 1-day lag compared to that without (2.2% [95% CI: 0.8, 3.5]). Unlike in those aged ≥ 75 yr, significantly higher risks were not observed with contributing respiratory causes in individuals aged <75 yr.

Bateson and Schwartz (2004): The association between PM_{10} and all-cause mortality in individuals aged ≥ 65 yr who were previously admitted to the hospital with a primary or secondary diagnosis of heart or lung disease was examined in this case-crossover study in Cook County, IL. A 1.14% (95% CI: 0.44, 1.85) excess risk was observed per 10 $\mu g/m^3$ increase in PM_{10} at a lag of 0 to 1 days. The effect of PM_{10} on the risk of mortality was higher among those with a prior diagnosis of myocardial infarction (1.98%), diabetes (1.49%), and congestive heart failure (1.28%).

Sullivan et al. (2003): In this case-crossover study in King County, WA, the association between PM and out-of-hospital sudden cardiac arrest in individuals with and without preexisting cardiovascular and respiratory disease was examined. $PM_{2.5}$ data was estimated using a nephelometric measure (PM_1). No consistent associations were observed between increased levels of $PM_{2.5}$ or PM_{10} and risk of primary cardiac arrest.

Holloman et al. (2004): To examine the association between cardiovascular mortality and estimated exposure to $PM_{2.5}$ in seven counties in North Carolina, a three-level hierarchical Bayesian model was used: (1) linking monitor readings to ambient levels over the region; (2) linking ambient levels to exposure levels (estimated using NHAPS); and (3) linking exposure levels to mortality. Significant associations were observed between cardiovascular mortality and $PM_{2.5}$ at a lag of 2 days. Results obtained by incorporating a simple exposure simulator into the model indicated that the effect of increased levels of exposure was not equivalent to that of ambient $PM_{2.5}$ on cardiovascular mortality.

Vedal et al. (2003): The associations between PM_{10} and all-cause, cardiovascular, and respiratory mortality were examined in Vancouver, Canada (PM_{10} concentration range 4.1 to 37.2 $\mu g/m^3$). During the summer, statistically significant effects on respiratory mortality were observed for PM_{10}, O_3, and SO_2, and the effects of NO_2 and CO were also nearly significant. Effects on total and cardiovascular mortality were only seen for O_3. During the winter, significant effects on total mortality were observed for PM_{10}, NO_2, and SO_2; NO_2 and SO_2 also

were associated with cardiovascular mortality. No significant associations with respiratory mortality were observed in the winter. The authors report that these findings may support the notion that no threshold pollutant concentrations are present, but they also raise concern that the observed effects may not be due to the measured pollutants themselves, but rather of some other factors present in the air pollution-meteorology mix.

Jerrett et al. (2004): Significant associations between CoH and all-cause mortality were observed in regions of lower SES status at various lags of exposure. Regions of higher SES status displayed no significant associations except at a multiday lag of 0 to 3 days. These findings suggest that the effect of PM on mortality may be modified by SES status. Low educational attainment and high manufacturing employment significantly and positively modified the effects of PM on acute mortality.

Additional Studies Examining Issues Related to Interpreting the PM-Mortality Relationship:

Forastiere et al. (2005): Using a case-crossover design, the associations between daily ambient air pollution levels (particle number concentration [PNC], PM_{10}, CO, NO_2, and O_3) and the occurrence of out-of-hospital fatal coronary events in Rome were examined. The association was statistically significant for PNC, PM_{10}, and CO, with the strongest effect observed on the same day. An IQR increase in PNC (27,790 particles/cm^3) and PM_{10} (29.7 $\mu g/m^3$) was associated with a 7.6% (95% CI: 2.0, 13.6) and 4.8% (95% CI: 0.1, 9.8) excess risk in mortality, respectively. Stronger effects were observed among people aged 65 yr, and possibly in those with hypertension and COPD.

Sunyer et al. (2002): This case-crossover study assessed the acute association between air pollution and all-cause mortality in a population-based cohort of subjects with asthma recruited from emergency room admissions for asthma exacerbation in Barcelona, Spain. No significant associations were observed between PM_{10} or BS and mortality. Slightly larger effect estimates were observed in subjects admitted more than once compared to those admitted only once to the emergency department for asthma, but differences were not significant. Stronger associations were observed for NO_2 and O_3.

Kan et al. (2005): Using time-series Poisson regression, the relationship between daily SARS mortality and ambient air pollution in Beijing was examined. An 10 $\mu g/m^3$ increase in PM_{10} (mean 149.1 $\mu g/m^3$ [SD 8.1]) over a 5-day moving average corresponded to a RR of 1.06 (95% CI: 1.00, 1.12). NO_2, but not SO_2, also was associated with daily SARS mortality (RRs of 1.22 [95% CI: 1.01, 1.48] and 0.74 [95% CI: 0.48, 1.13], respectively).

Goodman et al. (2004): In a Dublin, Ireland study, a constrained (6th order polynomial) distributed lag model used to examine BS effects through 40 days. Results were compared to effects estimated for a 0 to 2 day lag of BS exposure. Stronger associations with BS were consistently observed for all-cause, cardiovascular, and respiratory mortality using the extended follow-up period. Analyses suggest that studies on acute effects of air pollution have underestimated the total effects of PM on mortality.

Table A4. Effects of $PM_{2.5}$ on Daily Hospital Admissions

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{2.5}$						
Dominici et al. (2006) United States National Database1999-2002	A daily time-series analysis on hospital admission rates (from the Medicare National Claims History Files) for cardiovascular and respiratory outcomes and ambient $PM_{2.5}$ levels, temperature for 204 U.S. urban counties (population >200,000) with 11.5 million Medicare enrollees (aged >65 years) living an average of 5.9 miles from a $PM_{2.5}$ monitor.	$PM_{2.5}$ county annual mean: 13.4 $\mu g/m^3$ IQR (11.3-15.2 $\mu g/m^3$)	O_3	0-2	Nationally, short-term increase in hospital admission rates associated with $PM_{2.5}$ for all health outcomes except injuries. The largest association was for heart failure. Substantial homogeneity of fine particle matter concentration across geographic area. For cardiovascular disease, all estimates in the eastern U.S. were positive and generally statistically significant, while estimates in the western U.S. were close to 0 except for heart failure For respiratory disease, there was greater consistency between regions. The authors noted that they did not find evidence of the effect modification by average concentration of either $PM_{2.5}$ or O_3.	Excess risk per 10 $\mu g/m^3$: Heart failure 1.28% (0.78-1.78%) Annual reduction in admissions attributable to a 10 $\mu g/m^3$ reduction in daily $PM_{2.5}$ level for 204 counties in 2002 Cerebrovascular disease: 1836 (680-2992) Heart failure: 3156 (1923-4389) Respiratory tract infection: 2085 (929-3241)

Table A4 (cont'd). Effects of $PM_{2.5}$ on Daily Hospital Admissions

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)						
Lin et al. (2002) Toronto 1981-1993	Both case-crossover and time-series analyses used to assess the associations between various PM measures and asthma hospitalization among children 6-12 years old.	$PM_{2.5}$ mean: 17.99 µg/m^3 Min 1.22 Max 89.59	$PM_{10-2.5}$, PM_{10}, O_3, NO_2, CO, SO_2	1-7	Significant effects were not found for $PM_{2.5}$, but both analysis methods did find relationships with $PM_{10-2.5}$ for either sex. Individual $PM_{2.5}$ results showed some positive association but not after consideration of both weather conditions and gaseous co-pollutants.	$PM_{2.5}$ (IQR 9.3 µg/m^3) After controlling for gaseous pollutants effect estimates range from -7% to 1% with 95% CI all including 0% for both bidirectional case-crossover and time-series analysis.
Lin et al. (2005) Toronto 1998-2001	Examined the associations between pollutants and hospitalizations for respiratory infections among children younger than 15 years of age. Bi-directional case-crossover design used.	$PM_{2.5}$ Mean: SD 9.59 SD 7.06	$PM_{10-2.5}$, PM_{10}, CO, SO_2, NO_2, O_3		$PM_{2.5}$ showed no significant effects when other pollutants were considered. The effects for $PM_{10-2.5}$ were pronounced.	$PM_{2.5}$ (IQR 7.8 µg/m^3) single-pollutant: 10% (2-22) 4 day lag after adjustment for other pollutants: -6% (-19, 8)

Table A4 (cont'd). Effects of $PM_{2.5}$ on Daily Hospital Admissions

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)						
Yang et al. (2004) Vancouver, British Columbia Jun 1, 1995-Mar 31, 1999	Logistic regression was used to estimate the associations between PM and first hospitalization for children less than 3 years of age, a case-control approach. Also, analysis was conducted using bidirectional-case crossover analysis and time-series analysis.	$PM_{2.5}$ Mean 7.7 µg/m^3 SD 3.7 Range: 2.0-32.0	PM_{10}, $PM_{10-2.5}$, CO, O_3, NO_2, SO_2	0-7	The data indicated possible harmful effects from coarse PM on first hospitalization for respiratory disease. No significant association was found between $PM_{2.5}$ and first hospitalization for respiratory disease. $PM_{2.5}$ concentrations were relatively low. In this study, only the case-control and case-crossover approaches support the notion of effect of daily average $PM_{10-2.5}$ on first hospitalization for respiratory disease in early childhood. It is not clear if these two approaches overestimated or if the time-series analysis underestimated. For $PM_{2.5}$, the authors noted that differences in findings may be explained, in part, by TEOM measurements, which may be lower than those of filter-based samples.	No quantitative results reported.

Table A4 (cont'd). Effects of $PM_{2.5}$ on Daily Hospital Admissions

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)						
Chen et al. (2004) Vancouver, British Columbia Jun 1995-Mar 1999	A time-series analysis assessing the association between low levels of size-fractionated PM and hospitalization for chronic obstructive pulmonary disease (COPD) in the elderly. GAM and GLM models were used.	$PM_{2.5}$ Mean 7.7 µg/m^3 SD (3.7) Range: 2.0-32.0	PM_{10}, $PM_{10-2.5}$, CO, O_3, NO_2, SO_2	1-7	Particle-related measures were significantly associated with COPD hospitalizations in the Vancouver area, but the effects are not independent of other air pollutants.	For a 3-day average $PM_{2.5}$ 9% (3, 16%) This association was not significant when NO_2 included in the model.
Chen et al. (2005) Vancouver, British Columbia Jun 1, 1995-Mar 31, 1999	A time-series analysis was used to evaluate the associations between respiratory admissions and PM, looking at first, second, and overall hospital admission for respiratory disease among the elderly. 8,989 adults, ≥65 yr.	$PM_{2.5}$ Mean 7.7 µg/m^3 SD (3.7) Range: 2.0-32.0	PM_{10}, $PM_{10-2.5}$, CO, O_3, NO_2, SO_2	1-7	$PM_{10-2.5}$ had a larger effect on respiratory admissions than $PM_{2.5}$. For $PM_{10-2.5}$, the second and overall admission rates were higher than the first admission rate.	$PM_{2.5}$ adjusted for copollutants First admission Lag 1: 2% (-1, 6) Second admission: 1% (-3, 6)

Table A5. Effects of $PM_{10-2.5}$ on Daily Hospital Admissions

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{10-2.5}$						
Lin et al. (2002) Toronto 1981-1993	Both case-crossover and time-series analyses used to assess the associations between various PM measures and asthma hospitalization among children 6-12 years old.	$PM_{10-2.5}$ Mean 12.17 Range: 0-68	$PM_{2.5}$, PM_{10}, O_3, NO_2, CO, SO_2	1-7	Significant associations with $PM_{10-2.5}$ for either sex; no significant associations with PM2.5.	$PM_{10-2.5}$ (IQR 8.4 µg/m^3) After controlling for gaseous pollutants: 17% (3-3) 6d avg lag, bidirectional case-crossover 15% (6-25) 6d avg lag, time-series analysis.
Lin et al. (2005) Toronto 1998-2001	Examined the associations between pollutants and hospitalizations for respiratory infections among children <15 yr. Bi-directional case-crossover design used.	$PM_{1-10-2.5}$ Mean 10.86 (SD 5.37) Range: 0-45	$PM_{2.5}$, PM_{10}, CO, SO_2, NO_2, O_3		Significant associations with $PM_{10-2.5}$ for either sex; $PM_{2.5}$ showed no significant effects when other pollutants were considered.	$PM_{10-2.5}$ (IQR 6.5 µg/m^3) 6-day avg lag after adjustment for gases boys 15% (2-30) girls 18% (8-34)
Chen et al. (2004) Vancouver, British Columbia Jun 1995-Mar 1999	A time-series analysis assessing the association between low levels of size fractionated PM and hospitalization for chronic obstructive pulmonary disease (COPD) in the elderly. GAM and GLM models were used.	$PM_{10-2.5}$ Mean 5.6 µg/m^3 Range: 0.1-24.6	PM_{10}, $PM_{2.5}$, CO, O_3, NO_2, SO_2	1-7	Significant associations for $PM_{10-2.5}$ with COPD hospitalizations in the Vancouver area. Also statistically significant associations with PM_{10}, $PM_{2.5}$, and COH, but the effects are not independent of other air pollutants.	$PM_{10-2.5}$ (IQR 4.2 µg/m^3) 3-day avg lag 8% (2-15) Significance lost with CO, NO_2 and SO_2 but not O_3

Table A5 (cont'd). Effects of $PM_{10-2.5}$ on Daily Hospital Admissions

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{10-2.5}$ (cont'd)						
Yang et al. (2004) Vancouver, British Columbia Jun 1, 1995-Mar 31, 1999	Logistic regression was used to estimate the associations between PM and first hospitalization for children <3 yr, a case-control approach. Also, analysis was conducted using bidirectional-case crossover analysis and time-series analysis.	$PM_{10-2.5}$ Mean 5.6 µg/m^3 Range: 0-24.6	PM_{10}, $PM_{2.5}$, CO, O_3, NO_2, SO_2	0-7	The data indicated possible harmful effects from coarse PM on first hospitalization for respiratory disease. No significant association was found between $PM_{2.5}$ and first hospitalization for respiratory disease. $PM_{2.5}$ concentrations were relatively low. In this study, only the case-control and case-crossover approaches support the notion of effect of daily average $PM_{10-2.5}$ on first hospitalization for respiratory disease in early childhood. It is not clear if these two approaches overestimated or if the time-series analysis underestimated. For $PM_{2.5}$, the authors noted that differences in findings may be explained, in part, by TEOM measurements, which may be lower than those of filter-based samples.	$PM_{10-2.5}$ (IQR 4.2 µg/m^3) Respiratory hospital admissions, 3-day lag: mean $PM_{10-2.5}$ 12% (-2-25) *22% (2-48) max $PM_{10-2.5}$ 13% (0-27) *14% (-1-32) *after adjustment for gases Associations with asthma and pneumonia hospitalization not statistically significant.

Table A5 (cont'd). Effects of $PM_{10-2.5}$ on Daily Hospital Admissions

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{10-2.5}$ (cont'd)						
Chen et al. (2005) Vancouver, British Columbia Jun 1, 1995-Mar 31, 1999	A time-series analysis was used to evaluate the associations between respiratory admissions and PM, looking at first, second, and overall hospital admission for respiratory disease among the elderly. 8,989 adults, ≥65 yr.	$PM_{10-2.5}$ Mean 5.6 µg/m^3 Range: 0.1-24.6	PM_{10}, $PM_{2.5}$, CO, O_3, NO_2, SO_2	1-7	$PM_{10-2.5}$ had a larger effect on respiratory admissions than $PM_{2.5}$. For $PM_{10-2.5}$, the second and overall admission rates were higher than the first admission rate. (1) People with a history of respiratory admissions are at a higher risk of respiratory disease in relation to particulate air pollution in urban areas. (2) Analyses based on overall rather than repeated hospital admissions lead to lower estimates of the risk of respiratory disease associated with particulate air pollution.	$PM_{10-2.5}$ (IQR 4.2 µg/m^3) 3 day avg first admission 3% (-2-9) second admission 22% (0-36) overall 6% (2-11) No significant associations with $PM_{2.5}$

Table A6. Effects of $PM_{2.5}$ on Daily Emergency Department Visits

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{2.5}$						
Metzger et al. (2004) Atlanta, GA Aug 1998-Aug 2000	Emergency department visits for total and cause-specific cardiovascular diseases by age groups >19 yr and >65 yr. Time-series study. 4, 407, 535, EDV from 31 Atlanta hospitals.	$PM_{2.5}$ $\mu g/m^3$ Median: 17.8 Range: 8.9 to 32.3	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{10-2.5}$, ultrafine PM count, SO_4^{2-}, H^+, EC, OC, metals, oxygenated hydrocarbons	0-2	Poisson GLM regression used for analysis. A priori models specified a lag of 0 to 2 days. Secondary analyses performed to assess alternative pollutant lag structures, seasonal influences, and age effects. Cardiovascular visits were significantly associated with several pollutants, including NO_2, CO, and $PM_{2.5}$, but not O_3.	$PM_{2.5}$ per 10 $\mu g/m^3$ All ages: Total cardiovascular: 3.3% (1, 5.6) Dysrhythmia: 2.1% (-3, 7.0) Congestive heart failure: 5.5% (0.6, 10.5) Ischemic heart disease: 2.3% (-2, 6.4) Peripheral vascular and cerebrovascular disease: 5 (0.8, 9.3)
Peel et al. (2005) Atlanta, GA Aug 1998-Aug 2000	Emergency department visits for total and cause-specific respiratory diseases by age groups 0-1, 2-18, >19, and >65 yr. Time-series study.	$PM_{2.5}$ 19.2 ± 8.9 Range: 8.9 to 32.3	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{10-2.5}$, ultrafine PM count, SO_4^{2-}, H^+, EC, OC, metals, oxygenated hydrocarbons	0-2	Poisson GEE and GLM regression used for analysis. A priori models specified a lag of 0 to 2 days. Also performed secondary analyses estimating the overall effect of pollution over the previous 2 wk. Seasonal analyses indicated stronger associations with asthma in the warm months, especially for O_3 and $PM_{2.5}$ organic carbon. Quantitative results not presented for multipollutant, age-specific, and seasonal analyses.	$PM_{2.5}$ per 10 $\mu g/m^3$ All ages: All available data: Total respiratory: 1.6% (0, 3.5) Upper respiratory infections: 1.8 (0, 4.3) Asthma: 0.5 (-2, 3.3) Pneumonia: 1.1% (-2, 1.2) COPD: 1.5 (-3, 6.3)

Table A6 (cont'd). Effects of $PM_{2.5}$ on Daily Emergency Department Visits

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)						
Slaughter et al. (2005) Spokane, WA Jan 1995-Jun 2001	Study of hospital and ED visits for respiratory and cardiac condition in relation to PM_1, $PM_{2.5}$, PM_{10}, and $PM_{10-2.5}$ using a log-linear generalized linear model for lags 0 to 3 and compared results to a log-linear generalized additive model.	$PM_{2.5}$ 90% of concentration ranged between 4.2 and 20.2 $\mu g/m^3$	CO	1-3	No overall association with respiratory ED visits and any size fraction of PM nor with cardiac hospital admissions.	$PM_{2.5}$ ED visits (10 $\mu g/m^3$ increase) Lag 1: All respiratory: 1% (-2, 4) Acute asthma: 3% (-2, 9) Cardiac admissions: 0% (-4, 3)

Table A7. Effects of $PM_{10-2.5}$ on Daily Emergency Department Visits

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Quantitative Results
$PM_{10-2.5}$						
Metzger et al. (2004) Atlanta, GA Aug 1998-Aug 2000	Emergency department visits for total and cause-specific cardiovascular diseases by age groups >19 yr and >65 yr. Time-series study. 4, 407, 535, EDV from 31 Atlanta hospitals.	$PM_{10-2.5}$ Median: 9.1 $\mu g/m^3$ Range (10%-90%): 4.4-16.2	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{2.5}$, ultrafine PM count, SO_4^{2-}, H^+, EC, OC, metals, oxygenated hydrocarbons	0-2	Poisson GLM regression used for analysis. A priori models specified a lag of 0 to 2 days. Secondary analyses performed to assess alternative pollutant lag structures, seasonal influences, and age effects. Cardiovascular visits were significantly associated with several pollutants, including NO_2, CO, and $PM_{2.5}$, but not with $PM_{10-2.5}$ or O_3.	$PM_{10-2.5}$ per 5 $\mu g/m^3$ 3 day avg lag CVD visits: 1.2% (-1-4.0)
Peel et al. (2005) Atlanta, GA Aug 1998-Aug 2000	Emergency department visits for total and cause-specific respiratory diseases by age groups 0-1, 2-18, >19, and >65 yr. Time-series study.	$PM_{10-2.5}$ Median: 9.7 $\mu g/m^3$ Range (10%-90%): 4.4-16.2	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{2.5}$, ultrafine PM count, SO_4^{2-}, H^+, EC, OC, metals, oxygenated hydrocarbons	0-2	Poisson GEE and GLM regression used for analysis. A priori models specified a lag of 0 to 2 days. Also performed secondary analyses estimating the overall effect of pollution over the previous 2 wk. No significant associations with $PM_{10-2.5}$. Some significant associations with gaseous pollutants and PM_{10}. Quantitative results not presented for multipollutant, age-specific, and seasonal analyses.	$PM_{10-2.5}$ per 5 $\mu g/m^3$ 3 day avg lag Respiratory visits: 3% (-2-2.5)
Slaughter et al. (2005) Spokane, WA Jan 1995-Jun 2001	Study of hospital and ED visits for respiratory and cardiac condition in relation to PM_1, $PM_{2.5}$, PM_{10}, and $PM_{10-2.5}$ using a log-linear generalized linear model for lags 0 to 3 and compared results to a log-linear generalized additive model.	$PM_{10-2.5}$ 90% of concentration ranged between 4.2 and 20.2 $\mu g/m^3$	CO, PM_{10}, $PM_{2.5}$	1-3	No overall association with respiratory ED visits and any size fraction of PM nor with cardiac hospital admissions.	$PM_{10-2.5}$ ED visits (10 $\mu g/m^3$ increase) Lag 1: All respiratory: 1% (-2, 4) Acute asthma: 3% (-2, 8) COPD admissions: 1% (-7, 9)

Table A8. Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$					
Pope et al. (2004) Wasatch Front, UT Winter 1999-2000 and summer in Hawthorne and winter 2000-2001 in Bountiful and Lindon	Study of the effects of pollutants on autonomic function measured by changes in HRV and blood markers of inflammation in a panel of 88 elderly subjects using regression analysis.	$PM_{2.5}$ (TEOM) Mean (SD) 18.9±13.4	–	While this study observed statistical associations between $PM_{2.5}$ and HRV and C-reactive protein (CRP), most of the relevant variability in the temporal deviation of these physiological endpoints was not explained by $PM_{2.5}$. These observations therefore suggest that $PM_{2.5}$ may be one of multiple factors that influence HRV and CRP.	$PM_{2.5}$ 100 µg/m^3 increases −35 (SE = 8) in msec decline SDNN −0.81 (SE 0.17) mg/dL increase in CRP
Riedker et al. (2004) North Carolina Autumn 2001	Nine healthy North Carolina Highway Patrol troopers were monitored on 4 successive days for in-vehicle $PM_{2.5}$, roadside $PM_{2.5}$, and ambient $PM_{2.5}$. Ambulatory ECGs performed and various blood indicators measured.	$PM_{2.5}$ (ambient) 32.3 µg/m^3 Range: 9.9-68.9	O_3, CO, NO_2	The troopers showed significant and strong increases of HRV, ectopic beats, blood inflammation and coagulation markers, and MCV in association with the in-vehicle exposure to $PM_{2.5}$ as indication of increase of vagal activity.	$PM_{2.5}$ µg/m^3 In-vehicle 10 µg/m^3 decreased lymphocytes (−11%) increased neutrophils (6%) increased C-reactive protein (32%) ectopic beats (20%)

Table A8 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Schwartz et al. (2005b) Boston, MA 12 weeks during the summer of 1999	A panel study of 28 elderly subjects (age 61-89 years). Various HRV parameters were measured for 30 min once a week. Analysis using linear mixed models with log-transformed HRV measurements. To examine heterogeneity of effects, hierarchical model was used.	$PM_{2.5}$ during HRV measurement: Median: 10 µg/m^3 BC Median: 1.0 µg/m^3	BC,O_3, CO, SO_2, NO_2	HRV parameters examined included: SDNN, r-MSSD, PNN_{50}, and LF/HF ratio. Strongest association seen for BC, an indicator of traffic particles. The random effects model indicated that the negative effect of BC on HRV was not restricted to a few subjects. Subjects with MI experienced greater BC-related decrements in HRV parameters.	$PM_{2.5}$ 24 h Change in HRV parameters: SDNN: −2.6 (0.8, −6.0) r-MSSD: −10.1 (−2.8, −16.9) BC 24 h SDNN −5.1 (−1.5, −8.6) r-MSSD: −10.1 (−2.4, −17.2)
Park et al. (2005) Greater Boston area, MA Nov 2000-Oct 2003	Cross-sectional study examining the effect of pollutants on HRV in 497 adult males (mean age 72.7 years). Subjects were monitored during a 4-min rest period between 8 a.m. and 1 p.m. Pollutant levels measured at central site 1 km from study site. Exposure averaging times of 4, 24, and 48 h investigated. Modifying effects of hypertension, IHD, diabetes, and use of cardiac/anti-hypertensive medications also examined. Linear regression analyses. This subject group is from the VA Normative Aging Study.	$PM_{2.5}$ Mean (SD): 11.4 (±8.0) Range: 6.45-62.9	O_3, PNC, BC, NO_2, SO_2, CO	Of the pollutants examined, only $PM_{2.5}$ and O_3 showed significant associations with HRV outcomes. The 4-h averaging period was most strongly associated with HRV indices. The PM effect was robust in models including O_3. The associations between PM and HRV indices were stronger in subjects with hypertension (n = 335) and IHD (n = 142). In addition, calcium-channel blockers significantly influenced the effect of PM on low frequency power. Limitations of this study are the use of a short 4-min period to monitor HRV and the lack of repeated measurements for each subject.	$PM_{2.5}$ (8 µg/m^3) 48 h Change in low frequency power: Subjects with hypertension: −10.5% (−25.8, 7.9) Subjects without hypertension: −2.9% (−23.5, 23.2) Subjects with ischemic heart disease: 0.5% (−26.7, 37.7) Subjects without ischemic heart disease: −7.0% (−21.3, 9.9) LF/HF ratio increased 18.6% (95% CI 4.1-35.2%)

Table A8 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Wheeler et al. (2006) Atlanta, GA Fall 1999 and spring 2000	Examined pollutant effects on HRV in 18 subjects with COPD and 12 subjects with recent MI. Data collected 7 days in fall and spring. Associations examined using linear-mixed effect model. Age range 49-76 yrs.	$PM_{2.5}$ $\mu g/m^2$ Mean: 17.8	O_3, CO, SO_2, NO_2	For COPD patients, $PM_{2.5}$ exposure related to an increase in SDNN. The results for MI subjects were positive, but not significant. Effects were modified by medication use, baseline pulmonary function, and health status. The small numbers studied limit the study.	$PM_{2.5}$ 4-h IQR (11.65 $\mu g/m^3$) COPD 8.3% (1.7, 15.3) MI (IQR: −854 $\mu g/m^3$) 2.9% (−7.8, 2.3)
Rich et al. (2005) Boston, MA Jul 1995-Jul 2002	In 203 patients with implantable cardioverter defibrillators. Case-crossover study design used to examine association between air pollution and ventricular arrhythmias. For each case period, 3-4 control periods were selected. Various moving average concentrations of exposure considered – lags 0-2, 0-6, 0-23, and 0-47 h. Analysis using conditional logistic regression models.	$PM_{2.5}$ ($\mu g/m^3$) 1-h avg Median: 9.2 $PM_{2.5}$ ($\mu g/m^3$) 24-h avg Median: 9.28 IQR: 7.8	O_3, BC, CO, NO_2, SO_2	Associations were observed for $PM_{2.5}$ and O_3 with a 24-h moving average, and for NO_2 and SO_2 with a 48-h moving average. In two-pollutant analyses, only $PM_{2.5}$ and O_3 appeared to act independently.	Odds ratios: 24 h $PM_{2.5}$ per 7.8 $\mu g/m^3$ for ventricular arrhythmia 1.19 (1.02, 1.38) $PM_{2.5}$ with O_3 model: All events: 1.18 (1.01, 1.37)
Rich et al., (2006) Boston, MA Jun 1995-Dec 1999	In 203 patients with implantable cardioverter defibrillators, were 91 episodes of paroxysmal atrial fibrillation (PAF) in 29 subjects. Case-crossover design used to examining association between air pollutants and PAF, with matching control periods on weekday and hour within same calendar month. Conditional logistic regression models used.	$PM_{2.5}$ ($\mu g/m^3$) 1-h avg Median: 9.2 Max: 84.1 $PM_{2.5}$ ($\mu g/m^3$) 24-h avg Median: 9.8 Max: 53.2	O_3, BC, CO, NO_2, SO_2	Positive, but not significant, associations reported with $PM_{2.5}$, BC and NO_2. Significant associations reported with O_3. Authors note reduced statistical power for $PM_{2.5}$ and BC analyses due to missing data. Conclude PAF is associated with exposure to community air pollution.	$PM_{2.5}$ per 9.4 $\mu g/m^3$ IQR, 0-hour lag: OR 1.41 (0.82, 2.42) BC per 0.91 $\mu g/m^3$ IQR, 1-23 hour lag period: OR 1.46 (0.67, 3.17)

Table A8 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Dockery et al. (2005) Boston, MA Jul 1995-Jul 2002	Effect of air pollution on incidence of ventricular arrhythmias was examined in 203 patients with implantable cardioverter defibrillators using time-series methods. Mean follow-up period was 3.1 yr/subject. All subjects located <40 km of air pollution monitoring site. Two-day mean air pollution level used in analysis. Results analyzed by logistic regression using GEE with random effects. Modifying effects of previous arrhythmia within 3 days also examined.	$PM_{2.5}$ Median: 10.3 $\mu g/m^3$ IQR: 6.9 $\mu g/m^3$	O_3, BC, SO_4^{2-}, particle number, CO, NO_2, SO_2	No associations were observed between air pollutants and ventricular arrhythmias when all events were considered. When only examining ventricular arrhythmias within 3 days of a prior event, positive associations were found for most pollutants except for O_3. The associations suggest a link with motor vehicle pollutants.	$PM_{2.5}$ (6.9 $\mu g/m^3$) Odds ratios: All events: 1.08 (0.96, 1.22) Prior arrhythmia event <3 days: 1.60 (1.30, 1.96) Prior arrhythmia event >3 days: 0.98 (0.86, 1.12)

Table A8 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Rich et al. (2004) Vancouver, British Columbia, Canada Feb-Dec 2000	Case-crossover study design used to investigate association between air pollution and cardiac arrhythmia in patients aged 15-85 yr (n = 34) with implantable cardioverter defibrillators. Controls periods were selected 7 days before and after each case day. Analysis using conditional logistic regression.	$PM_{2.5}$ Mean: 8.2 µg/m^3 IQR: 5.2	O_3, EC, OC, SO_4^{2-}, CO, NO_2, SO_2	No consistent association between any of the air pollutants and implantable cardioverter defibrillators discharges.	Odds ratios were less than 1.0 at all lags (0, 1, 2, 3) for $PM_{2.5}$.
Gold et al. (2005) Boston, MA Summer of 1999	Study of associations between ambient pollutants and ST-segment levels in repeated measures involving 269 observations in 24 subjects 61-88 yr; each observed 12 times between June-September involving Holter recording. $PM_{2.5}$, BC, and CO were collected at 5 central sites 0.5 km from residences of subjects.	$PM_{2.5}$ 12 h Median: 9.8 µg/m^3 BC Median: 1.14 µg/m^3	CO, O_3, NO_2, SO_2	Elevated BC predicted increased risk of ST-segment depression with the strongest association being for the 5-h lagged value.	BC 12 h mean estimated overall ST-segment change: −0.08 mm p = 0.03

Table A8 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Dubowsky et al. (2006) St. Louis, MO Mar-June 2002	Investigation of ambient particles and markers of systemic inflammation among repeated measures from 44 subjects (≥60 yr). Trips from senior home in diesel bus into St. Louis. Analyzed using linear mixed model.	$PM_{2.5}$ Mean (SD) $\mu g/m^3$ 16 (6.0) Range 6.5-28	CO, NO_2, SO_2, O_3	Modest positive association found between fine particles and indicators of systemic inflammation with larger association suggested for individuals with diabetes, obesity, and hypertension. Positive associations found for longer moving averages.	$PM_{2.5}$ 4-h IQR (5.4 $\mu g/m^3$) 5-day mean $PM_{2.5}$ (6.1) 14% increased CRP (90% CI: 5.4 to 37%) for all individual and 81% (90% CI: 21, 172) for those with diabetes, obesity, hypertension

Table A8 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
O'Neill et al. (2005) Boston, MA May 1998-Jan 2000 Baseline period Time trial 2000-2002	270 patients with diabetes or at risk for diabetes were studied in relation to various pollutant levels and evaluated for association with vascular reactivity. Linear regressions were fit to the percent change in brachial artery diameter (flow-mediated and nitroglycerin-mediated) into particulate pollutant index and other factors.	$PM_{2.5}$ (1998-2002) Mean (SD): 11.5 (6.4) µg/m^3 Range: 1.1-40.0	SO_4^{2-}, BC, ultrafine	$PM_{2.5}$ was associated with nitroglycerin-mediated reactivity; an association was also reported with ultrafine particles. Effects were stronger in type II than type I diabetes. BC and SO_4^{2-} increases were associated with decreased flow-mediated reactivity among those with diabetes. Although the strongest associations were with the 6-day moving avg, similar patterns and quantitatively similar results appear in the other lags.	$PM_{2.5}$ 6-day moving average per IQR Nitroglycerin-mediated reactivity: −7.6%; 95% CI: 12.8 to −2.1
Schwartz et al. (2005a) Boston 2000	Examined the associations between $PM_{2.5}$ and HF in 497 subjects in Normative Aging Study (NAS) using linear regression controlling for covariates.	$PM_{2.5}$ Mean: 11.4 µg/m^3 (8.0 SD)	—	In subjects without the allele (for glutathione-*S*-transferase M1) an increase in $PM_{2.5}$ during the 48 h before HF (high-frequency component of HRV) measurement was associated with a decrease in HF. In subjects with the allele, no effect was noted. The effects of $PM_{2.5}$ on HR appear to be mediated by ROS, which may be a lag pathway for effects of combustion particles.	$PM_{2.5}$ µg/m^3 10 µg/m^3 increase HF −34% (−9%, −52%)
Sullivan et al. (2003) Western Washington State 1985-1994	A case-crossover study of 1,206 out-of-hospital cardiac arrest among persons with (n = 774) and without (n = 432) clinically recognized heart disease and daily measures of $PM_{2.5}$.	PM (nephelometry, km^{-1} bsp) Mean: 0.71 Min: 0.05 Max: 5.99	SO_2, CO	There was no consistent association between increased levels of fine particular matter and risk of primary cardiac arrest. This differs from results seen in other airsheds.	For cases with preexisting cardiac disease OR = 0.97 (0.89-1.07)

Table A8 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Mar et al. (2005) Seattle 1999-2001	Study of pollutants in relation to health parameters in 88 subjects (>75 yrs of age). HR, BP, and arterial oxygen saturation was examined using GEE.	$PM_{2.5}$ outdoor $\mu g/m^3$ range from 9.0 (±4.61) for healthy to 12.5 (±7.9) for CVD subjects	PM_{10}	Healthy subjects had decreases in HR associated with $PM_{2.5}$. SaO_2 does not have a consistent response to PM air pollution. Sample size was a limitation in this study.	$PM_{2.5}$ outdoor change in heart rate −0.75 bpm (−1.42, −0.07)
DeMeo et al. (2004) Boston July-August 1999	Investigated the association between $PM_{2.5}$ and oxygen saturation during a 12-wk repeated measures study of 28 older Boston residents using a fixed effects model/GLM.	$PM_{2.5}$ $\mu g/m^3$ IQR (11.45)	—	Demonstrated a statistically significant effect of ambient particle air pollution on decreased oxygen saturation at rest in a population of free-living older individuals with a more-significant interaction in those taking β-blockers. These small changes may be related to a pulmonary vascular and/or inflammatory cascade.	$PM_{2.5}$ Oxygen saturation (6-h rest period) −0.173% (−0.345, −0.001)
Lipsett et al. (2006) Coachella Valley, CA Feb-May 2000	Weekly ambulatory ECG's recorded, using Holter monitor, in 19 nonsmoking adults. Mixed linear regression models used with random effects parameters for inter-individual variation. Subjects' residences w/in 5 miles of one of two PM monitoring sites.	$PM_{2.5}$ $\mu g/m^3$ mean (range): Indio: 23.2 (6.3-90.4) Palm Springs: 14 (4.7-52)	PM_{10}, $PM_{10-2.5}$, O_3	No significant associations reported with $PM_{2.5}$; however were significant associations with $PM_{10-2.5}$.	Coefficient X1000 (p-value): SDNN: 24h $PM_{2.5}$: -1.63 (0.49) 6h $PM_{2.5}$: -1.21 (0.24) 4h $PM_{2.5}$: -0.55 (0.64) 2h $PM_{2.5}$: -0.37 (0.72)
Ebelt et al. (2005) Vancouver, Canada Summer 1998	Outcomes: FEV_1, ectopy, blood pressure, heart rate and variability 16 COPD patients, Vancouver, summer 1998, each subject measured 7 days mixed models	$PM_{2.5}$ Mean: 11.4	$PM_{10-2.5}$, and PM_{10} Ambient concentrations and exposures	$PM_{2.5}$ significantly associated with decreased systolic blood pressure and increased ectopic heart beats Use of ambient exposure instead of ambient concentration yields more meaningful results. Suggest that other Panel studies which depend on ambient concentrations or total personal exposure could fail to observe effects that existed. -day	No quantitative results reported. Results presented in figures only.

Table A9. Effects of Acute $PM_{10-2.5}$ Exposure on Cardiovascular Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{10-2.5}$					
Lipsett et al. (2006) Coachella Valley, CA Feb-May 2000	Weekly ambulatory ECG's recorded, using Holter monitor, in 19 nonsmoking adults. Mixed linear regression models used with random effects parameters for inter-individual variation. Subjects' residences w/in 5 miles of one of two PM monitoring sites.	$PM_{10-2.5}$ $\mu g/m^3$ Mean (difference between PM_{10} and $PM_{2.5}$): Indio: 23.2 (6.3-90.4) Palm Springs: 14 (4.7-52)	PM_{10}, $PM_{2.5}$, O_3	Significant associations between $PM_{10-2.5}$ (2h, 4h and 6h avg) and SDNN, SDANN. No significant associations reported with $PM_{2.5}$.	Coefficient X1000 (p-value): SDNN: 24h $PM_{10-2.5}$: 0.23 (0.81) 6h $PM_{10-2.5}$: -1.84 (0.006) 4h $PM_{10-2.5}$: -1.19 (0.024) 2h $PM_{10-2.5}$: -0.72 (0.017)
Ebelt et al. (2005) Vancouver, Canada Summer 1998	Outcomes: FEV_1, ectopy, blood pressure, heart rate and variability 16 COPD patients, Vancouver, summer 1998, each subject measured 7 days mixed models	$PM_{10-2.5}$ Mean: 5.6	$PM_{2.5}$ and PM_{10} Ambient concentrations and exposures	Associations between $PM_{10-2.5}$ and decreased systolic blood pressure and increased ectopic heart beats similar to $PM_{2.5}$ in size, but not statistically significant Use of ambient exposure instead of ambient concentration yields more meaningful results. Suggest that other Panel studies which depend on ambient concentrations or total personal exposure could fail to observe effects that existed.	No quantitative results reported. Results presented in figures only.

Table A10. Effects of Acute $PM_{2.5}$ Exposure on Various Respiratory Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$					
Gent et al. (2003) Southern New England Apr-Sept 2001	Panel study of 271 children (age <12 years) with active, doctor-diagnosed asthma followed over 183 days for respiratory symptoms. For analysis, cohort split into two groups: 130 who used maintenance medication during follow-up and 141 who did not, on assumption that medication users had more severe asthma. Logistic regression analyses performed.	$PM_{2.5}$ Mean: 13.1 (SD 7.9) $\mu g/m^3$	O_3	Correlation between daily $PM_{2.5}$ and 1-h max O_3 was 0.77 during this warm-season study. Significant associations between $PM_{2.5}$ and symptoms in some models, but not significant in two-pollutant models. Significant associations between O_3 and symptoms only in medication users, a group considered to be more sensitive.	$PM_{2.5}$ Shortness of breath OR for levels >19 $\mu g/m^3$ on previous day: 1.26 (1.02, 1.54) with O_3: 1.20 (0.94, 1.52)
Rabinovitch et al. (2006) Denver, CO winters 2001-2002 and 2002-2003	A school-based cohort study of children aged 6-13 years with physician-diagnosed asthma (n = 92), with data on bronchodilator use, urinary leukotriene E_4, and reported respiratory infections. Hourly and 24-h avg $PM_{2.5}$ data available from station 2.7 mi from school, using TEOM and FRM monitors.	$PM_{2.5}$ ($\mu g/m^3$) TEOM: Daily mean (SD) year 1: 6.5 (3.2) year 2: 8.2 (3.7) Morning mean (SD) year 1: 7.4 (4.7) year 2: 9.1 (5.0) Morning max (SD) year 1:15.5 (9.5) year 2: 18.4 (9.6) FRM: Daily mean (SD) year 1: 11.8 (7.2) year 2: 11.2 (5.5)	–	Peak $PM_{2.5}$ associated with bronchodilator use and urinary LTE4. Stronger associations reported with morning mean or max concentrations than daily mean; also stronger associations for severe asthmatics compared with mild/moderate asthmatics.	Morning max $PM_{2.5}$ per 12 $\mu g/m^3$: Increased bronchodilator use in severe asthmatics: 8.1% (2.9, 13.4) In mild/moderate asthmatics: 1.6% (-2.2, 5.4)
Mar et al. (2004) Spokane, WA Mar 1997-Jun 1999	Evaluated the effects of $PM_{2.5}$ on respiratory symptoms in both adults and children with asthma (16 adults, 9 children) using logistic regression.	$PM_{2.5}$ $\mu g/m^3$ Mean range over three years 8.1 to 11.0	PM_{10}, $PM_{10-2.5}$, PM_1	In children a strong association was reported between cough and PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, and PM_1. No association for symptoms in adults.	$PM_{2.5}$ (10 $\mu g/m^3$) Cough Lag 1 1.21 (1.00, 1.47)

Table A10 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Various Respiratory Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Jansen et al. (2005) Seattle 2002-2003	Study of 16 older asthma COPD patients' exposure to pollutants in relation to various health outcomes from data collected daily for 12 days analyzed using a linear mixed effect model.	$PM_{2.5}$ Outdoor IQR (SD) 10.47 (8.87) µg/m^3	BC, PM_{10}	FE_{NO} (fractional exhaled nitric oxide) increased in relation to increasing $PM_{2.5}$. No association was found between PM and changes in spirometry, blood pressure, pulse rate, or SaO_2 (oxygen saturation of blood).	$PM_{2.5}$ 10 µg/m^3 increase 4.2 ppb (95% 1.3-7.1) Increase in FE_{NO} for asthma subjects (n = 7)
Koening et al. (2005) Seattle, WA winter 2000 to spring 2001	Examined indoor-generated (E_{ig}) and outdoor generated (E_{ag}) PM pulmonary effects on 19 children with asthma using exhaled nitric oxide (eNO), using a linear model and also by GEE.	$PM_{2.5}$ Outdoor (E_{ag}) Mean: 11.1 µg/m^2 Range: 2.8-40.4	–	Based on a recursive model with a sample size of 8 children. E_{ag} was marginally associated with increases in eNO; no association reported with E_{ig}. Effects were only seen in children not using corticosteroid therapy.	$PM_{2.5}$ (10 µg/m^3) increase in eNO 5.6 ppb (CI: −0.6, 11.9) p = 0.08
Mar et al. (2005) Seattle, WA 1999-2001	Evaluated hourly exposures to $PM_{2.5}$ and FE_{NO} in 19 children with asthma using a polynomial distributed lag model, single and lag model taking into account ambient NO levels and use of inhaled corticosteroids.	$PM_{2.5}$ 1 h avg Ranges from 8.3 µg/m^3 at 3-h lag to 15.2 at 8-h lag	–	FE_{NO} was associated with hourly averages of $PM_{2.5}$ up to 10-12 h after exposure. No effects were seen in subjects on inhaled corticosteroids. Similar results were obtained for both analysis methods.	$PM_{2.5}$ (10 µg/m^3) Single lag 6.9 ppb (3.4 to 10.6)

Table A10 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Various Respiratory Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Adamkiewicz et al. (2004) Steubenville, OH Sept-Dec 2000	Breath samples collected weekly in panel of 29 elderly subjects, and analyzed for FE_{NO}. Indoor NO measured in study room at time of breath sample collection. Ambient measurements from a central monitoring site.	$PM_{2.5}$ ($\mu g/m^3$) Mean (max, IQR): 1h: 19.5 (105.8, 17.9) 24h: 19.7 (57.8, 17.7)	NO, NO_2, O_3, SO_2	Consistent positive, significant associations reported between FE_{NO} and $PM_{2.5}$, also with ambient and indoor NO levels. No associations reported with NO_2, O_3, or SO_2. In 2- and 3-pollutant models, $PM_{2.5}$ remains significant, while ambient and indoor NO associations are reduced and lose significance.	FE_{NO} change per IQR: 1h $PM_{2.5}$: 1.36 ppb change (0.58, 2.14) 24h $PM_{2.5}$: 1.45 ppb change (0.33, 2.57)
Giradot et al. (2006) Great Smoky Mountains NP, NC-TN Fall 2002, summer 2003	Investigated lung function in 354 adult-hikers over 71 days in relation to pollutant exposure using multiple linear regression models by ordinary least squares estimation. Hikers averaged 5.0 h of exercise.	$PM_{2.5}$ Average daily 13.9 ± 8.2 $\mu g/m^3$ Range 1.6-38.4 $\mu g/m^3$	O_3	Findings suggest that low levels of pollutant exposure over several hours may not result in significant declines in lung function in healthy adults engaged in exercise or work.	The coefficient for the percentage change in FEV_1 as a function of $PM_{2.5}$ adjusted for covariates $0.003\%/\mu g/m^3$ $p = 0.937$
Delfino et al. (2004) Alpine, CA Aug-Oct 1999, Apr-Jun 2000	Panel study of 19 asthmatic children (age 9-17 years) followed daily for 2 weeks to determine relationship between air pollutants and FEV_1. Linear mixed model used for analysis. Personal PM measurements made with dataRAM, which approximate $PM_{2.5}$ measurements.	$PM_{2.5}$ (24-h) Outdoor mean (SD) 10.3 (5.6) $\mu g/m^3$ Outdoor home: 11.0 (5.4) $\mu g/m^3$ Indoor home: 12.1 (5.4) $\mu g/m^3$ Personal PM: 37.9 (19.9) $\mu g/m^3$	PM_{10}, O_3	Significant declines in FEV_1 associated with various PM indices but not ambient O_3 levels. Stronger associations with multiday moving averages for both personal and stationary-site PM.	$PM_{2.5}$ Percent predicted FEV_1 with PM from previous 24 h: per 7.5 $\mu g/m^3$ central site: -0.7% (-1.9, 0.4) per 7.1 $\mu g/m^3$ outdoor home: -1.1% (-2.5, 0.1) per 6.7 $\mu g/m^3$ indoor home: -1.6% (-2.8, -0.4) per 30 $\mu g/m^3$ personal: -5.9% (-10.8, -1.0)

Table A10 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Various Respiratory Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Newhouse et al. (2004) Tulsa, OK Sep-Oct 2000	Panel study of 24 subjects aged 9-64 years with physician diagnosis of asthma. Performed PEF twice daily (morning and afternoon), and reported daily respiratory symptoms and medication use. Forward stepwise regression and Pearson correlation analysis.	$PM_{2.5}$ Mean (range): 13.07 (0.50-29.90) $\mu g/m^3$	O_3, CO, SO_2, pollen, fungal spores	Significant associations reported between O_3 and FEV_1 and various respiratory symptoms. In multi-pollutant models, including pollen and mold spores, maximum $PM_{2.5}$ negatively associated with cough, wheeze and shortness of breath; no discussion of these findings.	No quantitative results
Sinclair and Tolsma (2004) Atlanta, GA Aug 1998-Aug 2000	Respiratory medical visit data collected by Kaiser Permanente, including ambulatory care visits for asthma (adult and child), URI and LRI. ARIES air quality data used. Poisson GLM regression used for analysis. A priori models specified a lag of 0 to 2 days (average). Also performed analyses using average lag periods of 3-5 and 6-8 days.	$PM_{2.5}$ mean (SD) 17.62 (9.32) $\mu g/m^3$	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{10-2.5}$, ultrafine PM count, SO_4^{2-}, H^+, EC, OC, metals, oxygenated hydrocarbons (OHC)	Adult asthma visits associated with ultrafine number count, and negatively associated with $PM_{2.5}$ mass. Child asthma associated with OHC (0-2 day) and with PM_{10}, $PM_{10-2.5}$, EC and OC (3-5 day). LRI associated with $PM_{2.5}$ acidity and SO_2 (0-2 day) and with PM_{10}, $PM_{10-2.5}$, EC, OC and $PM_{2.5}$ water soluble metals. For URI, significant positive associations with ultrafine PM (0-2) and $PM_{10-2.5}$ (3-5 day) but negative associations with $PM_{2.5}$, SO_2 and sulfate.	$PM_{2.5}$ Quantitative results only for significant associations Adult asthma, per 9.32 $\mu g/m^3$ RR = 0.906 LRI visits: EC, per 1.38 $\mu g/m^3$ RR = 1.079 OC, per 2.2 $\mu g/m^3$ RR = 1.05 $PM_{2.5}$ acidity, per 0.02 $\mu g/m^3$ RR = 1.13 $PM_{2.5}$ water-soluble metals, per 0.03 $\mu g/m^3$ RR = 1.062

Table A10 (cont'd). Effects of Acute $PM_{2.5}$ Exposure on Various Respiratory Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$ (cont'd)					
Lewis et al. (2005) Detroit Winter 2001 thru Spring 2002	A longitudinal cohort study of primary-school age children with asthma, primarily African American and from low-income families, examined the relationship between lung function and PM and O_3 using GEE, considered effects modification by maintenance corticosteroid use and URI as recorded in diaries of 86 children in six 2-wk seasonal assessments for various lags.	$PM_{2.5}$ IQR 12.5 µg/m^3	O_3	Positive associations between $PM_{2.5}$ and O_3 with diurnal variability in FEV_1, and negative associations with lowest daily FEV_1; though many not statistically significant. Authors conclude that ambient air pollution exposure associated with adverse effects on pulmonary function among at-risk children with asthma in Detroit.	$PM_{2.5}$ Lag 1 Children on maintenance CS FEV_1 diurnal variability 1.61 (−0.50, 3.72) single pollutant model
Silkoff et al. (2005) Denver, CO winters 1999-2000 and 2000-2001	Two panels of adults with COPD (n = 16 and 18 for winters 1 and 2, respectively), with diary of twice-daily PEF and FEV_1, symptoms and bronchodilator use. 4-month study period included biweekly visits to collect data.	$PM_{2.5}$ (µg/m^3) Mean (SD): winter 1: 9.0 (5.2) winter 2: 14.3 (9.6)	PM_{10}, CO, NO_2	In winter 1, no evidence of detrimental effects on lung function; some significant associations between PM_{10}, NO_2 and CO with *increased* lung function. In winter 2, significant associations reported between PM_{10}, NO_2 and CO and increased medication use or symptoms. No significant associations reported with $PM_{2.5}$.	No quantitative results reported. Results presented in figures only.
Ebelt et al. (2005) Vancouver, Canada Summer 1998	Outcomes: FEV_1, ectopy, blood pressure, heart rate and variability 16 COPD patients, Vancouver, summer 1998, each subject measured 7 days mixed models	$PM_{2.5}$ Mean: 11.4	$PM_{10-2.5}$, and PM_{10} Ambient concentrations and exposures	Decrease in ΔFEV1 associated with ambient exposure for all PM components Use of ambient exposure instead of ambient concentration yields more meaningful results. Suggest that other Panel studies which depend on ambient concentrations or total personal exposure could fail to observe effects that existed.	No quantitative results reported. Results presented in figures only.

Table A11. Effects of Acute $PM_{10-2.5}$ Exposure on Various Respiratory Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{10-2.5}$					
Sinclair and Tolsma (2004) Atlanta, GA Aug 1998-Aug 2000	Respiratory medical visit data collected by Kaiser Permanente, including ambulatory care visits for asthma (adult and child), URI and LRI. ARIES air quality data used. Poisson GLM regression used for analysis. A priori models specified a lag of 0 to 2 days (average). Also performed analyses using average lag periods of 3-5 and 6-8 days.	$PM_{10-2.5}$ mean (SD) 9.67 (4.74) $\mu g/m^3$	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{2.5}$, ultrafine PM count, SO_4^{2-}, H^+, EC, OC, metals, oxygenated hydrocarbons (OHC)	Adult asthma visits associated with ultrafine number count, and negatively associated with $PM_{2.5}$ mass. Child asthma associated with OHC (0-2 day) and with PM_{10}, $PM_{10-2.5}$, EC and OC (3-5 day). LRI associated with $PM_{2.5}$ acidity and SO_2 (0-2 day) and with PM_{10}, $PM_{10-2.5}$, EC, OC and $PM_{2.5}$ water soluble metals. For URI, significant positive associations with ultrafine PM (0-2 day) and $PM_{10-2.5}$ (3-5 day) but negative associations with $PM_{2.5}$, SO_2 and sulfate.	$PM_{10-2.5}$ Per 4.74 $\mu g/m^3$ LRI visits: RR = 1.07 Child asthma: RR = 1.053 URI visits: RR = 1.021
Mar et al. (2004) Spokane, WA Mar 1997-Jun 1999	Evaluated the effects of $PM_{2.5}$ on respiratory symptoms in both adults and children with asthma (16 adults, 9 children) using logistic regression.	$PM_{10-2.5}$ Not reported	PM_{10}, $PM_{2.5}$, PM_1	In children a strong association was reported between cough and PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, and PM_1. No association for symptoms in adults. These findings also suggest that both larger and smaller particles can aggravate asthma symptoms	$PM_{10-2.5}$ (10 $\mu g/m^3$) Cough Lag 1 OR 1.06 (1.02, 1.10)
Ebelt et al. (2005) Vancouver, Canada Summer 1998	Outcomes: FEV_1, ectopy, blood pressure, heart rate and variability 16 COPD patients, Vancouver, summer 1998, each subject measured 7 days mixed models	$PM_{10-2.5}$ Mean: 5.6	$PM_{2.5}$ and PM_{10} Ambient concentrations and exposures	Decrease in ΔFEV1 associated with ambient exposure for all PM components Use of ambient exposure instead of ambient concentration yields more meaningful results. Suggest that other Panel studies which depend on ambient concentrations or total personal exposure could fail to observe effects that existed.	No quantitative results reported. Results presented in figures only.

Table A12. Effects of Acute $PM_{2.5}$ Exposure on Birth Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
$PM_{2.5}$					
Karr et al. (2006) South Coast Air Basin, CA 1995-2000	Linked hospital discharge for bronchiolitis during first year of life with $PM_{2.5}$ using closest measurements based on zip code. Case-crossover design used, with lag periods of 1-2, 3-5 and 6-8 days.	$PM_{2.5}$ Means range from 23.3 to 24.1 $\mu g/m^3$, for different lag periods	CO, NO_2	No significant associations reported for any of the pollutants.	$PM_{2.5}$ (10 $\mu g/m^3$) 1–2 day lag: OR 0.96 (0.94-0.99) 3-5 day lag: OR 0.98 (0.96, 1.00) 6-8 day lag: OR 0.96, (0.93, 0.98)

Additional Studies Examining Issues Related to Interpreting the PM-Morbidity Relationship:

U.S. and Canadian studies:

Liao et al. (2004): A population-based cross-sectional study of 5,431 members of the Atherosclerosis Risk in Communities cohort study in Minneapolis, MN; Jackson, MS; and Forsyth County, NC. Significant associations were reported between PM_{10} and decreased heart rate variability and increased heart rate. The mean PM_{10} concentration was 24.3 $\mu g/m^3$.

Delfino et al. (2002): Panel study of 22 asthmatic children (9-19 years) with diary of symptoms, medication use and presence of respiratory infection or hay fever for 61 days. Asthma symptoms were significantly associated with 1-h and 8-h PM_{10} (both lag 0 and 3-day average), but association with 24-h PM_{10} was not significant. Also significant associations were observed between asthma symptoms and 1-h ozone (lag 0) and 8-h max NO_2 (lag 0). Associations were stronger in children not using anti-inflammatory medication than in children on medication. Evidence of significant interaction between 1-h PM_{10} and 8-h max NO_2; but in 2-pollutant models, both lose significance.

Dugandzic et al. (2006): Linked 1998-2000 data from Nova Scotia Atlee Perinatal Database with air pollution data, using geocoding to link to monitoring site nearest the home. Significant associations were reported between LBW and exposures during the first trimester for PM_{10} (RR = 1.33, 1.02-1.74 for >75th percentile) and SO_2 (RR = 1.36, 1.04-1.78 for >75th percentile). No associations were reported with pollution exposures during the second and third trimesters. The mean PM_{10} concentration (trimester average) was 17 $\mu g/m^3$.

Letz and Quinn (2005): No correlation observed between Air Quality Index values for $PM_{2.5}$ or ozone with emergency department visits (n = 149) for asthma in military trainees.

Sagiv et al. (2005): Using a time-series analysis, this study investigated the effect of ambient outdoor PM_{10} on risk for preterm delivery counts in three Pennsylvania Counties and the City of Philadelphia from Jan 1, 1997-Dec 31, 2001. Results suggest an increase in preterm birth risk with exposure to PM_{10}, with a RR of 1.07 (0.98, 1.18) per 50 $\mu g/m^3$ PM_{10} (6 weeks preceding birth). The mean PM_{10} concentration was 25.3 $\mu g/m^3$.

International studies:

Romieu et al. (2005): A randomized double-blind trial, evaluating effect of supplementation with omega-3 fatty acids on reduction of $PM_{2.5}$-related HRV reduction. In 50 subjects living in nursing home with 6-month follow-up, HRV high-frequency change associated with 8 $\mu g/m^3$ $PM_{2.5}$ was -0.54% (95% CI -72, -24) with supplementation, and -7% (95% CI -20, +7) without supplementation. The mean $PM_{2.5}$ concentration was 19.6 $\mu g/m^3$.

Sorensen et al. (2003): In Copenhagen, personal exposure to $PM_{2.5}$ was associated with cardiovascular biomarkers (RBC count, hemoglobin) in women, but not men. No significant associations were observed with ambient $PM_{2.5}$ concentrations; however, personal exposure to carbon black was associated with plasma protein oxidation.

Boezen et al. (2005): In a panel of 327 elderly patients, symptom diaries and twice-daily PEF were collected for 3 months. Statically significant associations were reported for PM_{10}, BS and

NO_2 with respiratory symptoms in subjects with airway hyperresponsiveness and high IgE levels (AHR^+/IgE^+). There were no significant associations with the pollutants in the AHR^-/IgE^- subjects.

Chan et al. (2004): In Taipei, Taiwan, continuous measurements of ECG and personal exposure measurements of ultrafine particles ($NC_{0.02-1}$) (time period not indicated) were collected for a panel of nine young adults (19-29 years) and ten elderly patients (42-79 years). Decreases in HRV measures (SDNN, r-MSSD, LF, HF) were reported with personal exposure to $NC_{0.02-1}$ for both age groups.

Chuang et al. (2005): In Taipei, Taiwan, ECG and PM were measured continuously in a panel of 26 subjects (ten with coronary heart disease, 16 with hypertension) from November 2002 through March 2003; HRV measurements were used only for times when the subjects were awake. For all PM indicators, there were associations with decreases in several HRV measurements—SDNN, r-MSSD, LF, and HF—and positive associations with LF/HF. Associations were only significant for $PM_{0.3-1.0}$; the authors concluded that HRV was associated with $PM_{0.3-1.0}$, but not $PM_{1.0-2.5}$ or $PM_{2.5-10}$.

Lanki et al. (2006): In Helsinki, levels of $PM_{2.5}$ were related to ST-segment depression in 45 elderly (mean age 68.2 yrs [6.5]) nonsmoking subjects with stable coronary heart disease. Depression of ST-segment indicates a number of conditions including myocardial ischemia. The mass of fine particles was apportioned between five sources. ST-segment depression was associated with $PM_{2.5}$ originating from local traffic (RR = 1.53 [1.19-1.97] per 1 $\mu g/m^3$, at a 2-day lag) and long-range transport (RR = 1.11 [1.02, 1.20] per 1 $\mu g/m^3$). In multipollutant models where indicator elements were used for sources, only the absorbance (elemental carbon) indicator for local traffic and other combustion was associated with ST-segment depression. The mean $PM_{2.5}$ concentration was 12.8 $\mu g/m^3$

Penttinen et al. (2006): In a panel study of 57 adult asthmatics in Helsinki, subjects were followed for 181 days, and principal component analysis was used to evaluate source apportionment based on $PM_{2.5}$ mass. Decreases in morning PEF was linked to $PM_{2.5}$ from long-range transport and local combustion sources (1- and 2-day lags). There were no associations with $PM_{2.5}$ derived from oil combustion, soil, or sea salt.

Ruckerl et al. (2006): Blood parameters were measured in 57 male patients with coronary heart disease living in Erfurt, Germany, and positive associations were reported between elevated C-reactive protein and all measured pollutants – PM_{10}, $PM_{2.5}$, accumulation mode particles ($PM_{0.1-1}$), ultrafine particles, ED, OC, NO_2 and CO. The authors reported the strongest association with accumulation mode particles (3-day lag); significant associations were also observed with PM_{10}, ultrafine particles, NO_2 and CO (2-day lag strongest). Positive associations were also reported between ICAM-1 (indicator of endothelial dysfunction) and PM_{10}, $PM_{2.5}$, accumulation mode particles, EC and OC. No consistent associations were observed with various clotting factors.

Pekkanen et al. (2002): In three panels of elderly subjects in Amsterdam, Erfurt, and Helsinki (ULTRA study), biweekly submaximal exercise tests were done for six months. ST-segment depression was significantly associated with both $PM_{2.5}$ mass (OR 2.84, 1.42-5.66, 2-day lag) and ultrafine particles (OR 3.14, 1.56-6.32), and also with NO_2 and CO. No consistent associations were reported with thoracic coarse particles.

de Hartog et al. (2003): Three panels of elderly (aged 50+ years) subjects in Amsterdam, Erfurt, and Helsinki (ULTRA study) were followed for six months, with daily diaries and biweekly clinic visits. Prevalence of shortness of breath and phlegm were associated with $PM_{2.5}$, but not with ultrafine particles, CO or NO_2. The authors concluded that $PM_{2.5}$ was more closely correlated with cardiorespiratory symptoms than ultrafine particles.

Timonen et al. (2005): Repeated ECG measurements in panels of elderly subjects in Amsterdam, Erfurt, and Helsinki (ULTRA study) over six months. There were no consistent associations between HRV measurements and $PM_{2.5}$, but a pattern of generally positive associations between ultrafine particles and HF were reported, along with negative associations between ultrafine particles and LF/HF ratio.

Henneberger et al. (2005): Repeated ECG measurements in a panel of 56 patients with ischemic heart disease in Erfurt, Germany. $PM_{2.5}$ (6h average) was significantly associated with decreased T-wave amplitude, increased T-wave complexity and nearly significant with increased variability of the T-wave complex. Associations with 6h $PM_{2.5}$ were stronger than those with 24h $PM_{2.5}$ averages. Similar associations were seen with 6h ultrafine particles, accumulation mode particles, OC and EC, although most were not statistically significant. Significant associations were reported between OC and QT duration.

Table A13. Results of Epidemiologic "Intervention" Studies

Reference, Study Location and Period	Outcome Measure	Change in pollution/emissions	Reported PM Levels ($\mu g/m^3$)	Method/Design	Effect Estimates/Results
U.S. studies					
Lwebuga-Mukasa et al., 2003 Buffalo, NY	Hospital admissions and emergency department visits for respiratory illnesses	50% drop in total traffic at Peace Bridge following 9/11/2001			Statistically significant decreases in number of patients admitted to hospital or seen in emergency departments for respiratory illnesses.
European studies					
Bayer-Oglesby et al., 2005 9 Swiss communities 1991-2001	Respiratory symptoms via questionnaires, collected in 1992-1993 and 1998-2001	General air pollution abatement measures in Switzerland resulting in reduced PM_{10} concentrations	PM_{10} concentration declined an average of 9.8 $\mu g/m^3$ over all communities, ranged from 4.0 to 12.7 $\mu g/m^3$ declines. Mean PM_{10} concentrations in 1997-2000 ranged from 10 to 38 $\mu g/m^3$.	Multivariate logistic regression models used, including adjustment for covariates including indicators for SES, health status, indoor exposure factors, and avoidance behavior.	OR per 10 $\mu g/m^3$ decline in PM_{10}: chronic cough 0.65 (0.54, 0.79) bronchitis 0.66 (0.55, 0.80) common cold 0.78 (0.68, 0.89) nocturnal dry cough 0.70 (0.60, 0.83) conjunctivitis symptoms 0.81 (0.70., 0.95) No significant changes in prevalence of asthma, hay fever, wheeze or sneezing.

Table A13 (cont'd.). Results of Epidemiologic "Intervention" Studies

Reference, Study Location and Period	Outcome Measure	Change in pollution/emissions	Reported PM Levels ($\mu g/m^3$)	Method/Design	Effect Estimates/Results
European studies (cont'd)					
Frye et al., 2003 3 communities in East Germany 1992-1999	Pulmonary function measurements for 2,493 children 11-14 years of age, in 1992-1993, 1995-1996, and 1998-1999.	Reduction in air pollution concentrations following German reunification in 1990.	Mean TSP concentrations fell from 79 to 23 $\mu g/m^3$, while mean SO_2 concentration declined from 113 to 6 $\mu g/m^3$.	Linear regression using MIXED procedure in SAS, with log-transformed lung function measures and covariates including sex, height, season, lung function equipment, parental education, parental atopy, ETS exposure.	Percent change in lung function parameter per 50 $\mu g/m^3$ decrease in TSP: FVC: 4.7% (0.2, 9.5) FEV_1: 2.9% (-1.4, 7.3) Associations larger in magnitude and more often statistically significant for girls than for boys. Similar results reported with decreases in SO_2 concentration.
Heinrich et al., 2002 3 communities in East Germany 1992-1999	Respiratory symptom questionnaires for 4,949 children 11-14 years of age, in 1992-1993, 1995-1996, and 1998-1999.	Reduction in air pollution concentrations following German reunification in 1990.	In 1991, mean TSP concentrations range from 45 to 79 $\mu g/m^3$ in the three communities; in 1998, range from 25 to 33 $\mu g/m^3$. Fine particle concentrations ($NC_{0.01-2.5}$) reported for 1993 (11.7-12.6 $\mu g/m^3$) and 1999 (10.6-16.7 $\mu g/m^3$)	Two-stage analyses, using repeated-measures in generalized estimating equations. GEE logistic regression model used to compute symptom prevalences, adjusting for age, gender, parental education, parental atopy, and four indoor exposure factors (dampness/mold, gas cooking, ETS, cats); in second stage, logits of prevalence regressed against air pollution variables.	OR per 50 $\mu g/m^3$ TSP: Bronchitis: 3.02 (1.72, 5.29) Sinusitis: 2.58 (1.00, 6.65) Frequent colds: 1.90 (1.17, 3.09) Otitis media: 1.45 (0.89, 2.37) Febrile infections: 1.79 (0.92, 3.48) Cough in morning: 1.23 (0.82, 1.84) Shortness of breath: 1.33 (0.83, 2.12)

Table A13 (cont'd.). Results of Epidemiologic "Intervention" Studies

Reference, Study Location and Period	Outcome Measure	Change in pollution/emissions	Reported PM Levels ($\mu g/m^3$)	Method/Design	Effect Estimates/Results
European studies (cont'd)					
Neuberger et al. (2002) Linz, Austria 1985-1990	Lung function measured 2-8 times in 3,451 children in elementary and high schools, repeated measures over study time period.	Uniform decreases across districts of Linz for SO_2 and TSP; some areas report little changes and some dramatic decreases in NO_2 concentrations	NR	NR	Focus on lung function improvements with reduction in NO_2 concentrations; report that TSP and SO_2 do not act as confounders.
Sugiri et al. (2006) East and West Germany 1991-2000	Lung function measurements in 2,574 children aged 5-7 years	Dramatic decline in pollution in East Germany; smaller decline in West Germany	Annual average for TSP in year preceding measurement declined from 74 to 51 $\mu g/m^3$ in East Germany, from 54 to 44 in West Germany, average on the day of investigation decreased from 133 to 30 $\mu g/m^3$.	Linear regression with covariates as for Frye et al. (2003); included test for homogeneity of effects based on proximity to busy streets.	Lung function improved with reduction in air pollution; differences between East and West Germany vanished during study time period. Stronger associations reported for reactive airway measure with short-term TSP exposure measure, and with TLC with chronic TSP exposure measure. Per 40 $\mu g/m^3$ daily mean TSP: Raw: 0.969 (0.936, 1.004) per 40 $\mu g/m^3$ annual mean TSP: TLC: 0.938 (0.884, 0.996) Exposure to traffic also associated with reduced lung function.

Table A13 (cont'd.). Results of Epidemiologic "Intervention" Studies

Reference, Study Location and Period	Outcome Measure	Change in pollution/emissions	Reported PM Levels ($\mu g/m^3$)	Method/Design	Effect Estimates/Results
European studies (cont'd)					
Burr et al., 2003 North Wales, UK 1996-1999	Repeated questionnaires for respiratory symptom prevalence and PEF measures in 448 adults in congested and uncongested neighborhoods, before (1996-7) and after (1998-9) bypass opened and reduced traffic flow in area	Heavy goods vehicle counts and air pollution decreases with bypass opening	$PM_{2.5}$ mean before and after bypass in congested neighborhood : 21.2 $\mu g/m^3$ and 16.2 $\mu g/m^3$ (23.5% reduction) and in uncongested neighborhood: 6.7 $\mu g/m^3$ and 4.9 $\mu g/m^3$ (26.6% reduction) For PM_{10} in congested neighborhood : 35.2 $\mu g/m^3$ and 27.2 $\mu g/m^3$ (22.7% reduction) and in uncongested neighborhood: 11.6 $\mu g/m^3$ and 8.2 $\mu g/m^3$ (28.9% reduction) 46.9% reduction in heavy goods vehicles per hour	Percent subjects reporting improvement calculated for congested and uncongested streets and difference expressed as percent improvement.	% reduction in symptoms:: any wheeze -6.5 (-14.9, 2.0) # attacks -8.5 (-18.2, 1.2) No association with cough, phlegm, consulted doctor, rhinitis. Positive association with "affects activities" 10.3 (3.1, 17.3)

Toxicology studies:

Carvalho-Oliveira et al. (2004): Mutagenesis testing of particles collected during and after a bus strike in Sao Paulo, Brazil. Significant reduction in damage to DNA was observed, without significant changes in overt toxicity to cells, with exposure to PM collected during the strike. $PM_{2.5}$ mass concentrations were high (~40 $\mu g/m^3$) during strike; authors note "intense traffic jam" during this period. Concentrations of sulfur and BETX were lower on strike than non-strike days.

Somers et al. (2004): Study of heritable mutation rates in laboratory mice housed an urban-industrial area (near a major highway and two integrated steel mills) in Ontario, and mice housed in rural area. In both areas, one group of mice exposed to ambient air for 10 weeks and one group housed in a chamber with HEPA filtration system to remove 99.97+% of particles. HEPA filtration reduced heritable mutations in urban-industrial area, with larger effect on paternal mutation rates; no effect in rural area.

Table A14. Associations Between Source-related Fine Particles and Health Outcomes

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
Mar et al. (2006) Phoenix, AZ Feb 1995-Dec 1997	Mortality: All nonaccidental and cardiovascular causes; age 65 yr	$PM_{2.5}$: Estimated mean range across 9 independent analyses (24-h avg): SO_4^2: 1.3 to 3.6 Traffic: 4.0 to 7.7 Cu: 0.2 to 0.8 Sea salt: 0.1 to 0.2 Wood: 0.9 to 2.8 Soil: 0.8 to 2.6 Estimated 5^{th}-95^{th}% range across 9 independent analyses (24-h avg): SO_4^2: 2.5 to 6.9 Traffic: 10.3 to 16.1 Cu: 0.5 to 3.5 Sea salt: 0.2 to 0.6 Wood: 2.3 to 6.2 Soil: 2.0 to 7.9	None	0-, 1-, 2-, 3-, 4-day, or 5- lag	Time-series study. Poisson GLM with natural splines. Eight independent analyses performed. Daily $PM_{2.5}$ data collected using both gravimetric and TEOM samplers. Several teams of investigators used different source apportionment methods with $PM_{2.5}$ data. Traffic and secondary sulfate contributions, as estimated by different analyses, were well correlated.	Results from all investigators combined: Median % excess risk per 5^{th}-95^{th}% increment: (95% CI's not presented) <u>Cardiovascular</u>: Sulfate, lag 0: 16.0% Traffic, lag 1: 13% Cu smelter, lag 0: 12% Sea salt, lag 5: 10% Biomass/wood burning, lag 3: 9% No association reported with soil factor. Among all sources, the largest effect size for cardiovascular mortality observed for secondary SO_4^2, followed by traffic. Associations weaker for all-cause mortality. Variations in results across investigators/methods were small compared to the variations across source categories.

Table A14 (cont'd). Associations between Source-related Fine Particles and Mortality

Reference, Study Location and Period	Outcome Measure	Mean PM Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
Ito et al. (2006) Washington, DC Aug 1988-Dec 1997	Mortality: All nonaccidental, cardiovascular, and cardiorespiratory causes	$PM_{2.5}$: Estimated mean range across 9 independent analyses (24-h avg): SO_4^{2}: 5.1 to 10.7 Traffic: 1.6 to 4.7 NO_3^{-}: 1.6 to 6.7 Residual oil: 0.3 to 0.6 Wood smoke: 0.2 to 1.9 Incinerator: 0.3 to 1.0 Primary coal: 1.2 to 2.1 Sea salt: 0.2 to 0.9 Soil: 0.3 to 3.7 Estimated 5th% to 95th% range across 9 independent analyses (24-h avg): SO_4^{2}: 10.4 to 22.0 Traffic: 3.2 to 9.7 NO_3^{-}: 5.0 to 17.9 Residual oil: 0.9 to 3.3 Wood smoke: 0.6 to 5.7 Incinerator: 0.7 to 1.6 Primary coal: 3.2 to 3.8 Sea salt: 0.7 to 4.3 Soil: 0.9 to 4.8	None	0-, 1-, 2-, 3-, or 4-d lag	Time-series study. Poisson GLM with natural splines. Nine independent analyses performed. $PM_{2.5}$ gravimetric data collected on Thursday and Saturday only (U.S. Park Service, IMPROVE). Traffic contributions, as estimated by different analyses, were not well correlated; however, secondary sulfate contributions were fairly well correlated.	Results from all investigators combined: Median % excess risk per 5^{th}-95^{th}% increment: (95% CI's not presented) All causes: Sulfate, lag 3: 6.7% (1.7, 11.7) Traffic: 2.6% (-1.6, 6.9) Residual oil, lag 2: 2.7% (-1.1, 6.5) Primary coal, lag 3: 5.0% (1.0, 9.1) Soil: 2.1% (-1.8, 4.9) No significant associations were reported with the following factors: NO_3^{-}, wood burning, incinerator and sea salt. Among all sources, largest and most significant association with all-cause mortality observed for secondary SO_4^{2} at lag 3 d. Cardiovascular and cardiorespiratory mortality associations were generally similar to all-cause mortality. Variations in results across investigators/methods were small compared to the variations across source categories.

Table A14 (cont'd). Associations Between Source-related Fine Particles and Health Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean PM Levels	Copollutants Considered	Findings, Interpretation	Quantitative Results
Riediker et al. (2004) Wake County, NC Fall 2001	Cardiovascular outcomes: Nine healthy young non-smoking male troopers studied on 4 consecutive days, working 3PM to midnight shift. HRV measured with ambulatory ECG during shift and subsequent sleep phase. Blood parameters from blood sample drawn 15 min after work shift. Mixed effects regression models used.	In-vehicle $PM_{2.5}$ ($\mu g/m^3$) mean (SD): 23.0 (8.0)	—	Source apportionment of $PM_{2.5}$ mass identified 4 components: crustal material (Al, Si, Ca, Ti, Fe), wear of steel automotive components (Ti, Cr, Fe), gasoline combustion (benzene, CO), and speed-changing traffic (Cu, S, aldehydes). The "speed change" factor was significantly associated with increased heart cycle length, increased HRV, decreased % lymphocytes, decreased protein C and increases in von Willebrand factor, % neutrophils, mean red cell volume, and blood urea nitrogen. The "crustal" factor was significantly associated with increased uric acid. Nearly significant associations were seen between the "gasoline" factor and mean heart cycle length, decreased protein C and increased von Willebrand factor.	No quantitative results reported. Results presented in figures only.

Table A15. Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcome Measure	Mean Component Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
Burnett et al. (2004) 12 Canadian cities Jan 1981-Dec 1999	Mortality: All nonaccidental, cardiovascular, and respiratory causes	24-h avg SO_4^2: All 12 cities: 2.84 SD not provided.	$PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, NO_2, SO_2, CO, O_3	0-, 1-, or 2-d lag	Time-series study. Natural spline functions used to model nonlinear associations. SO_4^2 data determined from 75% of $PM_{2.5}$ filters. SO_4^2 data available on 9% of days with mortality data.	% excess risk per 2.84 $\mu g/m^3$: All causes: Single-pollutant model: Lag 1: 0.67% (0.00, 1.35) Two-pollutant model with NO_2: Lag 1: 0.46% (0.25, 1.18) NO_2 effect also nonsignificant in two-pollutant model.

Table A15 (cont'd). Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcome Measure	Mean Component Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
Goldberg et al. (2006) Montreal, Canada 1986-1993	Mortality: Diabetes, and nonaccidental mortality in subgroups with diabetes diagnosed at least 1 yr before death in adults >65. Also considered subgroups with cardiovascular diagnoses.	24-h avg measured SO_4^2: mean (SD) 3.3 (3.6) 24-h avg predicted SO_4^2 (from $PM_{2.5}$): mean (SD) 4.1 (3.6)	PM_{10}, TSP, coefficient of haze, $PM_{2.5}$, predicted $PM_{2.5}$, SO_2, NO_2, CO, O_3	0-, 1-, and avg of 0- to 2-day lags ("3-day mean")	Time-series study. Poisson regression using natural spline functions. Report results for SO_4^2 predicted from $PM_{2.5}$; used statistical model to estimate mass when measurements were not available; measured data available on 2680 days and predicted data for 3653 days.	Measured SO_4^2: % excess risk per 2.5 $\mu g/m^3$: mortality from diabetes: 5.1% (0.638, 9.71) nonaccidental mortality in subjects with diabetes: 2.31% (0.11, 4.56) Predicted SO_4^2: % excess risk per 2.9 $\mu g/m^3$: mortality from diabetes: 5.42% (0.44, 10.64) nonaccidental mortality in subjects with diabetes: 2.77% (0.23, 5.38) (all 3-day mean lag) Greater effects seen generally in the warm season. No significant association for nonaccidental mortality in subjects with diabetes, but without cancer, cardiovascular disease or airways disease. Associations reported for nonaccidental mortality in subjects with diabetes who also had any cardiovascular disease, chronic coronary disease, or atherosclerosis.

Table A15 (cont'd). Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcome Measure	Mean Component Levels ($\mu g/m^3$)	Copollutants Considered	Lag Structure Examined	Method/Design	Effect Estimates/Results
Klemm et al. (2004) Atlanta, GA Aug 1998-July 2000	Mortality: All nonaccidental, circulatory, respiratory, cancer, and other causes; age <65 yr and 65 yr	24-h avg mean (SD; range): SO_4^{2-}: 5.46 (0.79-19.34) EC: 2.03 (0.45.-9.76) OC: 4.54 (1.41-14.61) nitrates: 1.17 (0.15-5.40)	$PM_{2.5}$, $PM_{10-2.5}$, EC, OC, NO_2, NO_3^-, SO_2, CO, O_3, ultrafines, hydrocarbons, acid	Multiday lag of 0-1 d	Time-series study. Poisson GLM using natural cubic splines with quarterly, monthly, or biweekly knots. Default model used monthly knots. Analyses done by individual components, as well as three major $PM_{2.5}$ fractions: sulfate, carbon (OC and EC combined) and "balance" (remaining components combined).	% excess risk per 5.46 $\mu g/m^3$ SO_4^{2-}: All causes, age >65: Coefficient (t-statistic) for monthly knot models (lag 0-1): SO_4^{2-}: 0.00843 (1.54) EC: 0.01343 (1.54)) OC: 0.00529 (0.79) NO_3^-: -0.00103 (-0.06) For age >65, significant associations with $PM_{2.5}$ mass (quarterly and monthly knots; not significant for biweekly) but not with any individual $PM_{2.5}$ component. Results differ across model specifications (i.e., choice of lag and number of knots). No significant associations observed in those aged <65 yr.
Villeneuve et al. (2003) Vancouver, British Columbia, Canada Jan 1986-Dec 1998	Mortality: All nonaccidental, cardiovascular, respiratory, and cancer causes; SES status	24-h avg SO_4^{2-}: 2.7 10^{th}-90^{th}% 1.1-4.4 Range 0.4-9.0	$PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, TSP, coefficient of haze, SO_2, NO_2, CO, O_3	0-, 1-, or 2-d lag; multiday lag of 0-2 d	Time-series study. Poisson regression using natural spline functions. SO_4^{2-} data collected every 6th day.	% excess risk (95% CI) per 3.3 $\mu g/m^3$ SO_4^{2-}: All causes: Lag 0: 2.9% (-4.4, 10.8) Cardiovascular: Lag 0:. 3.2% (-14.1, 9.1) Respiratory: Lag 0: 8.3% (-12.3, 33.8) Cancer: Lag 0: 8.0% (-4.5, 22.1)

Table A15 (cont'd). Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean Component Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Effects (Relative Risk and 95% CI)
Metzger et al. (2004) Atlanta, GA Aug 1998-Aug 2000	Emergency department visits for total and cause-specific cardiovascular diseases by age groups >19 yr and >65 yr. Time-series study. 4, 407, 535, EDV from 31 Atlanta hospitals. Components included acidity (H^+), EC, OC, water-soluble (WS) metals, sulfates	Median ($\mu g/m^3$) (10-90% Range) SO_4^2: 4.5 (1.9-10.7) WS metals: 0.021 (0.006-0.061) OC: 4.1 (2.2-7.1) EC: 1.6 (0.8-3.7)	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, ultrafine PM count, oxygenated hydrocarbons	0-2	Poisson GLM regression used for analysis. A priori models specified a lag of 0 to 2 days. Secondary analyses performed to assess alternative pollutant lag structures, seasonal influences, and age effects. Cardiovascular visits were significantly associated with several pollutants, including NO_2, CO, and $PM_{2.5}$, but not O_3 or sulfates	Relative Risks for: SO_4^2 per 5 $\mu g/m^3$ WS metals per 0.03 $\mu g/m^3$ OC per 2 $\mu g/m^3$ EC per 1 $\mu g/m^3$ All ages: Total cardiovascular: SO_4^2 1.003 (0.968, 1.005) WS metals 1.027 0.998, 1.056) OC 1.026 (1.006, 1.046) EC 1.020 (1.005, 1.036) Congestive heart failure: SO_4^2 1.009 (0.938, 1.162) WS metals 1.040 (0.981, 1.051) OC 1.048 (1.007, 1.091) EC 1.035 (1.003, 1.068) Ischemic heart disease: SO_4^2 0.997 (0.936, 1.090) WS metals 1.000 (0.951, 1.051) OC 1.028 (0.994, 1.064) EC 1.019 (0.992, 1.046) Peripheral vascular and cerebrovascular disease: SO_4^2 1.025(0.964, 1.090) WS metals 1.043 (0.991, 1.036 OC 1.026 (0.990, 1.062) EC 1.021 (0.994, 1.049)

Table A15 (cont'd). Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcomes and Design	Mean Component Levels	Copollutants Considered	Lag Structure Examined	Method, Findings, Interpretation	Effects (Relative Risk and 95% CI)
Peel et al. (2005) Atlanta, GA Aug 1998-Aug 2000	Emergency department visits for total and cause-specific respiratory diseases by age groups 0-1, 2-18, >19, and >65 yr. Time-series study. Components included acidity (H^+), EC, OC, water-soluble (WS) metals, sulfates	Median ($\mu g/m^3$) (10-90% Range) SO_4^2: 5.5 (1.9-10.7) WS metals: 0.028 (0.006-0.061) OC: 4.5 (2.2-7.1) EC: 2.0 (0.8-3.7)	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, ultrafine PM count, oxygenated hydrocarbons oxygenated hydrocarbons	0-2	Poisson GEE and GLM regression used for analysis. A priori models specified a lag of 0 to 2 days. Also performed secondary analyses estimating the overall effect of pollution over the previous 2 weeks. Seasonal analyses indicated stronger associations with asthma in the warm months, especially for O_3 and $PM_{2.5}$ organic carbon. Quantitative results not presented for multipollutant, age-specific, and seasonal analyses.	All ages relative risks for: SO_4^2 per 5 $\mu g/m^3$ WS metals per 0.03 $\mu g/m^3$ OC per 2 $\mu g/m^3$ EC per 1 $\mu g/m^3$ All available data: Total respiratory: SO_4^2 0.998 (0.968, 1.028) WS metals 1.005 (0.981, 1.031 OC 1.011 (0.997, 1.025) EC 0.999 (0.987, 1.011) Upper respiratory infections: SO_4^2 1.001 (0.965, 1.039) WS metals 1.010 (0.980, 1.040) OC 1.011 (0.995, 1.028) EC 0.999 (0.985, 1.013) Asthma: SO_4^2 0.991 (0.949, 1.035) WS metals 1.007 (0.973, 1.043) OC 1.000 (0.978, 1.023) EC 0.993 (0.976, 1.011) Pneumonia: SO_4^2 1.013 (0.959, 1.069) WS metals 0.997 (0.958, 1.039) OC 1.028 (1.004, 1.053) EC 1.006 (0.987, 1.026) COPD: SO_4^2 1.004 (0.929, 1.085) WS metals 0.971 (0.913, 1.032 OC 0.996 (0.959, 1.035) EC 0.981 (0.952, 1.012)

Table A15 (cont'd). Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean Component Levels	Copollutants Considered	Findings, Interpretation	Effects
O'Neill et al. (2005) Boston, MA May 1998-Jan 2000 Baseline period Time trial 2000-2002	Cardiovascular Outcomes: 270 patients with diabetes or at risk for diabetes were studied in relation to various pollutant levels and evaluated for association with vascular reactivity. Linear regressions were fit to the percent change in BAD (flow-mediated and nitroglycerin-mediated) into particulate pollutant index and other factors.	SO_4^{2} mean: 3.3 μg/m^3 Range: 0.3 to 12.9	$PM_{2.5}$, BC, ultrafine	$PM_{2.5}$ was associated with nitroglycerin-mediated reactivity; an association was also reported with ultrafine particles. Effects were stronger in type II than type I diabetes. Black carbon and SO_4^{2} increases were associated with decreased flow-mediated reactivity among those with diabetes. Although the strongest associations were with the 6-day morning average, similar patterns and quantitatively similar results appear in the other lags.	Effect estimate per IQR SO_4^{2} 6-day morning average Nitroglycerin-mediated 6.2%; 95% CI, 11.5 to 0.6

Table A15 (cont'd). Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean Component Levels	Copollutants Considered	Findings, Interpretation	Effects
Sinclair and Tolsma (2004) Atlanta, GA Aug 1998-Aug 2000	Respiratory medical visit data collected by Kaiser Permanente, including ambulatory care visits for asthma (adult and child), URI and LRI. ARIES air quality data used. Poisson GLM regression used for analysis. A priori models specified a lag of 0 to 2 days (avg). Also performed analyses using avg lag periods of 3-5 and 6-8 days. Fine particle components included SO_4^2, H^+, EC, OC, water-soluble (WS) metals.	mean (SD) in $\mu g/m^3$: SO_4^2: 5.52 (3.5) H^+: 0.02 (0.02) EC: 2 (1.38) OC: 4.49 (2.2) WS metals: 0.03 (0.03)	NO_2, SO_2, CO, O_3, PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, ultrafine PM count, oxygenated hydrocarbons (OHC)	Adult asthma visits associated with ultrafine number count, and negatively associated with $PM_{2.5}$ mass. Child asthma associated with OHC (0-2 day) and with PM_{10}, $PM_{10-2.5}$, EC and OC (3-5 day). LRI associated with $PM_{2.5}$ acidity and SO_2 (0-2 day) and with PM_{10}, $PM_{10-2.5}$, EC, OC and $PM_{2.5}$ WS metals. For URI, significant positive associations with ultrafine PM (0-2 day) and $PM_{10-2.5}$ (3-5 day) but negative associations with $PM_{2.5}$, SO_2 and sulfate.	Risk Ratios per SD: Adult asthma visits: SO_4^2 NS H^+ NS EC NS OC NS WS metals NS Child asthma: SO_4^2 NS H^+ NS EC RR = 1.046 OC RR = 1.046 WS metals NS LRI visits: SO_4^2 NS H^+ NS EC RR = 1.079 OC RR = 1.05 WS metals RR = 1.062 URI visits: SO_4^2 RR = 0.976 H^+ NS EC NS OC NS WS metals NS Quantitative results provided only for statistically significant findings.

Table A15 (cont'd). Associations of Acute Exposure to Fine Particle Components with Health Outcomes

Reference, Study Location and Period	Outcomes and Methods	Mean Component Levels	Copollutants Considered	Findings, Interpretation	Effects
Delfino et al. (2003) Los Angeles, CA Nov 1999-Jan 2000	Respiratory outcomes: Panel study of 22 Hispanic children (10-15 yr) with asthma, living in the Huntington Park region of LA. Daily diary with symptoms, inhaler use, and PEF measurements made three times daily. GEE regression methods used.	Mean (range) in $\mu g/m^3$: EC: 5.09 (1.79-9.42) IQR = 2.91 OC: 9.47 (4.29-17.05) IQR = 4.64 (Measured in PM_{10})	NO_2, SO_2, CO, O_3, PM_{10}, numerous air toxics	Significant associations reported between increased asthma symptoms and PM_{10}, EC, OC, NO_2 and SO_2, acetaldehyde, benzene, ethylbenzene and tetrachloroethylene. Associations with PM10, EC, and OC generally decreased in size and lose significance in 2-pollutant models with air toxics. Authors conclude that their findings support the view that air toxics in the pollutant mix from traffic and industrial sources may have adverse effects on asthma in children.	Odds Ratio for asthma symptom per IQR: EC: lag 0: 1.85 (1.11-3.08) lag 1: 1.01 (0.66, 1.53) OC: lag 0: 1.88 (1.12, 3.17) lag 1: 1.08 (0.80, 1.46)

Additional U.S. and Canadian Studies:

Bennett et al. (2006): Assessed relationship between Asian dust event in April 1998 and hospital admissions. No statistically significant difference in hospital admissions rates for either respiratory or cardiovascular diseases between 4-day period in 1998 and corresponding 4-day period in 1997; methods include graphical display and chi-square test for difference.

Clairborn et al. (2002): This report includes discussion of ongoing research in Spokane, WA, that will examine relationships between health outcomes and particle sizes and fine and thoracic coarse particle metal concentrations. In addition, results of previous publications from this research group are discussed, and it is suggested that fine particulate metals, particularly Zn, are significantly associated with asthma hospital admissions.

Henneberger et al. (2005): Repeated ECG measurements in a panel of 56 patients with ischemic heart disease in Erfurt, Germany. $PM_{2.5}$ (6 h avg) was significantly associated with decreased T-wave amplitude, increased T-wave complexity and nearly significant with increased variability of T-wave complex. Associations with 6 h $PM_{2.5}$ were stronger than those with 24 h $PM_{2.5}$. Similar associations were observed with 6 h ultrafine particles, accumulation mode particles, OC and EC, although most were not statistically significant. A significant association was reported between OC and QT duration.

Moshammer and Neuberger (2003): In a panel of 78 children, biweekly lung function tests and daily symptom diaries were collected for 4 weeks. Ambient monitoring was conducted to determine "active surface" of particles by unipolar diffusion charging. The results of this study demonstrated that active surface correlates with PAH levels of particles. Significant associations reported between active surface of particles and evening cough, shortness of breath and wheeze.

Table A16: CAPs Studies with Source Apportionment or Components Analysis

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Factor or Principal Component Analysis					
Huang, Y-C.T et al. (2003)	Human, M (n = 35), F (n = 2) 26.2±0.7 yr	2 h with 15 min alternating rest and exercise ~50 L/min; assessed 18 h PE	Chapel Hill, NC air; HAPC; 72.2 μg/m^3 (range 0–311 μg/m^3) Median soluble components (μg/m^3): sulfate 17.6; V 2.1; Fe 42.6; Zn 66.4; Cu 13.1; As 2.2; Ni 1.2; Se 6.0; Pb 3.4	BALF: Cell counts Cell differential protein Cytokines PGE_2 Protein Fibrinogen NO Fibronectin Venous blood: CBC Ferritin Fibrinogen	Factor 1 (sulfate/Fe/Se) correlated with increases in BALF PMN. Factor 2 (Cu/Zn/V) correlated with elevated blood fibrinogen levels. BALF fibronectin correlated positively with BALF PMN. Factor 1 correlated highly with PM mass.
Batalha et al. (2002)	Rat, M, SD, 200–250 g; CB induced with SO_2	5 h/day for 3 consecutive days in 6 experimental sets; assessed 24 h PE	Boston, MA; HAPC; mean mass conc. 262.21±213 μg/m^3 (range 73.5–733) Elemental composition (μg/m^3); sulfate 66.9; EC 11.45; OC 57.73; Al 1.22; Si 4.62; S 25.61; Cl 0.68; K 1.68; Ca 1.82; Ti 0.20; V 0.05; Cr 0.01; Mn 0.09; Fe 3.47; Ni 0.05; Cu 0.10; Zn 0.26; As 0.01; Se 0.02; Br 0.07; Cd 0.02; Ba 0.73; Pb 0.12	Histopathology Morphometry for L/W ratios (muscular hypertrophy and constriction of vessels)	CAPs caused vasoconstriction of small pulmonary arteries. Exposure to CAPs in normal and CB rats resulted in decreased L/W ratio that was associated with CAPs mass, Si, Pb, sulfate, EC and OC. In normal rats exposed to CAPs, decreased L/W ratio was associated with sulfate and Si. In CB rats, decreases in L/W ratio were associated with Si and OC. No significant associations were observed between the L/W ratio and Day 1 of exposure (reported effects due only to Days 2 and 3).

Table A16 (cont'd): CAPs Studies with Source Apportionment or Components Analysis

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Factor or Principal Component Analysis (cont'd)					
Goldsmith et al. (2002)	Mice, Balb/c; sensitized to OVA on days 7 and 14, pretreated with OVA via inhalation on days 21, 22, and 23	5 h/day for 3 days (21, 22, and 23); exposure to CAPs only, O_3 only (0.3 ppm), or CAPs+O_3; assessed 24 or 48 h PE	Boston, MA; HAPC; mean mass conc. 302±58 μg/m^3; range 63.3–1569 μg/m^3 Elemental composition (μg/m^3): Al nd–17.2, Si 0.9–35.1, S 3.5–187, Cl nd–7.9, K 0.4–5.7, Ca 0.6–12.5, Ti nd–1.9, V nd–0.26, Cr nd–0.05, Mn 0.01–0.43, Fe 1.4–21.9. Ni nd–0.16, Cu 0.02–0.43, Zn 0.06–1.1, Br 0.01–0.24, Ba 0.04–0.83, Pb 0.001–0.34, As nd–0.31, Se nd–0.06, Cd nd	Pulmonary function BALF: Cell viability Cell counts Cell differentials	CAPs alone caused increases in penh (a measure of airway responsiveness) immediately following exposure, although the magnitude of response was small (approximately 0.9% for a 100 μg/m^3 increase in CAPs). CAPs+O_3 exposure resulted in elevated penh when sensitized animals were challenged with methacholine. An Al/Si component for daily and 3-day cumulative concentrations was associated with increased penh for OVA animals exposed to CAPs+O_3. A S component was associated with elevated penh for non-OVA mice exposed to CAPs only.
Wellenius et al. (2003)	Dog, F, retired mongrel; implanted balloon occluder on left anterior descending coronary artery	6 h/day; immediately PE a 5 min preconditioning occlusion followed 20 min later by a 5 min study occlusion	Boston CAPs; HAPC; mean mass conc. 345±194 (range 161–957) Elemental composition (μg/m^3): sulfate 77.90; BC 9.78; EC 21.48; OC 66.71; Al 2.13; As 0.028; Br 0.09; Ca 4.31; Cr 0.03; Cu 0.19; Fe 8.26; K 2.15; Mn 0.18; Ni 0.16; Pb 0.15; S 27.41; Se 0.02; Si 8.17; Ti 0.41; V 0.16; Zn 0.58	ECG: Peak and integrated ST-segment elevation Peak HR Incidence of arrhythmias	CAPs enhanced occlusion-induced peak ST-segment elevation. HR was not affected by CAPs. ST-segment elevation was associated with Si and other crustal elements. CAPs mass or particle number was not associated with any endpoint.

Table A16 (cont'd): CAPs Studies with Source Apportionment or Components Analysis

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Components (Elements, sulfate, nitrate, organic/elemental carbon)					
Gong et al. (2005)	Human, healthy (4F, 2M, 68±11 yr) and COPD (9F,9M, 72±7 yr); exposures were on separate days followed by at least 2 wks	2 h with 15 min alternating rest and exercise; assessed during, at 0h PE, 4 h PE, and day 2 (~22h PE)	Los Angeles, CA; HAPC Exposures to: (a) FA (b) 0.4 ppm NO_2 (c) CAPs - predominantly $PM_{2.5}$ at ~200 µg/m^3 collected with HAPC (d) CAPs + NO_2 <0.1 µm contributed ~6 µg/m^3 in all exp; >2.5 µm contributed ~6 µg/m^3 in FA or NO_2 exp and 12 µg/m^3 in CAPs and CAPs +NO_2 exp; CAPs and CAPs+NO_2 (1–2.5 µm) ~170 µg/m^3 Elemental composition (µg/m^3): Si 4.0; Fe 2.9; EC 10.1; Al 1.6; Ca 2.3; Na 2.0; K 1.1; Cl 2.5; NO_2 42 ppb	ECG SaO_2 Pulmonary function BP HR Sputum: Cell counts Cell differentials	For all exposure groups, there were no changes in symptoms, spirometry, or differential cell counts. In subjects exposed to CAPs and CAPs+NO_2, decrements in MMEF and SaO_2 (greater in healthy than COPD) were observed. Decreased percentages of columnar epithelial cells in sputum were also reported. For subjects exposed to CAPs+NO_2, FEV_1 and FVC decreases were associated with sulfate levels; total mass did not correlate with sulfate. HR increased for both CAPs groups post-exposure; for COPD subjects, the tendency of increased HR was lower with increasing mass. There was a decrease in self-reported symptoms during CAPs+NO_2 that were associated with elevated Fe concentration.
Urch et al. (2004)	Human, healthy (14M, 10F; 35±10 yr)	2 h CAP + O_3 (crossover design); O_3 conc. 120 ppb	Toronto CAPs; HAPC; mean mass conc.148 µg/m^3 (range 102–257) Major constituents (µg/m^3): C 22.7 (OC 19.7, EC 2.5), sulfate 14.2, nitrate 14.0, ammonium 5.4, Ca 0.78	BAD	A decrease in OC or EC concentration was associated with changes in BAD. When multiple linear regression analysis (MLRA) was conducted on the dose metric (a product of mean ventilation, exposure duration, and mass concentration), elevated OC+sulfate was associated with change in BAD (although p-value = 0.06 for sulfate in the MLRA). Sulfate was not associated with changes in BAD alone.

Table A16 (cont'd): CAPs Studies with Source Apportionment or Components Analysis

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Components (Elements, sulfate, nitrate, organic/elemental carbon) (cont'd)					
Urch et al. (2005)	Human, healthy (13M, 10F; 35±10 yr)	1 h CAP + O_3 (crossover design); O_3 conc. 121 ppb	Toronto CAPs; HAPC; mean mass conc.147±27 μg/m^3 (range 102–214); C 28.4 μg/m^3	BP HR	DBP increased an average of 6 mm Hg over the 2 h of exposure. A nonlinear relationship was reported between DBP change and estimated exposure concentration of OC; a similar correlation was observed between MAP and OC.
Dvonch et al. (2004)	Rat, BN, M; 7 rats/group	8 h/day for 3 consecutive days (22–24 July 2004); assessed 24 h PE	Urban Detroit CAPs; HAPC; mean mass conc. 354 μg/m^3 Elemental composition ranges (ng/m^3): sulfur 1393–26839, Mg 173–487; Ca 1137–2125; V 2–15; Fe 1035–2377; Ni 4.3–11.5; Cu 101–152; Cd 0.44–1.75; La 0.3–9.7; Ce 0.6–18.5; Sm 0.03–0.21; Pb 48.6–57.5	Plasma ADMA	Elevated levels of ADMA were observed in CAPs-exposed rats. CAPs mass concentration was the highest on the first day of exposure (4–5 times greater than Days 2 or 3). Increased PM mass was associated with elevated levels of S, V, La, Ce, and Sm. An industrial complex (coal combustion, oil refineries, coke ovens, iron/steel mills, sewage sludge incineration) was located SW of the study location.
Gurgueira et al. (2002)	Rat, SD, 250–300g	1, 3, or 5 h	Boston, MA; HAPC; conc. mass range 100–956 μg/m^3; mean mass conc. 300±60 μg/m^3	Organ CL (for ROS concentration); organ water content; LDH; SOD; catalase	Exposure to CAPs for 5 h resulted in increased oxidative stress in the lung, that was associated with the PM content of Fe, Mn, Cu, and Zn. Oxidative stress observed in the heart following exposure was associated with Fe, Al, Si, and Ti in CAPs. Organ water content and LDH activity also increased. Elevated levels of the antioxidants SOD and catalase were also reported following exposure.
Kodavanti et al. (2005)	Rat, WKY and SH, 10–12 wk old	SH one 4 h exp, assessed 1–3 h PE; SH and WKY 4h/day or 2 days, assessed 1 day PE	Research Triangle Park, NC; HAPC 1-day exp: 1138–1765 μg/m^3, size range 1.07–1.19, mean 1.12 μm 2-day exposure 144-2758 μg/m^3, size range 1.27–1.48, mean 1.39 μm	Pulmonary function BALF: Cell count Cell differentials Total protein, albumin, LDH, NAG, GGT, glutathione, ascorbic acid, cytokines Blood: CBC Plasma fibrinogen ACE activity CRP	In the 1-day exposure, no biologic effects were observed. In the 2-day exposure, WKY rats exposed to CAPs had decreased total cells and AM and increased PMN. Fibrinogen levels were also elevated in these animals. In the 2-day exposure, SH rats exposed to CAPs had increased total protein, GGT activity, ascorbate, UA, and PMN. Decreases in albumin were observed in these rats. For SH rats exposed to CAPs, plasma fibrinogen correlated with Zn and OC when expressed as mg/CAP.

Table A16 (cont'd): CAPs Studies with Source Apportionment or Components Analysis

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Components (Elements, sulfate, nitrate, organic/elemental carbon) (cont'd)					
Morishita et al. (2004)	Rat, BN, M; some sensitized to OVA (days 1-3) and challenged (days 14-16), n = 6/group	4 days after challenge; 10 h/day for either 4 days (July) or 5 days (Sept); assessed 24 h PE	Urban Detroit; HAPC; mean mass conc. 676 µg/m^3 (July), 313 µg/m^3 (Sept) Elemental composition (TWA in ng/m^3 in July): La 1.2; S 77716; V 17; Mn 206 Elemental composition (TWA in ng/m^3 in Sept): La 1.5; S 19272; V 46; Mn 309	BALF (left lung): Cell counts Cell differentials Leukocytes Total protein Right lung: trace elements by ICP-MS	CAPs caused increases in BALF eosinophils and protein in allergenic rats. Increased levels of La, V, Mn, and S in normal rats and greater increases in allergenic rats that were colocalized with eosinophilic infiltrates. For the September allergic CAPs-exposed rats, elevated eosinophils and protein were reported. Increased levels of La were reported in the lungs of rats in both CAPs groups in September. Increased levels of V and S were observed in the lungs of rats in the OVA/CAPs group in September. Heavy industrial source complex located 2 miles downwind of exposure site in September.
Rhoden et al. (2004)	Rat, SD, M, 250-300 g; control and NAC-pretreated	5 h, assessed 24 h PE	Boston, MA; HAPC; 1060300 µg/m^3 (range 150–2520 µg/m^3) Elemental composition (µg/m^3): Na 2.54; Mg 1.93; Al 5.21; Si 14.03; S 141.9; Cl 0.18; K 4.32; Ca 4.59; Ti 0.67; V 0.08; Cr 0.02; Mn 0.69; Fe 10.91; Ni 0.05; Cu 0.18; Zn 1.58; Br 0.20; Cd 0.01; Ba 0.83; Pb 0.10	TBARS Carbonyl BALF: Cell counts Cell differentials Edema	CAPs caused increases in TBARS, oxidized proteins, PMN, and edema. No change in BALF protein, total cells or LDH. NAC pretreatment attenuated increases in TBARS, edema, and PMNs. Component analysis: Al, Si, and Fe correlated with TBARS Cr and NA trended with carbonyl Cr, Zn, and Na trended with PMN

Table A17: Other Acute CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Humans					
Devlin et al. (2003)	Human, M&F (66.9±1.0 yr); healthy elderly subjects (n = 10)	2 h, alternating 15 min exercise and rest; HRV assessed pre-and post-exposure and 24 h PE; cross-over design	Chapel Hill, NC; HPAC; mean mass conc. 40.5 ± 8.6 μg/m^3 (range 21.2–80.3 μg/m^3)	HRV	CAPs caused significant decreases in time and frequency domain HRV parameters (PNN50 and HF) at 0 and 24 h PE. Individual subjects (n = 5) experienced abnormal beats (premature atrial contractions and/or bradycardia). Source apportionment not done.
Ghio et al. (2003)	Human, M (n = 14), F (n = 6), 25.3±0.8 yr; 5 to FA, 15 to CAPs	2 h alternating 15 min rest and exercise ~50L/min; assessed 0 or 24 h PE	Chapel Hill, NC; HAPC; mean mass 121±14.0 μg/m^3, range 15.0 to 358 μg/m^3	Venous blood: CBC Biochemical indices (total protein, albumin, UA, LDH, CRP) Cytokines ET-1 Fibrinogen and other clotting factors	CAPs caused decreases in WBC counts at 24 h PE, but no other changes CRC values. CAPs caused decreases in LDH at 24 h PE, but no other changes in blood chemistries. CAPs caused increases in fibrinogen, but other coagulation factors and inflammatory mediators were unchanged. Source apportionment not done.
Gong et al. (2004a)	Human, M and F; healthy (68±11 yr, n = 6) and COPD (73±8 yr, n = 13)	2 h, alternating 15 min exercise and rest; assessed just PE, at 4h, and at day 2. ECG before, during and after exposure	Los Angeles, CA; HAPC; mean mass conc. 194±26 μg/m^3; range 135–229 μg/m^3 >2.5 μm: 20±7 μg/m^3; range 7 –31 μg/m^3 0.1–2.5 μm: 167±27 μg/m^3; range 104–201 μg/m^3 <0.1 μm: 8±5 μg/m^3; range 3–23 μg/m^3 Mass percentages: 25% nitrate; 10% sulfate; 6% elemental carbon. Element composition (μg/m^3): silicon 4.1; iron 3.1; chlorine 2.7; sodium 2.4; calcium 2.3; aluminum 1.7; potassium 1.2	Pulmonary function SaO_2 BP Exhaled NO HRV Ectopic beat incidence Venous blood: WBC, platelet, and clotting factors Sputum: Cell counts	CAPS had no effect on symptoms, spirometry, or induced sputum. Decreased SaO_2 and increased peripheral basophils in healthy subjects. Modest increase in ectopic beats in COPD subjects. HRV was lower in healthy subjects than COPD subjects. Source apportionment not done.

Table A17 (cont'd): Other Acute CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Animals					
Gong et al. (2004b)	Human, M&F (19-51 yr); healthy (4) and mild asthmatics (12)	2 h, alternating 15 min exercise and rest; assessed immediately PE, at 4h, and at day 2. ECG before, during and after exposure	Los Angeles, CA; CPC; 80% coarse (2.5-10 µm), 20% fine (<2.5 µm); 157 µg/m^3 (range 56–218 µg/m^3) Elemental composition (%): silicon 19; sodium 18; iron 15; chlorine 11; sulfur 9; aluminum 7; potassium 4; magnesium 2; titanium 1; 16 others <1	Pulmonary function BP Exhaled NO HRV Sputum: Cell counts	CAPs caused reduction in overall HRV and increased HR 4-24 h PE. Greater responses in normal subjects. No changes in inflammation, spirometry, respiratory symptoms, or SaO_2. Source apportionment not done.
Campbell et al. (2005)	Mice, M, Balb/c (6 wk); 9 mice/group; pretreated daily with OVA (50 µg) via intranasal instillation prior to CAPs exposure; OVA challenge 1 and 2 wk PE, assessed 1 day after challenge	4 hr/day, 5 day/wk for 2 wk in whole body chambers	Los Angeles, CA; 150 m downwind of heavily trafficked highways; VACES UF (≤180 nm) or F (≤2.5 µm) UF: mass 282.5 µg/m^3; elemental composition (%): EC 5.7, OC 47.8, total metals 15.9, nitrate 8.8, sulfate 8.8 F: mass 441.7 µg/m^3; elemental composition (%): EC 2.8, OC 16.1, total metals 24.6, nitrate 17.0, sulfate 14.7	Brain: IL-1α TNF-α NF-κB	Elevated NF-κB in brain nuclear fraction of mice exposed to UF or F CAPs. Increased amount of IL-1α in cytoplasmic fraction of brain of mice exposed to UF or F CAPs; increased levels of TNF-α in mice exposed to F CAPs only.
Cassee et al. (2005)	Rat, M, SH (8–12 wk) or WKY (7 wk); a subset were preexposed to ozone for 8 h 1 day before CAPs	6 h, assessed 2 h PE	The Netherlands: Bilthoven (suburban), Utrecht (industrial), and freeway; HAPC For Wistar exposures: mean mass conc. 1104 µg/m^3; range 36–2085 µg/m^3 For SH exposures: mean mass conc. 1234 µg/m^3; range 270–3660 µg/m^3	BrdU for cell proliferation BALF: LDH NAG ALP UA Total protein Blood: WBC Fibrinogen CC16	In Wistar rats pretreated with ozone, CAPs induced increased protein, albumin and NAG activity in BALF and elevated Hb, Hct, and RBC in CBC. AM were significantly decreased. No observed effects were reported for antioxidants or cytotoxicity. In SH rats, CAPs caused increased PMN but no other effects were observed in BALF biochemical parameters. CAPs caused no changes in hematological parameters, but did cause increases in fibrinogen and CC16. For both strains, no robust concentration-effect relationship was observed for CAPS as a continuous variable.

Table A17 (cont'd): Other Acute CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Animals (cont'd)					
Chang et al. (2004)	Rat, M, SH, ~200 g, implanted with radiotelemetry transmitters	5 h/day in nose-only exposure chambers in spring (4 days total) and summer (6 days total)	Taipei suburb; VACES; mean mass conc. 202±68.8 μg/m^3 (spring) and 141±54.9 μg/m^3 (summer); particle number 2.30 × 10^5 particles/cm^3 (spring) and 2.78 × 10^5 particles/cm^3 (summer)	HR BP QAI	HR and BP significantly increased during spring CAPs exposure (maximum ↑52 bpm and ↑9 mm Hg, respectively). QAI decreased throughout the CAPs exposure in spring to a maximum of 1.6 msec.
Chang et al. (2005)	Rat, M, SH, ~200 g, implanted with radiotelemetry transmitters	5 h/day in nose-only exposure chambers in spring (4 days total)	Taipei suburb; VACES; mean mass conc. 202±68.8 μg/m^3; particle number 2.30 × 10^5 particles/cm^3	HRV	Statistically significant decreases in SDNN (60–85% of baseline period) were observed during PM exposure. The effects of CAPs on RMSSD were not significant, although there was a trend toward decreased HRV.
Cheng et al. (2003)	Rat, M,. SD, MCT-treated; implanted with telemetry transmitters	6 h/day in nose-only exposure chambers for 3 consecutive days, then rested 4 days; exposed to CAPs on wk 2,3, and 4 and to FA wk 1 and 5	Taipei suburb; VACES; mean mass conc. 240±77 μg/m^3; range 108 to 338 μg/m^3 Elemental composition (μg/m^3): Al 26.5; Mg 6.8; S 2.8; Si 2.7; Fe 1.4; Ga 0.7; P 0.5; Zn 0.2; Ni 0.07; Mn 0.03; Cu 0.02; Co 0.01; V 0.01	HR BP core temperature	An early decrease in HR (↓14.9 bpm) was observed, followed by a gradual increase in HR (↑8.6 bpm) to a maximum observed 11 h after the start of the exposure. BP initially decreased (↓3.3 mm Hg) during the first h of exposure, then returned to normal. No changes in core temperature were observed.
Kleinman et al. (2005)	Mice, Balb/c, M; pretreated with OVA via nasal instillation and challenge one and two weeks after exposure	WBI; 4 h/day for 5 day/wk for 2 wk; assessed 24 h after second OVA challenge; 4 experiments (July and October 2001, June and August 2002)	Los Angeles, CA; 50 or 150 m downwind of heavily trafficked roadway; VACES UF (≤150 nm) or F (≤2.5 μm) UF ranges: mass 283–442 μg/m^3; count 2.9–5.9×10^5 particles/cm^3; elemental composition (μg/m^3): EC 16–18, OC 135–189, total metals 45–51, nitrate 24.7–53.7, sulfate 25.0–35.5 F ranges: mass 313–498 μg/m^3; count 1.6–2.85×10^5 particles/cm^3; elemental composition (μg/m^3): EC 8.5–13, OC 86.0–253.8, total metals 10–109, nitrate 75.0–107, sulfate 25.3–76.9	BALF: Cell counts Cell differentials Cytokines Plasma: Cytokines IgE IgG1	Mice exposed to fine CAPs in 2001 at the 50 m location had elevated eosinophils and cytokines in BALF and elevated IgG1 in blood plasma compared to air controls. Mice exposed to UF CAPs in 2002 at the 50 m location had elevated IL-5 in BALF and increased IgG1 in blood plasma. Significant interactions were observed between treatment and location for IL-5, eosinophils, and IgG1 (i.e., mice exposed to CAPs at 50-m had higher levels of allergic response biomarkers than mice exposed to CAPs at 150-m downwind of the freeway).

Table A17 (cont'd): Other Acute CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Animals (cont'd)					
Lei et al. (2004a)	Rat, SD, M, 60 days old; 318.7±8.3 g; pretreated with single 60 mg/kg ip injection of MCT	6 h/day for 3 days; pulmonary function assessed 5 h PE; blood, lung and BALF 2 days PE	Taipei, Taiwan; VACES; mean mass conc. 371.7 μg/m^3 Elemental composition (μg/m^3): K 33.7;S 25.5; Al 6.1; Fe 4.7; P 2.7; Ca 2.3; Si 2.1; Zn 1.7; Mo 0.5; Ti 0.4; Cu 0.3; Mn 0.2; Pt 0.07; V 0.06; Co 0.04	Pulmonary function BALF: Cell counts Cell differentials Total protein LDH Cytokines	CAPs caused decreased *f* and increased V_T. CAPs caused increased BALF total cells, PMN percentage, protein, IL-6, and LDH. MCh challenge following exposure caused increased penh.
Lei et al. (2004b)	Rat, SD, M, 300–350 g; pretreated with single 60 mg/kg ip injection of MCT; 4 rat/group	Low - 6h; high - 4.5 h; assessed 36 h PE	Taiwan, Asian dust event particles; ACES Low: mean mass conc 315.6 μg/m^3; elemental composition (μg/m^3): Si 53.3; Al 14.0; S 6.25; Ca 6.1; K 3.1; Mg 2.7; Fe 2.1; As 2.1; Ni 0.09; W 0.9; V 0.2 High: mean mass conc 684.5 μg/m^3; elemental composition: Si 41.6; Al 10.7; K 3.6; As 2.9; Mg 1.2; Ca 1.7; W 1.4; V 0.1	BALF: Cell counts Cell differentials Total protein LDH IL-6 Blood: CBC	A dose-dependent increase in WBC was observed following exposure; no other blood parameters were altered. Dose-dependent increases in total cells, percent PMN, total protein, LDH and IL-6 were observed; no increase for AMs or lymphocytes.
Nadziejko et al. (2004)	Rat, M, F344, 18 mo; 6 rats/group, crossover design	4 h/day for 1 day; NOI; repeated twice for CAPs and ultrafine C (500 and 1280 μg/m^3) and 4 times for SO_2 (1.2 ppm)	Tuxedo, NY; centrifugal concentrator; 161 and 200 μg/m^3	HR Body temperature Activity Arrhythmia	Increases were observed in the number of delayed beats following CAPs exposure. No changes in arrhythmia frequency were observed following ultrafine C or SO_2 exposure.
Smith et al. (2003)	Rat, M, SD, 9–10 wk; 6 rats/group	4 h/day for 3 consecutive days in 6 experimental sets (3 weeks in fall, 3 weeks in winter); assessed immediately after exposure on day 3	Fresno, CA; VACES; fall mean mass conc. 260–847 μg/m^3 (number 1.1–1.2×10^5 particles/cm^3), winter mean mass conc. 190–815 μg/m^3 (number 0.9–1.2×10^5 particles/cm^3); largest contributors to PM mass were ammonium nitrate and OC (60–80%) Elemental composition ranges (μg/m^3); sulfate 13–51; nitrate 58–527; OC 61–141; EC 4–59; metals 8–38 (mostly Al, Si, S, Ca, and Fe); unexplained 30–174	BALF: Cell counts Cell differential Cell viability	Elevated PMN were observed following exposure during the first week of fall and the first week of winter. The highest levels of PM mass, nitrate, and OC were observed during these two weeks. The most consistent particle characteristics for all weeks were particle number, OC, Cl, Ti, Fe, Zn, Mn, and Pb. The particle characteristics that varied considerably across the exposure periods were mass, nitrate, sulfate, and trace elements (EC, Al, Si, S, K, Ca, Ba, Ni, Cu, Se, Cd).

Table A17 (cont'd): Other Acute CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Animals (cont'd)					
Zelikoff et al. (2002)	Rat, F-344, M, 7–9 mo, infected with *Streptococcus pneunoniae* (15–20 × 10^6) via IT; 4 rats/group	5 h/day for 1 day; NOI; assessed 4.5, 9, 18, 24, and 120 h PE	NYC; centrifugal concentrator; 65–90 µg/m^3	Lungs (affected rats): Absolute levels of bacteria Bacteria per g lung	Rats exposed to NYC CAPs had increased bacterial burdens at 9 h (10% above control), 18 h (300% greater than control), 24 h (70% above control), and 5 days (30% above control).

Table A18: Subchronic CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Factor Analysis					
Lippman et al. (2005c)	Mice, M, C57, ApoE$^{-/-}$	6 h/day, 5 day/wk for 5 mo.	Tuxedo, NY CAPs; VACES; mean mass conc. 113 µg/m^3 Source categories: 1. Secondary sulfate (SS)—high S, Si, and OC 2. Resuspended soil (RS)—high Ca, Fe, Al, and Si 3. Residual oil (RO)—V, Ni, and Se 4. Motor vehicle (MV) emissions and other	HR HRV (SDNN, RMSSD); data analyzed from 1600–1800 (afternoon) and 130–430 (night)	SS was the largest contributor to PM mass (56%), then RS (12%); MV/other were 30.9% and RO was 1.4%. RS (and PM mass) were associated with decreased HR during CAPs exposure in ApoE$^{-/-}$ mice. SS (but not PM mass) was associated with short-term decreases in HR in the afternoons following exposure in ApoE$^{-/-}$ mice; RS was associated with short-term increases in HR during the same period. MV traffic/other source category was associated with short-term decreases in RMSSD in the afternoons following CAPs exposures in C57. RO was associated with short-term decreases in SDNN and RMSSD in the afternoons following CAPs exposure in ApoE$^{-/-}$ mice. SS was associated with short-term decreases in SDNN and RMSSD (also PM mass) in nighttime following CAPs exposure in ApoE$^{-/-}$ mice. RS was associated with short-term increases in SDNN and RMSSD at night following CAPs exposure in ApoE$^{-/-}$ mice.
Maciejczyk et al. (2005)	BEAS-2B; 0, 100, 300, 500 µg/mL for 24 h 9 10^4 cells/well	Ambient (12.6±9.3 µg/m^3) and CAPs (108.6± 177.5 µg/m^3) filter samples collected 3/4–9/5/2003 M-F (900-1500)	Tuxedo, NY; VACES Source categories: 1. Secondary sulfate (SS)—S, Si, P, EC, and OC 2. Resuspended soil (RS)—K, Ca, Mn, Zn, Fe, Al, and Si 3. Residual oil (RO)—V and Ni 4. Motor vehicle (MV) emissions and other—Zn, Se, Br, Pb, nitrate	NF-κB	The NF-κB response was correlated with the RO source category. SS contributed on average 65% to overall PM mass, RS contributed 20%, and RO contributed 2%; 13% of the CAPs mass was unaccounted for and included high loadings of Pb, Br, Zn, Se, and nitrate. S and OC correlated well with each other.

Table A18 (cont'd): Subchronic CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Other					
Chen and Hwang (2005)	Mice, C57 and ApoE$^{-/-}$; 3–10 rats/group	6 h/day, 5 day/wk for 5 mo (4/11–9/5/2003)	Tuxedo, NY; VACES; mean mass conc. 110 µg/m^3	HR HRV (SDNN, RMSSD); data analyzed from 1600–1800 and 130–430	For ApoE$^{-/-}$ mice, SDNN gradually increased the first 6 wk of CAPs exposure, then slightly decreased for next 12 wk, and progressively increased at the end of study (1600–1800 and 130–430). No changes in evening HR or HRV were observed in C57 mice. Slight increases in SDNN were observed at nighttime after 6 wk of CAPs exposure. No lag effects were observed. There was no clear pattern between CAPs concentration and estimated acute effects (48 h).
Chen and Nadziejko (2005)	Mice, C57, ApoE$^{-/-}$, M&F ApoE$^{-/-}$ + LDL$^{-/-}$ (DK); 4–12 rats/group	6 h/day, 5 day/wk for up to 6 mo (3/10–9/5/2003); C57 6 mo, ApoE$^{-/-}$ 5 mo, DK 4 mo	Tuxedo, NY; VACES ; mean mass conc. 110±79, 120±90, and 131±99 µg/m^3	Heart: histopathology Aorta roots: total atherosclerotic lesion area, lipid contents, cellularity	20 DK mice died (lesions were indicative of myocardial infarction) during air or CAPs exposure. CAPs-exposed DK mice seemed to die earlier than air-exposed DK mice and females were more susceptible. No abnormal lipid deposition in coronary artery in C57 or ApoE$^{-/-}$ mice. More mice in the CAPs group had coronary artery disease (7/10) compared to the air (3/13) group. Similarly, more mice in the CAPs group had complex atherosclerotic lesions in the coronary artery (3/10) compared to the air group (0/13). All DK mice developed extensive lesions in the aortic sinus regions; plaque lesion cellularity was elevated in CAPs-exposed mice (28%). ApoE$^{-/-}$ and DK mice had severe atherosclerosis covering >40% of lumenal surface of aortic tree, which was significantly greater for CAPs-exposed ApoE$^{-/-}$ mice (66%).

Table A18 (cont'd): Subchronic CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Other (cont'd)					
Gunnison and Chen (2005)	Mice, M&F ApoE$^{-/-}$ + LDL$^{-/-}$ (DK); 3 rats/group	6 h/day, 5 day/wk for 4 mo (5/12–9/5/ 2003); sacrifice 3 or 4 days PE	Tuxedo, NY; VACES; median size of 4 exposure days 389±2 nm; mean mass conc. 131±99 μg/m^3 (range 13–441 μg/m^3)	Heart gene expression Lung gene expression	Many genes were up- or down-regulated following exposure to CAPs. The largest functional categories with alterations were heat shock proteins and other stress-response genes. Other genes related to DNA binding and regulation of transcription, defense responses, proteolysis, inflammatory response, and signal transduction and signaling pathways were changed. The Dbp gene associated with circadian rhythm was upregulated.
Hwang et al. (2005a)	Mice, C57 and ApoE$^{-/-}$; 3–10 rats/group	6 h/day, 5 day/wk for 5 mo (4/11–9/5/2003)	Tuxedo, NY; VACES; median size of 4 exposure days 389±2 nm; mean mass conc. 133 μg/m^3 (range 5–627 μg/m^3)	HR Core temperature Activity data analyzed from 130–430 (night) and 1100-1300 (morning)	Chronic CAPs exposure was associated with nighttime decreased HR (~34 bpm), body temperature (~1.0°C), and activity (2.4 count/min) in ApoE$^{-/-}$ mice starting 30 days after exposure began. There were few changes observed in HR, body temperature, or activity at night in C57 mice with CAPs. ApoE$^{-/-}$ mice had increased body temperature and activity during exposure (1100–1300) that was not associated with CAPs (chamber effect). Decreased HR (12.4 bpm) was associated with mean CAPs concentration during exposure. Fluctuation of HR in ApoE$^{-/-}$ mice within longer time intervals (4–7 h) increased 1.35-fold by the end of exposure; fluctuation within short term intervals (15 min) decreased 0.7 fold.
Lippmann et al. (200b)	Mice, C57, ApoE$^{-/-}$, M&F ApoE$^{-/-}$ + LDL$^{-/-}$ (DK)	Whole-body inhalation, 6 h/day, 5 day/wk up to 6 mo.; sacrifice 3 days after last exposure day	Tuxedo, NY; VACES	Same as Lippmann et al. (I)	Summary of results. No inflammation was observed in the lungs as measured by BALF.

Table A18 (cont'd): Subchronic CAPs Studies

Reference	Species	CAPs Exposure	CAPs Characterization	Endpoints	Results
Other (cont'd)					
Veronesi et al. (2005)	Mice, C57 and ApoE$^{-/-}$; 5-9 rats/group	6 h/day, 5 day/wk for 4 mo; sacrifice 3 or 4 days PE	Tuxedo, NY; VACES	Dopamine-containing neurons Astrocytes	In ApoE$^{-/-}$ mice exposed to CAPs, decreased tyrosine hydroxylase-stained neurons (29%) in the substantia nigra region of the brain were observed. Increased glial fibrillary acidic protein-stained astrocytes (8%) in nucleus compacta were observed in CAPs-exposed ApoE$^{-/-}$ mice. There were no effects of CAPs on neurons or astrocytes in C57 mice exposed to CAPs.
Sun et al. (2005)	Mice, M, ApoE$^{-/-}$ fed normal and high fat chow	6 h/day, 5 day/wk for 6 mo	Tuxedo, NY; VACES; mean mass conc. 85 µg/m^3	Composite atherosclerotic plaque in thoracic and abdominal aorta, vasomotor tone changes	The peak constriction due to serotonin or phenylephrine was enhanced in high fat chow mice exposed to CAPs and the half-maximal dose for dilation to acetylcholine was increased in the same group. The mean percentage positive areas of 3-nitrotyrosine and iNOS in aortic sections was observed in normal and high fat chow mice exposed to CAPs compared to the respective air controls; there were no differences in eNOS staining. Mice fed high fat chow and exposed to CAPs had elevated lipid content in the aortic arch. There was increased hydrogen peroxide generation in the aorta of mice exposed to CAPs.

Table A19: Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
Humans					
Schaumann et al. (2004)	Humans, 12 healthy subjects (8 F, 4 M); avg 27 yr	Instillation into lingula, 100 µg/10 mL; BALF collected 24 h PE	Ambient PM from Zerbst, Germany (agricultural sources) or Hettstedt, Germany (industrial and domestic sources); collected in 1999; $PM_{2.5}$	BALF: Cell counts Cell differentials AM surface markers Cytokines Total protein Albumin CL	Exposure to Hettstedt PM resulted in more numerous responses compared to Zerbst PM. Endotoxin levels were very low in both samples.
In Vivo					
Gavett et al. (2003)	Mice, Balb/c, F, 1–21 g; OVA sensitized, 2–12 mice/group	OA, 100 µg total in 50 µL saline (1 or 2 doses); assessed 18 h, 2 and 7 days after challenge 2 exposure protocols: 1) 10 µg OVA on Days 0 and 2 for sensitization 2 h prior to PM exposure on both days and 20 µg OVA on Day 14 for challenge 2) 20 µg OVA on Day 0 and PM exposure on Day 14 with OVA challenge 2 h later	Ambient PM from Zerbst, Germany (agricultural sources) or Hettstedt, Germany (industrial and domestic sources); collected in 1999; $PM_{2.5}$	Pulmonary function after MCh challenge Serum OVA-specific IgE BALF: Cell counts Total protein Albumin LDH NAG Cytokines	Allergic mice exposed to either PM had elevated penh at challenge and a number of BALF markers were increased 2 days post-challenge. Mice exposed to Hettstedt PM also had elevated penh, PMN, eosinophils, and IgE 2 days post-challenge and those exposed to Zerbst PM had increased IL-13. Hettstedt had much greater levels of Zn, Pb, Cu, Cd, Sn, and As. Neither Hettstedt nor Zerbst administered before sensitization enhanced allergic responses (except IgE in Hettstedt-exposed mice).

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vivo (cont'd)					
Corey et al. (2006)	Mice, ApoE$^{-/-}$, 11-12 mo, 2-3 mice/group	Nasal instillation, 1.5 mg/kg; assessed through 4 day PE	Seattle, WA $PM_{2.5}$ collected in close proximity to a freeway and industrial area	HR HRV (SDNN, RMSSD, HF, LF) Activity	Increased HR immediately following exposure; decreased HR on days 2 and 3. Decreased SDNN on days 2, 3, and 4 and decreased RMSSD on days 2 and 3. Lowered LF/HF ratio on days 3 and 4.
Gerlofs-Nijland et al. (2005)	Rats, SH, M, 250–350 g, 4–6 rats/group	IT, 0.3, 1, 3, and 10 mg/kg; assessed 4, 24, or 48 h PE	Road tunnel dust (RTD) collected outside a traffic tunnel in Netherlands; coarse and fine fractions were combined together prior to exposure	BrdU BALF (right lung); Cell counts Cell differentials MPO activity LDH NAG ALP UA Albumin Total protein CC16 GSH, GSSG Cytokines Fibrinogen Hematology ET-1 Histopathology (left lung)	Increased PMN and AM were observed in rats exposed to RTD at 24 h, regardless of dose. Increases in fibrinogen were observed in rats exposed to 10 mg/kg of RTD at 24 and 48 h. A number of BALF biomarkers were increased with exposure to RTD at all time points. There was a dose-dependent increase in the number of inflammatory foci at 24 and 48 h in rats exposed to 3 or 10 mg/kg RTD.
Gilmour et al. (2004)	Mice, F, CD1, 20–25 g, 5 mice/group	IT, 25 and 100 µg/mouse (approx. 1.25 and 5 mg/kg); assessed at 18 h PE	Coal fly ash derived from Montana (low-sulfur subbituminous; 0.83% sulfur, 11.72% ash content) or Western Kentucky (high-sulfur bituminous; 3.11% sulfur, 8.07% ash content); thoracic coarse, fine, and UF fractions	BALF: Cell counts Cell differentials Cell viability Cytokines	There were no differences in effects for either coarse particle types compared to saline. The UF fraction of combusted Montana coal induced greater neutrophilic inflammation and cytokine production than thoracic coarse or fine PM. The fine fraction of the western Kentucky fine PM caused increases in PMN, albumin, and protein.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vivo (cont'd)					
Nygaard et al. (2005)	Mice, BALB/cA, F, 5–9 mice/group	Subcutaneous injection of particles (100 µg) with or without OVA (50 µg) into hind footpads; 20 µL solution; assessed 5 days PE	Ambient PM from Oslo, Rome, Lodz, Amsterdam; spring, summer, and winter 2001/2002; thoracic coarse and fine fractions	Popliteal lymph node (PLN): Cell count Cell surface molecules Cell cytokines Histology	There was no observed difference between most of the coarse and fine fractions in the induction of IL-4 and IL-10. However, the Lodz coarse PM (+OVA) caused effects that were statistically significant compared to the Lodz fine PM (+OVA). Allergic mice exposed to PM had exacerbated effects compared to allergen alone or PM alone. Exposure to Rome or Oslo PM resulted in increased cytokine production. Exposure to Oslo PM caused alterations in PLN cell counts. Exposure to OVA+PM resulted in increased expression of surface molecules on B lymphocytes.
Rhoden et al. (2005)	Rat, SD, M, 300 g; pretreated with 1) atenolol or glycopyrrolate or 2) NAC	CAPs: WBI, 700 µg/m^3, 5 h; assessed immediately PE SRM 1649: IT, 750 µg; assessed 30 min PE	Boston CAPs Urban air particles; SRM 1649	Heart CL SDNN HR TBARS (heart) Wet/dry heart ratios	CAPs caused increases in TBARS, CL, and wet/dry heart ratio. SRM 1649 exposure resulted in elevated TBARS, CL, and SDNN during recovery. Pretreatment with NAC prevented changes in heart rate, SDNN, heart wet/dry ratio, and CL in SRM 1649- and CAPs-exposed rats. Administration of atenolol or glycopyrrolate prior to SRM 1649 or CAPs exposure prevented changes in CL and TBARS.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vivo (cont'd)					
Schins et al. (2004)	Rat, Wistar, F, 350–550 g; 5 rats/group	IT, 0.35 mg/rat (0.6–1 mg/kg); assessed 18 h PE	Ambient PM from Duisburg (D) and Borken (B) Germany collected in weekly intervals Feb–May 2000; thoracic coarse and fine fractions D: heavily-industrialized area; endotoxin 0.3 EU/mg for fine, 5 EU/mg for coarse B: Rural area; endotoxin 0.6 EU/mg for fine, 6.6 EU/mg for coarse	BALF: Cell differentials GSH, GSSG LDH Total protein Cytokines *In vitro* whole blood (WB) assay: Cytokines	Rats exposed to coarse PM (regardless of location) had increased percent PMN in BALF and TNF-α and IL-8 in the whole-blood assay. Only rats exposed to coarse Borken PM had depleted GSH levels and elevated TNF-α in BALF. Rats exposed to coarse Duisburg PM had increased MIP-2 in BALF.
Soares et al. (2003)	Mice, Balb/c, 8–10 weeks; 20 mice/group	WBI, 31–47 μg/m^3 (monthly average) for 120 days; for Sao Paulo SO_2 ranged from 12-20 μg/m^3, CO (8 h) ranged from 2.4–3.2 ppm, and NO_2 ranged from 97-108 μg/m^3	Urban air of Sao Paulo, Brazil (including gases) Urban air of Atibaia (AT) in rural Brazil, 65 km from Sao Paulo	Blood from tail vein: Micronuclei (MN) in peripheral erythrocytes	The greatest MN increase was observed at 90 days. Significant increases in MN frequency were observed for Sao Paulo mice compared to AT mice, with no significant time interaction. A positive association between all air pollution measures (PM_{10}, NO_2, and CO) and MN frequency difference was observed for the previous 8–14 days of exposure.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vivo (cont'd)					
Steerenberg et al. (2005)	Mice, Balb/cByJ.ico, M; 6–8 weeks; OVA sensitization (0.4 mg/ml) at days 0 and 14, challenge +/- PM on days 35, 38, and 41	IN, 0, 3, or 9 mg/mL PM with OVA (150-450 µg PM /mouse); assessed on day 42	Ambient PM collected during spring, winter, and summer from: (1) Oslo (near road), (2) Lodz (near heavy traffic), (3) Rome (rail station), (4) Amsterdam (near busy roadway), or (5) De Zilk (low traffic and natural allergens); thoracic coarse and fine fractions	Serum from abdominal aorta: IgE IgG1 IgG2a BALF: Total cells Cell differentials LDH Cytokines Lung histopathology	Spring and winter PM samples were more potent than summer PM samples. The order of mild response for IgE, IgG1, IgG2a, and eosinophil influx was (Lotz> Rome≥Oslo>Amsterdam). The coarse fraction induced greater adjuvant activity for De Zilk PM compared to the fine fraction. The coarse and fine fractions from Lodz or Rome with OVA exposure induced a number of effects including increased eosinophils, PMN, and monocytes. The adjuvant activity with immunoglobulins was greater with the fine than the coarse fraction. In general, the insoluble portion of the coarse PM was responsible for the observed adjuvant activity.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vivo (cont'd)					
Steerenberg et al. (2006)	Rat, Wistar, M, 8 rats/group (also mice, but data reported in other studies—Nygaard et al. 2005 and Steerenberg et al. 2005)	IT, 1 or 2.5 mg PM/rat; assessed 24-h PE	Ambient PM collected during spring, winter, and summer from: 1) Oslo (near road), 2) Lodz (near heavy traffic), 3) Rome (rail station), 4) Amsterdam (near busy roadway); thoracic coarse and fine fractions combined in the analysis	BALF: Albumin CC16 Cytokines	Correlations between the traffic and industry/combustion/ incinerator source cluster and pathology lesion occurrence and increased IgE were observed in the respiratory allergen model. The combustion of black and brown coal/wood smoke source cluster correlated with albumin in rats and IgE and pathology score in the respiratory allergen model. Crustal material source cluster correlated with CC16 in rats and IL-6, TNF-α, and MIP-2 in macrophage and type 2 cells (*in vitro*). Secondary inorganic/long-range aerosol source cluster correlated with IgE in the systemic allergen model. Sea spray source cluster correlated with CC16 in rats and IL-6 in macrophages (*in vitro*); the CC16 response also correlated with endotoxin.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vitro (cont'd)					
Becker et al. (2003)	Human AM (3×10^5 cell/mL)	50 µg/mL; 18–20 h	PM downwind of Utrecht (background site; collected March 1999) and west of Utrecht, Netherlands (influenced by light industrial activities and freeway traffic, esp. diesel; collected June 1999); thoracic coarse, fine, and UF fractions	Cytokines Phagocytosis CL Cell surface receptor expression	Increased IL-6, MIP-1α, and phagocytosis and decreased CL and CD11b receptor expression were greater for the thoracic coarse fraction than those observed with the other size fractions. Endotoxin was detected in water extracts of thoracic coarse particles.
Becker et al. (2005)	Human AM ($2–3 \times 10^5$ cells/cm^2) and normal bronchial epithelial (NHBE) cells (1×10^5 cells/cm^2)	AM: 50 µg/mL; NHBE: 11 µg/mL; 18–24 h	Chapel Hill, NC PM; collected Oct 2001, Jan 2002, Apr 2002, Jul 2002; thoracic coarse, fine, and UF fractions	Cytokines ROS CL	Thoracic coarse PM was more potent in inducing IL-6 and IL-8. For IL-6, Oct thoracic coarse PM caused the greatest response. The July thoracic coarse PM exerted the greatest production of ROS as measured in AM. Thoracic coarse Fe and Si were positively associated with IL-6 release in AM.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vitro (cont'd)					
Becker et al. (2005b)	Human AM ($2–3\times10^5$ cells/cm^2) and normal bronchial epithelial (NHBE) cells (1×10^5 cells/cm^2)	AM: 50 μg/mL; NHBE: 25, 50, 100, 250 μg/mL; 18–24 h	Chapel Hill, NC PM; collected for 72 h; thoracic coarse, fine, and UF fractions	Cytokines Gene expression	Thoracic coarse PM was more potent in inducing IL-8 release in NHBE cells. This response was blocked with an antibody for TLR2 was added. IL-6 release in AM was inhibited by addition of TLR4 agonist or an endotoxin-binding protein for all size fractions. Expression of TLR4 was increased in NHBE cells exposed to thoracic coarse PM only. Expression of TLR2 was increased in AM exposed to all three size fractions, although the largest increase was observed for the thoracic coarse fraction. A decrease in TLR4 expression was observed in AM exposed to thoracic coarse PM. Thoracic coarse PM was the most effective inducer of Hsp70 in NHBE cells. Fine PM also stimulated an increase in Hsp70 expression.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vitro (cont'd)					
Hetland et al. (2005)	WKY rat AM; 1.5×106 cells/mL	10, 20, 50, or 100 µg/mL; 20 h	Ambient PM collected during spring, winter, and summer 2001/2002 from: 1) Oslo (near road), 2) Lodz (near heavy traffic), 3) Rome (rail station), 4) Amsterdam (near busy roadway); thoracic coarse and fine fractions	Cytokines	Thoracic coarse PM collected during spring and summer from Lodz was the most potent for IL-6 release, followed by Rome and Oslo. Thoracic coarse PM collected from Amsterdam had the greatest IL-6 induction for the winter compared to thoracic coarse PM from other locations. The spring thoracic coarse PM from Rome and Lodz induced TNF-α release. The fine fractions did not induce a marked increase in TNF-α release in any city for any season. The thoracic coarse fractions had higher Fe, Cu, and Al content than fine PM. Endotoxin levels were also greater in the thoracic coarse fractions, but IL-6 release was similar when cells were treated with an endotoxin-binding protein (polymyxin).

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vitro (cont'd)					
Huang et al. (2003)	Human BEAS-2B and mouse RAW 264.7; 5×10^5 cells/mL	100 µg/mL; 8–16 h	PM from 4 different sites in Taiwan-background (B), urban (U), traffic (T), or industrial (I); thoracic coarse, fine, and UF fractions	BEAS-2B: IL-8 Lipid peroxidation RAW 264.7: TNF-α Cell viability	Increases in TNF-α due to $PM_{1.0}$ exposure correlated with Fe and Cr, although 77% of the response was attributable to the endotoxin content. For thoracic coarse PM, there was significant correlation between IL-8 and lipid peroxidation findings; Mn and Fe were more abundant in the thoracic coarse fraction compared to the other sizes. For the fine PM fraction, increases in IL-8 correlated with Mn and Cr and increases in lipid peroxidation were associated with EC and OC content. Cu and Zn were most abundant in $PM_{1.0 - 2.5}$. There were no differences in Ni, V, and Cr among size fractions.
Li et al. (2002)	RAW 264.7 and THP-1 cells	10–200 µg/mL; 8 h	CAPs from Downey, CA in Los Angeles basin using VACES from Mar 15-Dec 7 2000; thoracic coarse and fine fractions	HO-1 MnSOD JNK B-actin GSH/GSSG Apoptosis	The fine fraction induced a greater effect than thoracic coarse PM on all endpoints. Coarse PM collected in Sept and Dec resulted in increased HO-1 expression and cell cytotoxicity. The highest levels of OC were observed in December. Thoracic coarse PM collected from Jan–Feb 2001 induced HO-1 expression and had higher PAH content than the December thoracic coarse samples.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vitro (cont'd)					
Li et al. (2003)	Human BEAS-2B and mouse RAW 264.7	8–100 µg/mL (12.3 or 21.1 for coarse, 17.3 or 20.9 for fine, and 1.9 or 3.9 µg/m^3 for ultrafine); 16 h	CAPs from Los Angeles basin (USC as a typical urban site with vehicular traffic and Claremont as a receptor site) using VACES from Nov 2001–March 2002; thoracic coarse, fine, and UF fractions	HO-1 GSH/GSSG ROS	UF PM was the most potent in inducing oxidative stress which was associated with OC and PAH content. Thoracic coarse PM showed little toxic effects. Thoracic coarse PM collected in large cytoplasmic vacuoles in RAW 264.7 cells and UF particles lodged inside mitochondria.
Pozzi et al. (2003)	Mouse RAW 264.7	30 or 120 µg/mL (13.6 or 54.5 µg/cm^2); 5 or 24 h	Ambient PM from Rome, Italy (mainly traffic-derived) collected for 15 days in Sept 1999; thoracic coarse and fine fractions Endotoxin: Thoracic coarse = 7.68 EU/mg Fine = 1.92 EU/mg	LDH AA Cytokines	At 120 µg/mL, thoracic coarse PM induced significant release of LDH and fine PM did not result in any change in LDH release. Thoracic coarse PM fraction was slightly more effective in releasing AA and IL-6 compared to the fine fraction at 5 h. Thoracic coarse PM fraction at 30 µg/mL induced greater amounts of TNF-α production at 5 and 24 h.

Table A19 (cont'd): Size-fractionated and Collected Ambient PM Studies

Reference	Species (*in vivo*)/ Cell Type (*in vitro*)	Exposure	PM Characterization	Endpoints	Results
In Vitro (cont'd)					
Shi et al. (2003)	Human A549; 1.2×10^5 cells/ chamber	50 μg/mL; 2 h	Ambient PM from Dusseldorf, Germany from Jul–Dec 1999; coarse and fine fractions	Hydroxyl radical formation (using electron spin resonance) 8-Hydroxyde-oxyguanosine (8-OHdG) in A549 DNA or calf thymus DNA	Coarse PM had greater ability to generate hydroxyl radicals and 8-OHdG compared to fine PM at equal mass. Cu correlated with hydroxyl radical and 8-OHdG formation in coarse PM. For coarse PM, the autumn/winter samples induced nearly double the hydroxyl radicals generated by the summer samples. Both coarse and fine fractions induced 8-OHdG in A549 cells.
Vernanth et al. (2004)	BEAS-2B; 2.0×10^4 cells/cm^2	10, 20, 40, 80, 160 μg/cm^2; (≈25–400 μg/mL), 24 h	Dust $PM_{2.5}$ (0.3–3 μm): DD: desert dust (unpaved road) WM: west mesa (wind-generated dust area) R4: range 40 (unpaved road) UN: Uinta (wind and recreation activity)	Cell viability Cytokines TRPV1 receptor ROS	The cytotoxicity ranking was as follows: UN>WM>R4>DD. The IL-6 response was as follows at the highest dose: DD>R4>UN>WM. Heating the particles attenuated the IL-6 response. LPS induction of IL-6 and IL-8 release was significantly less than that from DD.
Veranth et al. (2006)	BEAS-2B; 3.5×10^4 cells/cm^2	10, 20, 40 or 80 μg/cm^2 (≈25–200 μg/mL); 24 h	Urban and rural surface soils (32) from the Southwestern U.S.; $PM_{2.5}$	Cell viability Cytokines	Rank order of potency was different at low and high PM concentrations. Coal fly ash samples did not affect IL-6 compared to soil-derived dusts. Strongest correlations for IL-6 and IL-8 were with low volatility EC and OC.

Table A20. Acid Aerosol Studies

Reference	Species	Exposure	Exposure Characterization	Endpoints	Sulfate Effects
Controlled human study					
Tunnicliffe et al. (2003)	Humans, healthy (7F, 5M; avg 34.5 yr) and mild asthmatics (5F, 7M; avg 35.7 yr; all using short-acting β agonists); double blind, random order design; prior to exposure subjects brushed teeth and gargled with mouthwash to reduce oral ammonia levels	1 h; head-only exposure system; measured during, pre- and/or post-exposure, or 5.5–6 h later	Six exposures: 1) FA 2) SO_2 (200 ppb) 3) sulfuric acid (200 µg/m^3; low) 4) sulfuric acid (2000 µg/m^3; high) 5) NH_4HSO_4 (200 µg/m^3; low) 6) NH_4HSO_4 (2000 µg/m^3; high) Particle exposures target MMD 0.3 µm, count mode ≈30 nm.	Self-reported symptoms Ventilation (breaths/min, V_T) Lung function Exhaled NO Nasal lavage (AA and UA)	Asthmatics exposed to SO_2 had increased respiratory rates. Asthmatics exposed to low or high concentrations of NH_4HSO_4 had increased exhaled NO levels. Healthy subjects exposed to low or high concentrations of sulfuric acid or NH_4HSO_4 had elevated UA levels in nasal lavage.
Animal toxicology studies					
Kleinman et al. (2003)	Rat, F344, 22–24 mo; 10–12 rats/group	4 h/day, 3 consecutive day/wk, 4 wk; NOI; 12 h PE	Four exposures: (1) FA (2) O_3 (0.2 ppm) (3) Low conc. particle mixture (50 µg/m^3 EC + 70 µg/m^3 NH_4HSO_4) +O_3 (0.2 ppm)–0.3 µm MMAD, 2.5 GSD (4) High conc. particle mixture (100 µg/m^3 EC + 140 µg/m^3 NH_4HSO_4) + O_3 (0.2 ppm)–0.3 µm MMAD, 2.3 GSD	Lung histology Cell replication in lung epithelial and interstitial cells BALF: Albumin mucus glycoprotein total protein AM Fc receptor binding AM function	Exposure to either concentration of the particle mixture resulted in elevated cell replication (290–340%) and decreased AM Fc receptor binding and respiratory burst activity. Greater cell replication was observed in the interstitial lung compared to the epithelial region. At the end of exposure, AM were activated but by 12 h, function was depressed. Increases in total protein were observed in the low concentration particle mixture group only.

Table A20 (cont'd). Acid Aerosol Studies

Reference	Species	Exposure	Exposure Characterization	Endpoints	Sulfate Effects
In Vitro					
Kleinman et al. (2006)	Rat, SD, M, 200 g; 5–15 rats/group	4 h; NOI; assayed 42 h post-exposure	Nine exposures: (1) FA (2) O_3–0.3 ppm (3) O_3–0.6 ppm (4) H_2SO_4–0.5 mg/m^3 (5) H_2SO_4–1.0 mg/m^3 (6) O_3 + H_2SO_4–0.3 ppm + 0.5 mg/m^3 (7) O_3 + H_2SO_4–0.3 ppm + 1.0 mg/m^3 (8) O_3 + H_2SO_4–0.6 ppm + 0.5 mg/m^3 (9) O_3 + H_2SO_4–0.6 ppm + 1.0 mg/m^3 Aerosol MMD 0.23–0.28 μm (GSD 2.1–2.3).	Lung histology DNA synthesis in nose, trachea, and lung AM Fc receptor binding AM function	Exposure to O_3 resulted in Type 2 lesions in the lung parenchyma at 0.6 ppm; co-exposure with H_2SO_4 attenuated this effect (significant interaction). O_3 and H_2SO_4 do not act synergistically in this study.
Beck-Speier et al. (2003)	Dog, AM (1×10^6/mL) and blood PMN	Sulfite and sulfate at pH 6 or pH 7; 30 min.	1.0 mM	PAF LTB_4 5-HETE 12-HHT TXB_2 PGE_2 PLA_2	Sulfite at pH 7 activates PLA_2 enzymes for release of arachidonic acid and synthesis of PAF. Sulfite activates $cPLA_2$ and $sPLA_2$ through signaling of the ERK1,2 pathway.

APPENDIX B

Bibliographies and Annotated Bibliographies for Recent Studies on the Health Effects of Particulate Matter Exposure

Recent Multicity Epidemiologic Studies
Epidemiologic Studies on Health Effects Associated with Exposure to Traffic
Toxicology Studies of Traffic, Diesel, or Vehicle Exhaust
Toxicology and Epidemiology Studies of Ultrafine Particles
Toxicology and Epidemiology Studies of Metals or Metal-Containing Particles
Toxicology Studies of Traffic, Diesel, or Vehicle Exhaust
Epidemiologic Studies on Health Effects Associated with Exposure to Traffic
Toxicology Studies of Endotoxin/LPS or Endotoxin/LPS-Containing Particles
Toxicology and Epidemiology Studies of Wood Smoke

Recent Multicity Epidemiologic Studies

The following three studies are described in detail in Tables 1 and 2. The remaining studies are grouped by the general issues being evaluated.

> Ostro B, Broadwin R, Green S, Feng W-Y, Lipsett M. 2006. Fine particulate air pollution and mortality in nine California counties: results from CALFINE. Environ Health Perspect 114: 29-33.
>
> Burnett RT, Stieb D, Brook JR, Cakmak S, Dales R, Raizenne M, Vincent R, Dann T. 2004. Associations between short-term changes in nitrogen dioxide and mortality in Canadian cities. Arch Environ Health 59:2280236.
>
> Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, Samet JM. 2006. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA 295:1127-1134.

Confounding by co-pollutants, weather, influenza epidemics:

Schwartz J. (2004a): Potential confounding of associations between PM_{10} and mortality by weather and season was assessed in 14 U.S. cities. A 0.36% (95% CI: 0.22, 0.50) excess risk in mortality per 10 $\mu g/m^3$ increase in PM_{10} was estimated using symmetrical sampling of control days. Results were little changed when control days were matched on temperature, the time stratified method was applied, or more lags of winter time temperatures were used. These results indicated that associations between PM_{10} and mortality risk are unlikely to be confounded by weather and season, and are robust to the analytical method.

Schwartz J. (2004b): Uses case-crossover design to assess potential confounding of associations between PM10 and mortality by gaseous co-pollutants in 14 U.S. cities. Significant associations reported with case-crossover matching for each of the 4 gaseous co-pollutants; effect estimate sizes range from 0.45% to 0.81% increases per 10 $\mu g/m^3$ PM_{10}.

Welty LJ, and Zeger SL. (2005): Used two flexible versions of distributed lag models to control for weather and season in 100 cities (1987-2000), with a 0-, 1- or 2-day lag for PM_{10}. Results were consistent with previous analyses, with effect estimates of approximately 0.2% increase in mortality per 10 $\mu g/m^3$ PM.

Touloumi G et al. (2005): Used data from 7 APHEA-2 cities and found that adjustment for influenza epidemics increased effect estimate for PM_{10}-mortality associations in most cases.

Concentration-response function and threshold evaluation:

Daniels MK et al. (2004): Applied flexible modeling strategies to daily time-series data for 20 U.S. cities (1987-1994). Spline model showed a linear relation without indicating a threshold for relative risks of death from all causes and for cardiovascular-respiratory cases with short-term PM_{10} exposure.

Evaluation of factors influencing heterogeneity:

Dominici F et al. (2003): City-specific and regional effect estimates provided for the 88-city analysis (1987-1994). The authors report "some modest variation in the relative risks across the nation . . . we were unable to explain the heterogeneity using descriptors of the population, air pollution characteristics, and reliability of the PM_{10} measurement data."

Martins et al. (2004): Significant associations were observed between PM_{10} and respiratory mortality in the elderly ($\geq$60 yr) in the combined analysis for six regions in Sao Paulo, Brazil, with an effect estimate of 5.4% (2.3, 8.6) excess risk per 10 $\mu g/m^3$ increase in PM_{10} at a multiday lag of 0 to 2 days. The greatest effect (14.2% [95% CI: 0.4, 28.0]) was found in the region with the highest % of slums, and the lowest % with college education and high monthly income. The effect of PM_{10} on respiratory mortality was strongly and negatively correlated with two SES indicators: % with college education and family income, and positively correlated with greater % living in slums.

Le Tertre A, et al. (2005): Used data from 21 cities (includes one non-APHEA city), reporting heterogeneity in associations between PM_{10} and mortality and calculates Bayesian estimates. A meta-regression method was then used to adjust for the identified sources of the heterogeneity. The authors state that the heterogeneity present in the data could be better taken into account by deriving an estimated underlying distribution that represents the dispersion observed between cities.

Medina-Ramon M, et al. (2006): Uses case-crossover design to evaluate effects of ozone and PM_{10} on respiratory hospital admissions and evaluate city characteristics that may explain heterogeneity in data from 36 U.S. cities. Significant associations found for both pollutants with pneumonia and COPD hospital admissions (effect estimates per 10 $\mu g/m^3$ PM_{10} of 1.47% and 0.84%, respectively). Effect estimates for PM_{10} reduced with greater air conditioning use in cities; little difference based on percentage of PM_{10} from traffic.

Samoli E, et al. (2005): Using data from 22 cities, found that association between PM_{10} or BS and mortality could be adequately estimated using a linear model. Tested thresholds at 10 and 20 $\mu g/m^3$ PM_{10} and found that linear models had better fit. The authors also report heterogeneity in associations between cities that is partly explained by several factors, with increased effect estimates associated with hotter climates, mean NO_2 concentration as an indicator of traffic emissions, and lower standard mortality rates (more elderly people in population).

Zeka A, et al. (2005): Using case-crossover design, significant associations were reported between PM_{10} and both cardiovascular and respiratory mortality in 20 U.S. cities that were stronger using 3-day cumulative distributed lag model. Associations were increased in size with increasing percent PM_{10} from traffic and with increasing summer temperature variability.

Zeka A, et al. (2006): Using data from 20 U.S. cities with case-crossover design, reported significant associations between PM_{10} and mortality from all causes, respiratory, and heart disease, and positive but not significant associations with MI and stroke deaths. Substantial effect modification was found for some sociodemographic factors (larger with >75 years, little difference for gender or race), location of death (larger for out-of-hospital), season (larger in

spring and fall) and coexisting medical conditions (e.g., secondary diagnoses of pneumonia, diabetes, heart failure).

Lag Structure:

Analitis A, et al. (2006): Used 2-stage hierarchical model with data from 29 APHEA-2 cities, and report significant associations with cardiovascular mortality (0.76% per 10 $\mu g/m^3$ PM_{10}) and respiratory deaths (0.58% per 10 $\mu g/m^3$ PM_{10}) using 0-1 day average lag. With distributed lag model effect sizes increase, particularly for respiratory mortality. The associations are independent of ozone, but reduced in size with adjustment for SO_2 and NO_2.

Roberts, S. (2005): This investigation finds that distributed lag models return particulate air pollution mortality effect estimates that are more robust and less prone to negative bias than single- and multi-day moving average exposure measures. The author concludes that distributed lag models should be preferred in future air pollution mortality time series studies and helps quantify the negative bias that can result from using single or multi-day moving average exposure measures.

Zanobetti A, et al. (2003): Using distributed lag models in 10 cities from the APHEA-2 project, effect estimate size for association with PM_{10} doubles for cardiovascular deaths and is five times higher for respiratory disease deaths compared with 1-day lag models.

Zeka A, et al. (2005): Using case-crossover design, significant associations were reported between PM_{10} and both cardiovascular and respiratory mortality in 20 U.S. cities that were stronger using 3-day cumulative distributed lag model. Associations were increased in size with increasing percent PM_{10} from traffic and with increasing summer temperature variability.

Mortality displacement:

Dominici F, et al. (2003): Used decomposed time series of PM_{10} data for 4 U.S. cities for which daily data were available (1987-1994), and reported larger relative rates of mortality associated with PM_{10} using longer timescale (14 days to 2 months) than shorter timescale (1 to 4 days), indicating that association does not represent advancement of death by just a few days for frail individuals.

Seasonal variation:

Peng RD, et al. (2005): Bayesian semiparametric hierarchical models for estimating time-varying effects of pollution on mortality in multisite time series studies. Effect estimates for winter, spring, summer, and fall were, respectively, 0.15%, 0.14%, 0.36% and 0.14% increases per 10 $\mu g/m^3$ PM_{10} (1-d lag), with an all-year estimate of 0.19% per 10 $\mu g/m^3$ PM_{10}. Effects were stronger in the summer for the Northeast and Industrial Midwest, but little difference across seasons in the southern regions and northwest.

New health outcomes:

Ballester et al. (2006): Significant associations reported between PM_{10} (lag 0-1 day) and emergency admissions for cardiovascular diseases and heart diseases. Significant associations

were also reported with ozone and CO, while associations with SO_2 and NO_2 were more sensitive in two-pollutant models.

Ibald-Mulli A, et al. (2004): Study of 131 adults in Helsinki, Erfurt and Amsterdam with biweekly clinic visits for 6 months. Results suggest decreased blood pressure (diastolic and systolic) and in heart rate.

Timonen KL, et al. (2006): Same cohort as above with analysis of heart rate variability (5-min measurement). Ultrafine particles associated with decreased LF/HF in pooled analysis; $PM_{2.5}$ associated with decreased HF and reduced LF/HF in Helsinki but opposite association in Erfurt, and no clear association in Amsterdam. Suggest that effects may be modified by location and characteristics of individual.

von Klot S, et al. (2005): In cohort of 22,000+ first MI survivors in Augsburg, Barcelona, Helsinki, Rome and Stockholm, significant associations were reported for cardiac hospital readmissions with PM_{10}, ultrafine particle number count, CO, NO_2 and O_3.

Wellenius et al. (2006a): Using case-crossover analysis, a significant association was reported between PM_{10} and hospital admissions for congestive heart failure in the elderly in 7 U.S. cities (7% increase [95% CI 0.35 to 1.10%] per 10 $\mu g/m^3$ PM_{10} [0-day lag]). Effect seemed to be smaller in those with secondary diagnosis of hypertension. No consistent effect modification observed for age, gender, race or other secondary diagnoses.

Wellenius et al. (2006b): Using case-crossover analysis, a significant association was reported between PM_{10} (3-day distributed lag) and hospital admissions for ischemic stroke (1.03% increase [95% CI 0.04 to 2.04%] per 10 $\mu g/m^3$ PM_{10}). No association was found for hemorrhagic stroke admissions.

Zanobetti A, and Schwartz J. (2005): Case-crossover analysis showed significant association between PM_{10} and emergency hospitalization for myocardial infarction in elderly people (0.65% [0.3-1.0] per 10 $\mu g/m^3$ PM_{10}) in 21 U.S. cities. Effect size doubled for subjects with previous admission for COPD or secondary diagnosis of pneumonia (difference in size not statistically significant).

Analytical methods:

Biggeri et al. (2005): A meta-analysis was conducted to examine the associations between PM_{10} and all-cause, cardiovascular, and respiratory mortality in six Italian cities. Daily PM_{10} data were collected in 2 cities; in the other cities, daily TSP collected. Conversion factors, estimated through validation studies, were applied to convert TSP to PM_{10}. Significant associations with PM_{10} were observed for all-cause (0.90% [95% CI: 0.21, 1.66] excess risk per 10 $\mu g/m^3$ increase in PM_{10} at a 0- to 1-day lag) and cardiovascular (1.11% [95% CI: 0.22, 2.19]) mortality. All other pollutants examined (NO_2, SO_2, CO, O_3) also were significantly associated with all-cause mortality. The effect of PM_{10} on mortality was greater during the warm season and for those aged $\geq$ 65 yr.

Daniels MJ, et al. (2004): Investigated impact of variance underestimation in both a simulation study and using NMMAPS data; report that underestimation as large as 40% had little effect on the national average relative risk of mortality.

Roberts S. (2005): Introduces model that uses information available in daily mortality time series to infer otherwise lost information about the effect of PM on mortality, considering that PM measurements may only be available every sixth day while the effect of PM on mortality may be spread over multiple days. Analyses use data from NMMAPS, a simulated data set, and daily PM measurements from Cook County, IL and Allegheny County, PA. New model produces more precise effect estimates compared with standard model.

Roberts S, and Martin, MA. (2006): New model tested use of moving total mortality time series that "allows inference on the information about the effect of PM on mortality that is lost when daily PM data is unavailable." Using the 100-city database (1987-2000), report results that are "consistent with those found in the NMMAPS analysis" with effect estimates of 0.12% increase in total mortality and 0.17% increase in cardiovascular and respiratory mortality per 10 $\mu g/m^3$ PM_{10}.

Simpson et al. (2005): Using three statistical methods—GLM, R, and a two-stage Poisson GAM with stringent convergence criteria—PM-related excess risks of total nonaccidental, cardiovascular, and respiratory mortality in Brisbane, Sydney, Melbourne, and Perth were estimated. Daily $PM_{2.5}$ data were collected using nephelometers in all four cities. Daily $PM_{2.5}$ data were available in all four cities, but Brisbane was excluded from the analysis as more than 40% of data was missing. Daily PM_{10} data were only available in Brisbane, Sydney, and Melbourne. Melbourne, which was included in all analyses, was missing ~30% of $PM_{2.5}$ and PM_{10} data. Significant associations were observed for all cause and cardiovascular mortality using the nephelometric data, but no associations were found with $PM_{2.5}$ or PM_{10}. Results using different statistical methods were similar. Mean $PM_{2.5}$ levels ranged from 9.00 $\mu g/m^3$ (Sydney and Perth) to 9.30 $\mu g/m^3$ (Melbourne) across the 3 cities.

Measurement error:

Zeka A and Schwartz J. (2004): Used 90-city database (1987-1994) and approach developed by Schwartz and Coull (2003) to test associations between pollutants and mortality, correcting for measurement error in the other pollutants. Effect estimates from models adjusting for the gaseous pollutants ranged from 0.14 to 0.35% increases in mortality per 10 $\mu g/m^3$ PM_{10}, with an overall effect of 0.24% per 10 $\mu g/m^3$ PM_{10}.

Review article:

Sandstrom T et al. (2005): Review article, concludes "The PM investigated generally induced significant biological responses, with both coarse (2.5-10 μm) and fine (0.1-2.5 μm) PM being able to induce toxic effects." Three studies briefly described: HEPMEAP (health effects of particles from motor engine exhaust and ambient air pollution) RAIAP (respiratory allergy and inflammation due to ambient particles) PAMCHAR (chemical and biological characterization of ambient air coarse, fine and ultrafine particles for human health risk assessment in Europe).

Epidemiologic Studies on Health Effects Associated with Exposure to Traffic

Mortality

Finkelstein MM, Jerrett M, Sears MR. (2004) Traffic air pollution and mortality rate advancement periods. Am J Epidemiol 160:173-177.

> Firestone Institute pulmonary function cohort (5228 adults), using residence w/in 50 m or major urban road or w/in 100 m of a highway as traffic index. CVD mortality significantly associated with pollution index [RR 1.06 (1.00-1.13)]; stronger association with deprivation index (RR 1.15) and traffic indicator (RR 1.40). In 2- and 3-variable models, pollution index reduced (RR 1.04 and nonsignificant) with little change in traffic indicator and some reduction for deprivation index. Deprivation and pollution indices were highly collinear, so created a combined (sum) index; both traffic and deprivation/pollution index were significantly association with CVD mortality (RR 1.05, 1.01-1.10)

Finkelstein MM, Jerrett M, DeLuca P, Finkelstein N, Verma DK, Chapman K, Sears MR. (2003) Relationship between income, air pollution and mortality: a cohort study. Can Med Assoc J 169(5):397-402.

> Firestone Institute pulmonary function cohort (5228 adults), using residence w/in 50 m or major urban road or w/in 100 m of a highway as traffic index. Significant association between mortality and residence w/in a road/highway buffer: RR 1.18 (1.02-1.38) for all subjects. By interpolation from Ontario life tables, estimated "rate advancement period" associated with traffic pollution of 2.5 years (0.2-4.8).

Finkelstein MM, Jerrett M, Sears MR (2005) Environmental inequality and circulatory disease mortality gradients. J Epidemiol Community Health 59:481-486.

Hart JE, Laden F, Schenker MB, Garshick E. (2006) Chronic obstructive pulmonary disease mortality in diesel exposed railroad workers. Environ Health Perspect 114:(in press)

Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA. (2002) Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. Lancet 360(9341):1203-1209.

Jerrett M, Burnett RT, Ma R, Pope CA III, Krewski D, Newbold KB, Thurston G, Shi Y, Finkelstein M, Calle EE, Thun MJ. (2005) Spatial analysis of air pollution and mortality in Los Angeles. Epidemiology 16:727-736.

American Cancer Society cohort, using traffic buffers of 500 and 100 m from freeway based on zip code centroids (22,905 subjects in 267 zip code areas). Significant association between

$PM_{2.5}$ and deaths from all causes; after adjustment for 44 covariates and freeways w/in 500 m, significant associations were reported with death from all causes (RR 1.17, 1.05-1.31) and IHD (RR 1.38, 1.11-1.72).

Lipfert FW, Wyzga RE, Baty JF, Miller JP. (2006) Traffic density as a surrogate measure of environmental exposures in studies of air pollution health effects: long-term mortality in a cohort of U.S. veterans. Atmos Environ 40:154-169.

Veterans cohort; traffic volume estimated from [vehicle-km traveled/county land area] using data from 1985, 1990 and 1997. Significant association with traffic (RR 1.176, 1.100-1.258 per 2.6 in 1999 data). In 3-pollutant models, traffic effect was little changed, with the $PM_{2.5}$ effect estimate reduced and not significant (RR 1.032) and $PM_{10-2.5}$ effect negative and nonsignificant.

Lipfert FW, Baty JD, Wyzga RE, Miller JP. (2006) $PM_{2.5}$ constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans. Inhal Toxicol (in press).

Veterans cohort; traffic volume estimated from [vehicle-km traveled/county land area], also $PM_{2.5}$ speciation data. Significant associations between mortality and traffic density, EC, nitrates, V and Ni, with the strongest effects for traffic density and EC. Positive, nonsignificant associations with $PM_{2.5}$ mass and sulfates. Negative nonsignificant associations with elements association with crustal particles (Al, Ca, Si).

Maheswaran R, Elliott P. (2003) Stroke mortality associated with living near main roads in England and Wales: a geographical study. Stroke 34(12):2776-2780.

Zeka A, Zanobetti A, Schwartz J. (2005) Short term effects of particulate matter on cause specific mortality: effects of lags and modification by city characteristics. Occup Environ Med 62:718-725.

Multicity study, associations for PM_{10} with cause-specific mortality in 20 U.S. cities. Heterogeneity in effect estimates partially explained by differences in city characteristics, including increased % PM_{10} from traffic.

<u>Respiratory morbidity:</u>

Brauer M, Hoek G, Van Vliet P, Meliefste K, Fishcer PH, Wijga A, Koopman LP, Neijens HJ, Gerritsen J, Kerkhof M, Heinrich J, Bellander T, Brunekreef B. (2002) Air pollution from traffic and the development of respiratory infections and asthmatic and allergic symptoms in children. Am J Respir Crit Care Med 166(8):1092-8.

The Netherlands: respiratory symptoms for 4,135 in birth cohort, 3,730 reassessed at 2 yr; numerous cities. Associations with NO_2, $PM_{2.5}$, soot; long-term average based on 2-wk samples. Positive, borderline significantly associations between all three pollutants and prevalence of wheeze, E, N, T infections, and flu/serious colds

Brunekreef B, Janssen NAH, de Hartog J, Harssema H, Knape M, van Vliet P. (1997) Air pollution from truck traffic and lung function in children living near motorways. Epidemiol 8(3): 298-303.

Buckeridge D, Gozdyra P, Ferguson K, Schrenk M, Skinner J, Tam T, Amrhein C. (1998) A study of the relationship between vehicle emissions and respiratory health in an urban area. Geogr Environ Modeling 2:17-36.

Buckeridge DL, Glazier R, Harvey BJ, Escobar M, Amrhein C, Frank J. (2002) Effect of motor vehicle emissions on respiratory health in an urban area. Environ Health Perspect 110(3):293-300.

> Three year hospitalization rates determined in SE Toronto; $PM_{2.5}$ emissions estimated from traffic data; modeled exposures. Hospitalization rate for subset of respiration diseases (asthma, bronchitis, COPD, pneumonia, URI) significantly increased with $PM_{2.5}$ emission density (RR 1.24, 1.05-1.45)

Burr ML, Karani G, Davies B, Holmes BA, Williams KL. (2004) Effects on respiratory health of a reduction in air pollution from vehicle exhaust emissions. Occupational and Environmental Medicine 61:212-218.

> PM_{10}, $PM_{2.5}$ via dichot, daily for 3-wk and 2-wk periods, before and after bypass; respiratory symptoms in 448 adults living in congested and uncongested neighborhoods. $PM_{2.5}$ means decreased between before/after bypass by 23.5% in congested and 26.6% in uncongested neighborhoods. Reduction in symptoms with decreased traffic for any wheeze -6.5% (-14.9, 2.0) and number of attacks -8.5% (-18.2, 1.2). No association with cough, phlegm, consulted doctor, rhinitis. Positive association with "affects activities" 10.3 (3.1, 17.3).

De Marco R, Poli A, Ferrari M, Accordini S, Giammanco G, Bugiani M, Villani S, Ponzio M, Bono R, Carrozzi L, Cavallini R, Cazzoletti L, Dallari R, Ginesu F, Lauriola P, Mandrioli P, Perfetti L, Pignato S, Pirina P, Struzzo P; ISAYA study group. (2002) Italian Study on Asthma in Young Adults. The impact of climate and traffic-related NO2 on the prevalence of asthma and allergic rhinitis in Italy. Clin Exp Allergy 32(10):1405-1412.

Delfino RJ, Gong H, Linn WS, Pellizzari ED, Hu Y. (2003) Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. Environ Health Perspect 111(4):647-656.

> Los Angeles, CA, community with high traffic density. Positive associations with both criteria pollutants and VOCs; two-pollutant models showed stronger association with EC or OC fractions of PM_{10} than PM_{10} mass. Suggest air toxics from traffic and industrial sources may have adverse effects on asthma in children.

Delfino RJ, Gong H, Linn WS, Hu Y, Pellizzari E. (2003) Respiratory symptoms and peak expiratory flow in children with asthma in relation to volatile organic compounds in exhaled breath and ambient air. J Expos Analysis Environ Epidemiol 13:348-363.

> Los Angeles, CA, community with high traffic density. Ambient VOCs, NO_2 and SO_2 associated with decreased peak flow in Hispanic children.

Fritz GJ, Herbarth O. (2004) Asthmatic disease among urban preschoolers: an observational study. Int J Hyg Environ Health 207:23-30.

Garshick E, Laden F, Hart JE, Caron A. (2003) Residence near a major road and respiratory symptoms in U.S. Veterans. Epidemiol 14(6):728-736.

U.S. male veterans in SE Massachusetts: persistent wheeze increased in men living w/in 50 m of major roadway, compared with those living >400 m away.

Gauderman WJ, Avol E, Lurmann, F, Kuenzli N, Gilliland F, Peters J, McConnell R. (2005) Childhood asthma and exposure to traffic and nitrogen dioxide. Epidemiology 16(6):737-743.

Children's Health Study in southern California; NO_2 (from 2000) as indicator of freeway-related pollutants and 3 traffic metrics: proximity to freeway, number of vehicles/day, modeling of traffic-related air pollution. Significant association between asthma history and distance to freeway (OR 1.89, 1.19-3.02) and model-based freeway pollution (OR 2.22, 1.36-3.63); positive nonsignificant association with traffic volume and model-based pollution from other roads.

Gehring U, Cyrys J, Sedlmeir G, Brunedreef B, Belander T, Fischer T, Bauer CP, Reinhardt D, Wichmann HE, Heinrich J. (2002) Traffic-related air pollution and respiratory health during the first 2 yrs of life. Eur Respir J 19(4):690-698.

Gordian ME, Hanuese S, Wakefield J. (2006) An investigation of the association between traffic exposure and the diagnosis of asthma in children. J Expo Sci Environ Epidemiol 16(1):49-55.

Anchorage, AK, survey of parents of children in kindergarten and 1st grade, traffic index based on GIS mapping of traffic density w/in 100 m of home. Increased risk of asthma diagnosis with medium and high exposure; significant for high-exposure group (OR 2.84, 1.23-6.51).

Heinrich J, Topp R, Gehring U, Thefeld W. (2005) Traffic at residential address, respiratory health, and atopy in adults: the National German Health Survey 1998. Environmental Research 98:240-249.

Heinrich, J.; Wichmann, H-E. (2004) Traffic related pollutant in Europe and their effect on allergic disease. Current Opin Clinical Epidemiol 4: 341-348.

Hirsch T, Weiland SK, von Mutius E, Safeca AF, Grafe H, Csaplovics E, Duhme H, Keil U, Leupold W. (1999) Inner city air pollution and respiratory health and atopy in children. Eur Respir J 14(3):669677.

Hirsch T, Neumeister V, Weiland SK, von Mutius E, Hirsch D, Grafe H, Duhme H, Leupold W. (2000) Traffic exposure and allergic sensitization against latex in children. J Allergy Clin Immunol. 106(3):573-8.

Ising H, Lange-Asschenfieldt H, Lieber GF, Weinhold H, Eilts M. (2003) Respiratory and dermatological diseases in children with long-term exposure to road traffic emissions. Noise Health 5:41-50.

Janssen NAH, Brunekreef B, van Vliet P, Aarts F, Meliefste K, Harssema H, Fishcer P. (2003) The relationship between air pollution from heavy traffic and allergic sensitization, bronchial

hyper responsiveness and respiratory symptoms in Dutch school children. Environ Health Perspect 111(12):1512-1518.

Kim JJ, Smorodinsky S, Ostro B, Lipsett M, Singer BC, Hogdson AT. (2002) Traffic-related air pollution and respiratory health: the East Bay Children's Respiratory Health Study. Epidemiol 13(4):S100.

Kim JJ, Smorodinsky S, Lipsett M, Singer BC, Hogdson AT, Ostro B. (2004) Traffic-related air pollution near busy roads: the East Bay Children's Respiratory Health Study. American Journal of Respiratory Critical Care Medicine. Am J Respir Crit Care Med 170:520-526.

> Respiratory symptoms for 1109 children in 10 schools, grades 3-5. Authors state positive, generally larger effect estimates for BC, NO_x and NO suggest effects of primary emissions more than regional pollutants for these outcomes.

Lee YL, Shaw CK, Su HJ, Lai JS, Ko YC, Huang SL, Sung FC, Guo YL. (2003) Climate, traffic-related air pollutants and allergic rhinitis prevalence in middle-school children in Taiwan. Eur Respir J 21(6):964-70.

Lewis SA. Antoniak M. Venn AJ. Davies L. Goodwin A. Salfield N. Britton J. Fogarty AW. 2005. Secondhand smoke, dietary fruit intake, road traffic exposures, and the prevalence of asthma: a cross-sectional study in young children. American Journal of Epidemiology. 161(5):406-11.

> UK study, 11,562 children 4-6 years of age, questionnaire at school on respiratory symptoms. Traffic index of living w/in 30, 60, 90, 120 or 150 m of main road; asthma prevalence not associated with proximity of home to main road.

Lin S, Munsie JP, Hwang SA, Fitzgerald E, Cayo MR. (2002) Childhood asthma hospitalization and residential exposure to state route traffic. Environ Res 88(2):73-81.

Livingstone AE, Shaddick G, Grundy C, Elliott P. (1996) Do people living near inner city main roads have more asthma needing treatment? Case-control study. BMJ 312:676-677.

Lwebuga-Mukasa JS, Ayirookuzhi SJ, Hyland A. (2003) Traffic volumes and respiratory health are utilization among residents in close proximity to the Peace Bridge before and after September 11, 2001. J Asthma 40(8):855-864.

> Buffalo, NY: Decrease in traffic on Peace Bridge (50%) after Sept 11, 2001 was associated with decreased hospital admissions or emergency department visits for respiratory illnesses.

Lwebuga-Mukasa JS, Oyana T, Thenappan A, Ayirookuzhi SJ. (2004) Association between traffic volume and health care use for asthma among residents at a U.S.-Canadian border crossing point. J Asthma 41(3):289-304.

> Buffalo, NY: Data on commercial traffic volume across Peace Bridge, and hospital discharges and outpatient visits for asthma. Highest asthma prevalence rates and health care use rates were in the two zip codes that surround the Peace Bridge.

Lwebuga-Mukasa JS, Oyana TJ, Johnson C. (2005) Local ecological factors, ultrafine particulate concentrations, and asthma prevalence rates in Buffalo, New York. J Asthma 42:337-348.

> Buffalo, NY: Cross-sectional survey of 2000 households, OR of 2.57 (1.85-3.57) for having at least one person with asthma in households on west side compared to east side. Ultrafine particle levels also higher in communities downwind of Peace Bridge.

McConnell R, Birhane K, Yao L, Jerrett M, Lurmann F, Gilliland F, Kunzli N, Gauderman J, Avol E, Thomas D, Peters J. (2006) Traffic, susceptibility, and childhood asthma. Environ Health Perspect 114:766-772.

> 13 Southern California communities: Cohort study of kindergarten and first grade children in 13 communities. Risk of asthma and wheeze was increased with residence within 75 m of a major road, also with exposure to nonfreeway traffic pollution (modeled) but not to freeway or total traffic pollution.

Montnemery P, Popovic M, Andersson M, Greiff L, Nybert P, Lofdahl CG, Svensson C, Persson CG. (2003) Influence of heavy traffic, city dwelling and socio-economic status on nasal symptoms assessed in a postal population survey. Respir Med 97(8):970-977.

Nicolai T, Carr K, Weiland SK, Duhme H, von Ehrenstein O. (2003) Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children. Eur Respir J. 21(6):956-63.

Oftedal B, Nafstad P, Magnus P, Bjorkly S, Skrondal A. (2003) Traffic related air pollution and acute hospital admission for respiratory diseases in Drammen, Norway 1995-2000. Eur J Epidemiol. 18(7):671-675.

Oyana TJ, Lwebuga-Mukasa JS. (2004) Spatial relationships among asthma prevalence, health care utilization, and pollution sources in neighborhoods of Buffalo, New York. J Environ Health 67:25-37.

> Buffalo, NY: Statistically significant association between proximity to source and diagnosed asthma. Asthma clusters located along major roadways, in communities near Peace Bridge, and in the west side of city.

Penttinen P, Vallius M, Tiittanen P, Ruuskanen J, Pekkanen J. (2006). Source-specific fine particles in urban air and respiratory function among adult asthmatics. Inhal Toxicol 18:191-198.

> EPIC, European multi-city study, deviation of peak expiratory flow in 78 adult asthmatics, during winter and spring seasons, 1996-1997. Used $PM_{2.5}$ data with source apportionment (long-range transport, local combustion, soil, heavy fuel oil, sea salt). Most consistent association with $PM_{2.5}$ from local combustion sources; significant association between decreased morning $\triangle$PEF and $PM_{2.5}$ from long range transport; positive nonsignificant association with $PM_{2.5}$ from soil.

Ryan, P.H.; LeMasters, G.; Biagnini, J.; Bernstein, D.; Grinshpun, S.A.; Shukla, R.; Wilson, M.S.; Villareal, M.; Burkle, J.; Lockey, J. (2005) Is it traffic type, volume, or distance? Wheezing in infants living near truck and bus traffic. J Allergy Clin Immunol 116: 279-284.

> Cincinnati allergy and air pollution study cohort: GIS and traffic classification used to categorize traffic exposures based on type (bus, truck), traffic volume and distance from road. Significant increase in prevalence of wheeze in infants living very near (<100 m) stop-and-go bus and truck traffic; no increase in infants living <400 m from high volume moving traffic; also greater risk for nonwhite infants compared with white infants.

Salam MT, Yi Y-F, Langholz B, Gilliand FD. (2004) Early life environmental risk factors for asthma: findings from the Children's Health Study. Environ Health Perspect 112(6): 760-725.

Sekine K, Shima M, Nitta Y, Adachi M. (2004) Long term effects of exposure to automobile exhaust on the pulmonary function of female adults in Tokyo, Japan. Occup Environ Med. 61:350-357.

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APPENDIX B

MEMORANDUM

SUBJECT: Review of TRC Comments on PM NAAQS

FROM: Roger W. Brode, Physical Scientist

TO: PM NAAQS Review Docket (OAR-2001-0017)

DATE: September 19, 2006

The purpose of this memorandum is to document a review of the dispersion and deposition modeling presented in the TRC "Comments on the Proposed Coarse Particulate Matter NAAQS," dated April 17, 2006, and submitted on behalf of the National Cattleman's Beef Association ("NCBA") and the National Mining Association ("NMA"). Figures 1 and 2 of the TRC comments present ISCST3 modeling results for a ground-level source and a source with a release height of 10m above ground for particle sizes of 2.5, 5, and 10 microns. These figures are provided here for reference in Attachment A. Based on these ISCST3 modeling results, TRC asserts on page 18 that the "area of influence of a source of $PM_{10-2.5}$ is less than 1,000 meters and less than 500 meters for the particles greater than 5 microns in diameter." While the term "area of influence" is not explicitly defined in the comments, a discussion on page 4 suggests that the criterion may have been when concentrations "fall to $1/100^{th}$ of the nearby concentrations." Other than the release heights and the particle sizes cited above, the TRC comment provides no other documentation regarding the specific source parameters and meteorological conditions used to generate the results presented in Figures 1 and 2 of the comments. Consequently, no assessment could be made of the reasonableness or representativeness of their modeling results.

In order to assess the legitimacy of their assertions regarding the area of influence for coarse particle emissions, an independent assessment was conducted using the AERMOD dispersion modeling, which was promulgated as EPA's preferred dispersion model in the Guideline on Air Quality Models (40 CFR Part 51, Appendix W) on November 9, 2005. TRC asserts (on page 3) that the ISCST3 model's treatment of deposition of coarse particles is the "state-of-the-science." The dry particle deposition algorithms in the AERMOD and ISCST3 models are very similar, with both accounting for particle settling and depletion of plume mass due to deposition processes. AERMOD includes an additional gustiness term, not included in ISCST3, which affects the quasilaminar sublayer resistance and increases deposition under convective conditions. The other main difference between the two models for particle deposition is in the dry depletion algorithm that accounts for removal of mass from the plume due to dry

deposition. The ISCST3 model includes a more refined method that adjusts the vertical profile of the plume as it is transported downwind to account for the fact that removal occurs at the surface. AERMOD currently utilizes a simpler dry depletion algorithm that does not adjust the plume vertical profile. However, the dry depletion algorithm in ISCST3 has shown significantly anomalous behavior under some conditions (documented in EPA's Model Change Bulletins for ISCST3). While the results presented in the TRC comments do not exhibit any evidence of this anomaly, this problem with ISCST3 has not yet been resolved.

Despite these few differences in the particle dry deposition formulations, the ISCST3 and AERMOD models will generally produce similar estimates of the dry deposition velocity under comparable meteorological conditions and source characteristics. As a result, the most significant difference between the two models for these types of sources is likely to be determined by differences in the basic plume dispersion algorithms. Given that AERMOD has been shown to be superior to ISCST3 in terms of plume dispersion, which is the basis for EPA promulgating AERMOD as a replacement for ISCST3, one could make the case that AERMOD is therefore the "better" model for deposition as well. Unfortunately, there is a lack of sufficient field study data available for deposition to clearly substantiate (of refute) such a claim.

The AERMOD tests presented in Attachment B are based on three test meteorological conditions (convective, neutral, and stable) for a rural setting. Maximum ground-level centerline concentrations were estimated for five particle sizes representative of both fine and coarse particles (0.1, 1, 2, 5, and 10 micron aerodynamic diameter). The AERMOD results for the ground-level source for each of the meteorological conditions are presented in Figures B-1 through B-3, and AERMOD results for the 10-meter release height are shown in Figures B-4 through B-6. These results show, as expected, that coarse particles do "deposit out" more rapidly than fine particles under some, but not all conditions, and there is a noticeable dependence of this effect on meteorology. More specifically, Figures B-1 and B-4 indicate that under convective conditions the differences in fine and coarse particle concentrations are insignificant at distances of 1 to 3 km. The ISCST3 plots presented in the TRC comments look most similar to the AERMOD plots for neutral conditions (Figures B-2 and B-5). It's also worth noting here that the AERMOD impacts for stable conditions are several times higher than impacts for neutral or convective conditions, and will therefore contribute significantly to 24-hour average impacts for these sources.

The AERMOD test results presented in Figures B-1 through B-6 are based on non-buoyant point (stack) releases for simplicity. Similar tests were performed for ground-level and elevated area source releases, and the results are comparable to those presented here for point source simulations. However, since the TRC comments specifically address the representativeness of $PM_{10-2.5}$ monitors in urban areas, additional comparison tests were performed for urban conditions using an urban population of 2.5 million. Figures B-7 and B-8 show the urban test results for stable conditions for the ground-level and 10-meter point sources, respectively. The overall peak ground-level concentrations for the urban tests are lower than the rural results, as expected due to the enhanced turbulence for the urban case. However, the area of influence for coarse particles, both in terms of absolute magnitude and relative to fine particles, is larger for the urban case, especially for the ground-level source.

Overall, the results of this independent assessment using the AERMOD dispersion model do not support the assertion in the TRC comment that the "area of influence" of coarse PM sources is limited to 1,000m (or less than 500m for particles greater than 5 μm). The area of influence, expressed in terms of ground-level concentration, shows a significant dependence on meteorological conditions, with a larger area of influence expected under stable conditions. Most of the drop-off of concentration with distance exhibited for low-level sources of coarse PM is due to dispersion of the plume rather than deposition of the particles.

Attachments

ATTACHMENT A

Industrial Source Complex (ISC) Modeling Results Presented with TRC "Comments on Proposed Coarse Particulate Matter NAAQS," dated April 17, 2006

Figure 1. Concentrations of Coarse Particles vs Downwind Distance (Groundlevel Source)

Figure 2. Coarse Particle Concentration vs Distance (10 Meter High Source)

FIGURE 1. Concentrations of Coarse Particles vs Downwind Distance (Groundlevel Source)

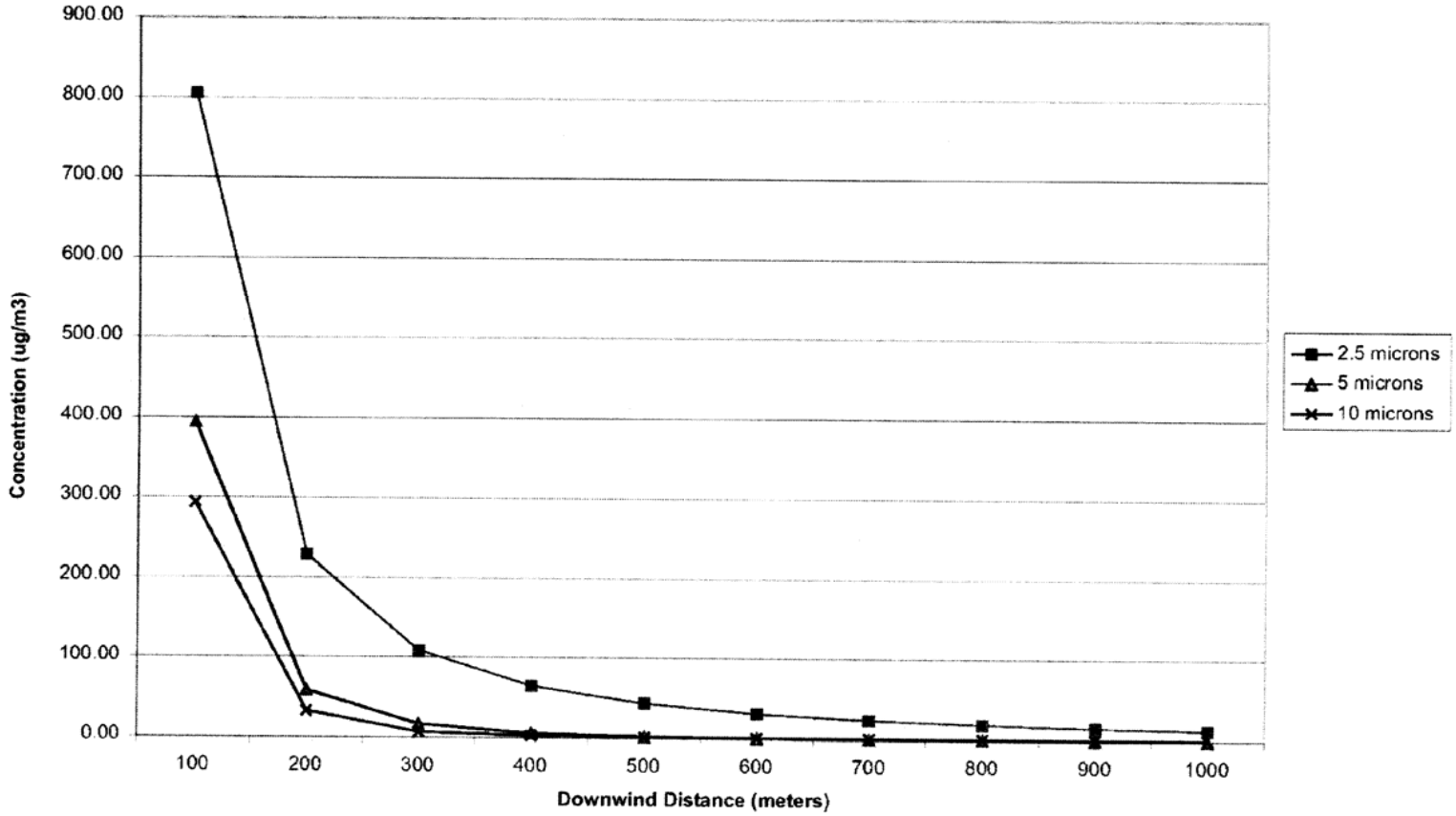
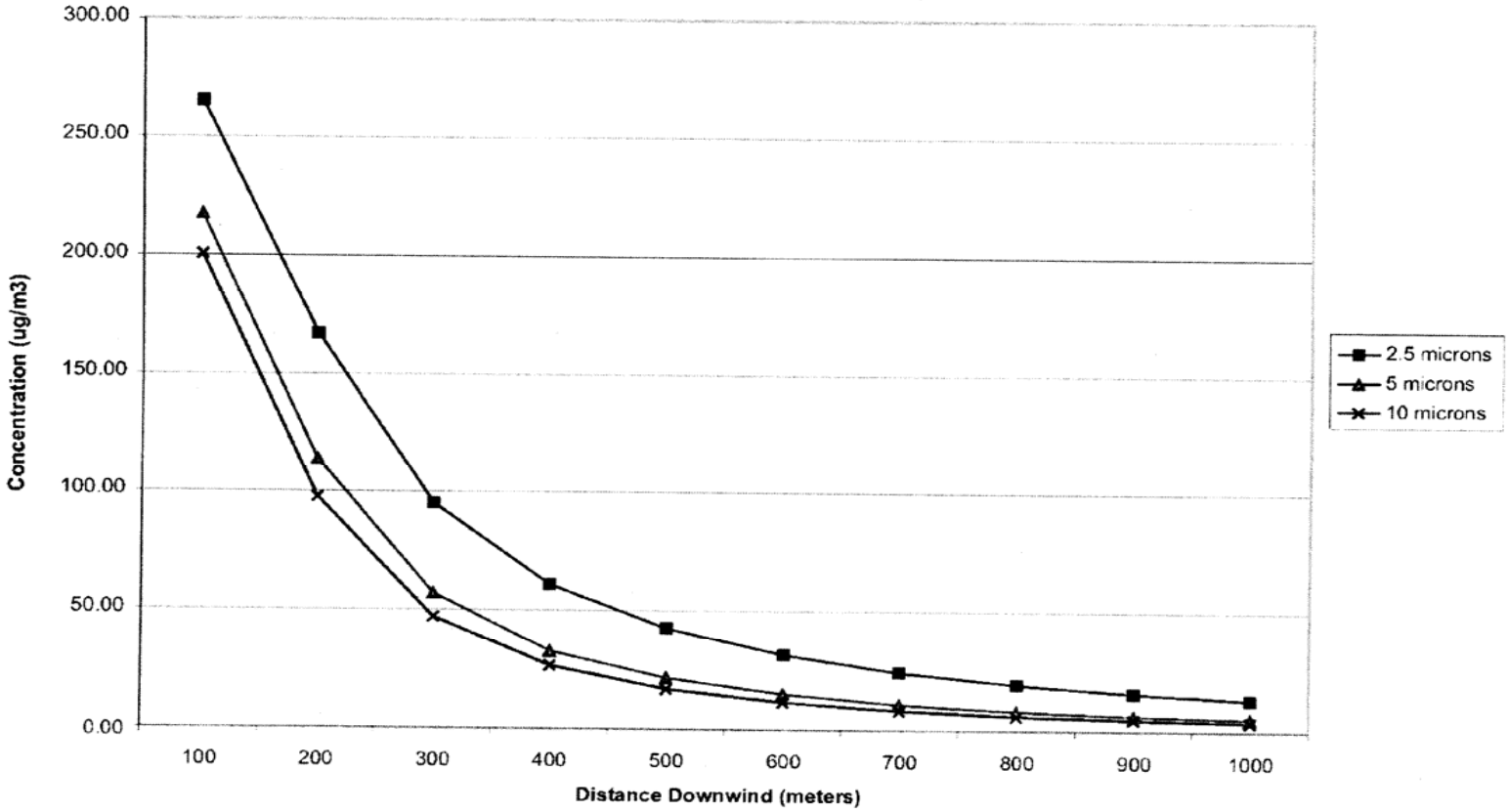


FIGURE 2. Coarse Particle Concentration vs Distance (10 Meter High Source)



ATTACHMENT B

AERMOD Model Estimates of Particulate Matter Concentrations by Particle Size for Ground-level and 10-Meter Release Heights

Figure B-1. AERMOD Concentrations by Particle Size, Ground-level Point Release Convective Conditions

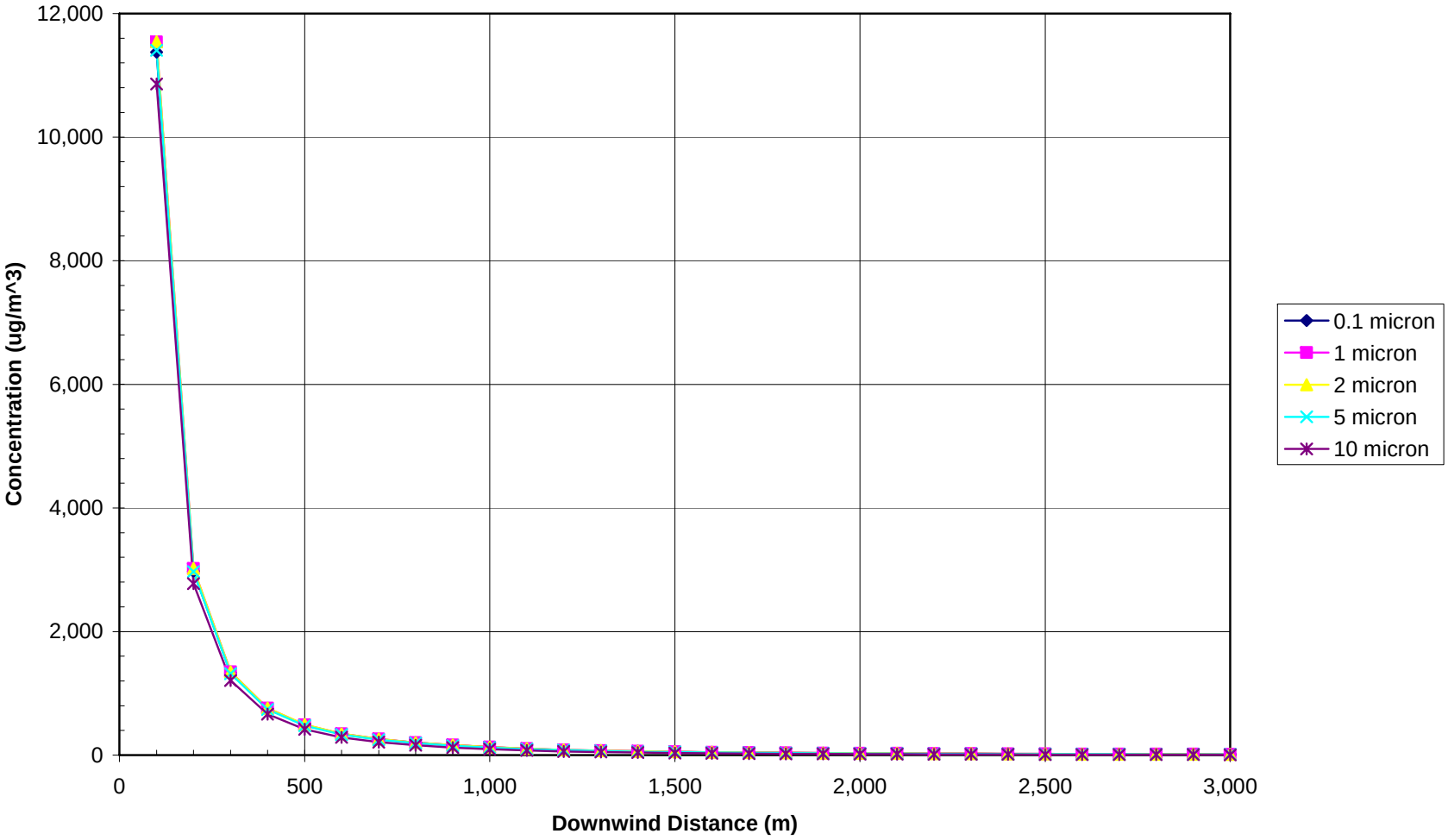


Figure B-2. AERMOD Concentrations by Particle Size, Ground-level Point Release
Neutral Conditions

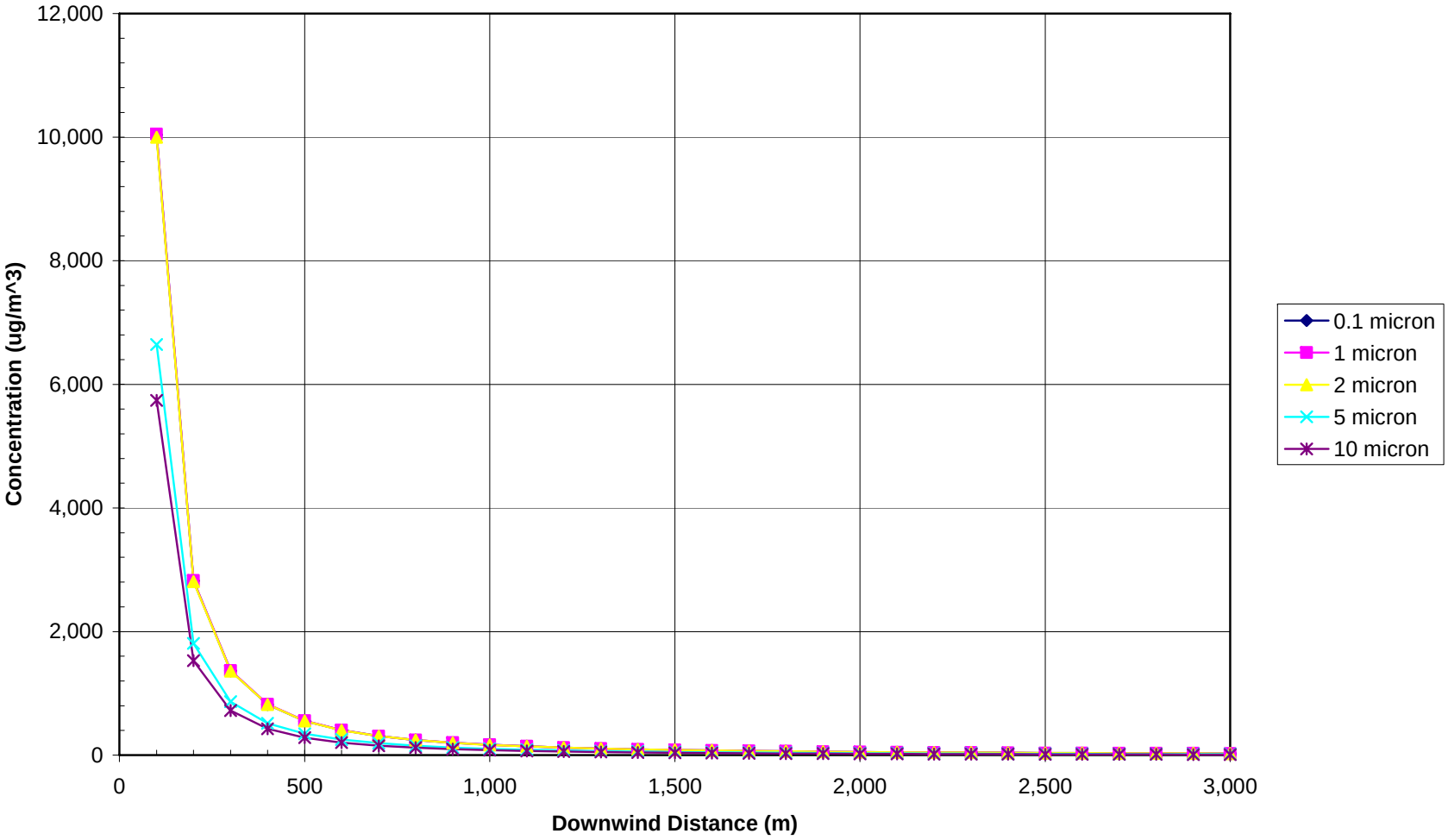


Figure B-3. AERMOD Concentrations by Particle Size, Ground-level Point Release Stable Conditions

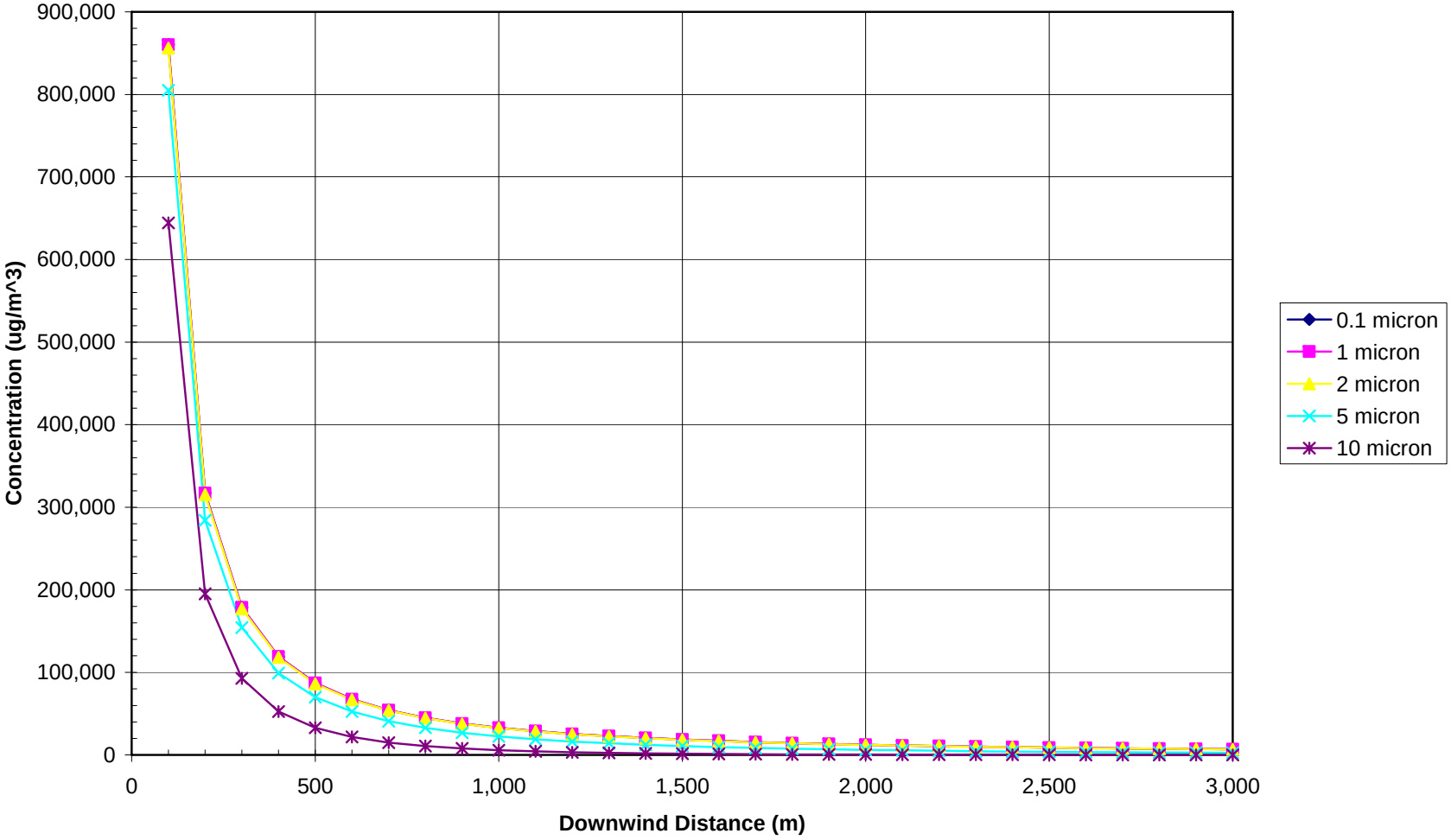


Figure B-4. AERMOD Concentrations by Particle Size, 10m Non-buoyant Stack Convective Conditions

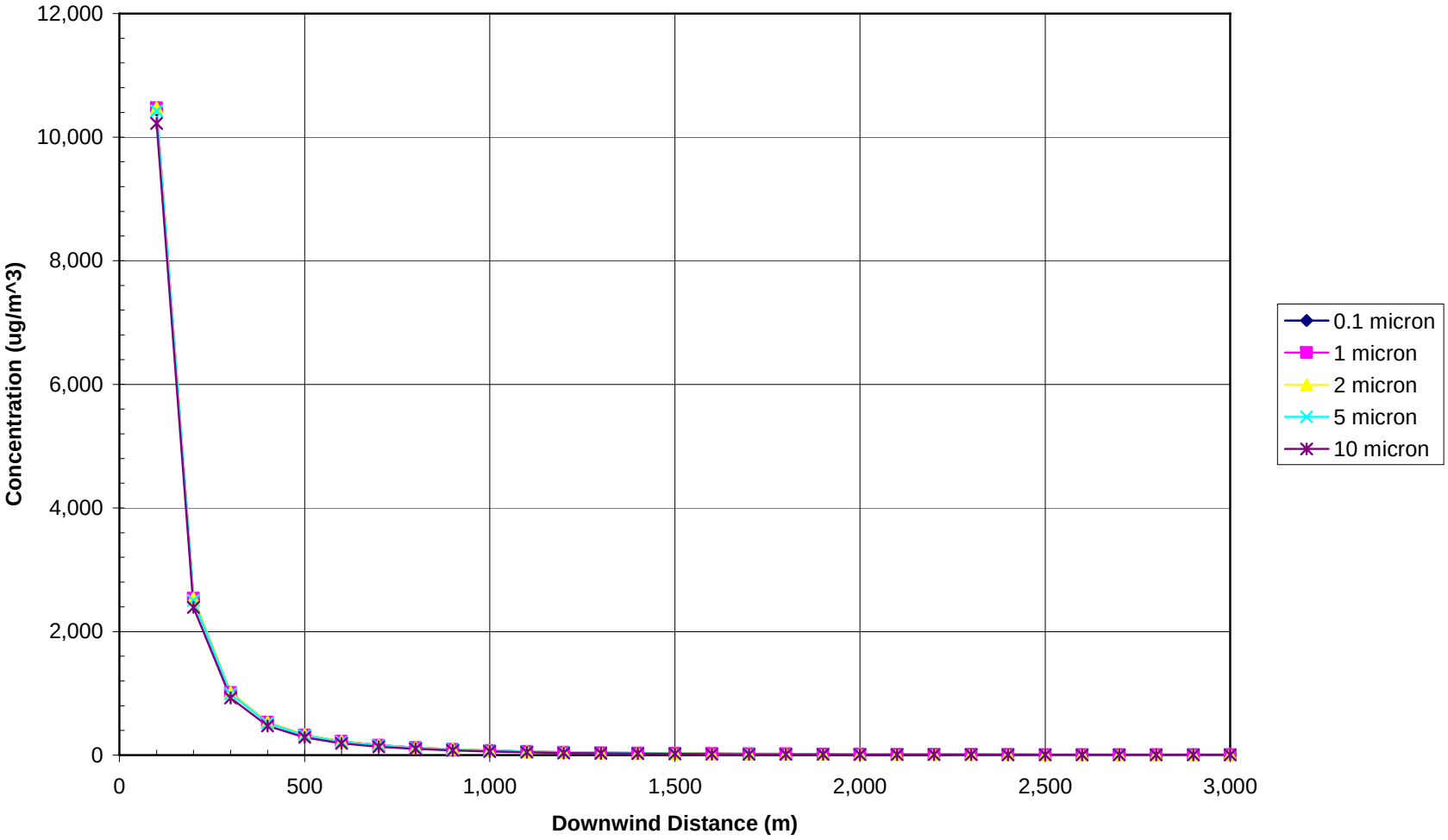


Figure B-5. AERMOD Concentrations by Particle Size, 10m Non-buoyant Stack Neutral Conditions

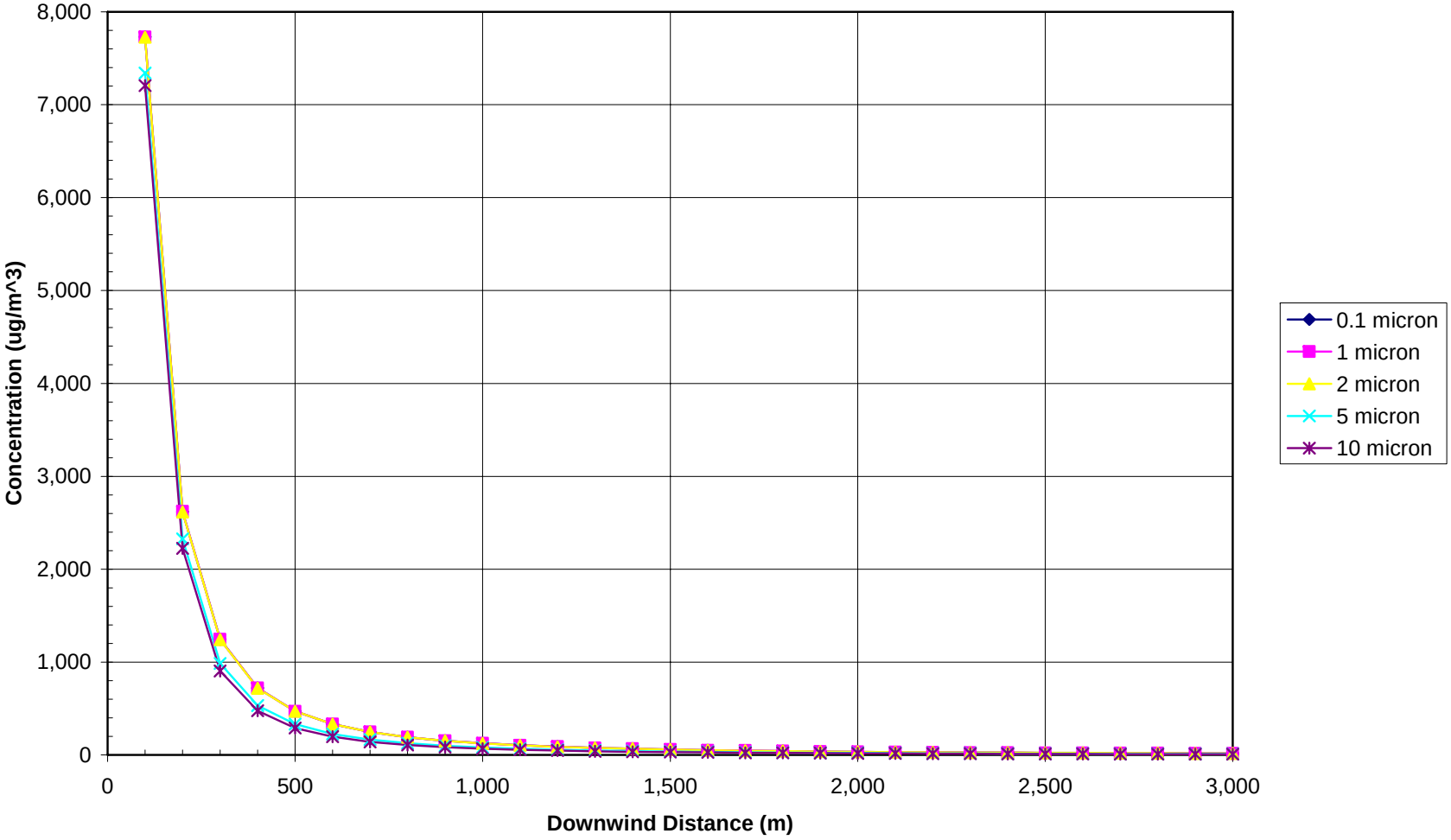


Figure B-6. AERMOD Concentrations by Particle Size, 10m Non-buoyant Stack Stable Conditions

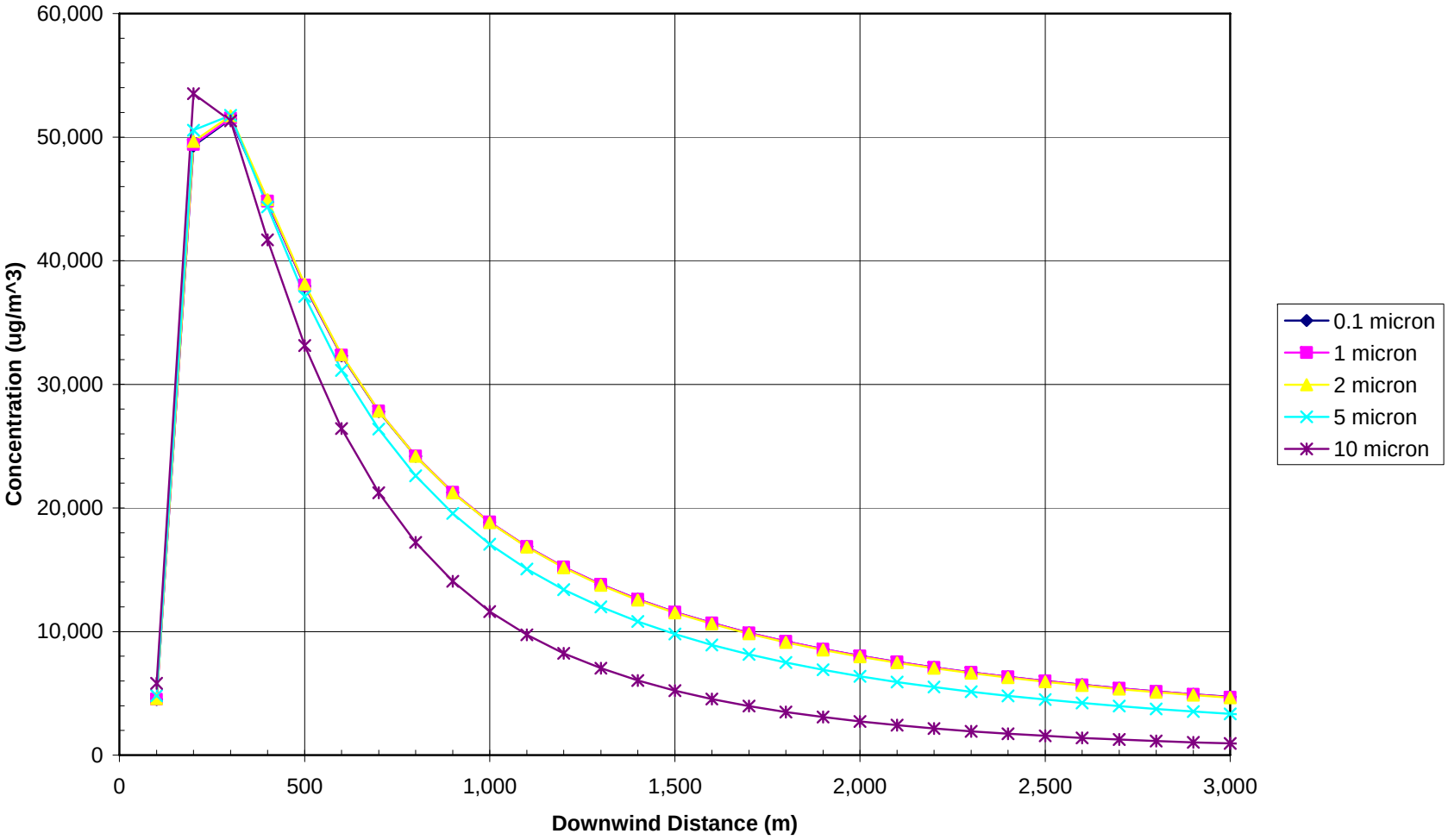


Figure B-7. AERMOD Concentrations by Particle Size, Ground-level Point Release
Stable Conditions - Urban

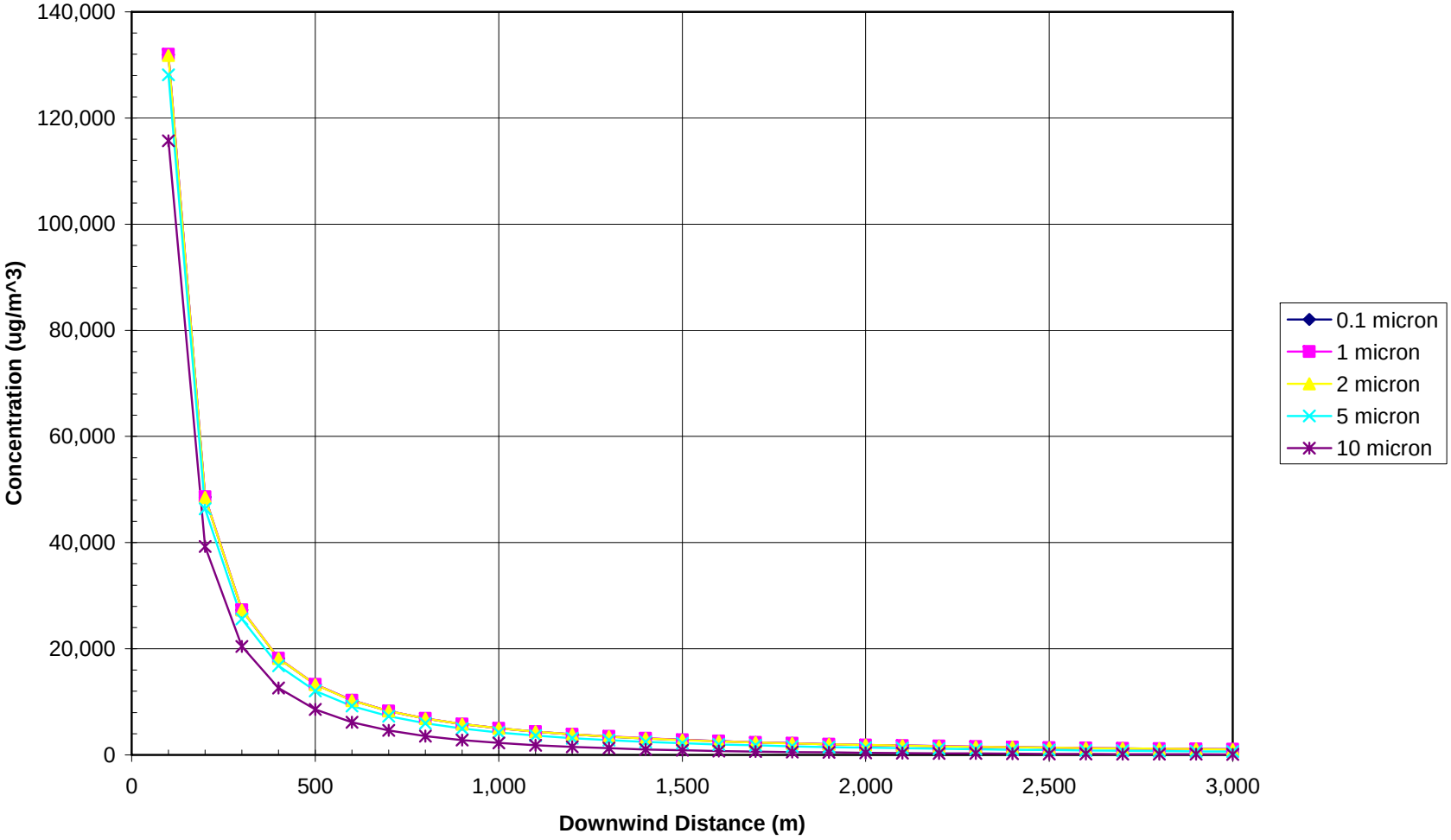
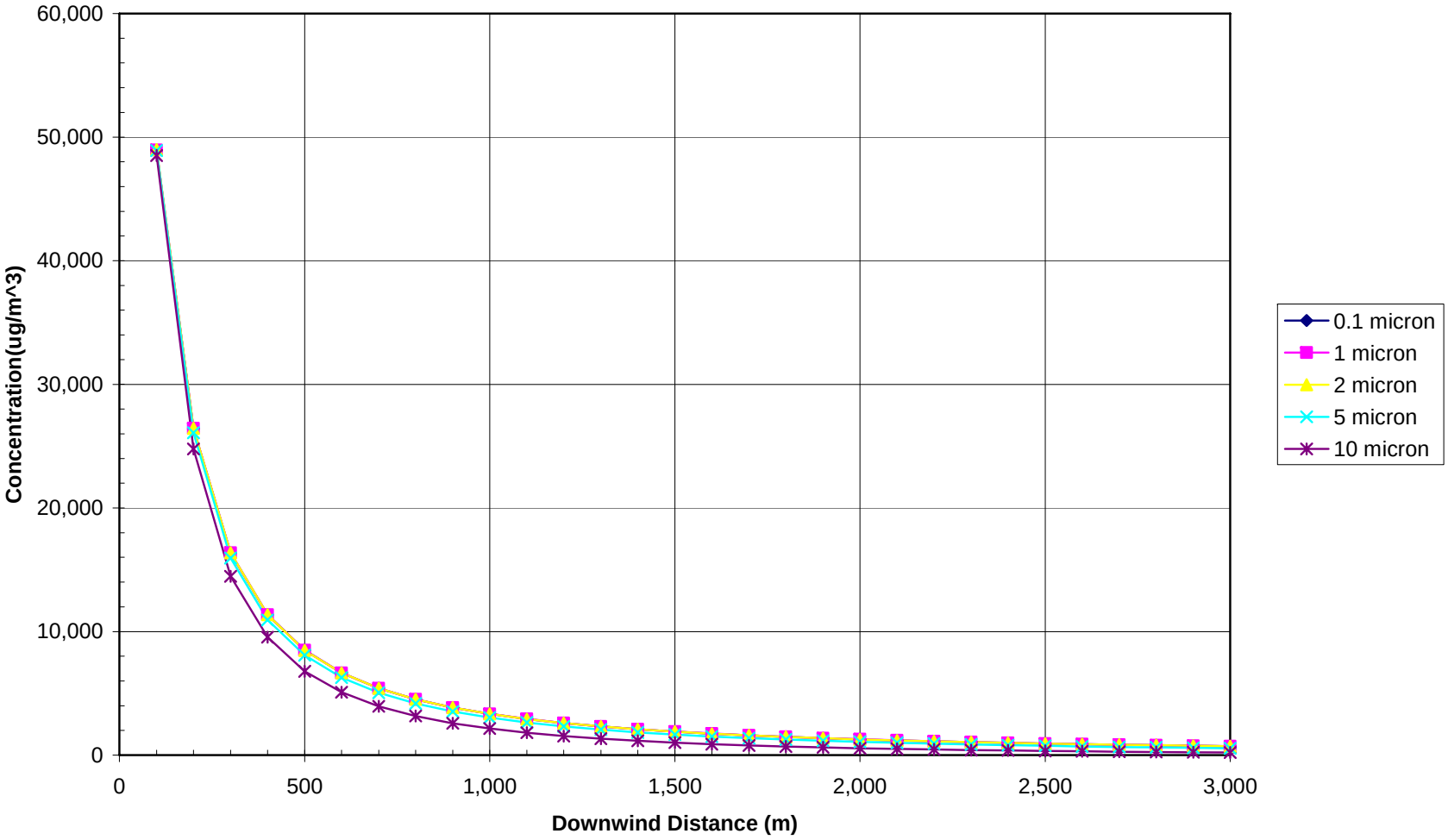


Figure B-8. AERMOD Concentrations by Particle Size, 10m Non-buoyant Stack
Stable Conditions - Urban



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Office of Air Quality Planning and Standards (OAQPS)
Research Triangle Park, North Carolina 27711

September 21, 2006

MEMORANDUM

SUBJECT: PM_{10} Annual and 24-Hour Design Values, 2003-2005

FROM: Mark Schmidt, OAQPS

TO: PM NAAQS Docket, OAR-2001-0017

General

PM_{10} design values are typically updated each year after data in the Air Quality System (AQS) are certified by State officials and preliminary outputs are reviewed and approved by EPA staff in Regional Offices. An 'official' design value summary is generally made publicly available by late summer or early fall (i.e. before the time of this memo). This year, there have been some delays in the official process. Preliminary 2003-2005 PM_{10} design values, however, were utilized in recent deliberations pertinent to the PM NAAQS review. This memo documents the preliminary PM_{10} design values and highlights an important analytic aspect of the data. Final design values will subsequently be released by EPA and posted on the EPA "Air Trends" internet web site (http://www.epa.gov/air/airtrends). The important analytic aspect highlighted in this memo is the fact that although there are two PM_{10} NAAQS metrics, one based on annual means and the other based on an expected number of 24-hour ("daily") exceedances, only the latter metric appears to have merit in the context of the established regulatory levels. That is, with an annual PM_{10} NAAQS level of 50 $\mu g/m^3$ and a 24-hour PM_{10} NAAQS level of 150 $\mu g/m^3$, the 24-hour NAAQS metric is obviously the "controlling standard".

Preliminary PM_{10} Design Value Tables

Design values for the 87 designated PM_{10} nonattainment areas are shown in Attachment (Table) 1. Design values for additional violating areas are shown in Attachment (Table) 2. These tables are subject to change!

Controlling Standard Analyses

As shown is Attachment 1, 17 designated areas violated the PM_{10} NAAQS for 2003-2005. Although four of these 17 areas violated the annual metric, all 17 violated the 24-hour exceedance-based metric. Thus, none of the designated PM_{10} areas violated only the annual NAAQS. As shown in Attachment 2, 21 additional (non-designated)

areas also violated the PM_{10} NAAQS. While only one of the 21 areas violated the annual NAAQS with complete data, all 21 areas violated the 24-hour NAAQS with sufficient data to show nonattainment (per CFR 40 Part 50, App. K). Thus, none of the additional violating areas violated solely the annual NAAQS.

Attachment 3 shows a scatter plot of monitor 24-hour concentration design values versus annual design values. Although a limited number of concentration-based 24-hour design values exceed 900 $\mu g/m^3$, the y-axis scale was constrained to that level due to readability concerns. Reference lines are plotted for the two NAAQS metrics: a y-axis reference line is plotted at 155 and an x-axis reference line is plotted at 51. (For regulatory purposes, a 24 hour level is only considered an exceedance if it rounds to 160 $\mu g/m^3$ by 10's; an annual design value must round to at least 51 by 1's in order to be considered a violation.) The two reference lines create four quadrants. The bottom left quadrant contains monitors that have design values below both NAAQS levels; most monitors are plotted in this quadrant. The top left quadrant contains monitors that have a 24-hour design value above the level of the 24-hour standard but have an annual design value below the level of that standard. There about approximately 3 dozen monitors in this quadrant. The top right quadrant contains monitors that violate both NAAQS metric levels. There are about a half dozen monitors plotted in this quadrant. Thus, approximately six-fold the number of monitors that violated both NAAQS levels, violate just the 24-hour NAAQS level. The bottom right quadrant is where monitors that violate the annual NAAQS metric but not the 24-hour NAAQS would be plotted. There are no monitors plotted here. Thus, this confirms the results from Attachment 1 and Attachment 2; there are no monitors/areas that violate only the annual PM_{10} standard.

The figure in attachment 3 also shows a linear regression plot line (red) and a 3/1 reference plot line (green). The 3/1 reference plot line is meant to represent the ratio of the 24-hour NAAQS to the annual NAAQS (150/50). The red line lies above the green line indicating a higher slope. The regression slope coefficient is, in fact, closer to 4 than to 3 (specifically, 3.9).

Attachment 4 shows two sets of statistics for (monitor-based) distributions of the ratio of the 24-hour design value to the annual design value. The first set of statistics is for all monitors in the 2003-2005 PM_{10} design value database. For this dataset, the ratio mean is about 4.0 and the ratio median is about 3.2. The second set of statistics is for monitors with "high" concentrations. An arbitrary level of 100 $\mu g/m^3$ (for the 24-hour design value) was used as the "high" threshold. The ratio mean for this set of monitors was 4.4 and the ratio median was also 4.4. 75% of the monitors with "high" concentrations had a ratio of 3.6 or higher. These two sets of data seem to indicate that true ratio of 24-hour design value to annual mean design value is greater than 3 and the ratio is higher for higher concentrations. This fact implies that a 24-hour NAAQS level of $\mu g/m^3$ is "stronger" (i.e., more controlling) than an annual NAAQS level of 50 $\mu g/m^3$.

4 Attachments

Table 1. Areas previously designated nonattainment for PM_{10}

State	Designated Area	EPA Region	Status	Classification	2003-2005 Annual Design Value [1]	2003-2005 Expected Number of Estimated Exceedances [1]	2003-2005 24-hour Design Value [1]	Met NAAQS 2003-2005?
AK	Eagle River	10	Nonattainment	Moderate	18	0	90	yes
AK	Juneau	10	Nonattainment	Moderate	10	0	42	incomplete
AZ	Ajo	9	Nonattainment	Moderate	22	0	139	yes
AZ	Bullhead City	9	Maintenance	Moderate	18	0	49	incomplete
AZ	Douglas	9	Nonattainment	Moderate	30	0	86	yes
AZ	Hayden/Miami	9	Nonattainment	Moderate	31	0	128	incomplete
AZ	Nogales	9	Nonattainment	Moderate	46	10.2	280	no
AZ	Paul Spur	9	Nonattainment	Moderate	22	2.1	207	no
AZ	Payson	9	Maintenance	Moderate	22	0	99	incomplete
AZ	Phoenix	9	Nonattainment	Serious	62 [3]	13.1 [3]	240	no
AZ	Rillito	9	Nonattainment	Moderate	37	0	118	yes
AZ	Yuma	9	Nonattainment	Moderate	38	0	127	incomplete
CA	Coachella Valley	9	Nonattainment	Serious	47	4	227	no
CA	Coso Junction [2]	9	Nonattainment	Moderate	18	1.2	118	no
CA	Imperial Valley	9	Nonattainment	Moderate	63	11.1[3]	211	no
CA	Indian Wells Valley [2]	9	Maintenance	Moderate	23	2[3]	162	no
CA	Mammoth Lakes	9	Maintenance	Moderate	22	0	86	incomplete
CA	Mono Basin	9	Nonattainment	Moderate	70 [3]	22.2 [3]	5283	no
CA	Owens Valley	9	Nonattainment	Serious	89	23.5	4125	no
CA	Sacramento County	9	Nonattainment	Moderate	26	0	110	yes
CA	San Bernardino	9	Nonattainment	Moderate	29	1.3 [3]	162	no
CA	San Joaquin Valley	9	Nonattainment	Serious	46	0.3	150	yes
CA	South Coast Air Basin	9	Nonattainment	Serious	54	1.1	149	no
CA	Trona [2]	9	Nonattainment	Moderate	19	0.5	136	yes
CO	Aspen	8	Maintenance	Moderate	19	0	103	yes
CO	Canon City	8	Maintenance	Moderate	14	0	32	incomplete
CO	Denver	8	Maintenance	Moderate	37	0	111	yes
CO	Lamar	8	Maintenance	Moderate	25	0	113	yes
CO	Pagosa Springs	8	Maintenance	Moderate	24	0	89	incomplete
CO	Steamboat Springs	8	Maintenance	Moderate	23	0	94	yes
CO	Telluride	8	Maintenance	Moderate	20	0	97	incomplete
CT	New Haven	1	Maintenance	Moderate	41	0	130	incomplete
ID	Boise	10	Maintenance	Moderate	22	0	88	yes
ID	Fort Hall	10	Nonattainment	Moderate	24	0.8	134	yes
ID	Pinehurst	10	Nonattainment	Moderate	20	0	85	yes
ID	Portneuf Valley	10	Maintenance	Moderate	22	0	88	yes
ID	Sandpoint (Bonner County)	10	Nonattainment	Moderate	17	0	71	incomplete
ID	Shoshone County	10	Nonattainment	Moderate	20	0	85	yes
IL	Granite City	5	Maintenance	Moderate	39	0	105	yes
IL	Lyons Township	5	Maintenance	Moderate	32	0	92	yes
IL	Oglesby	5	Maintenance	Moderate	25	0	91	yes
IL	Southeast Chicago	5	Maintenance	Moderate	33	0	87	yes
IN	Lake County	5	Maintenance	Moderate	32	2.7	183	no
IN	Vermillion	5	Maintenance	Moderate	ND	ND	ND	incomplete
ME	Presque Isle	1	Maintenance	Moderate	15	0	63	yes
MI	Detroit	5	Maintenance	Moderate	39	4.8 [3]	193	no
MN	Rochester	5	Maintenance	Moderate	ND	ND	ND	incomplete
MN	Saint Paul	5	Maintenance	Moderate	32	0	83	yes
MT	Butte	8	Nonattainment	Moderate	19	0	69	yes
MT	Columbia Falls	8	Nonattainment	Moderate	22	0	125	yes
MT	Kalispell	8	Nonattainment	Moderate	24	0	105	yes
MT	Lame Deer	8	Nonattainment	Moderate	24	0.7	117	incomplete
MT	Libby	8	Nonattainment	Moderate	27	0	103	yes
MT	Missoula	8	Nonattainment	Moderate	22	0	110	yes
MT	Polson	8	Nonattainment	Moderate	20	0	105	yes
MT	Ronan	8	Nonattainment	Moderate	17	0	61	incomplete
MT	Thompson Falls	8	Nonattainment	Moderate	13	0	48	incomplete
MT	Whitefish	8	Nonattainment	Moderate	25	0	104	yes
NM	Anthony	6	Nonattainment	Moderate	30	0.7	148	yes
NV	Las Vegas	9	Nonattainment	Serious	42	3.8 [3]	274	no
NV	Reno	9	Nonattainment	Serious	42	3.6 [3]	173	no
NY	New York	2	Nonattainment	Moderate	ND	ND	ND	incomplete
OH	Cuyahoga County	5	Maintenance	Moderate	37	2.6	221	yes
OH	Mingo Junction	5	Maintenance	Moderate	32	0	95	yes
OR	Eugene/Springfield	10	Nonattainment	Moderate	18	0	50	yes
OR	Grants Pass	10	Maintenance	Moderate	16	0	56	yes
OR	Klamath Falls	10	Maintenance	Moderate	22	0	110	yes

Table 1. Areas previously designated nonattainment for PM_{10}

State	Designated Area	EPA Region	Status	Classification	2003-2005 Annual Design Value [1]	2003-2005 Expected Number of Estimated Exceedances [1]	2003-2005 24-hour Design Value [1]	Met NAAQS 2003-2005?
OR	La Grande	10	Maintenance	Moderate	22	0	61	yes
OR	Lakeview	10	Maintenance	Moderate	19	0	84	yes
OR	Medford	10	Maintenance	Moderate	23	0	70	yes
OR	Oakridge	10	Nonattainment	Moderate	18	0	76	yes
PA	Clairton	3	Maintenance	Moderate	39	0.7	152	yes
PR	Guaynabo	2	Nonattainment	Moderate	35	0	115	yes
TX	El Paso	6	Nonattainment	Moderate	49	17.3 [3]	504	no
UT	Ogden	8	Nonattainment	Moderate	27	0.7	125	yes
UT	Salt Lake County	8	Nonattainment	Moderate	40	2.1	421	no
UT	Utah County	8	Nonattainment	Moderate	27	0.3	111	yes
WA	Kent	10	Maintenance	Moderate	18	0	46	incomplete
WA	Olympia	10	Maintenance	Moderate	14	0	42	incomplete
WA	Seattle	10	Maintenance	Moderate	25	0	70	incomplete
WA	Spokane	10	Maintenance	Moderate	27	0	142	yes
WA	Tacoma	10	Maintenance	Moderate	20	0	68	incomplete
WA	Wallula	10	Maintenance	Serious	31	0	134	incomplete
WA	Yakima	10	Maintenance	Moderate	24	0	105	yes
WV	Follansbee	3	Maintenance	Moderate	26	0	72	yes
WV	Weirton	3	Maintenance	Moderate	28	0	121	yes
WY	Sheridan	8	Nonattainment	Moderate	31	0	137	yes

Underlined values are based on incomplete data. Either 1) there are no other sites in the area with complete data for this three-year period; 2) the incomplete data are considered valid (see footnote #3); or a complete site(s) is located in the area but has an expected estimated exceedance value of zero and an incomplete site in the area registered the non-zero value shown.

[1] The updated design values are computed for the 2003-2005 period using federal reference or equivalent PM_{10} data reported by the Tribes and the State and local governments to EPA's Air Quality System (AQS) as of July 10, 2006. Concentrations flagged by States and Tribes as natural events (e.g. high winds, wildfires, volcanic eruptions) or exceptional events (e.g. construction, prescribed burning) and concurred by the EPA Regional Office are not included in the calculation of these design values. The computation procedures follow EPA guidance for calculating design values (40 CFR Part 50 Appendix K and the *PM10 SIP Development Guideline* EPA 450/2-86-001). No regulatory decisions on attainment status have been made for areas based upon this data. In some cases the data are still under review.

[2] On August 6, 2002, EPA finalized certain actions affecting the Searles Valley, California, PM-10 nonattainment area, which is located in the rural high desert and includes portions of Inyo, Kern, and San Bernardino Counties. The action splits the Searles Valley nonattainment area into three separate areas: Coso Junction, Indian Wells Valley and Trona. EPA's action also determines that the Trona area attained the PM-10 standards by December 31, 1994. On May 7, 2003, EPA finalized approval of the Indian Wells Moderate Area and Maintenance Plan and redesignated the area from nonattainment to attainment for particulate matter (PM-10). Source: http://www.epa.gov/region9/air/searlespm/index.htmla

[3] Although these values are based on incomplete data, they are considered valid for regulatory usage per 40 CFR Part 50 Appendix K 2.3(c). An incomplete expected number of estimated exceedances is valid if zeros are assumed for the unmonitored periods and the the 3-year metric still exceeds 1.0. An incomplete annual standard design value is valid if by substituting one half the minimum detectable concentration for missing values in deficient quarters (i.e., those with less than 75% data capture) the recalculated 3-year metric still exceeds 50. (For the latter noted situation, the substitution is implemented in the deficient quarters until the capture rate reaches 75%.). In both instances (expected estimated exceedances or annual design value), the intiially calculated metric value is shown and not the recalculated metric containing the low values.

ND = No Data

Table 2. Additional areas failing to meet the PM_{10} NAAQS in 2003-2005

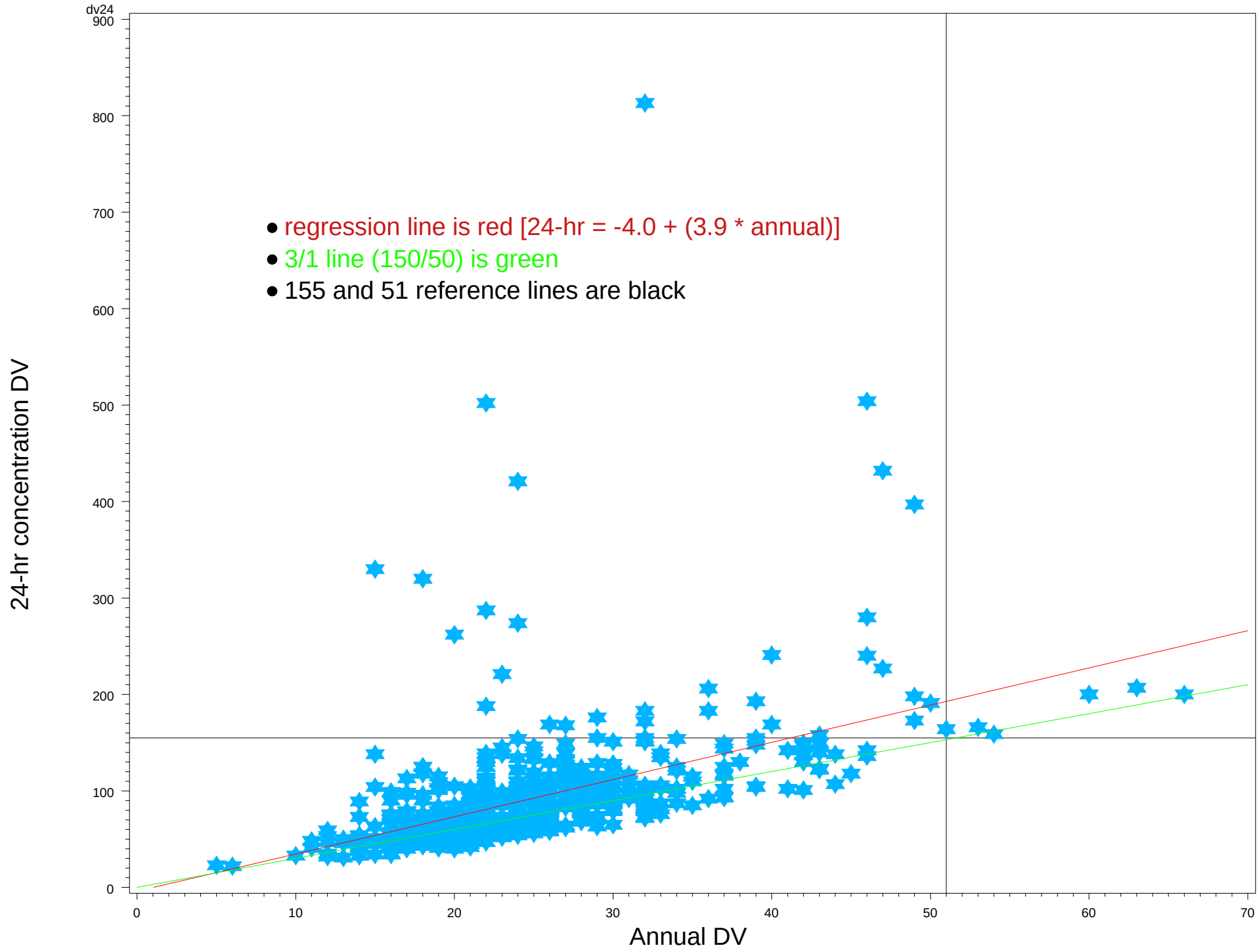
State	County	EPA Region	2003-2005 Annual Design Value [1]	2003-2005 Number of Estimated Exceedances [1]	2003-2005 24-hour Design Value [1]
AL	Jefferson	4	53	3.1 [3]	179
AZ	Maricopa [2]	9	54	3.2 [3]	158
AZ	Pinal [3]	9	34	8.1 [3]	289
CA	San Diego	9	30	3.1 [3]	155
CA	Yolo	9	26	2	169
CO	Mesa	9	31	4 3	198
MN	Kandiyohi	5	37	6.1 [3]	209
MO	Jasper	7	32	1.1	152
MO	St. Louis (City)	7	50	7.7	191
MT	Glacier	8	18	3 [3]	195
NM	Dona Ana [2]	6	42	6.1 [3]	205
NM	Sandoval	6	26	2.9 [3]	165
NV	Nye	9	37	4.9 [3]	252
OH	Scioto	5	20	2.8 [3]	210
SC	Georgetown	4	38	1.2 [3]	157
TN	Union	4	39	1.1	148
WY	Campbell	8	30	1.1 [3]	159
WY	Carbon	8	24	7.4 [3]	167
WY	Lincoln	8	23	4.4	221
WY	Natrona	8	19	2.1 [3]	194
WY	Sweetwater	8	24	6 3	306

Underlined values are based on incomplete data. Either 1) there are no sites in the area with complete data for this three-year period; 2) the incomplete data are considered valid (see footnote #3); or a complete site(s) is located in the area but has an expected estimated exceedance value of zero and an incomplete site in the area registered the non-zero value shown.

[1] The updated design values are computed for the 2003-2005 period using federal reference or equivalent PM_{10} data reported by the Tribes and the State and local governments to EPA's Air Quality System (AQS) as of July 10, 2006. Concentrations flagged by States and Tribes as natural events (e.g. high winds, wildfires, volcanic eruptions) or exceptional events (e.g. construction, prescribed burning) and concurred by the EPA Regional Office are not included in the calculation of these design values. The computation procedures follow EPA guidance for calculating design values (40 CFR Part 50 Appendix K and the *PM10 SIP Development Guideline* EPA 450/2-86-001). No regulatory decisions on attainment status have been made for areas based upon this data. In some cases the data is still under review.

[2] These counties are near or, in some cases, overlap previously designated PM10 nonattainment areas. However, the monitoring sites from which these design values are derived are located outside the boundaries of the nonattainment area. Therefore, these counties are listed here as "additional areas".

2003-2005 PM10 DV's - 24-hr vs. annual



Ratio statistics (ratio of 24-hr design value / annual design value

all data

minimum	2.0
p5	2.4
q1	2.7
median	3.2
mean	4.0
q3	4.0
p95	6.2
maximum	46.7

24-hr gt 100 µg/m3

minimum	2.4
p5	2.9
q1	3.6
median	4.4
mean	4.4
q3	5.6
p95	17.5
maximum	46.7