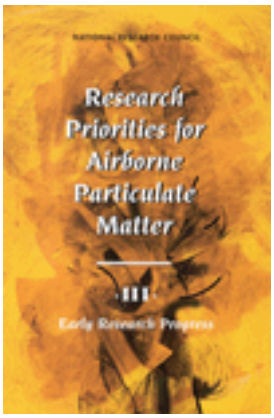

Research Priorities for Airborne Particulate Matter: III. Early Research Progress

Committee on Research Priorities for Airborne Particulate Matter, National Research Council

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Research Priorities for Airborne Particulate Matter

• III •

Early Research Progress

Committee on Research Priorities for Airborne Particulate Matter
Board on Environmental Studies and Toxicology
Commission on Life Sciences
Commission on Geosciences, Environment, and Resources
National Research Council

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Preface

The U.S. Environmental Protection Agency (EPA), other federal and state government agencies, and nongovernment organizations are conducting a major multiyear research program to improve scientific understanding of airborne particulate matter and its effects on human health. An overall objective is to reduce uncertainties in the scientific evidence used to guide regulation of airborne particulate matter in the United States. At the request of Congress and EPA, the National Research Council's (NRC's) Committee on Research Priorities for Airborne Particulate Matter proposed, in its first report, a conceptual framework to guide the formation of that program, and the committee is now independently monitoring the program's implementation.

The first of the committee's four planned reports, *Research Priorities for Airborne Particulate Matter: I. Immediate Priorities and a Long-Range Research Portfolio*, was released in 1998. It identified 10 high-priority research topics linked to key policy-related scientific uncertainties and presented a 13-year “research investment portfolio” containing recommended short-term and long-term phasing and estimated costs of research on each topic. Congress, EPA, and the scientific community have given strong support to the committee's recommendations and have implemented substantial changes in research efforts in response to them.

The committee's second report, *Research Priorities for Airborne Particulate Matter: II. Evaluating Research Progress and Updating the Portfolio*, released in 1999, described the committee's plans for monitoring the progress of re

search. In addition, the research recommendations from the committee's first report were updated, and recommendations related to emissions and air-quality models were substantially revised.

This, the committee's third report, monitors the progress of the research begun in 1998 or later to address the priority research topics identified by the committee. Although much research has been initiated, not enough time has elapsed for many of the projects to be completed and their results reported. Therefore, this report should be viewed as an interim assessment of research progress. In preparing its fourth report, which is due near the end of 2002, the committee will have the opportunity to evaluate a more extensive body of research results.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report: Arthur DuBois, Yale University Medical School, New Haven, Connecticut; Robert Frosch, Harvard University, Cambridge, Massachusetts; Carol Henry, American Chemistry Council, Arlington, Virginia; George Hidy, ENVAIR, Placitas, New Mexico; Morton Lippmann, New York University Medical School, Tuxedo, New York; Thomas Peterson, University of Arizona, Tucson, Arizona; Robert Phalen, University of California, Irvine, California; and George Wolff, retired, Farmington, Michigan.

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by Donald Mattison, March of Dimes Birth Defects Foundation. Appointed by the National Research Council, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

The committee gratefully acknowledges John Bachmann, Judith Graham, Lester Grant, Peter Preuss, Kenneth Reid, Lawrence Reiter, Richard Scheffe, John Vandenberg, and James Vickery of EPA for making presentations or

providing information to the committee. In addition, we are grateful to Maria Constantini and others at the Health Effects Institute for developing an internet-based inventory of particulate matter research projects.

We are grateful for the assistance of the NRC staff in preparing the report. Staff members who contributed to this effort are Raymond Wassel, principal staff officer for the committee; James J. Reisa, director of the Board on Environmental Studies and Toxicology; Kulbir Bakshi and K. John Holmes, senior staff officers; Eileen Abt and Laurie Geller, staff officers; Norman Grossblatt, editor; Ruth Crossgrove, publications manager; Mirsada Karalic-Loncarevic, information specialist; Tracie Holby and Emily Smail, senior program assistants; and Ramya Chari, project assistant.

Finally, I would like to thank all the members of the committee for their dedicated efforts throughout the development of this report.

Jonathan Samet, *Chair*

Committee on Research Priorities for Airborne Particulate Matter

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Executive Summary

This is the third in a series of reports by the Committee on Research Priorities for Airborne Particulate Matter. The committee was convened by the National Research Council (NRC) in January 1998 at the request of the U.S. Environmental Protection Agency (EPA) following directions from Congress in EPA's fiscal year 1998 appropriations report. The congressional request for this study arose from the uncertainties in the scientific evidence used by EPA in reaching the July 1997 decision to establish new National Ambient Air Quality Standards (NAAQS) for particulate matter (PM) less than 2.5 µm in aerodynamic diameter ($PM_{2.5}$). Anticipating the next scheduled review of the standards in 2002 and every 5 years thereafter, Congress appropriated substantial funds for a major research program to reduce the scientific uncertainties. It also directed EPA to arrange for this independent NRC study to provide guidance for planning the research program and then monitoring research progress for the 5 years of 1998-2002.

THE COMMITTEE'S 1998 AND 1999 REPORTS

The committee's first report, *Research Priorities for Airborne Particulate Matter: I. Immediate Priorities and a Long-Range Research Portfolio*, was released in 1998. It proposed a conceptual framework for a na

tional program of PM research, identified 10 high-priority research topics linked to key scientific uncertainties relevant to setting policy, and presented a 13-year, integrated "research investment portfolio" including recommended short- and long-term scheduling and estimated costs of the research. In developing its research recommendations, the committee did not undertake to judge the adequacy of the scientific foundation for EPA's 1997 decision to establish the new PM standards, recognizing that such policy considerations extend beyond the realm of science, and the committee was neither charged nor constituted to undertake a review of the standards.

In its second report, *Research Priorities for Airborne Particulate Matter: II. Evaluating Research Progress and Updating the Portfolio*, released in 1999, the committee described its plans for monitoring the progress of the research. In addition, the research recommendations from the committee's first report were updated, and two of the recommended research topics were substantially revised.

THE PARTICULATE-MATTER RESEARCH PROGRAM

Congress and EPA have given strong support to the recommendations presented in the committee's first two reports, as indicated in Table ES-1, which shows funding levels budgeted during fiscal years 1998-2001 for EPA's PM research and related technical work. In contrast, the fiscal year 1997 funding level for PM research and related technical work was about $21 million. EPA's Office of Research and Development (ORD) has shifted its PM research program to respond

TABLE ES-1 EPA Funding for PM Research and Related Technical Work (millions of dollars)

	Enacted Budget			
	FY 1998	FY 1999	FY 2000	FY 2001
PM research	42.0	47.3	53.7	59.0
Related technical work	8.2	8.3	8.7	6.3

to the research priorities identified by this committee in its first two reports. The overall effort involves inhouse research studies at EPA laboratories and centers, EPA funding of university-based research centers and investigator-initiated competitive research grants, and enhanced collaboration with other agencies and organizations. The majority of the funding has been used to support inhouse studies in EPA. Substantial research is also being funded by other governmental and nongovernmental agencies.

REVIEW OF PROGRESS AND STATUS OF RESEARCH

In preparing this, the third report, the committee began the task of assessing the progress made in implementing the PM research program. The committee has matched the PM research projects sponsored by EPA and other institutions against the committee's recommended research portfolio to assess the extent to which ongoing research is addressing the major issues that decisionmakers will consider as they review the scientific evidence relevant to the PM NAAQS. For each of its 10 priorities, the committee then evaluated current and planned research activities with six criteria: scientific value, decisionmaking value, timing and feasibility, multidisciplinary interaction, integration and planning, and accessibility of information. The first three criteria were applied to the specific priorities while the last three were considered as overarching and applying to the full program.

The committee reviewed the progress made in implementing PM research from 1998 (the year in which the research portfolio was first recommended by the committee) until the middle of 2000. Because this period represents the initial stage of the PM research program, the committee's assessment necessarily focused more on current and planned research projects than on published results. Therefore, the committee's evaluation should be viewed as an interim review of the PM research program which will be updated and modified in the committee's final report in 2002.

Research Topic 1. Outdoor Measures Versus Actual Human Exposures

In its first report, the committee recommended that information be obtained on relationships between total personal exposures to particles (the exposure measured by placing a monitor directly on a person) and outdoor concentrations of PM. Specifically, the committee recommended that groups of 10-40 persons should be studied over time to examine the relationship between their personal exposures to particles and the corresponding outdoor concentrations. There was also a recommendation that these studies include not only healthy persons, but persons considered to be "susceptible" [1] to PM.

Considerable research is under way on the relationship between ambient particle concentrations and personal exposures. While more time than expected has been taken to initiate these studies, many of the elements of research topic 1 are being addressed. Collectively, the studies are assessing general population exposures to PM and gaseous copollutants (such as ozone) and potentially susceptible subpopulations (such as asthmatics). Personal exposures are correlated with outdoor ambient exposures, but the correlations differ among people depending on their activities and other factors. The current studies are expected to expand greatly the database on personal exposures and the influencing factors, such as indoor PM concentrations, human activities, and characteristics of the places where people spend time (microenvironments).

Preliminary results from the studies have contributed to understanding of the relationship between personal exposures and outdoor concentrations and have added data from potentially susceptible groups. However, the pattern of findings is still based on a small number of studies, and replication of the results will be needed from current or recently completed studies in other cities before firm conclusions can be drawn.

[1] In using the term "susceptibility," the committee refers to an increased risk at a particular exposure that is greater for "susceptible" people than for healthy people.

Research Topic 2. Exposures of Susceptible Subpopulations to Toxic Particulate-Matter Components

The committee previously recommended that after obtaining and interpreting results of studies from research topic 1, studies be conducted to examine human exposures to specific chemical constituents of PM considered relevant to health effects. The recommendation included exposures to both the general population and potentially susceptible subpopulations. Methods of measuring some characteristics of the particles to which people are exposed are available and being field-tested for this purpose, including various physical properties (such as particle number and size) and chemical characteristics (such as presence of sulfate, nitrate, and carbon and other specific elements). In addition, methods for measuring personal exposures to some gaseous pollutants —such as ozone, nitrogen dioxide, and sulfur dioxide—are available.

The results of the studies in research topic 1 should facilitate the design of cost-effective protocols for future population-exposure studies related to priority 2 that focus on PM components considered in determining toxicity. These studies will be directed at properties of particles found to be important in toxicological and epidemiological studies. Because the research needed to determine PM toxicants is still in progress, the committee expects that research activities related to priority 2 will not begin for a few years.

Research Topic 3. Characterization of Emission Sources

The third research topic recommended by the committee was measurement of the size distribution and chemical composition of PM emissions from key sources. In addition, characterization of the emission rates of reactive gases that can form particles on reaction in the atmosphere is needed, including emission data on sulfur oxides, nitrogen oxides, volatile organic compounds, and ammonia.

Although the scientific merit of the work under way to develop new source-testing methods is high, potentially greater benefits for decisionmaking would emerge from more-complete and more-accu

rate knowledge of particle emissions by size and composition. To obtain the needed data, EPA should expand its source-testing program substantially over the next several years. At the same time, EPA should develop a comprehensive plan for systematically using the emissions test results to create a comprehensive emission inventory for the nation based on standardized tests of pollution sources. There is still ample opportunity to plan and conduct such a program over the next 5 years, and the results will be needed to develop cost-effective programs for reducing PM exposures.

Research Topic 4. Air-Quality Model Development and Testing

Source-oriented models are used to estimate the concentration of airborne particles at specific locations. Receptor-oriented models look backwards from a location towards the sources of particles. Research topic 4 calls for research to develop, test, and evaluate source-oriented and receptor-oriented models that represent the linkages between emission sources and ambient concentrations of PM. Comprehensive source-oriented models for PM are still under development. However, before such models are ready for regulatory applications, they require more-certain emission inventories (as described under the previous research topic) and an improved knowledge of the chemical and physical processes that determine the size distribution and chemical composition of ambient particles. To enhance receptor-oriented models we need better mathematical tools for identifying informative patterns in the spatial and temporal variability of particle concentration and composition. To be used with confidence, the results from receptor models and source models should be cross-compared and also validated against observations from intensive field-measurement campaigns.

Current studies are expected to make substantial contributions to our understanding of chemical and physical processes that determine the size distribution and chemical composition of ambient particles. However, additional research is needed to develop, test, and evaluate source-oriented and receptor-oriented models. In general, there has

not been sufficient effort to evaluate and compare the models developed by EPA and others. There has been inadequate attention to organizing and carrying out field studies to provide the data needed for thorough evaluation of existing models.

The ambient-PM monitoring program should provide an essential foundation on which intensive field-measurement campaigns can be built. However, little effort is being given by EPA to leveraging its investments in the PM monitoring program in order to provide field data for model evaluation.

Research Topic 5. Assessment of Hazardous Particulate-Matter Components

The committee's previous reports outlined an agenda to improve understanding of the role that specific PM characteristics (such as particle-size distribution, shape, and chemical constituents) play in determining toxicity for the health outcomes associated with PM exposures. Research was also recommended to develop experimental models, including PM surrogates, for use in toxicity studies. As the committee's recommendations are followed, epidemiological research will assume increasing importance because of the need to establish linkages in the population between PM sources and health effects as a basis for setting standards and implementing control strategies.

To date, new work on this subject has been based largely on toxicological approaches. The question of whether biological responses to PM are nonspecific—that is, are due merely to inhalation of any particle—or depend on specific PM properties is a critical focus of current research. There is considerable research evaluating physiochemical properties of PM in relation to biological effects. However, the effort has generally focused on only a few chemical characteristics, with the largest body of work involving metals—which are found at very low concentrations in the atmosphere. Other potentially important PM characteristics (such as particle number, concentration, and surface area, as well as specific particle constituents, including bioaerosols and organic compounds) have received less attention.

Current work is beginning to address the issue of exposure and dose measures other than mass concentration, although most studies continue to evaluate health effects in relation to total or size-specific mass concentration during exposure. The committee is unable to identify any studies under way that incorporate experimental PM surrogates that can mimic daily, seasonal, and regional variabilities of particle characteristics. Such experimental agents are needed so that research can be focused on specific components. Timely research is also needed to develop animal models that more closely mimic human heart and lung diseases. Study designs should give greater consideration to the relevance of the high doses used in many controlled-exposure studies and the typically low exposure levels to some components of ambient PM.

In epidemiological investigations, because insufficient monitoring data for specific particle characteristics have been available, opportunities for testing hypotheses related to the characteristics have also been somewhat insufficient, and few studies have incorporated substantial monitoring of both particle concentration and other specific characteristics of particles.

Epidemiological studies need to include sufficient exposure assessment to provide findings to guide toxicological studies of PM characteristics. However, because the populations in prospective epidemiological studies are often large, it is generally not feasible to obtain personal exposure measurements for all subjects. Opportunities should be sought to apply research models that combine toxicological and epidemiological research. In addition, consideration should be given to new population-based approaches that could be useful for hypothesis-testing and eventually surveillance. A number of studies in progress should provide information on the risks posed by ultrafine particles.

Research Topic 6. Dosimetry: Deposition and Fate of Particles in the Respiratory Tract

In its first report, the committee recommended studies to improve scientific understanding of the deposition, translocation, and clear

ance of particles deposited in the respiratory tract. Although the dosimetric studies under way are at a level of effort meeting the committee's recommendations, there is not yet sufficient focus on the specific information needs described by the committee. To the extent that those research needs are being addressed and in light of the previous lack of dosimetry data for persons who have respiratory abnormalities or in animal models of those conditions, the scientific value of the work is generally high. Nearly all the work builds on previous knowledge in an incremental way and will lead to a more integrated understanding of PM-related health effects.

Only a small portion of the work has addressed characteristics other than age and sex; there has been insufficient work on the impact of respiratory diseases. The committee called for development and validation of mathematical models for predicting deposition and clearance in abnormal lungs. However, there has been only modest advancement in the modeling of dosimetry in potentially susceptible people and very little effort to validate the models. Efforts to improve interspecies-extrapolation models continue in a few laboratories, but there has been little effort to validate the models. There has also been little effort to assess dosimetry of any type in animal models of human respiratory abnormalities. Many potentially important aspects of respiratory abnormalities—such as microdosimetry in tissues and cells, bioavailability of particleborne compounds, translocation and clearance, and handling of diverse particle types—have been addressed very little.

Research Topic 7. Combined Effects of Particulate Matter and Gaseous Pollutants

Because ambient PM is part of a pollutant mixture also containing gases, any biological effects attributed to PM in an observational study might also reflect contributions of gaseous pollutants. Research relevant to this topic should include toxicological and clinical studies that examine the effects of gaseous copollutants on the toxicity of PM.

Although research to assess if gaseous copollutants can affect the toxicity of PM has been increasing, the current controlled-exposure

research on this topic is not adequate. Particles can be concentrated in urban air for research in experiments, including exposures of human volunteers. The concentrated particles are referred to as concentrated ambient PM (CAP). The particle concentrators do not concentrate gases; approaches should be sought to augment CAP with concentrated gaseous pollutants or to scrub out specific unconcentrated gases from CAP. Furthermore, there appears to be insufficient toxicological research effort on the role of gases in influencing particle toxicity in comparison to the effort directed at studies of specific components of PM, absent gaseous copollutants. However, the epidemiological research portfolio for this topic is relatively strong; most epidemiological studies of PM include data on gaseous copollutants. Although the array of PM exposure indicators across the studies is broad, most include results of monitoring the principal gaseous pollutants of concern, including ozone, nitrogen dioxide, sulfur dioxide, carbon monoxide, and irritant hydrocarbons. Sample sizes of the studies range from obviously too small (and consequently uninformative) to adequate, so that some studies should have enough data to provide insights into combined effects.

Most research for this priority is directed at acute effects of relatively short-term (modeled or directly measured) exposures to ambient particles. In its second report, the committee recommended that increased efforts be undertaken to conduct epidemiological studies of the effects of long-term exposures to particle constituents, including ultrafine particles. However, effects of chronic exposure are being considered in only a few studies, and the current studies model long-term exposure on the basis of relatively recently measured exposures combined with historical extrapolations. There does not yet appear to be a systematic, sustained plan for implementing human chronic-exposure studies, including examining ultrafine particles.

Research Topic 8. Susceptible Subpopulations

Several groups in the population have been considered susceptible to air pollution in general and to PM specifically. In each subpopu

lation, there is likely to be a range of susceptibility. Taken together, current research efforts are expected to provide a rigorous evaluation of PM risks to susceptible subpopulations with chronic diseases, such as asthma, chronic obstructive pulmonary disease, coronary arterial disease, heart failure, and hypertension. The evidence exists primarily in relation to PM mass as an exposure index. A complete understanding of risks in susceptible subpopulations will require research that cuts across several areas, including exposure, dosimetry, toxicity mechanisms, and epidemiology. There is a general need for improved and validated animal models of human disease. In much of the experimental work, the investigators are studying relatively young animals, perhaps in the first fourth of their normal life span. In contrast, a substantial portion of the human diseases of concern occurs in the last quarter of the normal life span.

Research Topic 9. Mechanisms of Injury

The major potential biological responses which have been suggested as underlying the reported human health effects from ambient PM exposures include oxidative stress, pulmonary inflammation, airway hyperreactivity, and alterations in the cardiovascular system, such as changes in blood viscosity, heart rate and pattern of beating, and heart rate variability. The issue of mechanistic plausibility has been addressed with a number of approaches: animal models, in vitro systems, and clinical models. In studies examined by the committee, about half of the studies on mechanisms involve animal toxicology, and the other half are roughly evenly divided between clinical and in vitro studies.

It is encouraging that numerous animal models are being used to measure the effects of exposure to PM. However, a substantial number of studies have reported exposing healthy normal animals to particles; this may not be an informative approach for modeling the consequence of exposure of susceptible humans. Even though animal models of cardiac and lung diseases are being used to investigate the

effect of particles, their relevance to humans must be carefully considered. Before they are used, the models need to be well characterized and validated relative to human disease.

Many laboratories can conduct in vitro studies. The current and planned in vitro studies are designed to investigate several components of PM with a number of outcomes, such as inflammatory cytokines, chemokines, release of oxidants, and oxidative stress responses. The issue of age-dependent responses, as well as modulation of responses in cells from susceptible subjects, is also being investigated. A few studies have been designed to assess dose-response relationships. However, the committee is unable to identify any current in vitro studies that have used relevant low doses to test the validity of conclusions for specific mechanisms but instead have used unrealistic high doses. Despite those shortcomings, which need to be rectified, comparative in vitro toxicity studies to establish concepts and elucidate mechanisms of PM toxicity are valuable additions to the database.

The current and planned studies of human volunteers are designed to investigate CAP and several specific characteristics of PM (such as size, acidity, and associated metals) with a number of local and systemic end points. Studies are under way in potentially susceptible populations and are planned in other subgroups with pre-existing diseases. Despite the small number of facilities available for carrying out human exposures, the array of studies under way should provide valuable information on PM toxicity.

Research Topic 10. Analysis and Measurement

In its previous reports, the committee outlined several methodologic issues that need further study. They included the choice of statistical methods for analyzing data obtained from studies, especially epidemiological studies. Because more than one method can be used to analyze data, it is important to understand the extent to which use of alternative methods might influence the analytical results. There is a critical need for analytical methods that will aid in

characterizing exposure-response relationships at low exposures, including the range of concentrations found in ambient environments in the United States.

The recent research appears to address the research gaps and needs identified by the committee. That is especially true of measurement error and harvesting issues. [2] This research is new, however, and experience needs to be gained with the methods as they are refined and used to analyze data sets. Data that will allow further testing applications of the methods are either available or being collected. The value of the research will increase as it is applied to more—and in some cases better—data sets. The value will also increase when the various studies, methods, and results can be compared and synthesized.

OVERARCHING ISSUES RELATED TO IMPLEMENTATION OF THE PARTICULATE-MATTER RESEARCH PROGRAM

The committee identified several overarching issues based on application of its three evaluation criteria (that is, multidisciplinary interaction, integration and planning, and accessibility of information) for assessing the implementation of the PM research program.

Disincentives and Incentives for Multidisciplinary Interaction Among Particulate-Matter Researchers

Institutional and cultural obstacles often discourage attempts to perform research across disciplines, agencies, and institutions (including public, private, and nongovernmental organizations). Such obsta

[2] Harvesting issues are concerned with questions of whether deaths occurring in response to air pollution are those of people who are highly susceptible and near death or the air pollution advances the deaths of people who are not otherwise near death.

cles tend to sustain historical tendencies to conduct research within particular disciplinary or organizational boundaries (for example, toxicology versus epidemiology, EPA versus DOE, or government versus industry).

In viewing such disincentives as they apply to the inter-related tasks of conducting PM research, the committee recommends that a series of incentives be established, or in some cases continued, to orient professional and institutional policies, practices, and behavior in favor of joint planning and information exchange. These incentives should include the following:

- Encouraging federal-agency PM research programs to give greater priority to integrated, multidisciplinary projects.
- Developing a unified, cross-agency federal budget for key PM research initiatives (that is, a "virtual-agency or multiagency budget" for PM research). The committee is aware that the Air Quality Research Subcommittee of the interagency Committee on Environment and Natural Resources (CENR) [3] has undertaken such budgetary coordination for PM research. The subcommittee is encouraged to extend this coordination to the greatest extent practicable.
- Conducting regular and frequent multisponsor, multidisciplinary gatherings to build a common community of PM investigators with the goal of determining whether or not the research under development is being adequately integrated for the purpose of achieving the principal goals of the PM research program. A series of triennial colloquia and other meetings have largely met this goal.

[3] CENR is part of the National Science and Technology Council. The overall aim of the Air Quality Research Subcommittee is to enhance the effectiveness and productivity of the U.S. air quality research, and to provide a better scientific basis for decisionmaking on policies designed to improve air quality.

Integration and Planning Particulate-Matter Research Across Federal Agencies

The committee has emphasized the critical need for the federal government to provide comprehensive and integrated management of the PM Research Program. Without such management in place, it is likely that many useful individual research projects will not be synthesized into a coordinated, multidisciplinary program to ensure that key PM research questions are answered.

Since the committee's second report, measurable progress has been made in several aspects of integrating and planning the conduct of the PM Research Program:

- EPA established a formal management structure, led by a senior PM program manager within ORD. This has enabled the initial development of multiyear research budgets (an important initiative) and regular reporting of budget priorities and progress toward addressing the committee's research portfolio. In addition, the assistant administrator for ORD had tasked its Board of Scientific Counselors to review the management of the program in detail and provide specific recommendations on how to improve it.
- Across the federal government, the charter of the Air Quality Research Subcommittee of the CENR has been expanded, and efforts are under way, as a critical first step in creating an integrated federal strategy, to create a complete federal inventory of PM research and to make it available through the Particulate Matter Research Activities web site (www.pmra.org). On the basis of the inventory, the subcommittee is now developing a strategy for integrating PM research that is sponsored by federal agencies.

Those efforts have provided the PM research program with the potential to be well integrated and well planned. Although it is too early to assess the effectiveness of current management efforts fully, several aspects of the current management structure pose potential challenges to successful implementation of the PM research program.

ORD has put in place a formal management structure that should help to ensure program success, and there have been initial efforts to integrate health, exposure, and atmospheric research interests into the ambient air monitoring system. EPA's Office of Air and Radiation (OAR) has responsibility for the monitoring program and participates in EPA's PM research management structure. Although it has taken steps to integrate research needs into the implementation of the ambient monitoring program, OAR should strive to develop a stronger management system for its PM technical program which is comparable to the PM management system within ORD. An enhanced management structure for the PM technical program within OAR is needed to ensure full coordination with ORD, to catalyze active involvement of the state air agencies in developing and managing the speciation network (a key source of future data to support health research), and to develop fully the source-emission inventories needed for accurate source apportionment.

Also, past efforts to coordinate federal research have shown that this type of unified management strategy cannot be readily achieved. Sustained efforts on the part of the CENR Air Quality Research Subcommittee will be needed to ensure that these next, more-challenging steps are accomplished.

On balance, many of the elements for successful integration and planning of the PM research program have already been put in place. Successful efforts to address these remaining planning and integration challenges are critical to ensure that the maximum research return is obtained from the sizeable investments currently under way.

Connecting Research Management to Standard Implementation

The continuing process of planning and applying research in ambient air-quality standard development is part of an established process that includes preparation of EPA's air-quality criteria documents and the staff papers to inform the review of air quality standards. Both documents undertake a synthesis of existing peer-reviewed scientific information and present technical implications relevant to selecting

among the policy options for standard setting. The scientific community and the broader public have long participated in the process of reviewing the adequacy of scientific information and its application in the above documents.

There is a need to extend more effectively the application of research planning and management and scientific review into the standards-implementation process. This need exists because of the many scientific uncertainties associated with implementation, including how to account for regional variations in airborne PM characteristics and long-term changes in PM air quality due to changes in economic activities. Therefore, the committee recommends that EPA develop a research-management strategy to address key uncertainties concerning implementation of air-quality standards for PM.

Accessibility of Information

The committee has found the ongoing research-projects inventory initiated by the EPA and Health Effects Institute (HEI) to be a useful means for interested parties to track research in progress as the body of PM research continues to grow. The database can also be used to identify and plan future research. Efforts should continue to develop and maintain the database, and make it widely known and used by scientists in government, the private sector, and universities, as well as the broader public.

In addition to the PM research inventory database, the committee identified the need for the PM research program to provide information on its planning, budgets, progress, and results to parties that have an interest in PM research. Such parties could include other research organizations, public-health and environmental organizations, industry groups, health professionals, the interested public, and the news media. Information about PM research plans and results should be easily and effectively accessible. And, enhanced efforts should be used to inform and engage interested parties in understanding the multidisciplinary aspects of research results.

Throughout the PM research program, there have been efforts to

enhance accessibility to publicly funded data for scientists and others, as evidenced by the provisions of the "supersite" program and other elements of the air-quality measurement program for central archiving and public data access. In response to legislation, recent revisions to federal grant-making rules have broadened access to the data created by federally funded research.

Overall Evaluation of Particulate-Matter Research Progress

Although the initial phases of the nation's PM research program have shown promise, and a substantial number of peer-reviewed publications are forthcoming, there is as yet insufficient evidence for the committee to predict the program's ultimate effectiveness. In general, the PM research program, following on the committee's priorities, is appropriately addressing many of the key uncertainties. However, as discussed in this report, there are a number of critical specific subjects that should be given greater attention. Because research results are coming more slowly than originally expected, managers of the research program may need to adjust the timing of future research activities.

EPA and other organizations have made progress in integrating the full range of research approaches into the implementation of the national PM air-quality measurement system. However, key shortcomings (such as inadequate efforts to provide for data analysis) have limited the agency's ability to plan for and take full advantage of the wealth of new data on air quality likely to emerge from the system. EPA and other organizations will need to support research to ensure that success is achieved.

What Is Success?

As the committee continues its evaluation of PM research progress over the next two years, it will seek information to determine the extent to which the research program has provided measurable

growth in knowledge that informs the policy-relevant issues that scientists and decisionmakers must resolve in reviewing the NAAQS for airborne PM. It will also assess the full scope of research results obtained from the individual scientific disciplines in relation to the 10 research priorities; its overall assessment will consider how much understanding has been advanced in the committee's paradigm from sources of PM exposures to health effects. In addition, the committee will consider the degree of acceptance by public and private decisionmakers and interested parties of the quality and relevance of the scientific information obtained. A key determinant will be the extent to which the research findings inform the setting of future NAAQS for PM, namely, identification of the indicator (such as $PM_{2.5}$), concentration of the indicator in air, time over which measurements are made or averaged, statistical form of the standard used to determine the allowable number of exceedences, and the effective and efficient implementation of emission-control programs to achieve the NAAQS. In the future, it will also be important to ask whether the PM research and this committee's role offer a model for conducting major research initiatives on other key areas, such as endocrine-disruption effects of chemicals and potential health impacts of genetically engineered organisms.

1

The Committee's Task and the Particulate-Matter Research Enterprise

THE COMMITTEE'S TASK

The Committee on Research Priorities for Airborne Particulate Matter was convened by the National Research Council (NRC) in January 1998 at the request of the U.S. Environmental Protection Agency (EPA) pursuant to directions from Congress in EPA's fiscal year 1998 appropriations report. The congressional request for this independent NRC study arose from scientific uncertainties in the data used in EPA's July 1997 decision to establish new National Ambient Air Quality Standards (NAAQS) for airborne particulate matter (PM) smaller than 2.5 μm in aerodynamic diameter (EPA 1997). [1] Contemplating the next and later reviews of the new standards in 2002 and every 5 years thereaf

[1] PM_{10} refers to particulate matter collected by a sampling device with a size-selective inlet that has a 50% collection efficiency for particles with an aerodynamic diameter of 10 μm. $PM_{2.5}$ is similarly defined except with reference to a 2.5-μm size cut. “Total suspended particles” (TSP) was defined as the particle mass collected by a sampling device with a size-selective inlet that has a 50% collection efficiency for particles with an aerodynamic diameter of about 30 μm.

ter and EPA's proposed schedule for regulatory implementation of the new standards (Table 1.1), Congress mandated and appropriated substantial funds for EPA to conduct a major research program to reduce the scientific uncertainties. It also directed the EPA administrator to arrange for the NRC to provide independent guidance for planning the research program and monitoring its implementation. Specifically, the committee was charged to assess research priorities, and develop a conceptual research plan, and monitor research progress made over the 5 years 1998-2002 toward improved understanding of the relationships among airborne PM, its various sources, and its effects on public health. The committee's formal statement of task is presented in Appendix B. This is the committee's third report; a fourth report is scheduled for the end of 2002.

TABLE 1.1 EPA's Review and Implementation Timetable for Particulate-Matter Standards [a]

Past Actions	
1971	EPA issues TSP NAAQS
1979-1987	Criteria and standards are reviewed
1987	EPA issues PM_{10} NAAQS
1994-1997	Criteria and standards are reviewed
1997	EPA issues $PM_{2.5}$ and revised PM_{10} NAAQSs
1999	EPA designates areas as “unclassifiable” regarding attainment of NAAQS for $PM_{2.5}$
1998-2000	$PM_{2.5}$ monitors are placed nationwide
Planned Actions	
1998-2003	$PM_{2.5}$ monitoring data to be collected nationwide
2002	EPA will complete 5-year scientific review of $PM_{2.5}$ standards, leading to possible revision
2002-2005	EPA will designate nonattainment areas for $PM_{2.5}$
2005-2008	States will submit implementation plans for meeting $PM_{2.5}$ standard.
2012-2017	States will have up to 10 years and two 1-year extensions to meet $PM_{2.5}$ standards

[a] The impact of the U.S. Supreme Court decision on this timetable is unknown. That decision is pending at the time of completion of this report.

Because the committee has been directed to focus on human health effects, it did not include consideration of research on the effects of airborne PM on nonhuman biota and the environment (see Text Box 1.1). The committee's focus has been on contributions to ambient PM from human activity. Of course, airborne PM includes a natural component and some of those particles (such as pollen) have shown adverse health effects.

The committee's first report, *Research Priorities for Airborne Particulate Matter: I. Immediate Priorities and a Long-Range Research Portfolio*, was released in 1998 (NRC 1998). It proposed a conceptual framework for a national program of PM research (see Figure 1.1) identified 10 high-priority research topics linked to key policy-related scientific uncertainties (see Table 1.2); and presented a 13-year integrated "re

TEXT BOX 1.1 NONHUMAN EFFECTS OF AIRBORNE PARTICLES

In addition to effects on human health, airborne particles have other important effects. Light scattering and absorption in the atmosphere can reduce visibility and cause discoloration of the sky. Interference with solar radiation and particleborne nutrient and acid fluxes can affect ecosystem and agricultural productivity because of reduction or redistribution of light or chemical substances in the environment. Particle deposition onto surfaces leads to the discoloration of historic buildings, monuments, and museum collections. Particle deposition also can accelerate the corrosion of metal structures as varied as bridges and outdoor sculptures. And, there can be direct or indirect health effects on wild and domesticated animals. EPA has the responsibility under the Clean Air Act to consider secondary national ambient-air-quality standards that provide appropriate protection from the "welfare" effects of air pollutants, such as those listed above. The work of this NRC committee has been directed solely at providing the design of a research program that elucidates the human health effects of airborne particles. The committee notes that EPA has the further obligation to conduct research on the nonhealth effects of airborne particles, and it urges EPA to design and implement its own research program to that end.

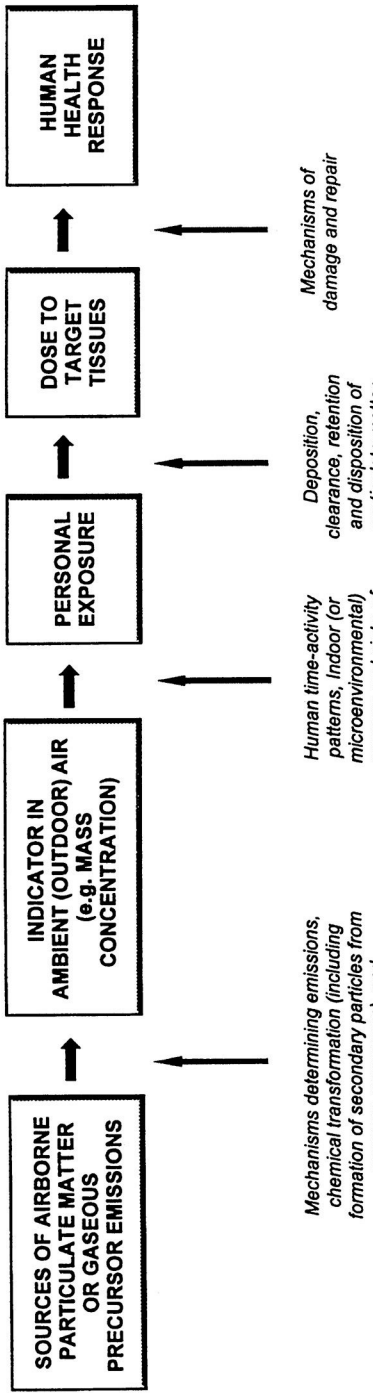

FIGURE 1.1 A general framework for integrating particulate-matter research. Note that this figure is not intended to represent a framework for research management. Such a framework would include multiple pathways for the flow of information. Sources: Modified from NRC (1983, 1994), Lioy (1990), and Sexton et al. (1992).

TABLE 1.2 Key Scientific Uncertainties Related to the Source-to-Response Framework

Source → Concentration (or other indicator)

- Contribution of various emission sources to ambient and indoor particulate-matter concentrations
- Relative contribution of various sources to the most toxic components of particulate matter

Concentration (indicator) → Exposure

- Relationship between ambient (outdoor) particulate matter and the composition of particles to which people are exposed
- Contribution of ambient particulate matter to total personal exposure for:
  - Susceptible subpopulations
  - General population
- Variation in relationship of ambient particulate-matter concentrations to human exposure by place
- Variation in contribution of ambient particulate matter to total human exposure over time
- Covariance of particulate-matter exposures with exposures to other pollutants
- Relationship between outdoor ambient and personal exposures for particulate matter and copollutants

Exposure → Dose

- Relationship between inhaled concentration and dose of particulate matter and constituents at the tissue level in susceptible subjects
  - Asthma
  - Chronic obstructive pulmonary disease (COPD)
  - Heart disease
  - Age: infants and elderly
  - Others

Dose → Response

- Mechanisms linking morbidity and mortality to particulate-matter dose to or via the lungs
  - Inflammation
  - Host defenses
  - Neural mechanisms

search investment portfolio" containing recommended short- and long-term phasing of research and estimated costs of such research.

In its second report, *Research Priorities for Airborne Particulate Matter: II. Evaluating Research Progress and Updating the Portfolio*, the committee described its initial plans for monitoring the progress of research (NRC 1999). In addition, the research recommendations from the committee's first report were reviewed and updated, and two of the recommended research topics were substantially revised. The committee's updated research investment portfolio for fiscal years 2000-2010 is shown in Table 1.3. The committee's estimates for technical support are presented in Table 1.4.

In response to the committee's first two reports, Congress and EPA made substantial changes in EPA's research program and other technical activities related to PM. In fiscal year 1997, EPA's enacted budget for PM research and related technical work was about $21 million. However, for fiscal years 1998-2001, that amount was increased substantially by Congress: $50.2 million, $55.7 million, $62.4 million, and $65.3 million, respectively. Table 1.5 summarizes the levels of resources allocated to the 10 categories of research recommended by this committee for fiscal years 1998-2001. The table shows the amounts of funding allocated to intramural and extramural research funding for each category. Most of the funding has been used to support intramural studies within EPA.

It is important to note that the work of the committee is separate from the process of reviewing the PM NAAQS. The committee's work is intended to provide advice on the PM research program, which informs the review process. Therefore, the committee was neither charged nor constituted to evaluate the adequacy of the scientific foundation of EPA's 1997 decision to issue new PM standards; in addition to scientific information, such a decision involves policy judgments beyond the realm of science. As part of the NAAQS review process, EPA has prepared a draft "criteria document" that reviews the latest scientific information to be used as the scientific basis of reevaluation of the PM NAAQS. Drawing from the criteria document, EPA's "staff paper" is being prepared to provide a written assessment of the most policy-relevant scientific information and technical analyses that form the basis of recommendations and decisions about the NAAQS.

TABLE 1.3 Committee's Research Investment Portfolio for FY 2000-2010: Timing and Estimated Costs a ($ million/year in 1998 dollars) of Recommended Research on Particulate Matter

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
SOURCE, CONCENTRATION, and EXPOSURE											
1. Outdoor vs. human exposure	3.0										
2. Exposure to toxic PM components											
2a. Methods	1.0										
2b. Studies		4.0	4.0	4.0	4.0	4.0					
3. Emission sources	2.5	2.5	2.5	2.5							
4. Models											
4a. Source-oriented [b]	4.5	4.5	4.5	4.5	4.5	4.5	4.5				
4b. Receptor-oriented	1.0	1.0	1.0								
EXPOSURE and DOSE-RESPONSE RELATIONSHIP											
5. Assessment of hazardous PM components											
5a. Toxicologic and clinical studies	8.0	8.0	8.0								
5b. Epidemiology	1.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0
6. Dosimetry	1.5	1.5									
7. Effects of PM and copollutants											
7a. Copollutants (toxicology)	4.0	4.0	4.0	4.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
7b. Copollutants, long term (epidemiology)	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	3.0	3.0
8. Susceptible subpopulations	3.0	3.0	3.0	3.0	3.0	3.0					
9. Toxicity mechanisms											
9a. Animal models	3.0	3.0	3.0	3.0							
9b. In vitro studies	3.0	3.0	3.0	3.0							
9c. Clinical studies	3.5	3.5	3.5	3.5							
ANALYSIS AND MEASUREMENT											
10a. Statistical analysis	1.0	1.0	1.0	1.0							
10b. Measurement error	1.5	3.0	2.0	2.0							
SUBTOTALS	47.5	54.0	51.5	42.5	28.5	28.5	21.5	17.0	17.0	14.0	14.0
RESEARCH MANAGEMENT COST [c] (ESTIMATED AT 10%)	4.8	5.4	5.2	4.3	2.9	2.9	2.2	1.7	1.7	1.4	1.4
TOTALS	**52.3**	**59.4**	**56.7**	**46.8**	**31.4**	**31.4**	**23.7**	**18.7**	**18.7**	**15.4**	**15.4**

[a] The committee's rough but informed collective-judgment cost estimates for the highest-priority research activities recommended in this report. See Chapter 3 of NRC 1999 and Chapter 4 of NRC 1998 for explanations. These estimates should *not* be interpreted as a recommended total particulate-matter research budget for EPA or the nation, for reasons explained in NRC 1998.

[b] These estimates are in addition to costs for EPA's "supersite" program and expansion of the nationwide speciation network, as well as likely expenditures by states, local agencies, and industries for source-emissions inventories and field-measurement campaigns in support of model— evaluation studies (see Table 1.4).

[c] Research management includes research planning, budgeting, oversight, review, and dissemination, cumulatively estimated by the committee at 10% of project costs.

TABLE 1.4 Committee's Technical-Support Estimates: Timing and Estimated Costs a ($ million/year in 1998 dollars) of Additional Technical Work Needed for Implementation of Emissions Control Programs for Airborne Particles

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
ACTIVITY											
1. Source testing by regulatory programs			5.0	5.0	5.0	5.0	5.0				
2. Compilation of interim PM emission inventory	1.0	1.0	1.0	1.0							
3. Compilation of PM emission inventory based on results of new source information	1.0	1.0	1.0								
4. Field studies in support of air-quality model evaluation and testing		20.0	20.0	20.0	20.0	20.0					
TOTALS	**1.0**	**21.0**	**26.0**	**26.0**	**25.0**	**25.0**	**6.0**	**1.0**	**1.0**		

[a] Technical-support expenditures by all public and private sponsoring organizations.

TABLE 1.5 EPA Intramural and Extramural PM-Research Enacted Budgets and Implementation for FY 1998-2001 ($ million/year in actual dollars) a

NRC Committee Recommended Research Topic	Recipient [b]	FY 1998	FY 1999	FY 2000	FY 2001
1. Outdoor vs. human exposure	**Total**	**$6.3**	**$8.2**	**$8.1**	**$5.3**
	Intramural	$4.1	$8.2	$7.6	$4.8
	Extramural	$2.2	$0.0	$0.5	$0.5
2. Exposure to toxic PM components	**Total**	**$0.5**	**$0.0**	**$0.6**	**$0.6**
	Intramural	$0.0	$0.0	$0.0	$0.0
	Extramural	$0.5	$0.0	$0.6	$0.6
3. Emission sources	**Total**	**$5.5**	**$7.0**	**$4.7**	**$4.5**
	Intramural	$3.6	$5.6	$4.2	$4.0
	Extramural	$1.9	$1.4	$0.5	$0.5
4. Air-quality models	**Total**	**$0.5**	**$0.4**	**$6.6**	**$7.2**
	Intramural	$0.0	$0.4	$6.0	$6.7
	Extramural	$0.5	$0.0	$0.6$0.6	
5. Assessment of hazardous PM components	**Total**	**$7.9**	**$7.9**	**$8.1**	**$6.7**
	Intramural	$4.1	$3.3	$4.8	$4.5
	Extramural	$3.8	$4.6	$3.2	$2.2
6. Dosimetry	**Total**	**$1.5**	**$0.6**	**$1.3**	**$1.1**
	Intramural	$1.0	$0.6	$0.8	$0.6
	Extramural	$0.4	$0.0	$0.5	$0.5
7. Effectsof PM and copollutants	**Total**	**$2.3**	**$7.4**	**$6.4**	**$11.7**
	Intramural	$0.0	$2.6	$2.3	$4.7
	Extramural	$2.3	$4.9	$4.1	$7.0

8. Susceptible subpopulations	**Total**	**$8.4**	**$2.7**	**$2.9**	**$2.7**
	Intramural	$3.9	$2.4	$1.9	$1.7
	Extramural	$4.6	$0.3	$1.0	$1.0
9. Toxicity mechanisms	**Total**	**$5.6**	**$8.3**	**$8.2**	**$8.4**
	Intramural	$2.5	$2.7	$3.0	$3.6
	Extramural	$3.1	$5.7	$5.2	$4.8
10. Analysis and measurement	**Total**	**$1.6**	**$1.2**	**$1.0**	**$1.0**
	Intramural	$1.1	$1.2	$0.5	$0.5
	Extramural	$0.5	$0.0	$0.5	$0.5
SUBTOTAL		**$40.1**	**$43.8**	**$47.8**	**$49.3**
INTRAMURAL		20.3	27.0	31.1	31.1
EXTRAMURAL		19.8	16.9	16.7	18.2
Management expenses [c]		**$1.9** [d]	**$3.6** [e]	**$5.9** [e]	**$1.7**
Working capital and operating expenses		— [d]	— [e]	— [e]	$8.0
TOTAL FOR NRC RECOMMENDED RESEARCH		**$42.0**	**$47.3**	**$53.7**	**$59.0**
Implementation-Related Activity [f]					
Technical support	**Total**	**$2.9**	**$3.4**	**$3.2**	**$1.7**
	Intramural	$2.9	$3.4	$3.2	$1.7
	Extramural	$0.0	$0.0	$0.0	$0.0
Supersites				$2.9	$2.0
Emissions characteristics, factors, and controls	**Total**	**$4.0**	**$3.5**	**$1.2**	**$1.0**
	Intramural	$3.7	$3.2	$1.2	$1.0
	Extramural	$0.4	$0.4	$0.0	$0.0

Criteria document development	**Total Intramural**	**$1.3**	**$1.4**	**$1.4**	**$1.6**
TOTAL FOR IMPLEMENTATION		**$8.2**	**$8.3**	**$8.7**	**$6.3**
INTRAMURAL		$7.9	$8.0	$5.8	$4.3
EXTRAMURAL		$0.4	$0.4	$2.9 (supersites)	$2.0 (supersites)
GRAND TOTAL FOR RESEARCH AND IMPLEMENTATION		**$50.2**	**$55.7**	**$62.4**	**$65.3**

[a] Sums of intramural and extramural costs may differ from their respective totals shown in the table because of round-off error.

[b] Extramural consists of competitive and noncompetitive awards. It includes the Science to Achieve Results (STAR) Program, PM centers, interagency agreements, cooperative agreements with universities, and supersite funding. The distribution of research efforts of PM centers to the NRC topics is based on input from each center. Intramural includes EPA personnel salaries and expenses, contracts, and cooperative agreements.

[c] Management expenses includes salaries and expenses for EPA management personnel.

[d] In FY 1998, working capital and operating expenses were tracked under a different budget element than that for PM.

[e] Working capital and operating expenses for scientific infrastructure are allocated to EPA laboratories and EPA centers based on program need. Those expenses are included under "Management expenses" for FY 1999 and FY 2000. Other expenses have been included under research topic areas.

[f] Not identified by committee as among highest priorities.

The criteria document and the staff paper are reviewed in draft form by the public and by EPA's Clean Air Scientific Advisory Committee.

On May 14, 1999, a panel of the U.S. Court of Appeals for the District of Columbia Circuit remanded several NAAQS issued by EPA in July 1997, including the new standards for $PM_{2.5}$ (EPA 1997). The court required EPA to provide more explanation of its decisionmaking process and criteria in setting the standards. The U.S. Supreme Court was later asked to consider this case and heard oral arguments on November 7, 2000. The potential impact of the court's upcoming decision on EPA's implementation schedule for the PM NAAQS (see Table 1.1) is unknown. That decision is pending at the time of completion of this report.

As stated in its second report, the committee believes strongly that the PM research program should continue to move forward expeditiously. Whatever the resolution of the legal proceedings, the public health and regulatory issues concerning PM will remain. The scientific uncertainties related to those issues are of paramount importance to public policy, and a promising national research effort to reduce the uncertainties has been initiated at great effort and expense. If stopped, a research program of this scope could not easily be started again, and any substantial disruption in the current and planned research efforts might be very costly to the nation in economy and public health.

THE PARTICULATE-MATTER RESEARCH PROGRAM

EPA's Office of Research and Development (ORD) has aligned its PM research program to respond to the set of research priorities identified by this committee. The overall research effort involves inhouse studies at EPA laboratories and centers, EPA funding of university-based research centers and investigator-initiated competitive research grants, and enhanced collaboration with other agencies and organizations. Several components of the research program are discussed below. Because this overall program has been in existence for only a few years, much of the research initiated as part of it is still in progress. Much relevant research is also being funded by other governmental and nongovernmental agencies.

Research Centers

In fiscal year 1998, Congress urged EPA to establish as many as five university-based research centers focused on PM and provide additional funding to expand PM research efforts. The PM research centers were solicited to construct integrated programs that address PM research needs in exposure, dosimetry and extrapolation modeling, toxicology, and epidemiology. These centers were established as part of EPA's Science to Achieve Results (STAR) Program through a competitive award process. EPA issued a request for applications that encouraged the proposals to include a multidisciplinary approach and, in carrying out the proposed research, to take advantage of existing air-quality databases and major new databases as they become available. Each of the following centers received an award of about $8 million to be expended over a 5-year period: New York University School of Medicine; University of Rochester; University of California, Los Angeles; Harvard University School of Public Health; and University of Washington.

Ambient-Air Monitoring

The air-quality measurement system now being implemented includes several key elements: an extensive network of PM mass monitors installed on a population-weighted basis and intended primarily to measure compliance of different metropolitan areas with the 1997 NAAQS for $PM_{2.5}$; a much smaller number of continuous $PM_{2.5}$ monitors in key metropolitan areas; a network of speciation monitors to provide basic and comparable speciation of $PM_{2.5}$ samples; and the supersites, which involve intensive shorter-term sampling efforts at selected sites around the country. [2]

To commence the PM supersite program, EPA selected two phase I sites: Atlanta, GA and Fresno, CA. Seven phase II sites were awarded cooperative agreements in January 2000: New York, NY; Pittsburgh, PA; Baltimore, MD; St. Louis, MO; Houston, TX; Los Angeles, CA; and

[2] Chapter 4 of this report represents a brief case study concerning implementation of the supersite and speciation programs.

Fresno, CA. The work in Atlanta for phase I has been completed and EPA is considering additional work at this site. Funding for the supersites is provided by EPA's Science and Technology appropriations, including funds provided through the Office of Air and Radiation and ORD. The primary objectives of the supersites are to obtain atmospheric measurements for the following purposes:

- To characterize PM and its constituents, precursors, copollutants, atmospheric transport, and source categories that affect airborne PM.
- To address research questions and scientific uncertainties about PM source-receptor-exposure-effects relationships.
- To compare and evaluate different methods of characterizing PM (such as different sampling and monitoring techniques).

Particulate-Matter Management Infrastructure

In its first two reports, the committee emphasized the critical need for the federal government to provide overarching and integrated management for the PM research program. Without such management, it is likely that useful and interesting individual research projects will lack synthesis into a coordinated, multidisciplinary program to ensure that key PM research questions are answered. To accomplish integrated management, the committee recommended, in its second report, that the proposed expansion of the charter of the Air Quality Research Subcommittee of the Interagency Committee on Environment and Natural Resources (CENR) [3] be "encouraged to promote greater coordination of the resources of the federal government

[3] CENR is part of the National Science and Technology Council. The overall aims of the Air Quality Research Subcommittee are to enhance the effectiveness and productivity of U.S. air-quality research and to provide a better scientific basis for decisionmaking on policies designed to improve air quality.

on PM research." Specifically, the committee called for a coordinated, peer-reviewed, interagency strategy that would include the following:

- A process and budget to implement the PM research portfolio recommended by the committee.
- The specific methods that would be used to coordinate research across agencies on a continuing basis.
- Strategies and mechanisms for leveraging funding within the federal sector, state governments, and the private and nonprofit sectors.

The committee was pleased to hear at its May 2000 meeting that the CENR Air Quality Research Subcommittee charter had been expanded and that efforts were under way, as a critical first step in creating an integrated federal strategy, to establish a complete federal inventory of PM research and to make it available through the Particulate Matter Research Activities web site (www.pmra.org). (See Chapter 2 for a description of the inventory.) On the basis of the inventory, the Air Quality Research Subcommittee is developing a strategy for integrating federal research on PM. Successful completion of these efforts continues to be a key to the success of the PM effort.

In its second report, the committee also noted that EPA is the agency with the largest mandate and budget for PM research. The committee recommended that EPA implement an effective management structure to ensure multidisciplinary integration of its research and air-quality monitoring efforts. Specifically, the report recommended that "top EPA research and policy officials should participate and provide management guidance during all major decision points in planning, managing, implementing, and evaluating the PM research program."

EPA has taken several important steps to implement the structure necessary for the success of the PM research effort. Specifically, it has established a formal management structure, led by an ORD PM research program manager; this has enabled the initial development of multiyear research budgets (an important innovation) and regular reporting of budget priorities and progress toward addressing the

research priorities. The agency has also continued to commit resources comparable with those proposed in the committee's research portfolio. And the assistant administrator for ORD had tasked EPA's Board of Scientific Counselors to review the management of the research effort in detail and provide specific recommendations on how to improve management.

At the same time, EPA's Office of Air and Radiation (which has important responsibility for monitoring, supersites, and emission inventories) participates in the EPA management structure for PM programs and has undertaken some valuable efforts to integrate research needs into the implementation of the monitoring and supersite program. However, there needs to be a strong senior-level commitment to sustaining and managing these efforts over the long term. (See the discussion and recommendations in Chapter 4.) Mechanisms for ensuring better cross-agency implementation of scientific initiatives have been recommended in a recent report of the NRC Committee on Research and Peer Review in EPA (NRC, 2000).

ORGANIZATION OF THIS REPORT

In the next chapter, the committee discusses its six evaluation criteria and the approach it used for evaluating progress of the PM research program. Chapter 3 presents the committee's review of progress made in each of the 10 topics in the research portfolio. Chapter 4 summarizes findings and recommendations resulting from the committee's evaluation of progress made in research on PM. The chapter also addresses general issues related to the program's implementation, providing a briefcase study in EPA's implementation of the speciation and supersite air-monitoring program.

2

Evaluating Implementation and Progress of Research

In its first two reports (NRC 1998, 1999), the committee offered criteria for evaluating various qualities of research and its policy relevance for informing the review of the national ambient air quality standards (NAAQS) for airborne particulate matter (PM). In preparing this, its third report, the committee began the task of applying the evaluation criteria to determine whether progress has been made in implementing the PM research program and to assess the rate of progress, in each priority subject. The evaluation effort should help to ensure that the PM research program provides quantitative guidance on key issues, such as the dose-response relationships of PM and the association of PM characteristics with health effects. It should also help to ensure that the PM research program provides qualitative guidance on some topics, such as physiological mechanisms of PM toxicity and atmospheric processes that lead to airborne-particle formation. And the committee's evaluation has the goal of helping to ensure the effective implementation of the research program.

APPLYING THE COMMITTEE'S RESEARCH CRITERIA

The committee arrayed the PM research projects sponsored by the Environmental Protection Agency (EPA) and other institutions against

the committee's recommended research portfolio to assess the extent to which research is addressing the major issues that decisionmakers need to consider as they review the scientific evidence relevant to the PM NAAQS. It then evaluated current and planned research activities with six criteria, which are described below. The first three —scientific value, decisionmaking value, and timing and feasibility [1] —are research-outcome criteria, and they were applied to research in each of the committee's 10 topics (see Chapter 3). The last three—multidisciplinary interaction, integration and planning, and accessibility of information—are research-planning criteria, and they were applied more generally than the other three (see Chapter 4).

Where possible and appropriate, the committee applied quantitative indicators to evaluate progress in implementing PM research, but most of the indicators were qualitative and were based on professional judgment.

Research-Outcome Criteria

The first three evaluation criteria guided the development of the committee's research portfolio, including recommended research topics, estimated budgets, and approximate periods for conducting research (see Table 1.3). The committee concluded that these criteria serve equally well as outcome measures for evaluating progress in obtaining research results that decisionmakers will use in determining whether to revise the PM NAAQS in 2002.

Scientific Value

How well does the research build on previous scientific findings to address key scientific uncertainties in a source-to-effect framework (see Figure 1.1)? The research should contribute to the development

[1] "Timing and feasibility" are treated as one criterion.

of a scientifically credible and integrated understanding of the health effects of PM and gaseous copollutants. The investigations should address testable hypotheses and provide reproducible results that can be generalized, to some degree, beyond the immediate study being performed. Specific indicators of progress for this criterion include the following:

- Number and distribution of research projects that address key uncertainties within each research-priority topic. There should not be overemphasis on a few kinds of uncertainty while others, which could be addressed, are not covered.
- Adequacy of studies in considering the heterogeneous nature of particles.
- Adequacy of addressing specific potential characteristics of PM and other factors that appear to be involved in PM-induced health effects.
- Usefulness of study results for forming hypotheses for future studies and for helping to build new research capacity and skills that might be valuable for addressing future questions about PM and other air pollutants.
- Extent to which new results of studies strengthen the bases of existing conclusions that lack a clear interpretation.
- Extent to which collective judgment of expert groups, such as EPA's Clean Air Scientific Advisory Committee and other scientific bodies, indicates a substantial increase in the scientific value of completed research.

Decisionmaking Value

How well does the research contribute to reducing key uncertainties associated with regulatory standard-setting and risk-management decisions for the next scheduled review of the NAAQS in 2002 and for later reviews? New research should provide more-accurate and more-substantial knowledge to address uncertainties about sources of PM, biologically important PM constituents and mechanisms, ambient

concentrations, personal exposures, dose-response relationships, and the extent of short-term and long-term risk to human health. Performance indicators for this criterion include the following:

- Usefulness of results in identifying the magnitude of uncertainty in the scientific information provided to decisionmakers. Studies should be evaluated on the basis of the extent to which results provide a means of testing the reliability of analytical tools, such as newly developed air-quality models.
- Usefulness of results in defining adverse effects and susceptible subpopulations.
- Usefulness of results in informing decisions concerning the setting and implementation of standards, including all four elements of a standard:

  — Indicator—the specific measurement (for example, mass, chemical form, or size fraction, such as $PM_{2.5}$) of airborne particles that is important to control for protection of public health.
  — Concentration—the amount per unit volume of air.
  — Averaging time—the period over which measurements are made or averaged (for example, annual or 24-hour periods).
  — Form—the statistical nature of the standard, used for determining the allowable number of exceedences per averaging time (for example, the 98th percentile).

- Usefulness of results for implementation of strategies for achieving the NAAQS for PM and other pollutants, including identification of emission sources and development of emission-control strategies.

Feasibility and Timing

Is the research technically, operationally, and financially feasible? The technical methods needed to conduct the research should be available. There should be sufficient research capacity and expertise to achieve the research objectives, and the research objectives should

be achievable within reasonable budgets. Indicators of performance include the following:

- Sequencing of research projects in such a way that the results of early investigations can be used advantageously in the planning and conduct of later research and regulatory reviews.
- Conduct of research in a timeframe responsive to decisionmakers' needs.
- Availability of new scientific information for the air-quality criteria document, staff paper, and standards development.
- When appropriate, conduct of research to develop the capability of addressing a key uncertainty that had not been technically feasible to address.
- Adequacy of funding for high-priority research and adequate agreement of allocations of research funding with resource estimates across the research portfolio.

Research-Planning Criteria

The final three criteria are relevant to evaluating the planning, management, and implementation of the recommended research to ensure that criteria 1-3 are achieved. The first three criteria address the question, Is the needed information being obtained? The final three ask, Is the information being effectively sought and made available?

Multidisciplinary Interaction

How well do scientists involved in PM research collaborate across scientific disciplines? This criterion is highly pertinent to the effective involvement of science managers during the planning and funding of scientific research. The success of the PM research program depends heavily on the ability of government and extramural scientists in a variety of institutions to collaborate across disciplines and organiza

tions and to communicate the status and progress of their research in an effective and accessible manner. Success in meeting this criterion will enhance the timing and feasibility of the planned research. Specific performance indicators include the following:

- Specification of disciplines and skills needed to achieve explicit research objectives.
- Use of resources in a cooperative manner or, where appropriate, for mutually funded research.
- Extent to which hypotheses based on data in one domain are tested in another, complementary domain (for example, evidence obtained in the laboratory is tested by observing the population).
- Consistent use of terminology and measures, for example names for the size fractions of PM characteristics, so that study comparisons are possible not only between disciplines, but also between control studies.
- Encouragement of investigators to be broadly aware of the information that their research can provide to researchers in other disciplines.
- Proportion of completed projects and peer-reviewed publications that have multidisciplinary participation.

Integration and Planning

How well are research planning, budgeting, and management integrated to optimize the use of financial resources, scientific talent, and infrastructure across governmental and private organizations? The diversity of sponsors and the many kinds of scientific investigations under way increase the need for federal interagency coordination and management of the effort. This criterion represents both preliminary planning and postproject analyses to fit the various pieces of the research puzzle together to provide timely guidance and feedback for achieving scientific and decisionmaking value. Performance indicators include the following:

- Effective use of available financial and human resources and, where appropriate, leveraging of resources with other scientific studies (leveraging is the degree to which the results of a research activity can increase the value of other research results).
- Formal statement of research objectives and timeframes for each of the major research activities that address PM.
- Differentiation between the kinds of research that can be conducted intramurally and extramurally, including research best sponsored jointly with the private sector, other federal agencies, or nonprofit research institutions.
- Data-sharing among scientific investigators, when feasible, to aid research planning.
- Planning to design and coordinate research projects within EPA and between EPA and other institutions and to include relevant activities from other research programs, and use of planning to address the process by which needed results will be interpreted and used as they become available.
- Speed and effectiveness of evaluation of new information and its incorporation into decisionmaking.

Accessibility of Information

How effectively is information concerning research planning, budgeting, progress, and results communicated and shared among research organizations and other interested parties? This criterion represents a measure of the continuing ability of research sponsors, scientists, decisionmakers, and other interested parties to gain access to and use information appropriate to their needs. Performance indicators for this criterion include the following:

- Availability of research plans to interested parties.
- Maintenance of an inventory of current PM research projects, which (as described later in this chapter) should be continually updated to serve as a status report of research in progress.

- Publication of periodic reports that synthesize the status of research activities and the progress being made to reduce key uncertainties; such reports should be integrated summaries that enable PM investigators, the broader scientific community, regulatory decisionmakers, Congress, and the public to understand major accomplishments and identify key challenges still to be met.

Considerations in Applying the Criteria

In conducting its evaluation, the committee applied its criteria to research activities in the 10 priority areas. The committee recommended adjustments in the implementation of the research program with respect to key uncertainties, rather than specific studies.

The committee has applied the six criteria in a flexible, commonsense fashion that relies on professional judgment and recognizes the practicalities of conducting a large research program in support of public-policy decisions. In addition, the committee is aware that not every research project conducted through this program should be expected to meet the criteria to the same degree. For example, different timeframes for applying specific criteria must be taken into account.

The committee is applying the criteria with a near-term perspective, such as the rapid startup of a large number of exposure-assessment studies, and with a long-term perspective, such as the effectiveness of the interagency Committee on Environment and Natural Resources (CENR) as a planning mechanism for PM research. However, the preliminary nature of many of the results emanating from application of the committee's research portfolio by EPA and other agencies places constraints on the present application of the evaluation criteria. Thus, the committee's evaluation represents an interim review of the PM research program and is subject to update and modification as additional data become available. Also, because of such constraints, the committee did not attempt to determine if any changes should be made to the resource estimates of the research portfolio.

SOURCES OF INFORMATION

The committee used various sources of information to assess progress in PM research, including published papers and abstracts from scientific meetings, such as the Health Effects Institute (HEI) annual conferences of 1999 and 2000 (HEI 1999; 2000), the Third Colloquium on Particulate Air Pollution and Human Health held in June 1999 (Phalen and Bell 1999), and the PM2000 Conference held in January 2000 (AWMA 2000). EPA representatives provided briefings, documents, and responses to committee questions. The committee examined published reports and written descriptions of ongoing research projects to sort relevant studies into appropriate research topics within the committee's research portfolio. Some studies were found to be relevant to more than one topic. The committee did not attempt to use its evaluation criteria as means of selecting studies to be in this report.

The principal source of information on research begun in response to the committee's research portfolio is the PM research inventory database. Beginning with its first report, the committee has recommended, as an essential element of the PM research program, the development and maintenance of an “evergreen” inventory of all PM research. That inventory now exists at an Internet site (www.pmra.org) developed and maintained by HEI in collaboration with EPA. The inventory contains a searchable database of descriptions of nearly 500 current PM research projects in a variety of disciplines throughout the world; it is being used by about 1,200 visitors per month. Most recently, the entire federal government program of PM research was added as a result of efforts of the CENR Air Quality Subcommittee. In addition to the current projects accessible through the Web site, all completed projects are maintained in an archive that will allow a complete evaluation of the PM research effort.

The establishment of the inventory has been an important step in implementing the current PM research effort. At the same time, the need to draw on disparate reports from various research-funding agencies to compile the inventory has, of necessity, resulted in some duplication and potential omission. Thus, although the inventory

clearly gives a sound overall picture of the current PM research program, there will undoubtedly be some inaccuracies in the descriptions of individual projects. Among the tasks set out by HEI and EPA for the next steps are development of procedures for regularly updating and improving the accuracy of the entries and development of a mechanism for tracking research results that emerge from the projects under way.

3

Review of Research Progress and Status

INTRODUCTION

In this chapter, the committee reviews the progress made in implementing the particulate-matter (PM) research portfolio over the period from 1998 (the year in which the portfolio was first recommended by the committee) to the middle of 2000. Because that period represents the initial stage of the PM research program, the committee's assessment necessarily focused more on continuing and planned research projects than on published results.

For each of the 10 topics in the research portfolio, the committee first characterizes the status of relevant research and progress, including the approximate numbers of studies in progress on various subtopics (the committee did not attempt to list all relevant research projects but did attempt to capture the major studies across the spectrum of the research in progress), then considers the adequacy of the current research in addressing specific needs as identified in its first two reports, and finally applies the first three evaluation criteria discussed in Chapter 2: scientific value, decisionmaking value, and feasibility and timing. The remaining three criteria—largely cross-cutting—are considered in more general terms in Chapter 4. The committee's next report, due near the end 2002, will consider research in relation to these criteria in more detail.

RESEARCH TOPIC 1. OUTDOOR MEASURES VERSUS ACTUAL HUMAN EXPOSURES

What are the quantitative relationships between concentrations of particulate matter and gaseous copollutants measured at stationary outdoor air-monitoring sites and the contributions of these concentrations to actual personal exposures, especially for subpopulations and individuals?

In its first report (NRC 1998), the committee recommended that information be obtained on relationships between total personal exposures and outdoor concentrations of PM. Specifically, the committee recommended longitudinal panel studies, in which groups of 10-40 persons would be studied at successive times to examine the relationship between their exposures to PM and the corresponding outdoor concentrations. The studies were intended to focus not only on the general population, but also on subpopulations that could be susceptible [1] to the effects of PM exposures, such as the elderly, children, and persons with respiratory or cardiovascular disease. It was recommended that some of the exposure studies include measurements of PM with an aerodynamic diameter of 2.5 μm or less ($PM_{2.5}$), PM with an aerodynamic diameter of 10 μm or less (PM_{10}), and gaseous copollutants. It was expected that the investigations would quantify the contribution of outdoor sources to personal and indoor exposures. The design and execution of studies were to take about 3 years, and the suggestion was made to conduct the studies at various geographical locations in different seasons.

Research Progress and Status

Substantial research is in progress, and some studies, started before the committee's first report, have been completed. Results of

[1] The committee is aware that there are several definitions of "susceptibility" (Parkin and Balbus 2000). in using the term in this report, the committee refers to an increased risk at a particular exposure that is greater for susceptible people than for healthy people.

recent panel studies of personal exposure conducted in Wageningen, Netherlands (Janssen et al. 1999), Boston, MA (Rojas-Bracho et al. 2000), Baltimore, MD (Sarnat 2000; Williams et al. 2000), and other places suggest that 12-15 measurements per person are sufficient to examine relationships between personal exposures and outdoor PM concentrations. These longitudinal panel studies have increased the understanding of the relationships between personal exposures and outdoor concentrations more than did earlier cross-sectional exposure studies. Several additional longitudinal panel studies are going on in other U.S. cities, including New York, NY; Atlanta, GA; Los Angeles, CA; Research Triangle Park, NC; and Seattle, WA. A number of research and funding organizations—including academic institutions, the U.S. Environmental Protection Agency (EPA), the Health Effects Institute (HEI), the Electric Power Research Institute (EPRI), and the American Petroleum Institute (API)—already have been engaged in this effort. Collectively, the studies should provide an understanding of the relationships between personal exposures and outdoor pollutant concentrations in a large number of geographic areas in the United States.

Several insights have been gained from the results of completed studies (Janssen et al. 1999, 2000; Ebelt et al. 2000; Rojas-Bracho et al. 2000; Sarnat et al. 2000; Williams et al. 2000). These studies have observed significant differences among study participants in the relationship between personal exposures and outdoor concentrations. When such relationships were analyzed for each person, substantial variability was found. Because outdoor concentrations exhibited little spatial variability, the heterogeneity was attributed to differences in indoor concentrations. Indeed, indoor concentrations were found to be an excellent predictor of personal exposures for most study participants, independently of city (Baltimore or Boston), season (winter or summer), and panel (elderly; chronic obstructive pulmonary disease, or COPD; or children). The finding that indoor concentration is an excellent predictor of personal exposure is not surprising, in that people spend more than 80% of their time indoors (EPA 1996a). Apart from exposures to tobacco smoke and emissions from cooking, which produce long-term increases in PM exposures of around 30 $\mu g/m^3$ (Spengler et al. 1981) and 15-20 $\mu g/m^3$ (Ozkaynak 1996), respectively,

home activities that were expected to produce particles, such as vacuum-cleaning and dusting (EPA 1996; Ozkaynak 1996), were found to explain very little of the total variability in personal exposures (Rojas-Bracho et al. 2000). In general, indoor sources tend to operate intermittently and, when measured by continuous monitors, can produce indoor concentrations as high as several hundred micrograms per cubic meter (Abt et al. 2000). The impact of these indoor (or other microenvironmental) peak concentrations can be captured only by real-time or semicontinuous personal monitors (Howard-Reed et al. 2000). However, when such short-term increases in concentration are averaged, their contributions to the average 24-hr indoor concentrations or personal exposures are estimated to be small.

Analyses of data from the study of elderly people in Baltimore (Sarnat et al. 2000) and the study of COPD patients in Boston (Rojas-Bracho et al. 2000) have demonstrated that ventilation (rate of exchange of indoor with outdoor air) is the measure that most strongly influences the relationship of personal-exposure to outdoor concentration. Personal exposure data were classified into three groups based on reported home ventilation status, a surrogate for the rate of exchange of indoor with outdoor air. Homes were classified as "well," "moderately," or "poorly" ventilated, as defined by the distribution of the fraction of time that windows were open while a person was in an indoor environment. When the PM datasets were stratified into these ventilation groups and analyzed cross-sectionally, strong relationships between personal exposures and outdoor concentrations were observed for well-ventilated homes and, to a lesser extent, for moderately ventilated homes. However, a low correlation coefficient was found for the poorly ventilated homes. Those findings suggest that for homes with no smokers and little cooking activity most of the variability in indoor concentrations, as well as in personal exposures of occupants, is due to the varied impact of outdoor sources on the indoor environment. That effect is underscored by the influence of air-exchange rates on the relationship between indoor and outdoor concentrations when no activities are occurring in the homes. For instance, for well-ventilated homes, indoor-to-outdoor particle ratios are close to 1.0, whereas for homes with low rates of exchange and

no activities, indoor-to-outdoor ratios can be substantially lower (about 0.4-0.6) (Abt et al. 2000; Long et al. 2000).

Home ventilation rates are expected to vary with season, geographical location, and home characteristics; that implies that the relationship of human exposures to outdoor PM concentrations will also vary with these factors. Therefore, PM risk relationships estimated from epidemiological studies might differ by city, season, and overall home characteristics. However, the additional influence of personal activity patterns on the overall relationship between human exposure and outdoor PM concentrations is also relevant to interpretation of the results of observational studies. The pattern of reported findings is still based on a small number of studies, and replication of the results will be needed from current or recently completed studies in other cities before firm conclusions can be drawn.

Adequacy of Current Research in Addressing Research Needs

Considerable effort is going into examining the relationship between ambient particle concentrations and personal exposures. Several longitudinal panel studies are being conducted in various geographic locations, including New York, NY; Atlanta, GA; Los Angeles and Fresno, CA; and Seattle, WA (see Table 3.1). Collectively, these studies are assessing exposures of healthy subjects and susceptible subpopulations (such as those with COPD; myocardial infarction, or MI; or asthma) to PM and some gaseous copollutants (such as ozone, sulfur dioxide, and nitrogen dioxide). The studies are expected to greatly expand the database on personal exposures, indoor and outdoor concentrations, human activities, and home characteristics. They are also expected to improve understanding of factors that influence the relationship between ambient concentrations and personal exposures. Therefore, as new information from the panel studies accumulates, it appears that, in spite of the time needed to initiate them, many of the elements of research topic 1 are being addressed. Most of the studies have not been completed; their findings are expected to appear in the peer-reviewed literature in the next several years.

TABLE 3.1 Current Studies Relevant to Research Topic 1

Funding Agency [a]	Research Group [b]	Location	Proposed Cohort [c]
EPA	New York University	New York, NY	16 asthmatic, 16 COPD
		Anaheim, CA	16 asthmatic, 16 COPD
		Seattle, WA	16 asthmatic, 16 COPD
EPRI and API	Harvard University	Nashville, TN	10 COPD
		Boston, MA	18 COPD
EPA	University of Washington	Seattle, WA [d]	48 COPD and elderly
			48 COPD and elderly
			48 MI
			48 MI
			24 COPD and elderly, 24 MI
			25 COPD and elderly, 24 MI
EPRI and API	Harvard University	Baltimore, MD [d]	15 elderly
HEI and Mickey Leland	EOHSI, UMDNJ, and Rutgers University	Elizabeth, NJ	50 healthy adults
		Houston, TX	50 healthy adults
		Los Angeles, CA	50 healthy adults
HEI	Harvard University	Baltimore, MD [d]	15 children
		Baltimore, MD [d]	15 COPD, 15 children
		Boston, MA [d]	15 children, 15 elderly
EPA and EPRI, [e]	Harvard University	Boston, MA [d]	15 MI, 15 MI spouses
			15 healthy adults
CARB [f]	Emory University	Atlanta, GA [d]	15 COPD
	Rutgers University and UMDNJ	Los Angeles, CA [d]	15 COPD
EPA	EPA and RTI	Baltimore, MD	15 elderly
		Fresno, CA	5 elderly
		Fresno, CA	60 elderly
EPA [g]	EPA and RTI	Research Triangle Park, NC	15 MI, 15 low-SES healthy adults
CARB	University of California, Berkeley	Fresno, CA [h]	25 asthmatic children
CARB and EPA (planned)	Harvard University, Rutgers University, and IES	Los Angeles, CA [d]	16 healthy adults (nonsmoking)

HEI	Wagenigen University	Helsinki, Finland and Amsterdam, Netherlands	50 healthy adults
DOE, OCDO, EPRI, API, and EPA	Harvard University and CONSOL Energy Inc.	Steubenville, OH [d]	25 elderly 15 children
EPRI and EPA	Harvard University and Washington University	St. Louis, MO	Not determined

[a] API = American Petroleum Institute
CARB = California Air Resources Board
DOE = U.S. Department of Energy
EPA = U.S. Environmental Protection Agency
EPRI = Electric Power Research Institute
HEI = Health Effects Institute
Mickey Leland = Mickey Leland National Urban Air Toxics Research Center
OCDO = Ohio Coal Development Office
[b] EOHSI = Environmental and Occupational Health Sciences Institute
IES = Integrated Environmental Sciences
UMDNJ = University of Medicine and Dentistry–New Jersey
RTI = Research Triangle Institute
[c] COPD = chronic obstructive pulmonary disease
MI = myocardial infarction
SES = socioeconomic status
[d] Copollutants (NO2, O3) also measured
[e] Funding for Atlanta panel study to be provided by EPRI
[f] Cofunding for Los Angeles panel provided by CARB
[g] Information is preliminary
[h] Copollutants (CO, O3, SO2, NO2) also measured

Many of the recently completed and current studies examine the relationship between ambient concentrations of gaseous pollutants and personal exposures. Understanding that relationship will provide profiles of multipollutant exposures that can inform understanding of research topic 7 (combined effects of PM and gaseous pollutants). In

addition, understanding of differences between personal exposure and ambient concentrations for a suite of gaseous pollutants and PM will provide input into analyses of measurement error in a multi-pollutant context (see research topic 10, analysis and measurement).

Application of Evaluation Criteria

Scientific Value

The current panel exposure studies are straightforward and have expanded on findings from previous investigations. They have used well-established research tools for conducting personal and micro-environmental measurements. They have also relied on field protocols developed as part of previous exposure studies, (such as the Particle Total Exposure Assessment Methodology (PTEAM) study (Pellizzari et al. 1993). The studies are generally designed to assess the range of exposures including those that occur in the home, in the workplace, and while traveling. To a large extent, the scientific value of these investigations will be judged by the appropriateness of their design. It appears that the study designs, (such as repeated measurements of a small number of people) can adequately address the scientific questions in research topic 1.

Completed studies have indicated key factors that influence outdoor-personal relationships. Preliminary results suggest that for homes with no smokers and little cooking activity, home ventilation rate (or air-exchange rate) is the most important modifier of personal exposure. To a great extent, ventilation rate controls the impact of both outdoor and indoor sources on the indoor environment, where people spend most of their time. If correct, this observation implies that such entities as home characteristics, season, and location could be more important determinants of personal exposure than activities and type of susceptible subpopulation studied.

The panel studies will also produce a large set of data on human activities and home characteristics. These data will substantially enrich the existing information and will be available to other researchers

involved in human-exposure assessment investigations (such as EPA's National Human Exposure Assessment Survey).

Decisionmaking Value

Exposure assessment is of paramount importance for understanding the effects of ambient particles and for developing cost-effective exposure-control strategies. The current studies should allow the scientific community and decisionmakers to understand the factors that affect the relationship between personal exposure and outdoor concentrations. That will be accomplished through the continued development of personal-exposure monitoring tools that allow a better understanding of the sources of exposure, physical and chemical properties of PM, and sampling durations that could be relevant to the subpopulations being studied. Although the panel studies are based on small numbers of participants (10-50 per panel), they are addressing factors that influence relationships between outdoor air and personal exposures. This is the first step in attempts to develop a comprehensive exposure model, which is a key research tool in the source-exposure-dose-response paradigm.

Feasibility and Timing

Sampling and analytical procedures, time-activity questionnaires, and other related methods necessary for conducting the panel studies have been adequately tested. They have been implemented successfully in various geographical locations by various research groups (such as Janssen et al. 1999, 2000; Ebelt et al. 2000; Rojas-Bracho et al. 2000; Sarnat et al. 2000; Williams et al. 2000). Therefore, it is expected that the current longitudinal panel studies will be completed without great difficulty. Although there was some delay in initiating some of the studies, abundant personal and microenvironmental measurements have been collected. Reporting of results from research related to this topic began during the summer of 2000, and the re

maining studies should be reported.within about 2 years, a year later than originally planned.

RESEARCH TOPIC 2. EXPOSURES OF SUSCEPTIBLE SUBPOPULATIONS TO TOXIC PARTICULATE-MATTER COMPONENTS

What are the exposures to biologically important constituents and specific characteristics of particulate matter that cause responses in potentially susceptible subpopulations and the general population?

The committee recommended that after obtaining and interpreting results of studies from research topic 1 human exposure-assessment studies examine exposures to specific chemical constituents of PM considered relevant to health effects. To make research topic 2 investigations more practicable, it will be necessary to characterize susceptible subpopulations more fully, identify toxicologically important chemical constituents or particle-size fractions, develop and field-test exposure-measurement techniques for relevant properties of PM, and design comprehensive studies to determine population exposures.

Methods of measuring personal exposures to particles of various physical properties (such as particle number and size) or chemical properties (such as sulfate, nitrate, carbon, and other elements) are available and are being field-tested. Methods of measuring personal exposures to some gaseous copollutants—such as ozone, nitrogen dioxide, and sulfur dioxide—are also used. As interest in personal-exposure measurements increases, new sampling and analytical techniques will probably emerge.

The results of the longitudinal panel studies discussed under research topic 1 should facilitate the design of cost-effective protocols for future exposure studies that focus on PM components considered in determining toxicity. These studies will be based on toxicity and epidemiological studies that are successful in identifying particle properties of interest over the next few years; because they will prob

ably not get under way for several years, the committee is planning to evaluate their progress in its next report.

RESEARCH TOPIC 3. CHARACTERIZATION OF EMISSION SOURCES

What are the size distribution, chemical composition, and mass-emission rates of particulate matter emitted from the collection of primary-particle sources in the United States, and what are the emissions of reactive gases that lead to secondary particle formation through atmospheric chemical reactions?

In its second report, the committee created a separate set of research recommendations that address measurement of the size distribution and chemical composition of PM emissions from sources. Characterization of the emission rates of reactive gases that can form particles on reaction in the atmosphere was also emphasized, including the need to maintain emission data on sulfur oxides, nitrogen oxides, ammonia, and volatile organic compounds (VOCs) (specifically those components that lead to particle formation).

The committee noted that traditional emission inventories have focused on representing PM mass emissions summed over all particles smaller than a given size, without detailed accounting of the particle-size distribution or chemical composition. Health-effects research recommended by the committee emphasized identification of the specific chemical components or size characteristics of the particles that are most directly related to the biological mechanisms that lead to the health effects of airborne particles. Detailed information on the size and composition of particle emissions from sources is important for this process of hazard identification and effective regulation. In the near term, toxicologists and epidemiologists need to know the size and composition of particles emitted from key emission sources to form hypotheses about the importance of particle characteristics and to give priority to their evaluation in laboratory- and field-based health-effects studies. In the longer term, detailed information on

particle size and composition will be needed for the design of effective air-quality control programs if those programs become more precisely targeted at the most biologically active components of the atmospheric particle mixture.

Detailed data on the particle size distribution and chemical composition of emissions from sources are also needed to support the application and evaluation of air-quality models that relate source emissions to ambient-air pollutant concentrations and chemical composition. These models are central to the process of evaluating emission-control strategies in advance of their adoption. Source-oriented models for particle transport and new particle formation can require detailed data on particle size and composition for use in condensation-evaporation calculations. Chemical mass-balance (CMB) receptor-oriented air-quality models determine source contributions to ambient particle concentrations by computing the best-fit linear combination of source chemical-composition profiles needed to reconstruct the chemical composition of atmospheric samples. These CMB models inherently require the use of accurate data on the chemical composition of particle emissions at their source. Finally, emissions data on particle chemical composition and size will be needed in the future to support detailed studies of air-quality model performance. Even when the regulated pollutant is fine-particle mass, assurances are needed that air-quality models are getting the right answers for the right reasons. Model-evaluation studies conducted in a way that tests a model's ability to account for ambient particle size and chemical composition can be used to confirm that the model has arrived at agreement between the predicted and observed mass-concentration values for the correct reasons.

In light of those needs for data on the size and chemical composition of particle emissions from sources, the committee's second report outlined the following set of research needs: establish standard source-test methods for measurement of particle size and chemical composition, characterize primary particle size and composition of emissions from the most important sources, develop new measurement methods and use of data to characterize sources of gas-phase ammonia and semivolatile organic vapors, and translate new source-

test procedures and source-test data into comprehensive national emission inventories.

Research Progress and Status

Establish Standard Source-Test Methods for Measurement of Particle Size and Chemical Composition

Research into the establishment of new source-test methods for measurement of fine- particle chemical composition is under way at EPA. A dilution source sampler for measurement of emissions from stationary sources has been built and tested. It permits measurement of particle size distributions and elemental carbon, organic carbon, speciated organic compounds, inorganic ions, and trace elements. The inorganic ions typically would include sulfates, nitrates, ammonium, and chlorides. Catalytic trace metals are included among the more than 30 trace elements that will be measured. These measurements are aligned with many of the potentially hazardous characteristics of the particles that have been identified by the committee and include determination of size-fractionated PM mass, PM surface area, PM number concentration, transition metals, soot, polycyclic aromatic hydrocarbons (PAHs), sulfates, nitrates, and some copollutants. It is not clear whether plans are being made to measure strong acids, bioaerosols, peroxides, or free radicals, which constitute other categories of concern to the health-effects community in determining the toxicity of particles. The methods being developed can be used to collect data on volatile and semivolatile organic vapor emissions and could be adapted to measure ammonia emissions. Methods for dilution source sampling of diesel exhaust particles are also under development.

EPA has conducted field tests of these advanced emission-measurement methods for open biomass burning, residential wood stoves, heavy-duty diesel trucks, and small oil-fired boilers. Construction dust emissions have also been measured. Plans for the near future include measurement of PM emissions from diesel trucks, wood-

fired boilers, large residual oil-fired boilers, jet aircraft engines, and coal-fired boilers. In addition, dilution source sampling to determine particle size and composition by comparable methods is being supported by EPA through the Science to Achieve Results (STAR) grants program (biomass smoke), American Petroleum Institute (API) (petroleum-refinery processes), the Coordinating Research Council or CRC (diesel trucks), the California Air Resources Board, the National Park Service (NPS), the Department of Defense (motor vehicles, boilers, and so on), and the Department of Energy.

Those dilution source-sampling methods have been developed for research purposes and are being used to gather data to prepare accurate emission inventories. However, the new methods have not yet replaced earlier methods for testing to establish and enforce emission limits. EPA's Office of Air and Radiation (OAR) is evaluating a dilution-based source-testing procedure for $PM_{2.5}$ compliance source-testing that might be proposed in the 2002 *Federal Register.*

Characterize Primary Particle Size and Composition of Emissions

In its second report, the committee advised EPA that development of new source-test methods would probably require substantial attention during FY 2000 and 2001. It was suggested that the new methods be used to characterize a larger number of sources over a 5-year period, beginning in FY 2002, because this information will be needed to revise the nation's emission inventories. EPA's method-development effort is well under way as recommended, but it is too early to expect large-scale application of the new methods.

In the course of development and testing of the new source-measurement methods, emissions from about six important source types have been characterized by EPA according to their particle size distributions and chemical composition, and another six will be characterized in the near future. Beyond those advances, EPA OAR reports that current resources will not support plans to conduct measurements of PM emissions from other stationary sources with either newly developed or more traditional source-test methods. Historically, few states

have devoted substantial resources to source testing for the purposes of emission-inventory development. Some source testing has been supported by government agencies other than EPA (such as CARB, the state of Colorado, NPS, and DOE) and by industry (for example, CRC, EPRI, and API). The committee located more than 150 projects related to source testing either under way or recently completed, with studies generally distributed as shown in Table 3.2. However, few of these studies use methods, such as the dilution source-sampling system being developed by EPA, that fully characterize particle size and chemical composition.

The small number of sources scheduled for full characterization falls far short of a well-designed comprehensive testing program that would lead to more-accurate emission inventories. EPA has noted its reply to the committee's questions about the range of sources to be tested that "ORD can only test a limited number of source categories annually with currently available staff and funding. In addition, the ORD method development effort is unable to test sources within any one category under the full range of operating conditions typically encountered in the field. As previously stated, the number and diversity of sources means that, at any foreseeable resource level, many years would be needed to test a representative sample of all distinctive types of sources" (EPA response to questions from the committee

TABLE 3.2 PM Emissions-Related Research

Category	EPA-Funded Projects	Projects Funded by Other Organizations
Mobile sources	11	50
Fugitive sources	9	23
Stationary-source fuel combustion	3	10
Industrial processes	2	6
Other (such as mixtures of sources)	1	8
Inventory simulation	3	13
Ammonia	1	12

dated June 2000). In its second report, the committee recommended that EPA plan to systematically achieve nearly complete characterization of emissions by particle size and composition for sources that contribute about 80% of the primary particle emissions nationally. The committee notes that now is the time to begin planning the selection of sources to be tested during the 5-year cycle beginning in FY 2002 to achieve that objective.

In its second report, the committee specifically recommended an expanded source-testing program at the level of an additional $5 million per year, beginning in FY 2002. That recommendation, if followed, will remove the program's current financial constraints. Therefore, it is appropriate to begin planning for a comprehensive source-testing program that will systematically measure the particle size distribution, particle chemical composition, and gaseous particle precursor emissions characteristics of a reasonably complete set of the relevant sources over a 5-year period. Consultations should be held with researchers in health effects, exposure, source-oriented air-quality modeling, and receptor-oriented air-quality modeling to solicit recommendations on sources to be tested and any additional chemical and physical dimensions that should be measured during the national source-testing program.

Develop New Measurement Methods and Use of Data to Characterize Sources of Gas-Phase Ammonia and Semivolatile Organic Vapors.

Methods for measurement of ammonia from nonpoint sources, such as hog-feeding facilities and highway operation of motor vehicles, have been tested by EPA ORD during the last year. Additional measurements of ammonia emissions from animal husbandry are planned for next year. Semivolatile organic compound emissions are among the dimensions listed as measurable by the research-grade dilution source-sampling procedures developed by ORD. As in the previous discussion of fine-particle emission characterization, there appears to be no program in place that will characterize more than a

handful of the relevant emission source types within the foreseeable future. Before FY 2002, a plan should be put into place for a comprehensive source-testing program that will lead to the creation of a national ammonia emission inventory based on credible and recent experimental data.

Translate New Source-Test Procedures and Source-Test Data into Comprehensive National Emission Inventories

EPA maintains a national regulatory emission inventory for $PM_{2.5}$, PM_{10}, and gases that act as particle precursors. The PM emission inventory is primarily a mass-emission inventory that does not extend to particle size distributions and particle chemical composition. EPA maintains a file of source chemical-composition profiles that can be used to estimate particle chemical-composition in many cases. These source chemical-composition profiles need to be brought up to date through a continuing program of literature review and additional source testing.

Funds appear to be available to incorporate data from new emission measurements into the national emission inventory. Although the new data are incorporated into the inventory continuously as they are collected, there is no specific date for completion of a truly new inventory. This process might appear to be one of continuous improvement, but that is not necessarily the case. Technologies used in various types of emission sources change over time. As a result, older emission data can become obsolete faster than the program of continuous improvement can keep up with the changes, especially if the emission inventory program does not have a systematic schedule for review and replacement of existing data. Highway diesel engines, for example, could be scheduled for new source-characterization experiments, but it is possible that many other diesel-engine types used in heavy-duty off-highway applications—such as construction equipment, railroad locomotives, and ships—are represented by obsolete source-test data as these technologies change over time.

The committee has recommended the compilation, beginning in

FY 2006, of a thoroughly revised national emission inventory for PM as a function of particle size and composition, and for gaseous particle precursors based on the new source-test data generated in accordance with the above recommendations. The infrastructure exists to support this work, and the committee has recommended new funds of $1 million per year to finance the effort over several years, beginning in FY 2006.

Application of Evaluation Criteria Scientific Value

Scientific Value

There is great scientific value to the research under way to develop new source-test methods and demonstrate their capabilities to measure particle size, particle chemical composition, and rates of emission of ammonia and semivolatile organic compounds. This information is needed to guide exposure-assessment studies and help toxicologists and epidemiologists form potential hypotheses about components of PM that could be hazardous to human health. The emission data are also needed to support tests of advanced air-quality models that seek to relate pollutant emissions to ambient-air quality. Emission data that describe particle size and chemical composition are needed to permit the calculation of gas-to-particle conversion rates and support calculations of heterogeneous chemical reactions that occur clouds in clouds, haze, and fog. Furthermore, when emission data on particle size and composition are available, air-quality models that account for particle size and composition can be put to very demanding tests that ensure that they are producing the right answers for the right reasons.

Decisionmaking Value

Decisions about alternative emission-control policies have to be based on an accurate understanding of the relative strength and possible toxicity of emissions from various sources. Accurate emission

inventories are absolutely fundamental to the decisionmaking process. Although there is scientific merit in the work that is under way to develop new source-test methods, the potentially important benefits to the decisionmaking process of more-complete and accurate knowledge of particle emissions evaluated according to size and composition can be realized only if EPA proceeds to expand its present source-testing program substantially by FY 2002, in accordance with the committee's recommendations. EPA should now develop a comprehensive plan for systematically translating the new source-test methods into a completed comprehensive national emissions inventory based on contemporary source tests of comparable quality. There is still ample opportunity to plan that future source-test program. The first step would involve the systematic creation of a master list of sources that most need to be tested over a specific period. The timeline for this testing must allow for the incorporation of revised and updated data into an overall emission inventory of predetermined quality and completeness by the time the next round of PM implementation plans must be drafted.

Feasibility and Timing

In the committee's second report, it was estimated that five to 15 source-testing campaigns would need to be directed at different source types each year for a 5-year period beginning in FY 2002 to bring new source-test methods to bear in creation of a reasonably complete emission inventory for particle size and composition based on contemporary data of high quality. EPA ORD is conducting about six such testing campaigns per year, at a cost of about $2.3 million per year while it is in the method-development phase that precedes the work of source testing for an emission inventory. That is reasonably consistent with the committee's recommendation that about $2.5 million per year should be spent during FY 2000 and 2001 on method-development research. On the basis of the observation that EPA ORD alone has been able to conduct about six source-test campaigns per year with an annual budget of $2.3 million, it seems reasonable that funds of $5-$7.5 million per year, as recommended by the committee

for FY 2002-2006, will be sufficient to support the proposed testing needed for a thorough upgrade of the emission inventory. With the FY 2002-2006 timeline, EPA has at least a year in which to draft a plan that identifies the sources to be tested in the future to ensure reasonably complete representation (a goal of about 80% coverage on a mass basis) of the national fine- particle emission inventory. Although some of the remarks by EPA in reply to committee questions appear to assume that a reasonably complete reworking of the emission inventory is beyond the planning horizon of the agency, the goal of a high-quality inventory for particle size and chemical composition is not out of reach. Drafting of a comprehensive plan that preselects sources to be tested and sets priorities for the work to be done over about a 5-year period will help to ensure the success of the research effort.

RESEARCH TOPIC 4. AIR-QUALITY MODEL DEVELOPMENT AND TESTING

What are the linkages between emission sources and ambient concentrations of the biologically important components of particulate matter?

The focus of this research topic is development and testing of source-oriented and receptor-oriented models that represent the linkages between emission sources and ambient concentrations of the most biologically important components of PM. Comprehensive source-oriented models for PM are still under development; before they are ready for regulatory applications, they require more-certain emission inventories (see research topic 3) and an improved understanding of the chemical and physical processes that determine the size distribution and chemical composition of ambient particles. Receptor-oriented models have been used to apportion particle mass measurements to primary emission sources through a mathematical comparison of chemical profiles of ambient PM samples with the profiles of emission-source types. However, better mathematical tools and chemical tracers are needed to resolve additional sources and to handle secondary species. Before the models can be used with suffi

cient confidence, both the receptor-oriented and source-oriented approaches need to be tested with observations from intensive field programs and then compared with each other.

Air-Quality Model Development

Source-Oriented Models

EPA has developed its major new modeling platform, MODELS 3, over the last decade. MODELS 3 is just beginning to be deployed and has not yet been extensively tested. It has been developed in a specific configuration, Community Model for Air Quality (CMAQ), primarily for modeling ozone. Scientific reviews of MODELS 3 have focused primarily on its ability to provide adequate representations of chemical processes to estimate ozone. Only recently has there been active consideration of incorporating PM formation and transport into the model.

The atmospheric-science community had limited interaction with EPA during the development of MODELS 3. In EPA's response to the committee's questions, the agency suggested that there was limited interaction because EPA faces relatively few major uncertainties about atmospheric processes and it is simply a matter of time before all the science that is needed to produce adequate estimates will be incorporated into the model. The committee did not get an indication as to whether MODELS 3 had been sufficiently tested with regard to PM formation and transport.

Table 3.3 presents a summary of the current studies identified by EPA and others as sources of information on atmospheric processes. These studies demonstrate the efforts under way to understand the processes governing atmospheric phenomena. However, the committee does not believe that current or planned efforts are sufficiently organized to effectively assess and use the information obtained through these studies.

EPA has developed a second model, the Regulatory Modeling System for Aerosols and Deposition (REMSAD), that is designed to simu

late the concentrations and chemical composition of primary and secondary $PM_{2.5}$ concentrations, PM_{10} concentrations, and depositions of acids, nutrients, and toxic chemicals. To reduce computational time and costs, REMSAD uses simpler chemistry and physics modules than MODELS 3. REMSAD has been applied to model concentrations of total $PM_{2.5}$ and $PM_{2.5}$ species (sulfate, nitrate, organic carbon, elemental carbon, and other directly emitted $PM_{2.5}$) over the conterminous United States for every hour of every day in 1990. Annual, seasonal, and daily averages from the 1990 base case have been compared with data from the Interagency Monitoring of Protected Visual Environments (IMPROVE) network and the Clean Air Status and Trends Network (CASTNET). Sensitivity analyses have also been conducted for changes in SOx, NOx, ammonia, and directly emitted $PM_{2.5.}$ Because of the lack or sparseness of available data on many areas of the United States (for example, IMPROVE provided only two 24-hour-average concentrations per week for a few dozen sites in 1990), there has not been an effective national evaluation of the model for PM. It is not clear whether REMSAD's simplified representations of chemistry adequately capture the complex atmospheric processes that govern observed particle concentrations.

TABLE 3.3 Summary of Current Studies Identified by EPA as Sources of Information on Atmospheric Processes

Study Topic	No. EPA-Funded Projects	No. Projects Funded by Other Agencies
Meteorology	1	1
Ultraviolet photometry	0	1
Fog	0	0
Semivolatile compounds	6	8
Acid precipitation	2	3
VOC-oxidant	2	2
Plume chemistry	1	0
Dry and wet deposition	1	2
Source characterization, soil	0	4
Source characterization, smoke	1	4

A number of other source-oriented PM models are being developed by individual investigators at universities or consulting companies. Seigneur et al. (1998, 1999) reviewed 10 Eulerian grid models: seven for episodic applications and three for long-term applications. The episodic models are the California Institute of Technology (CIT) model, the Denver Air Quality Model (DAQM), the Gas, Aerosol, Transport, and Radiation (GATOR) model, the Regional Particulate Model (RPM), the SARMAP Air Quality Model with Aerosols (SAQM-AERO), the Urban Airshed Model Version IV with Aerosols (UAM-AERO), and the Urban Airshed Model Version IV with an aerosol module based on the Aerosol Inorganic Model (UAM-AIM). The long-term models are the REMSAD, the Urban Airshed Model Version IV with Linearized Chemistry (UAM-LC), and the Visibility and Haze in the Western Atmosphere (VISHWA) model. In addition, several university groups are developing additional PM models that are primarily extensions of the CIT model to other areas of the country.

It appears that none of the models reviewed by Seigneur et al. (1998, 1999) is suitable for simulating PM ambient concentrations under a wide range of conditions. The following limitations were identified in both episodic and long-term models:

- Most models need improvement, albeit to various extents, in their treatment of sulfate and nitrate formation in the presence of fog, haze, and/or clouds.
- All models need improvement, albeit to various extents, in their treatment of secondary organic particle formation.
- The urban-scale models will require modifications if they are to be applied to regional scales.
- All models but one lack subgrid-scale treatment of point-source plumes.

In addition to the limitations identified above, the reliability of the simplified treatments of chemistry used for estimating the effect of emission changes on PM concentrations in the long-term models has

not been sufficiently tested. An alternative approach for predicting annual average PM concentrations has also not been adequately tested. This approach—to be used by EPA in applications of MODELS 3/CMAQ—is to approximate a full year by combining several typical meteorological scenarios with appropriate weighting factors and applying an episodic model separately to each scenario. The validity of the approach depends on, among other things, the meteorological representativeness of the selected scenarios. The approach has not yet been the subject of a comprehensive evaluation, so its validity is unknown.

In addition to the limitations indicated above regarding the formulations of PM source models, it must be noted that the application of PM source models requires input data for emission, meteorology, and ambient concentrations of PM and gases. For example, it might be possible to improve the models by incorporating more information on atmospheric processes, but any apparent improvements will need to be tested for their success in reproducing observations during specific meteorological situations. Substantial uncertainties are still associated with PM emission inventories, as described under research topic 3. Ammonia and VOC emission inventories involve large gaps that will affect the predictions of secondary PM, and uncertainties in natural and anthropogenic emissions of mineral dust will affect the predictions of primary PM. Moreover, the most comprehensive modeling input databases are for California regions, and there are insufficient data on other states.

Emission and process data related to specific components of PM are notably lacking. A long-term research goal is to identify specific physical or chemical components in PM that are primarily responsible for the adverse health effects. EPA models focus on total mass concentrations and major PM constituents, such as sulfate and nitrate. However, future models could expand their focus to size distributions and other chemical constituents.

Efforts are under way at academic and other research institutions (such as EPRI) to improve air-quality models. Efforts are also under way to link and integrate air-quality models with exposure and dose

models. However, it appears that there is no coordinated effort to compare the various models with one another or to use improvements developed for one or another model to improve the others, particularly those earmarked for regulatory applications. It is not clear that the appropriate commitment is being made to have the best models available at the local air-quality management levels for use in PM planning efforts.

Receptor-Oriented Models

There has been very little support for the development and testing of new receptor-oriented models. Such models are used to identify and quantitatively appropriate an ambient PM sample from a given location (receptor) to its sources. The CMB model has been rewritten to run under the Windows operating system, and EPA has supported factor-analysis model development under a single STAR grant. Both products are now in the process of external review, with probable release at the end of 2000. A new version of the EPA source-profile library will run under modern PC operating systems. However, only 16 profiles have been added to the library since its revision in 1992—an indication of the lack of incorporation of recently published source profiles. Seigneur et al. (1998, 1999) reviewed existing receptor models, including back-trajectory-based analyses to locate candidate source areas, alternative factor-analysis models based on least-squares fitting, and alternative solution methods for the CMB. However, further development and testing are required before they can be widely distributed for air-quality management purposes.

There is a particular need for data-analysis tools to handle newly emerging monitoring technologies, such as aerosol mass spectroscopy. A number of approaches have been presented in the literature, but they are typically applied to only a single location or region. There has not been an extensive effort to test the effectiveness of these alternative methods or to review their potential use in future development of air-quality management strategies.

Air-Quality Model Testing

To test the predictive capability of models, it is necessary to have both the model input data and appropriately detailed sets of air-quality observations to compare with the model outputs. Earlier field campaigns —such as the Southern Oxidants Study (SOS; www2.ncsu.edu/ncsu/CIL/southern_oxidants/index.html), the Northern Front Range Air Quality Study (NFRAQS; www.nfraqs.colostate.edu/index2.html), the Southern California Air Quality Study (SCAQS; Lawson 1990), and the San Joaquin Valley Air Quality Study (SJVAQS; Lagarias and Sylte 1991; Chow et al. 1998)—provide the necessary data for model testing. (SOS, until recently, and SJVAQS have limited utility for PM models because they focused primarily on ozone.) Although those earlier efforts provided insights into basic atmospheric processes, only some of the supersite monitoring stations can possibly have sufficient data to validate regional-scale air-quality models. It is clear that more field campaigns are needed to provide data to test the predictive capability of state-of-the-science PM models.

A number of large studies are just starting, such as the supersite efforts, and continuing studies, such as SOS. However, there do not appear to be plans to use these databases fully for testing air-quality models. ORD personnel have suggested that EPA will use the data to test MODELS 3/CMAQ, but it is not clear to the committee that there will be effective internal and external review. The committee is aware of no defined plans to compare MODELS 3/CMAQ with any of the other similar-scale models. Such comparisons are needed, and a plan for evaluation and revision of the EPA model should be developed as part of EPA's PM research program.

This lack of effort to use available data effectively highlights the need for EPA to be active in defining the nature of the data needed to test Models 3/CMAQ fully and compare it with other independently developed models. There is now an agreement among the Baltimore, New York City, and Pittsburgh supersites and the NARSTO NE-OPS (Northeast Oxidant and Particle study) program in Philadelphia to operate in an intensive mode during July 2001. There will be only sparse upper-air measurements using LIDAR in Baltimore and Philadel

phia. Although it might be too late to organize extensive additional upper-air measurements for those particular studies, this is one example of the kind of opportunity that EPA should be actively seeking, particularly in the eastern and southeastern United States, where such large-scale, detailed data are lacking.

It might be possible to build on the speciation network, once it is in place, to develop appropriate field campaigns. By operating these systems more intensively (more frequently than daily) and supplementing the speciation network monitors with particle-size measurement devices, it would be possible to provide a suitable database for regional-scale model testing.

The testing of receptor models is similarly incomplete. It appears that there has been no clear plan for development, testing, and deployment of additional receptor-modeling tools. CRC recently supported an effort to evaluate receptor models for VOCs, using grid models to produce test data. EPA has had a small effort to compare factor-analysis models, but a more extensive program will be needed to provide the full range of tools necessary for a comprehensive analysis, particularly for $PM_{2.5.}$

Application of Evaluation Criteria

Scientific Value

There is substantial support of current studies that are expected to make substantial contributions to the understanding of atmospheric processes. The development of source-oriented models represents the codification of a portion of new knowledge into an organized framework for application. The testing of individual models and the comparison of the results of multiple models can help to identify the effects of different approaches to incorporation of the knowledge into prediction based upon models. Such comparisons will help to refine the available knowledge. The development of better algorithms for source- and receptor-oriented models will also be substantial scientific advances.

Decisionmaking Value

Air-quality models are essential for making regulatory decisions. They provide the critical information required to develop the effective and efficient air-quality management strategies that are needed for state implementation plans (SIPs), which are developed when areas are found to be in nonattainment of the PM National Ambient Air Quality Standards (NAAQS). Regional-scale models are needed for reducing visibility impairment, acid precipitation, and other adverse environmental effects. Improved models would also provide critical exposure-related data that could be used in health studies to examine the relationships between ambient PM concentrations and health. There is insufficient effort to test the models developed by EPA and others or to use extensive comparison with other models to ascertain the differences and similarities in the results. Such efforts would provide further improvements in the models and greater confidence in the decisions based on the model results. In addition, it is important to link air-quality models with exposure models. EPA is collaborating with other organizations to develop a population exposure model for PM to provide such a linkage.

Feasibility and Timing

The development and testing of models is highly feasible. The increase in computational power permits the incorporation of greater numbers of observations and understanding of atmospheric processes into source-oriented models. The same computational power permits much more sophisticated methods for data analysis to be used in receptor-oriented models.

The new PM monitoring program provides a base from which data can be obtained for testing of the models. If research topic 3 is appropriately implemented, the necessary source data and source-oriented models will be readily available. The source profiles developed under research topic 3 will also provide data to introduce into recep

tor-oriented models. Thus, the plan for testing models presented in the committee's second report can be used to provide the necessary tests and improvements for models. However, the planning process should be started immediately to allow time for important regional-scale field studies. It should be noted that the data needed for model testing and evaluation are not necessarily the same as data needed for developing exposure metrics, which is discussed later in this chapter.

There is also time to develop, test, and deploy advanced receptor models more fully before requirements arise from the SIP process. However, there must be a more concerted effort to recognize the need for improved models and improved data for existing models.

Integration and Planning

There appears to be insufficient effort in organizing and carrying out the field studies that would provide the data for thorough evaluation of existing models; only a small effort to leverage the investment is being made in the PM monitoring program to provide these data. There is a large body of historical data that would be of great value in model testing if they could be processed in a standard way into a central repository from which they can be easily accessed. It appears that EPA does not yet recognize the need for full model testing, so it has not mobilized the needed resources.

It appears that there has been no comprehensive planning for the development and deployment of receptor-oriented models. The current ad hoc approach to receptor-model development will not provide the additional tools essential to develop future state implementation plans. With the development of several new factor-analysis models, there has been some effort to compare them, but there is still no evidence of a plan for developing and implementing improved models in the context and timeframe of what will be needed for the $PM_{2.5}$ SIP process.

RESEARCH TOPIC 5. ASSESSMENT OF HAZARDOUS PARTICULATE-MATTER COMPONENTS

What is the role of physicochemical characteristics of particulate matter in eliciting adverse health effects?

The initial research portfolio (NRC 1998) outlined a research agenda designed to improve the understanding of the roles of specific characteristics of ambient PM (such as particle size distribution, particle shape, and chemical constituents) in determining the toxicity for underlying adverse health outcomes associated with PM exposure. The research plan indicated not only studies aimed at determining the relevance of those characteristics, but also work designed to evaluate the dose metrics that have been used to relate PM exposure to health effects in epidemiological and toxicological evaluations. Research was needed to develop PM surrogates, that is, material with specified characteristics for use in toxicity studies. In its second report, the committee (NRC 1999) reconfirmed the importance of this kind of investigation.

The nature of the chemical or physical characteristics of ambient PM that might account for its biological activity remains a critically important component of the PM research portfolio. In addition to providing mechanistic plausibility for epidemiological findings related to PM, an understanding of the relationship between mechanisms of biological action and specific PM characteristics will be a key element in selecting future control strategies. The following list of particle characteristics potentially relevant to health risk is large and possibly variable across health effects:

Size-fractionated PM mass concentration
PM surface area
PM number concentration
Transition metals
Acids
Soot and organic chemicals
Bioaerosols

Sulfate and nitrate

Peroxides and other free radicals

Those particle characteristics may be associated with cardiovascular disease, acute respiratory infection, chronic obstructive pulmonary disease, asthma, and morbidity. Inspection of this list, which could be expanded, makes clear the challenge that is faced by the investigative community and by research managers who need to focus resources toward the key relationships between particle characteristics and health effects.

In addressing this research topic, both toxicological and epidemiological approaches are needed. Hypotheses advanced from data in one domain need to be tested in the other, complementary domain. Greater certainty will be achieved as evidence from the laboratory and the population converges and as integrative research models merge the population and laboratory data into a common framework. For example, particles obtained from filters in the Utah Valley, the site of epidemiological studies of health risks posed by particles from a steel mill, have been assessed for toxicity in laboratory systems (Frampton et al. 1999; Soukup et al. 2000; Dye et al. in press). The availability of particle concentrators could also facilitate the implementation of integrative research models, in that animals and people can be exposed to a comparable mixture of real-world particles.

The general methodological issues arising in connection with this research topic are akin to the problem of assessing the toxicity of a mixture and determining the specific characteristics that are responsible for its toxicity. Particles, in fact, constitute a mixture: urban atmospheres are contaminated by diverse sources, and the characteristics of particles can change and vary among regions. The difficulties of studying mixtures have been addressed by numerous panels, including committees of the National Research Council (NRC 1988). Accepted and informative research models have not yet been developed, and even attempting to characterize several toxicity-determining characteristics of mixtures has proved challenging.

One objective of research related to this topic was to assess relevant dose metrics for PM to explain adverse health outcomes. EPA

routinely measures size-specific mass concentration, previously PM_{10} and now $PM_{2.5}$ as well. The selection of these concentrations and the timeframe over which they are measured (24 hours) reflect technological feasibility to a greater extent than fit with time-exposure-response relationships of PM with health risk. Routine regulatory monitoring provides only 24-hour averaged mass concentrations, but special monitoring programs—including those instituted in support of epidemiological studies, the speciation sites, and the supersites program—offer the opportunity to explore alternative dose (exposure) metrics. Newer techniques to monitor $PM_{2.5}$ over shorter periods, and even continuously, are being developed and tested.

Another objective, to evaluate the role of particle size in toxicological responses to PM and that related to epidemiological outcomes, focuses on the size of particles that are relevant to the health effects observed in the epidemiological studies. To date, the associations of PM with both illness and death have been demonstrated in studies using indexes that incorporate particles with a large range of sizes (such as total suspended particles, or TSP, and PM_{10}). These studies have drawn on the available data. PM_{10}, of course, includes particles in all smaller size categories and thus includes $PM_{2.5}$ and ultrafine particles (those smaller than 0.1 μm in diameter). Ultrafine particles probably make up a very small fraction of PM_{10} mass, but pathophysiological considerations and some initial toxicological findings have focused attention on the hypothesis that such smaller particles may be responsible for some toxicological responses that lead to the epidemiological findings.

Research Progress and Status

Toxicology

New work directed at this research topic has been based largely on toxicological approaches. Forty-eight toxicology projects described in the HEI database were identified as potentially related to the topic.

Ambient PM is a complex mixture that contains various chemical components in various size fractions. Evaluation of whether biologi

cal responses to PM are nonspecific—that is, are due merely to inhalation of any particle—or depend on specific PM properties is a critical focus of current research. Regarding the latter possibility, research performed in the recent past has indicated some specific potential characteristics that appear to be involved in PM-induced health effects. A compilation of these (Mauderly et al. 1998) is as follows: size-fractionated particle mass concentration; particle surface area; particle number concentration, which is generally related to the ultrafine component of PM; transition metals (especially the fraction soluble in vivo); acids; organic compounds (especially PAHs); bioaerosols; sulfates and nitrates, typically existing in ambient air as ammonium or sodium compounds; peroxides and free radicals that can accompany, and help to form, particles; soot (elemental carbon, black carbon, or light-absorbing carbon); and correlated cofactors (such as the presence of gaseous pollutants and variations in meteorology). The current toxicological research portfolio as reported in the HEI database was examined with regard to each of those specific chemical or physical characteristics.

- *Size-Fractionated Particle Mass Concentration.* The mass concentration—the mass (weight) of collected PM per unit volume of sampled air, generally within some selected particle-size range or below some upper size cutoff—was the exposure metric most commonly evaluated in relation to health effects in the studies in the HEI database. More-recent epidemiological studies of ambient particles have generally focused on the 0.1- to 2.5-μm size range, although there have been a few studies of coarse particles. In a number of cases, the particle-size cutoffs used in toxicity studies differed from those commonly used to define size fractions obtained with ambient monitoring networks, namely $PM_{2.5,}$ coarse PM (PM_{10} minus $PM_{2.5}$), and PM_{10}, and TSP. For example, some toxicity studies have used mass in sizes termed $PM_{1.7}$ and $PM_{3.7\text{-}20}$, whereas others have included particles of up to 4 μm in the definition of "fine" particles. Definitions of specific size fractions, such as "fine" and "coarse," used in toxicological research should be consistent with those used in ambient monitoring studies and in epidemiological studies.

- *PM Surface Area.* A few studies in the HEI database address particle surface area in the context of particle size, specifically in terms of its relation to health effects. Surface area is also relevant to the absorption of gases onto particle surfaces.
- *PM Number Concentration.* A few studies address the issue of particle number concentration, which is generally used to describe exposures to the ultrafine particles in ambient PM. These include in vivo and in vitro studies, the former including clinical-exposure studies and involving particles ranging from 0.01 to 0.1 μm.
- *Transition Metals.* The transition metals include titanium (Ti), vanadium (V), chromium (Cr), manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), copper (Cu), zinc (Zn), cadmium (Cd), and mercury (Hg). Some—Cr, Mn, Co, Ni, Cd, and Hg—are both transition metals and listed as EPA hazardous air pollutants. Although a number of studies address the issue of toxic metals, many use material containing a mix of various metals, and few specify single metals for evaluation. For example, residual-oil fly ash particles containing nickel and vanadium are commonly used in toxicity studies related to PM; such studies have involved both animal in vivo and in vitro study designs. Other studies have examined pulmonary inflammation related to Fe, V, Zn, and Ni; DNA damage related to Cr(VI); and oxidative stress after exposure to Fe. In general, however, exposure doses in these studies have been high and not relevant to ambient exposure. Metal concentrations found in ambient and source samples should serve as broad exposure guidelines for these experiments. Because in vitro studies often involve material extracted from ambient-air filters, methods of filter extraction (for example, water extraction vs. acid digestion) and analysis need to be standardized.
- *Acids.* Health effects of exposure to acid aerosols have been extensively studied and are specifically addressed in the current controlled-exposure research portfolio in only a few studies reported in the HEI database. However, ambient acidity is generally not analyzed in filters obtained from studies that use ambient-particle concentrators. Such data would be valuable for comparison with pub

lished epidemiological data on health effects. Furthermore, little information on specific types of acids is given in the project descriptions in the HEI database.

- *Soot, Organic Compounds, and Associated PAHs.* The effects of PAHs are specifically addressed in only one in vivo study described in the HEI database. Characteristics of combustion-related organic chemicals will be explored further by the EPA-sponsored PM centers. Studies of diesel exhaust, diesel soot, and black carbon focus mainly on elemental carbon. More research with emphasis on organic speciation is needed to evaluate potential health effects. Because there are so many organic compounds in ambient PM, a subset specifically related to pollution sources needs to be defined for in vivo and in vitro studies.
- *Bioaerosols.* One of the subjects clearly in need of evaluation is the role of biological agents in adverse health effects related to ambient PM exposure. Biological agents that might be involved in PM-induced response are diverse, and few are being evaluated. One class, endotoxins, has been identified as having the ability to induce or potentiate adverse health effects induced by PM, and some studies are addressing this issue. Another antigen being evaluated for its role in PM-related health effects is that derived from dust mites. Although exposure to dust mites largely occurs indoors, it may offer an informative example.
- *Sulfates and Nitrates.* Sulfate has been examined in several studies, but nitrate and other nitrogen species have been largely ignored except as components of complex particle mixtures.
- *Peroxides and Other Free Radicals.* One in vivo study addresses the role of peroxide in PM toxicity. This is a subject on which further research is needed.
- *Copollutants.* There is an increasing effort in the research portfolio to evaluate the potential for interaction between PM and gaseous copollutants. The gases of potential concern include O_3, NO_2,

SO_2, CO, and irritant hydrocarbons. Data on precursor gases (especially HNO_3, NH_3, and SO_2) are important to relate ambient secondary particles to health effects. This subject is discussed further with regard to research topic 7.

The committee is unable to identify any studies reported in the HEI database that address the issue of experimental PM surrogates that can mimic daily, seasonal, and regional particle characteristics. Specific in vivo and in vitro tests provide snapshots of adverse effect. Understanding of the role of PM characteristics in eliciting biological responses, measurements of PM components or analyses of aerosol filters should include extensive chemical speciation, consistent with the national $PM_{2.5}$ chemical-speciation network, in which mass, elements (40 elements from sodium to uranium), ions (nitrate, sulfate, ammonium, and water-soluble sodium and potassium), and carbon (organic and elemental) are determined. Furthermore, there needs to be a reconciliation of ambient concentrations with the exposures used in controlled studies. Concentrations of specific chemical compounds in PM vary widely. For example, V and Ni are often found at less than 0.01 $\mu g/m^3$ in ambient samples, although most other metals are typically found at 0.01-0.5 $\mu g/m^3$. But crust-related materials (such as aluminum (Al), silicon (Si), calcium (Ca), Fe, and Mn) are often present at 0.5-10 $\mu g/m^3$, and many toxicity studies use concentrations as high as about 100-5,000 $\mu g/m^3$. The relevance of such high-exposure studies for materials present at much lower concentrations in ambient air must be considered in controlled-exposure studies. Furthermore, the ratio of specific chemical species in ambient air to those occurring in experimental atmospheres must be considered in experimental-study designs.

Epidemiology

Epidemiologists have approached the problem of mixtures or, in this instance, the toxicity-determining characteristics of particles, by evaluating risk in relation to heterogeneity in exposure, whether over time or across geographical regions. For example, time-series studies identified particles in urban air as a key determinant of morbidity and

mortality by evaluating risk for events on a day-by-day basis in relation to changing daily concentrations of particles and other pollutants. Statistical models, such as Poisson regression, are used to "separate" the effects of one pollutant from those of another. Comparisons have also been made across regions that have different pollution characteristics. Panel studies can also be used for this purpose.

In applying the epidemiological approach in investigating particle characteristics, there is a need to have measurements of particles in general and of the specific characteristics of interest over the period of the study. Because monitoring for particle characteristics of specific interest has been limited, opportunities for testing hypotheses related to those characteristics have also been somewhat limited, and few studies that incorporate substantial monitoring of both particle concentration and other specific characteristics have been carried out. One example is afforded by the work carried out in Erfurt, Germany, where particle mass, concentration, and numbers have been carefully tracked for a decade. The resulting data have been used to support several epidemiological studies of health effects in that community (Peters et al. 1997). EPA's supersite program will also offer a platform for carrying out observational studies on particle characteristics related to health risk.

Epidemiological data, if sufficiently abundant, can be used for testing alternative dose metrics. Statistical modeling approaches can be used to test which exposure metrics are most consistent with the data; with this general approach, the fit of the statistical model to the data is compared across exposure metrics, and the metric that best fits the data is given preference, assuming that its biological plausibility is at least equivalent to that of alternatives. For example, 2-day running averages might be compared with 24-hour averages, or peak values obtained with continuous monitoring might be contrasted with averages over longer periods. If a strong preference for one metric over alternatives is to be gained, the data requirements of this approach are substantial. Epidemiological studies relevant to this research topic need to be large and require data on the exposure metrics to be compared.

Table 3.4 shows that the number of potentially informative epidemiological studies is small. Studies in Erfurt, Germany, and in Atlanta

TABLE 3.4 Number of Epidemiological Studies Relating Health Outcomes to Target Pollutants a

Health Outcome	PM [b]	PM, Copollutants [c]	PM Metals	PM, Ultrafines [d]	PM, Ultrafines, Copollutants [c]	PM, Ultafines, [d] Metals
Asthma onset	1				1	
Asthma, exacerbation of symptoms	4	4		1		1
Respiratory outcomes, children under 10 years old	3	2			1	
Respiratory outcomes, children 10-19 years old	7	3			1	
Pulmonary function, children 10-19 years old	2	5			1	
Respiratory outcomes, normals		3				
Minority groups		1				
Respiratory outcomes, people over 65 years old	7		1			
Pulmonary function, people over 65 years old	3					
Morbidity and mortality, respiratory elderly	1	7		2		
Morbidity and mortality, cardiac elderly	5	11	2	2		
Total mortality	4	8			1	2
Total	37	44	3	5	5	3

[a] Some studies consider more than one health outcome. The quality of a study and its ability to address the research priorities are not considered here.

[b] Denotes various size fractions of PM, including $PM_{2.5}$, PM_{10}, TSP, and unspecified size fractions.

[c] Copollutants include SO_2, O_3, NO_2, and CO.

[d] ines refers to PM with a diameter equal to or less than 0.1 µm.

capture mass concentrations, particle counts, and acidity; other studies are addressing ultrafine particles and risk of myocardial infarction in Augsburg, Germany, and in Atlanta. Several time-series studies include measurements of sulfate and acid aerosols, and a number of panel studies also incorporate measurements of a variety of particle characteristics. PM components are being considered in a small number of existing or planned studies. More data will probably be needed, particularly to obtain evidence related to the general issue of exposure metrics as applied to population risk. A number of current studies should provide information on the risks posed by ultrafine particles; these risks are the focus of one of the PM centers. Panel studies conducted by EPA will also contribute useful information.

Adequacy of Current Research in Addressing Research Needs

There is considerable effort in evaluating physiochemical properties of PM in relation to biological effects. However, it has generally been concerned with only a few chemical characteristics; the largest body of work involves metals. Other potentially important PM characteristics as illustrated in Table 3.4, have received less attention. Current work is beginning to address the issue of exposure or dose metrics other than mass concentration, although most studies continue to evaluate health effects in terms of total mass concentration during exposure. The relevance of high doses used in many controlled exposure studies to the low exposures to some components of ambient PM remains a subject that must be more adequately considered in study design than it is now.

In its second report, the committee noted that although most of the research activities recommended in its first report were being addressed or planned by EPA or other organizations, studies in one cross-cutting research topic of critical importance did not yet appear to be adequately under way or planned: studies of the effects of long-term exposure to PM and other major air pollutants. The committee recommended that efforts be undertaken to conduct epidemiological studies of the effects of long-term exposures to particle constituents, including ultrafine particles. There does not yet appear to be a sys

tematic, sustained plan for implementing studies of human chronic exposure, including examining ultrafine particles.

Application of Evaluation Criteria

Scientific Value

This research topic is a key scientific question in the understanding of PM and health: Are effects of PM nonspecific—that is, determined only by the mass dose delivered to target sites—or do they depend on the specific physical and/or chemical characteristics of the particles? Data relevant to this question would be informative as to cardiopulmonary and/or systemic effects and therefore would guide mechanistic research. Thus, the scientific value of this research topic remains high. Identification of characteristics that produce adverse responses in controlled studies will allow comparison with PM properties obtained from epidemiological evaluations and will thus provide important confirmation of the role of specific properties in adverse health outcomes. There should be coordination between toxicological and epidemiological studies, including use of a consistent terminology for such PM characteristics as specific size fractions, so that study comparisons are possible not only between the two disciplines, but also among different controlled-exposure studies.

Integration across exposure assessment, toxicology, and epidemiology will be critical for obtaining a comprehensive body of evidence on this research topic that can guide decisionmakers from health effects back to responsible emission sources. Epidemiological studies need to include sufficient exposure assessment to guide toxicity studies of PM characteristics. Opportunities should be sought to apply hybrid research models that combine toxicological and epidemiological research.

Decisionmaking Value

Evidence on the particle characteristics that determine risk could have a profound influence on decisionmaking. At present, an ap

proach of regulating particle mass in general is followed, in the recognition that particles vary substantially in size, makeup, and chemical properties. There are multiple sources of PM, and decisionmakers need guidance on whether some sources are producing more hazardous particles or whether all sources produce particles of equivalent toxicity.

Epidemiological research alone will not provide sufficiently certain evidence on this research topic; joint toxicological and epidemiological study is required. However, epidemiological data will be critical for decisionmakers, in that such data will confirm laboratory- based findings and hypotheses.

Feasibility and Timing

This is one of the most challenging research topics in the committee's research portfolio. In the laboratory setting, characteristics of particles can be controlled through experimental design, so carefully measured studies of particles that have specific characteristics can be assessed. In the population setting, in contrast, participants in epidemiological studies inhale PM that has multiple sources and that changes in characteristics as participants move from location to location over the day and possibly even in one location at different times. Data on substantial numbers of persons will be needed to test hypotheses related to particle characteristics. Nonetheless, epidemiological studies can be carried out for this purpose; one of the most effective approaches is likely to be the panel study, with specific, tailored monitoring for particle characteristics of interest. Such studies are feasible, as shown, for example, by the studies in Erfurt (Peters et al. 1997).

RESEARCH TOPIC 6. DOSIMETRY: DEPOSITION AND FATE OF PARTICLES IN THE RESPIRATORY TRACT

What are the deposition patterns and fate of particles in the respiratory tract of individuals belonging to presumed susceptible subpopulations?

The committee's recommended research portfolio (NRC 1998) outlined research needed to improve understanding of the deposition of particles in the respiratory tract, their translocation, and their clearance. The recommendations encompassed the development of new data and predictive models and the validation of the models for respiratory-tract structure; respiratory variables; total, regional, and local deposition; and particle clearance. Also included were the micro-dosimetry of particles and particle-derived hazardous chemical species and metabolites in intrapulmonary and extrapulmonary tissues.

Information on dosimetry is important for decisionmaking because it is critical to understanding of the exposure-dose-response relationship that is key to setting the NAAQS. It is also important for understanding of how exposure-dose-response relationships differ between normal and especially susceptible subpopulations, if the standard is to be adjusted to protect sensitive people. Knowledge of interspecies differences is important for extrapolating results from animals to humans.

The committee's recommendations focused on dosimetry in people potentially more susceptible to particles because of respiratory abnormalities or age (children and the elderly). A large portion of the population is in one or more of the categories of concern. Most people spend at least one-fourth of their lives in stages during which lungs are developing or senescent. In 1997, an estimated 44.3 million adults were former smokers and 48 million were current smokers (ALA 2000a); many smokers develop some degree of airway abnormality. Asthma afflicts over 17 million Americans, including 5 million children whose lungs are still developing (ALA 2000b). COPD afflicts about 16.4 million people (ALA 2000c). All respiratory diseases together kill one of seven Americans (ALA 2000d). The focus of past dosimetry research—almost entirely on normal young adult humans and animals—leaves us with little ability to estimate exposure-dose-response relationships in the above subpopulations.

In its second report (NRC 1999), the committee confirmed its initial recommendations, added a recommendation for research to bolster interspecies dosimetry extrapolation models, and re-emphasized the need for dosimetric research in animals to focus on models of human susceptibility factors.

Several sources of information were examined to assess current research and recent research progress on the dosimetry of PM. The review of current research centered on the HEI-EPA database on PM research. The database was examined as of August 2000 for research projects and programs, including dosimetric research in the abstracts. Numerous additional past or current projects were evident from published reports, but because of uncertainty as to whether these projects were continuing, only those listed in the HEI database were included in Table 3.5. In all, 22 project descriptions were identified as apparently responsive to the dosimetry research needs.

New information since the 1996 criteria document was assessed by examining published papers and abstracts from meetings. A search of the recent published literature was conducted by using numerous

TABLE 3.5 Summary of Dosimetry Projects and Reports

Topic	No. of Projects [a]	No. of Reports [a]
Deposition:		
Influence of susceptibility conditions on deposition	15	26
Quantitative data on structure and respiration	7	8
Effects of particle size and hygroscopicity, and respiratory variables	1	23
Development and validation of mathematical models	5	13
Interspecies differences, especially for ultrafines	3	5
Translocation and clearance:		
Translocation, clearance, and bioavailability	5	24
Disposition of ultrafine particles after deposition	1	2
Interspecies differences	0	5
Total	37	106

[a] Projects (from HEI database) and reports (abstracts of papers and presentations) might be listed in more than one category if they address multiple issues. For example, the 37 "projects" were derived from a total of 22 individual project descriptions.

key words pertaining to the research recommendations. The first external review draft of the new criteria document for PM (EPA 1999) was examined for its portrayal of new information since the last criteria document, published in 1996. References added to the revised dosimetry chapter as of September 2000 were also reviewed. Published abstracts from 1999 and 2000 meetings of the American Thoracic Society (ATS 1999, 2000), HEI (HEI 1999, 2000), and the Society of Toxicology (SOT 1999, 2000) were examined for relevant research, as were the abstracts from the 1999 meeting of the International Society for Aerosols in Medicine (ISAM 1999). The abstracts and papers from the Third Colloquium on Particulate Air Pollution and Human Health in June 1999 (Phalen and Bell 1999) and from the "PM2000" conference in January 2000 (AWMA 2000) were also examined for relevant completed research. The evaluation of reports was limited to reviewing of abstracts. Published papers were not reviewed in detail, and authors were not queried.

In all, 62 papers and 59 presentation abstracts were identified as potentially relevant to the dosimetry research needs as set forth by the committee. On review of abstracts, some proved to fall outside the scope of the recommended research portfolio, and many more related to the recommendations only indirectly. A total of 96 reports were considered relevant to the dosimetry research needs. Although this review undoubtedly missed some potentially relevant reports, it was considered sufficient to provide a reasonable evaluation of the extent to which the recommendations are being addressed. The results of the review are summarized below, by categories according to the committee's research recommendations (in italics). A numerical summary of the projects and reports is presented in Table 3.5.

Deposition

1. *Conduct research on deposition of particles in the respiratory tracts of individuals having respiratory abnormalities presumed to increase susceptibility to particles, and on the differences in deposition between these susceptible subpopulations and normals.*

a. Obtain quantitative data on lung morphology and respiration for individuals of different ages and having respiratory abnormalities.

Research using advanced imaging and reconstruction techniques is producing new information on the effects of age, sex, and several types of abnormalities on airway dimensions. This information can serve as the foundation of mathematical models of deposition in abnormal airways. Some researchers are using stereolithography to construct physical models of airways from stereo images and computer-controlled etching of solid media. Other researchers are using magnetic resonance imaging to create airway images and develop digital data from which structures can be modeled or physical replicas can be machined. These techniques show promise for obtaining new morphological data useful for modeling deposition in a broad range of airway abnormalities. It is likely that, in some cases, these approaches will allow acquisition of data for more varied subjects and at a greater rate than is practical with traditional postmortem airway casting.

A modest amount of work is continuing with the more traditional methods of evaluating solid casts made from cadaver lungs and airways and measurements of airway dimensions with light microscopy of lung sections.

Information on the effect of age and respiratory abnormalities on breathing patterns and dosimetry in humans has been expanded substantially in the last 2 years. The EPA intramural program is the strongest contributor in this field. Laboratories working in this field are addressing the variables of age, sex, asthma, COPD, and cystic fibrosis. Inclusion of a broader range of susceptibility factors and particle types is needed. For example, there is little emphasis on people who have respiratory infections or edema related to cardiopulmonary failure. Most studies have measured only total particle uptake; information on regional and local dosimetry is also needed.

b. Determine the effects on deposition of particle size, hygroscopicity, and respiratory variables in individuals with respiratory abnormalities.

New information has been obtained on the influence of sex on regional (pulmonary vs. tracheobronchial and extrathoracic) fractional deposition and on differences between children and adults, and these data are being extended by current projects. Work on the effects of respiratory abnormalities on regional or local deposition has been limited largely to modeling or work with airway replicas. There has been little validation of the models with measurements of living subjects. An important advance has been the finding that total fractional deposition is greater in people who have asthma and COPD and in smokers than in people who have normal lungs. Total fractional deposition has been found to be similar in normal elderly people and young adults. More emphasis is needed on regional and local deposition in lungs and airways of susceptible subjects.

The influences of particle size and hygroscopicity on deposition have been addressed by some studies, but only a small portion of this work has included subjects or airway replicas that have abnormalities or different ages. There appears to be little emphasis on the influence of particle and respiratory variables on deposition in susceptible people or on the development of predictive models that incorporate these variables. In addition, only a few particle types and only a few of the many common combinations of ambient particle sizes and compositions have been studied.

As in the past, there continues to be only modest effort aimed at identifying the type and location of particles retained in lungs at autopsy. Although the locations are sometimes characterized as reflecting sites of particle deposition, the results typically reflect sites of retention of only the most biopersistent classes of deposited particles and might not reflect accurately the sites of deposition or the dose of the full spectrum of inhaled particles. When coupled with evaluations of accompanying tissue changes, this approach provides useful information on the relationship between long-term particle retention and disease.

c. Develop mathematical models for predicting particle deposition in susceptible individuals and validate the models by measurements in individuals having those conditions.

Several recently completed or current efforts have led, and will continue to lead, to the development and refinement of models for predicting deposition in abnormal lungs. Most efforts have focused on the effect of flow limitation in conducting airways and on the heterogeneity of local particle deposition.

Very few efforts have included validation of models by measurements in living subjects. Only two of the reports in this category involved validation experiments—one for deposition in asthmatics and one for the effect of particle size on deposition in rats. More emphasis is needed on model validation and on modeling a greater range of susceptibility factors.

2. *Develop information on interspecies differences and similarities in the deposition of ultrafine particles in abnormal vs. normal respiratory tracts.*

Although this recommendation focused on ultrafine particles, there is a dearth of information on deposition of particles of any size in animals that have respiratory abnormalities. As noted in the toxicology sections that follow, continued effort is needed to develop, refine, and validate animal models of human respiratory abnormalities. Progress has been made, but it has been accompanied by little effort to examine particle dosimetry in the models. Although a few laboratories are attempting to develop and refine mathematical models for interspecies adjustments in particle deposition, there is still little attempt to validate the models by comparing deposition in animals and humans directly, and only one group is generating comparative data on the deposition of ultrafine particles.

Several projects have developed models to predict comparative deposition in normal rats and humans, and most can be adapted for ultrafine particles. Other animal species have been largely ignored. The committee's first report recommended increased development and use of animal models of human susceptibility factors, as described in other sections. Because differences in deposited dose can contribute substantially to differences in the models' response, there is a need for more work on particle deposition in animal models of respiratory abnormalities.

Translocation, Clearance, and Bioavailability

1. *Conduct research on the translocation and clearance of particles and the bioavailability of particle-borne compounds in the respiratory tracts of individuals having respiratory abnormalities presumed to confer increased susceptibility. Determine differences in the disposition of particles between these susceptible subpopulations and normals.*

New information is beginning to accumulate that shows that respiratory abnormalities can have variable effects on short-term clearance of inhaled particles deposited on conducting airways. As is the case for deposition, information on clearance is being developed in both the pharmaceutical and environmental fields. There are data on short-term airway clearance in adult humans who have asthma, chronic bronchitis, and COPD, including comparisons with normal subjects.

Although the available information is still sketchy, it reveals both the potential importance and the complexity of the issue. For example, Svartengren et al. (1996) did not find that clearance from small ciliated airways of unprovoked asthmatics differed from that of normal people, but later (Svartengren et al. 1999) found that more particles were retained in airways of asthmatics than of normal subjects when the allergic asthmatics were challenged with allergen before deposition of the particles. There is little information on the influence of respiratory abnormalities on longer-term clearance from the pulmonary region and little information on age-related differences. Some data suggest that there is little influence of age or sex on particle clearance in normal humans.

Several recent studies have demonstrated the importance of the bioavailability (solubility) of particleborne metals in eliciting adverse responses. A modest amount of work is being done on the bioavailability of particleborne organic compounds. Little if any effort is being expended to determine differences in bioavailability or the importance of bioavailability between normal and abnormal respiratory tracts.

It appears that differences in particle clearance are not yet being incorporated into models for predicting differences between normal

and susceptible people in the dosimetry of particles or particle-associated compounds.

2. *Determine the disposition of ultrafine particles after deposition in the respiratory tract, and whether respiratory abnormalities alter the disposition pathways or rates.*

Despite the current interest in potential differences between the disposition of fine and ultrafine particles after deposition in the respiratory tract, little progress has been made, and little work appears to be under way. The technical difficulty of measuring small amounts of ultrafine particles in various intrapulmonary and extrapulmonary locations continues to be a deterrent to progress. The recent development of ^{13}C-labeled ultrafine carbon particles is likely to advance this field, and tracer technologies need to be developed and applied for use with other types of ultrafines.

Sufficient work has been done to confirm that solid ultrafine particles can penetrate into the circulatory system and reach other organs, but quantitative data are still lacking. There has been no apparent effort to study the dosimetry of nonsolid ultrafine condensates. Moreover, there has been no work on the disposition of ultrafines in either humans or animals that have respiratory abnormalities. As investigative techniques are developed, it is important that they be applied to both normal and abnormal subjects.

3. *Develop information on interspecies differences and similarities in the translocation, bioavailability, and clearance of particles in abnormal vs. normal respiratory tracts.*

Little research appears to have been completed recently or to be under way addressing interspecies differences in particle clearance, translocation, or bioavailability in either normal or abnormal respiratory tracts. Recent work demonstrated marked differences in the sites of retention of fine particles in lungs of normal rats and nonhuman primates, but at lung loadings much higher than would result from environmental exposures. There are some new data and reviews on

particle clearance in different species, but the committee is unable to identify any direct intercomparisons among species or comparisons in the presence of respiratory abnormalities.

Adequacy of Current Research in Addressing Information Needs

Although the volume of dosimetric work shown in Table 3.5 reflects a level of effort commensurate with the committee's recommendations, there is not yet an adequate focus on the specific information needs described by the committee. Only a portion of the work has addressed characteristics other than age and sex; there has been insufficient work on the impact of respiratory abnormalities. The committee called for development and validation of mathematical models for predicting deposition and clearance in abnormal lungs. There has been only modest advancement in the modeling of dosimetry in susceptible people and little effort to validate the models. Efforts to improve interspecies extrapolation models continue in a few laboratories but, again, little effort to validate the models. There has been little effort to assess dosimetry of any type in animal models of human respiratory abnormalities. Many potentially important aspects of respiratory abnormalities—such as microdosimetry in tissues and cells, bioavailability of particleborne compounds, translocation and clearance, and handling of diverse particle types—have been addressed little or not at all. Although the level of effort might appear adequate, the degree of focus is not yet adequate.

Among the many programs, studies, and recent reports contributing new information on the dosimetry of particles, only a portion are focused specifically on dosimetric issues. Much of the information was produced as a byproduct of research focused on health responses to inhaled particles, rather than on particle dosimetry. That is appropriate, but effort is needed to make investigators broadly aware of the need for dosimetric information to encourage them to develop and publish the data as a specific, albeit opportunistic, product of their research. In a related vein, our review demonstrated that relevant information is being produced as a byproduct of pharmaceutical re

search. That suggests the importance of looking beyond the traditional environmental research community when searching for and summarizing information relevant to environmental dosimetric issues.

The information on particle deposition in potentially susceptible subgroups has grown since the 1996 PM criteria document; results have demonstrated important differences in total fractional deposition in some disease states. The findings support the importance of the committee's recommendations. Work is needed on a wider range of susceptibility conditions, and more emphasis is needed on regional and local deposition (deposition "hot spots") in susceptible people.

Much less information has been, or is apparently being, produced on differences in the clearance and translocation of deposited particles and in bioavailability of and cellular response to particleborne compounds due to age or respiratory abnormalities. Although many adverse responses might be most strongly moderated by deposition, some might be more strongly influenced by the amount and location of retained dose. Translocation and bioavailability issues remain important for an understanding of response mechanisms.

The research recommendations noted ultrafine particles as a specific class on which more dosimetric information is needed. The effort focused on ultrafines is modest and addresses a narrow range of ultrafine-particle types. Like coarse and fine particles, ultrafines include diverse physiochemical classes that can be expected to behave differently when deposited.

There is not yet an adequate effort to determine the dosimetry of particles of any type in animals that are used to study characteristics of human susceptibility. If the animal models of susceptibility are to be useful, differences in particle deposition and disposition, as well as differences in response, must be considered. Not only might differences in dosimetry help to explain differences in response on a total or regional dose basis, but the models might also be useful for predicting the influences of abnormalities on local deposition in susceptible people on whom such data might never be obtained directly. Research sponsors need to explicitly encourage investigators to evaluate dosimetry as an integral component of the characterization of the responses of animal models.

Application of Evaluation Criteria

Scientific Value

The scientific value of this research is generally high. Nearly all the work noted above builds on previous knowledge in a logical way that will lead to a more integrated understanding of PM-related health effects. Most of the dosimetric data collected in response to PM research needs will also have high value for other purposes, such as understanding and predicting the dosimetry of inhaled pharmaceuticals in normal vs. abnormal respiratory tracts and in animal models vs. humans. Findings pointing toward differences in respiratory control, anatomy, and defenses are raising issues likely to lead to more studies that will provide a more complete understanding of respiratory-tract structure and function.

Although insufficient effort is being expended to evaluate dosimetry in animal models of respiratory abnormalities, the resulting data will have high scientific value for determining the extent to which differences in health responses between normal and susceptible people are due to differences in dose and differences in responsiveness. This information is important for the selection and interpretation of the animal models.

Considering the previous lack of data on dosimetry in people who have respiratory abnormalities or animal models of these conditions, almost any such data would have scientific value. As results accumulate, it will be important to focus on more-specific and more-detailed issues, for example, on local and regional deposition rather than total deposition.

Decisionmaking Value

The results of this research will have a direct bearing on the setting of air-quality standards in two principal ways: providing the dose component of dose-response information required to set the standard, and providing information on the dose component of susceptibility as input into the adjustment of the standard for protection of sensitive subpopulations.

Knowledge of differences between the deposited doses received by normal people and those who have respiratory abnormalities will play a direct role in the estimating of safe and hazardous PM exposures. In this role, dosimetry is an equal partner in the exposure-dose-response paradigm that is integral to risk assessment. In addition, knowledge of dosimetry in animal models of susceptibility will play an indirect role in decisionmaking by influencing the selection of appropriate models, the interpretation of results of the use of the models, and the understanding of the role of dose variables in the susceptibility of humans.

Feasibility and Timing

Lack of feasibility is not impeding the progress of dosimetric research. As noted in the committee's first report (NRC 1998), there are few technical limitations on obtaining the needed data. An exception might be current technical limitations on detecting ultrafine particles in tissues and fluids.

The research gaps identified above result from inadequate coverage of topics, not from inadequate research tools or personnel. It remains true, as stated in the first report, that with the combination of modest funding and its direction toward key information gaps, most dosimetric issues could be resolved soon. It is clear that not all important topics are being covered, although most of the time originally projected for this work has been spent. Without greater attention to targeting particular gaps, key issues might not be adequately resolved.

RESEARCH TOPIC 7. COMBINED EFFECTS OF PARTICULATE MATTER AND GASEOUS POLLUTANTS

How can the effects of particulate matter be disentangled from the effects of other pollutants? How can the effects of long-term exposure to particulate matter and other pollutants be better understood?

Research Progress and Status

Toxicology

PM exists in outdoor air in a pollutant mixture that also contains gases. Thus, biological effects attributed to PM alone in an observational study might also include those of other pollutants that arise independently or through interactions with PM. There might be chemical interactions between gases and PM, or gases can be adsorbed onto particles and thus carried into the lung. Interactions can also occur in the process of deposition on lung airway surfaces and later through lung injury. Research relevant to this topic includes toxicological and clinical studies that examine the effects of gaseous copollutants on the health impacts of PM.

The committee's first two reports (NRC 1998, 1999) indicated that it is important to consider the effects of combined exposures to particles and copollutants when characterizing health risks associated with PM exposure. This research topic remains of critical importance because epidemiological studies might not be able to characterize fully the specific contributions of PM and gases in causing health outcomes. Thus, mechanistic studies are needed to determine the relative roles that various components of ambient pollution play in observed health effects of exposure to atmospheric mixtures.

The HEI database was examined to determine the research status of this topic. A number of current studies involve pre-exposure to high levels of ambient gases (such as ozone and sulfur dioxide) to induce pulmonary pathology in animals so that effects of PM in a compromised host model can be assessed. However, those types of studies are not considered to fit this research theme. A number of studies are using concentrated ambient PM (CAP), and such exposure atmospheres might include ambient gases unless they are specifically scrubbed out before entering the exposure system. However, it was often not possible from a study description in the database to determine whether the effects of these gases on response to PM were being examined. One group of researchers is exposing animals specifically to highly complex emission atmospheres to determine the rela

tive contributions of PM and gaseous copollutants to various health effects.

Studies of interactions of gaseous copollutants with PM are being conducted with both animal and controlled human-exposure studies. Fewer studies are examining such effects in vitro. Endpoints span the array of effects observed in populations but focus largely on cardiovascular effects, inflammatory response, and mediators. Some animal studies and some human studies also involve the use of compromised hosts to compare effects with those occurring in normal animals and humans. As with all animal toxicity studies, it is important to be able to relate responses to human responses. That is specifically addressed as a goal in only one study program being performed at one of the EPA-sponsored PM centers.

One of the gaseous copollutants of major concern with regard to interaction with PM is ozone, and this copollutant is the subject of the greatest research effort. That is evident in Table 3.6, which shows the list of gaseous pollutants being studied and the number of research projects addressing them. However, some attention is also being given to other gases of potential concern, such as sulfur dioxide and nitrogen dioxide. Other suggested modulators of PM-induced effects are receiving little attention. The role of ambient gases should receive more attention in studies with CAP because these types of expo sures are the most realistic and do not require the generation of "sur

TABLE 3.6 Gaseous-Copollutant Studies

Gaseous Copollutant	No. of Animal Toxicity Studies	No. of Human-Exposure Studies
O_3	12	7
SO_2	4	0
NO_2	3	1
NH_3	1	0
CO	1	0
Unspecified	5	1

rogate" atmospheres. Opportunities should be sought to augment CAP with concentrated gaseous pollutants or to scrub out specific residual gasses.

Epidemiology

PM in outdoor air is one component of a complex mixture that varies over time and also geographically on both small and large spatial scales. PM is one of the six pollutants in outdoor air regulated as "criteria pollutants." In part, driven by the needs of evidence-based regulation, epidemiologists and other researchers have attempted to separate the effects of PM from those of other pollutants, even though they are often components of the same mixtures and their concentrations are often correlated, reflecting their shared sources. The effects of the individual components of the mixture can be assessed in time-series approaches with multivariate statistical methods or in designs that incorporate contrasts in exposures to mixtures by drawing participants from locations that have different pollutant mixtures (for example, with higher and lower ozone concentrations).

In addressing the "combined effects" of PM and other pollutants, one of the scientific questions of interest is whether the risks to health associated with PM exposure vary with the concentrations of other pollutants. For example, are risks posed by PM to children who have asthma higher in communities that typically have higher background concentrations of ozone than in other communities? Epidemiologists refer to this phenomenon as "effect modification," and its presence is generally assessed with statistical methods that test for interaction in multivariable models. Effect modification that is positive, or synergistic, results in greater risks than would be predicted on the basis of estimates of risk posed by PM itself. Studies of effect modification need substantial sample sizes if statistical power is to be sufficient.

Studies on combined effects need to include information on PM and the copollutants of interest. Epidemiological studies of diverse design are potentially relevant to this topic. As for studies of mixtures

generally, a precise characterization of combined effects requires a substantial body of data.

Examination of the HEI research inventory shows that many studies in progress should provide relevant information on modification of PM risks by other pollutants. The range of PM indicators across the studies is broad, but most studies include monitoring results for the principal gaseous pollutants of concern. Samples range from too small and consequently uninformative to large enough to provide insights into combined effects.

Adequacy of Current Research in Addressing Research Needs

Although attention to the issue of effects of gaseous copollutants on the toxicity of PM is increasing, the current controlled-exposure research portfolio aimed at assessing the role of gaseous pollutants in health effects of PM is not adequate. The use of CAP can provide valuable information on effects of exposure to complex mixtures. Furthermore, the research effort in evaluating the role of gases in influencing particle effects seems to be lagging behind the effort in studying of specific components of PM in the absence of gaseous copollutants. The epidemiological research portfolio on this topic is relatively substantial; as most epidemiological studies of PM include data on gaseous copollutants. There does not yet appear to be a systematic, sustained plan for implementing studies of chronic exposure.

Application of Evaluation Criteria

Scientific Value

The criteria pollutants have long been addressed as though their effects on health were independent, with recognition that they exist as components of complex mixtures in the air. Rather than seeking to characterize mixture toxicity overall, researchers have sought to determine, experimentally or in observational data, whether the pres

ence of one pollutant changes the effect of another (a phenomenon referred to in epidemiology as "effect modification"). Findings on effect modification inform estimates of risk posed by mixtures and suggest hypotheses for followup laboratory investigation.

Decisionmaking Value

Present regulations are based on the tenet that effects of individual pollutants are independent and that public-health goals can be met by keeping individual pollutants at or below mandated concentrations. Epidemiological demonstration of effect modification for PM effects by other pollutants, such as ozone, would indicate that the regulatory structure does not fully reflect the actual risks to the population.

Feasibility and Timing

Epidemiological and controlled-exposure studies of effect modification or interaction can be carried out; in fact, most contemporary studies include the requisite data on other pollutants. Thus, studies could be readily carried out now to explore whether other prevalent pollutants affect risks posed by PM. Methods for experiments involving mixed atmospheres are available. Analytical information derived from evaluation of atmospheres in epidemiological studies can help to determine specific components of mixed atmospheres to be used in controlled-exposure protocols.

RESEARCH TOPIC 8. SUSCEPTIBLE SUBPOPULATIONS

What subpopulations are at increased risk of adverse health outcomes from particulate matter?

A number of subgroups within the population at large are postulated to be susceptible to the effects of inhaled PM. They include

people who have COPD, asthma, or coronary heart disease; the elderly; and infants. Also, fetuses are possibly susceptible. Those groups have long been assumed to be susceptible to the effects of air pollution, in general, and therefore assumed to be at risk from PM. Epidemiological data support that assumption, as does understanding of the compromised organ systems of people with chronic heart and lung diseases and of the physiologic and immunologic vulnerability of infants and the elderly. A number of epidemiological and controlled-exposure investigations are now directed at characterizing health effects of PM in those subpopulations. Other populations might also be at excess risk from PM, and the committee considers that this research topic includes both subpopulations already considered susceptible and others yet to be identified.

In susceptible subpopulations, there is likely to be a range of vulnerability reflecting the severity of underlying disease. For example, in persons with asthma, there is a broad distribution of level of lung function and of increased nonspecific airway responsiveness, a hallmark of the disease. The degree of susceptibility can also depend on the temporal exposure pattern. However, data to support such biologically based speculations are still notably lacking. For example, whether all children are equally at risk or only children who are exercising or who have specific predisposing factors, such as a history of atopy or asthma or other respiratory disease history, is unknown. In adults, the interplay among factors that determine susceptibility, such as the presence of both COPD and coronary heart disease, is not yet understood. Findings of both acute and chronic morbidity and mortality studies suggest that those with prior respiratory disease are more susceptible to acute changes in ambient PM concentrations.

Although from the early days of air-pollution research hypotheses have been proposed related to increased susceptibility of selected fractions of the population, much of that work has been directed at identifying acute morbid events during acute exposures. For example, research in London in the 1950s followed up on the observation that many of the excess deaths noted in the December 1952 fog were of persons who were already quite sick, many with heart or lung disease. Panels of people with chronic bronchitis were followed during the 1950s and 1960s with monitoring of pulmonary function and symp

toms. Those studies followed a design now referred to as a panel study, which involves following a susceptible subpopulation with relatively detailed tracking of their status. This model is particularly useful for assessing acute effects of exposure and can provide evidence relevant from both the clinical and the public-health perspectives. More recently, work has been directed toward testing whether exposure to particles can contribute to initiation of disease, as well as exacerbating existing conditions. To date, the collective evidence indicates that there are susceptible subpopulations, particularly of people who have chronic heart or lung diseases.

Research Progress and Status

Controlled-Exposure Studies

The committee identified 53 animal and human studies in the HEI database that specifically addressed the issue of subpopulations susceptible to PM-induced diseases (Table 3.7). In several cases, a study identified more than one susceptible subpopulation; for these, each population group was entered into the table.

Almost all the studies concern with diseases of the respiratory and cardiac systems; only one concerns increased susceptibility to cancer induction. Twelve studies concern age as a risk factor. The disease states of concern include pulmonary allergies, asthma, bronchitis, emphysema, COPD, and cardiac disease. Twenty-four of the studies involve human subjects, and 29 use animal models intended to mimic human disease.

The particulate atmospheres most frequently being used for toxicity studies are those with CAPs, carbon black, and residual-oil fly ash delivered via inhalation or intratracheal instillation. The duration of the exposures is variable but typically only hours or a few days; this contrasts with epidemiological studies that involve chronically exposed populations.

A strength of the studies is their focus on the major human diseases that have been identified by epidemiological studies as placing

people at risk from exposure to PM. An additional strength is that epidemiological studies in which exposures cannot be controlled are complemented with controlled-exposure studies of humans and laboratory animals.

TABLE 3.7 Controlled-Exposure Studies on Effects of PM on Susceptible Subpopulations

Susceptibility Factor	Humans	Laboratory Animals
Disease		
Allergies	1	1
Asthma	9	1
Bronchitis	—	7
Emphysema	—	3
Cardiac	1	8
Chronic obstructive pulmonary disease	8	1
Cancer	—	1
Age		
Infants	1	2
Children	3	—
Elderly	1	5

There are difficulties in investigating susceptible populations. The effect of PM exposure is not large enough to be readily and precisely detected without carrying out fairly large studies. Identifying study participants can be difficult, particularly if emphasis is placed on the most susceptible persons. Frail elderly persons and persons with advanced heart and lung disease, for example, might be reluctant to participate if study protocols are demanding. In contrast, experimental studies involve very small populations and typically short observation periods. In laboratory-animal studies, investigators typically attempt to circumvent this issue of population size by increasing the level of exposure or dose. It is common for all the treated animals to manifest disease or some other response. However, a critical ques

tion is whether the disease states observed and the underlying mechanisms of pathogenesis with short-term high exposures (doses) studied over periods of days, and occasionally weeks, are relevant to assessing the risks posed by exposure over long periods, even at high ambient doses.

Beyond the extrapolation issue, the adequacy of the design of each toxicity study must be addressed. For example, in most cases, the investigators are typically studying relatively young animals, usually in the first fourth of their normal life span, whereas in humans a substantial portion of the disease of concern occurs in the last fourth of the normal life span. Many of the human diseases of concern are chronic, with periods of acute exacerbation. It is crucial that additional effort be directed at evaluating the animal models to assess the degree to which they mimic human disease.

Rationales for selection of the exposure atmospheres, exposure concentrations, and exposure durations were not always readily apparent from the project descriptions. There is also a special need to articulate the relevance of using intratracheal instillation, which delivers a large dose of particles at once, in contrast with the chronic exposures of concern for human populations.

Epidemiology

A general concern for the health effects of air pollution, including particles, on susceptible persons has permeated epidemiological research on air pollution. This concern has become increasingly focused as the body of evidence has expanded and led to hypothesis-driven studies of susceptible subpopulations. In addition, with the recognition that much of the morbidity and mortality associated with PM exposure appears to have been from cardiovascular diseases, the efforts to understand susceptibility have expanded greatly beyond considerations of chronic respiratory conditions, particularly asthma and COPD, to include persons with underlying heart disease.

About 70 funded studies using epidemiological databases were reviewed to identify those directed to understanding the impact of

particulate pollution on susceptible subjects, patients, or populations. In general, the studies can be divided into those related to people who have an underlying chronic condition (such as asthma, COPD, or pre-existing coronary arterial disease), those related to persons free of disease but considered to be at increased risk because of a relatively high pollution dose resulting from exertion or exercise, and those related to persons generally at risk for increased morbidity or mortality (such as the elderly). Across the studies, a wide variety of measures of exposure are used, and insights can be gained on some aspects of particle characteristics and toxicity. However, only a few of the strata of the matrix defined by subpopulation and particle characteristics are being addressed.

Taken together, the efforts under way indicate that a rigorous evaluation of risks posed by PM exposure of susceptible subpopulations with established diseases—such as asthma, COPD, coronary arterial disease, heart failure, and hypertension—can be expected. The evidence will be primarily in relation to PM mass as the exposure metric. The groups that have been or are being studied, as summarized in the examined HEI database, include subjects potentially at risk and patients. Few studies are identified specifically as targeted to ethnic minority populations.

Efforts are also under way to explore pathogenesis and intermediate markers of risk, including changes in blood concentrations of inflammatory markers and clotting factors; additional predictors of cardiac risk, including changes in heart-rate variability; and other risk factors for sudden death.

Several studies directed toward an understanding of mechanisms of putative cardiac effects in humans are being carried out in the EPA, at several of the EPA-sponsored PM centers, and through other funding agencies. These include panel studies and clinical studies of healthy persons and potentially high-risk persons exposed to ambient PM and to CAP. These studies are being conducted by multidisciplinary teams that include expertise in exposure assessment, epidemiology, and clinical toxicology. Investigating the role of PM in initiating disease is more challenging, and less progress can be expected in understanding how susceptibility plays a role in initiation of chronic

diseases, simply because the susceptible groups have been less well defined.

In all the studies mentioned above, most of the efforts are directed to explaining acute effects of relatively short-term modeled or directly measured exposures to ambient particles. In a few instances, copollutants or other gases are also being considered. In only a very few cases are effects of chronic exposure being considered; in those cases, long-term exposure is being modeled for relatively recently measured exposures and historical extrapolations of known industrial or ambient particles. Better modeling of past exposure is needed, to develop new efforts directed toward the understanding of chronic effects in potentially susceptible groups. Such data would also be useful in conjunction with studies of factors that determine the development of susceptibility.

Adequacy of Current Research in Addressing Research Needs

There is increasing use of animal models and humans with chronic heart or lung disease in studies to evaluate effects of PM exposure. However, the animal studies need to mimic the human disease state of interest properly. Better modeling of past exposure is needed to develop new efforts to understand chronic effects in potentially susceptible subpopulations. Collection of such data in conjunction with studies of factors that determine the development of susceptibility would be useful.

Application of Evaluation Criteria

Scientific Value

The hypothesis that particular groups in the population have increased susceptibility has been long advanced and supported by substantial epidemiological evidence. In fact, a general acceptance of the hypothesis has led to focusing of effort in a large number of projects

on the assessment of acute air-pollution effects on morbidity and mortality in selected groups of potentially susceptible persons. The results have been relatively consistent in demonstrating modest effects of particles as measured by mass. The same susceptible subpopulations will need to be reinvestigated, and previously unrecognized subpopulations will need to be considered as hypotheses concerning toxicity-determining characteristics of particles are increasingly refined.

Decisionmaking Value

Data on susceptible populations are critical to decisionmakers because the Clean Air Act requires that protection against risks posed by air pollution be extended to almost all persons. Standards are, in fact, intended to provide protection with "an adequate margin of safety." Sufficient studies are under way to identify and reduce uncertainty related to susceptible groups with respect to acute effects of particle mass. However, for each individual study and for the studies as a group, it is important to anticipate how the results will influence decisions in establishing a NAAQS for PM—that is, will the information obtained provide an improved scientific basis for a decision on appropriate standards for ambient PM? It appears that few of the investigators have adequately considered this matter in a critical manner, especially for the controlled-exposure studies.

Feasibility and Timing

The only practical way to increase the number of investigations with regard to either acute or chronic exposures is to undertake studies in conjunction with current supersite or speciation-site data collections or with the use of additional exposure-data sources in the future. There is continuing development of animal models that mimic various aspects of potentially susceptible human conditions. Thus, this field continues to evolve.

RESEARCH TOPIC 9. MECHANISMS OF INJURY

What are the underlying mechanisms (local pulmonary and systemic) that can explain the epidemiologicalal findings of mortality/morbidity associated with exposure to ambient particulate matter?

Epidemiological studies have associated various health outcomes with exposure to ambient PM. Controlled-exposure studies are attempting to provide plausible underlying biological mechanisms for these health effects. The results have indicated a number of potential biological responses by which PM could underly possible pulmonary or systemic responses to PM exposures, many of which have been related to specific particulate characteristics, such as chemical or particle size. The major potential biological responses which have been suggested as underlying the reported human health effects from ambient PM exposures include oxidative stress, pulmonary inflammation, airway hyperreactivity, and alterations in the cardiovascular system, such as changes in blood viscosity, rate and pattern of heartbeat, and heart-rate variability. The issue of mechanistic plausibility has been addressed with animal models, in vitro systems, and clinical models. Of the studies described in the HEI database, about 50% involve animal toxicology, and the other 50% are roughly evenly divided between in vitro and clinical and studies. The relative apportionment of research effort for specific mechanisms of PM-induced responses and the allocation of these efforts among the three research approaches are indicated in Table 3.8.

Research Topic 9a. Animal Models

What are the appropriate animal models to use in studies of particulate matter toxicity?

As previously noted, epidemiological studies suggest that exposure to low concentrations of PM is associated with morbidity or mortality in susceptible people and not in normal healthy people.

Experimental data show that healthy animals exposed to similar low concentrations of PM also show little to no effect. Animal models are needed to mimic susceptible human subpopulations, because, without supporting data from animal studies, it is difficult to identify individual toxic materials in ambient PM and the mechanisms by which they induce damage to human and pulmonary and cardiovascular systerms. The occurrence of some pathological conditions in an exposed population can establish the probability that some of or all the pollutants produce damages but, in any reasonable time frame, it cannot always differentiate the effects, if any, of specific pollutants or the mechanisms of their action. That will ultimately require controlled exposures of animals to individual pollutants and relevant mixtures and then

TABLE 3.8 Mechanistic Studies

	Experimental Approach [a]		
Mechanism Examined	Animal Toxicology	In Vitro	Human Clinical
Pulmonary			
Inflammation	20	9	14
Airway reactivity	5	—	3
Oxidative stress	4	4	—
Pulmonary function	1	—	4
Infection, immunology (includes asthma)	11	1	5
Other [b]	12	3	4
Cardiovascular			
Heart-rate pattern, variability	3	—	2
Blood coagulation	3	—	1
Other	16	—	7

[a] Number of studies from HEI database. Some studies might be examining more than one endpoint.
[b] In many cases, the specific mechanism examined was not indicated in the description in the database.

measurements of response. In the initial stages of investigating the toxicity of PM and copollutants, it was sufficient to determine a correlation between their presence in inspired air and disease. Now, however, animal models are clearly needed to establish causality, help to unravel cellular mechanisms, and help to elucidate specific PM components that produce responses.

Research Progress and Status

In assessing progress toward the development of animal models, the committee found projects to be distinguished by their heterogeneity. Of the 47 relevant studies identified, most used young normal animals, which were not models for susceptible disease. Fewer studies used older animals as models to evaluate the effects of age, and others used animal models of disease, such as asthma and hypersensitivity, chronic lung diseases, and cardiac dysfunction. Normal or mutant animals were used in some studies.

There are a number of difficulties in developing animal models of human diseases. Deposition of particles in animal lungs differs in both rate and location from that in human lungs, and there is a need for detailed knowledge of the distribution of deposition in animal lungs so that it can be related to deposition in human lungs (see research topic 6). Advanced scaling and modeling of the lung airways in animals should be encouraged. The cellular mechanisms by which the pertinent lung and cardiovascular diseases are produced in humans and by which particles exacerbate or initiate these conditions are not understood so it is difficult to produce analogous pathological conditions in animals. The lung contains more types of cells than most other organs and thus provides the opportunity for numerous types of interactions between cells exposed to PM atmospheres and increases the complexity of particle-tissue interaction.

It has been possible to mimic some aspects of specific human diseases in animals. Therefore, it might be necessary to be satisfied with modeling and studying only part of a disease constellation at a time. For example, “asthma-like” allergic conditions have been mod

eled by sensitizing animals to various foreign proteins. That might produce marked contraction of airway smooth muscle on appropriate challenge but not involve other aspects of human asthma, such as inflammation and mucus gland hypertrophy.

Adequacy of Current Research in Addressing Research Needs

It is encouraging that numerous animal models are being used to measure the effects of exposure to PM. However, a substantial number of studies exposed healthy normal animals to particles, and this is not necessarily a useful model of exposure of susceptible humans. Even though animal models of cardiac and lung disease are being used to investigate the effect of particles, relevance to the human situation must be considered. Research to develop models that more closely mimic the natural history of human diseases caused by air pollution should be emphasized. Models need to be well characterized and validated before use.

Application of Evaluation Criteria

Scientific Value

The use of animal models that mimic susceptible human populations is important for the study of effects of ambient or surrogate PM. However, all models must be validated for their relevance to the human condition. Validated models will provide important insights into the mechanisms of action of ambient PM and associated pollutants.

Decisionmaking Value

Studies that use validated animal models will assist in the evaluation of particle characteristics that underlie human health effects of exposure to ambient PM. They will provide input into the standards-

setting process by contributing information needed to determine margins of safety for exposure.

Feasibility and Timing

Continued development and use of appropriate animal models are required. The necessary tools for such development are readily available.

Research Topic 9b. In Vitro Studies

What are the appropriate in vitro models to use in studies of particulate-matter toxicity?

In vitro studies are important in helping to determine underlying toxicological mechanisms. They remain a necessary complement to animal and clinical evaluations.

Research Progress and Status

The HEI database and the proceedings of the PM 2000 meeting list 34 studies related to this research topic. However, three of the studies do not deal with in vitro methods, and four are not relevant to the PM issue, but rather address issues of occupational and fibrogenic particle exposure. Most in vitro studies with PM are still conducted without considering the important issue of relevant doses to be used or, at a minimum, the use of a study design incorporating dose-response assessments. Many studies also focus on only one particle type collected from different ambient sources without including any control particles; in general, this type of study design should be avoided.

Several in vitro studies reported in the database are based on findings of animal studies that use very high doses of a specific particle type. Although state-of-the-art methods of cellular and molecular

toxicology are applied, the lack of an adequate justification for doses, the lack of control particles, and the presence of insufficient discussion of these important issues make the interpretation of results difficult. The results, contrary to what investigators of those studies conclude, will not be directly applicable to an understanding of pathophysiological mechanisms of PM action, nor will they be useful for the validation of high-dose animal studies as models of human respiratory-tract responses to much lower doses. Conclusions that are based on high doses do not provide arguments for the biological plausibility of effects of ambient PM. At best, the studies could contribute mechanistic information on PM effects in occupationally exposed workers whose lungs are generally exposed to a particulate compound at several milligrams per cubic meter.

On the positive side, several studies that are under way do use appropriate dose-response designs. Recognizing the need to use lower doses, these studies compare the toxicity of different particle types and responses in animal vs. human cells; this facilitates extrapolation of in vivo responses in animals to humans. Although high doses are also delivered, the studies are valuable with respect to a toxicological evaluation of potentially reactive components, but will require followup studies with more realistic doses. Another well-designed study includes a comparison of responses in airway biopsy cells from normals and asthmatics for an in vitro determination of relative sensitivities to ambient PM. One study in this category of comparative in vitro studies evaluated the response of human bronchial epithelial cells to PM collected before and after a steel mill closure; the goal was to identify the importance of differing PM composition—in this case related to transition metals—for inducing adverse health effects.

Several other studies use methods of in vitro priming—for example, with lipopolysaccharides—of specific respiratory-tract cells, including alveolar macrophages and epithelial cells, to compare responses of oxidative stress induction by PM in sensitized cells and normal cells. These studies are aimed at assessing mechanistic concepts of PM toxicity and contribute to the establishment of a good basis for designing further in vivo studies.

Two planned in vitro studies are designed to investigate age differences by using cells from young and old animals and applying a variety

of doses down to very low ones. Plans of one group of investigators include delivery of particles in the airborne state to in vitro cell cultures so that the dosing will be similar to in vivo conditions. The importance of coculture of different cell types is realized in one study in which an in vitro lung-slice technology is used to compare responses to a variety of PM of different sources and to surrogate control particles. One in vitro study is aimed at evaluating mutagenic effects of airborne PM and associated organic compounds, addressing long-term effects. However, administered doses and the use of a dose-response design are not indicated, and it is necessary to consider these issues in studies addressing potential long-term effects.

Adequacy of Current Research in Addressing Research Needs

The current and planned in vitro studies are designed to investigate several components of PM by using a number of end points, such as changes in the levels of inflammatory cytokines, and chemokines, release of oxidants, and oxidative stress responses. The issues of age-dependent responses and modulation of responses in cells from susceptible subjects are also being investigated. However, many current in vitro studies do not use or consider appropriate doses but, instead, are using unrealistic high doses; a dose-response design is still the exception in these types of studies. Despite those shortcomings, which need to be rectified, comparative in vitro toxicity studies to establish concepts and elucidate mechanistic events of PM toxicity are valuable additions to the database.

Application of Evaluation Criteria

Scientific Value

Specific mechanistic hypotheses related mainly to PM-induced effects are being tested at several laboratories. Although in vitro models are used for investigating mechanisms of PM-induced toxicity, the relevance of identified mechanistic pathways is highly question

able when they are based on high doses, as is the case in most of the current studies. A major gap is a lack of testing of the validity of conclusions for specific mechanisms by using relevant low doses; this is due in large part to the lack of a demonstrated causal relationship between relatively low PM exposures and adverse effects in controlled in vivo studies. Thus, in vitro studies have their greatest scientific value when they are designed on the basis of results of controlled whole-animal or clinical studies, involve relatively realistic exposures, and test specific mechanistic hypotheses.

Decisionmaking Value

Mechanistic information at the cellular and molecular levels obtained from well-designed in vitro studies can contribute to the weight of evidence regarding a causal relationship between PM exposure and health effects. That will reduce uncertainties related to the plausibility of observed adverse PM effects. Knowledge gained about mechanisms of PM toxicity will contribute greatly to the scientific justification of the PM standards.

Feasibility and Timing

In vitro studies clearly are feasible in many laboratories. It is important for special attention to be directed toward the use of relevant doses. Moreover, the development of appropriate new methods for in vitro studies should be encouraged, including airborne-particle exposures of cell cultures, use of cells from compromised lungs, and use of genetically modified cells. Because the developmental phase of these models is potentially long, useful results might not become available very soon.

Research Topic 9c. Clinical Models

What are the appropriate clinical models to use in studies of particulate matter toxicity?

Clinical studies are controlled exposures of humans. In the case of PM, such studies are designed to use laboratory-generated surrogate particles or concentrated ambient-air particles. The use of human subjects avoids the need to extrapolate results from other species. Both normal and susceptible subpopulations can be studied, and physiologic, cellular, immunologic, electrocardiographic and vascular end points, as well as symptoms, can be assessed. Elucidation of responses in humans is key to understanding the importance of ambient pollution and determining the nature of adverse health effects of PM exposure.

Research Progress and Status

Review of the HEI database and proceedings of the PM 2000 meeting identified about 10 active human-exposure studies. All are using particles of concern, which include CAP, ultrafine carbon, ultrafine acidic sulfates, diluted diesel exhaust, and smoke from burning of vegetable matter. Studies are under way in healthy volunteers, asthmatics, and atopic people. Studies in people who have COPD or cardiac disease are planned. The clinical studies focus on evaluation of pulmonary and systemic responses, such as pulmonary inflammation and injury to epithelial cells; cardiac rhythm, rate, and variability; initiation of the coagulation cascade; and symptoms.

Few laboratories are equipped to perform clinical studies of PM. However, the similarities in their protocols enhance the likelihood of obtaining useful data. For example, studies with CAP and ultrafine particles have incorporated prolonged electrocardiographic monitoring after exposure. All studies include physiologic assessments of lung function, and indicators of airway inflammation in nasal or bronchoalveolar lavage fluid, induced sputum, or exhaled air (such as nitric oxide). In addition, coagulation indexes in blood are examined in some of the studies. In selected cases, efforts have been made to centralize analytical studies in a core laboratory for standardization of techniques.

There are a number of difficulties in establishing clinical models to study PM. Although the particle concentrators allow exposure to

relevant atmospheres, the mixtures vary from day to day and, typically, minimal chemical analyses of the particles are performed. If responses to CAP are variable, it is not possible to determine whether the variability resulted from differences in human susceptibility or in particle chemistry. In contrast, studies with surrogate particles result in reproducible exposures but mimic only selected aspects of ambient particulate pollution. Furthermore, the epidemiological data suggest that the most severely ill are at risk of pollutant effects; these subgroups cannot be used in controlled clinical studies. Because clinical studies by design are limited to short-term exposures, they will rarely be able to contribute to an understanding of development of chronic disease secondary to exposure to particles.

The particle-exposure systems used in clinical studies include environmental chambers, facemasks, and mouthpieces. Each design offers specific advantages, but the mouthpiece studies with ultrafine particles have incorporated measurements of total particle deposition. One clinical study will investigate the interaction of particles with ozone, another plans to incorporate metals into the particles, and virtually all include some level of exercise to enhance minute ventilation, thus increasing the inhaled dose of pollutants.

Adequacy of Current Research in Addressing Research Needs

The current and planned clinical studies are designed to investigate CAP and several specific components of PM (such as size, acids, metals, and diesel exhaust) with a number of pulmonary and systemic end points. Studies are under way in susceptible subpopulations and are planned in other subgroups with pre-existing disease. Despite the limited facilities available for clinical research, the array of studies under way should provide valuable information on PM toxicity.

Application of Evaluation Criteria

Scientific Value

Clinical studies present an opportunity to examine responses to

PM in both healthy and susceptible subpopulations. Carefully designed controlled exposures provide information on symptomatic, physiologic, and cellular responses in both healthy and at-risk groups. They also provide important insights into mechanisms of action of PM. Such studies can provide needed information on PM deposition and retention in healthy and susceptible subpopulations (see research topic 6).

Decisionmaking Value

Clinical studies often provide important information for regulatory decisions. Assessing acute responses in groups that have chronic diseases will establish important insights into plausible mechanistic pathways. In addition, they provide crucial data on relative differences in responsiveness between healthy and potentially at-risk populations.

Feasibility and Timing

Studies are under way in several laboratories. They should provide highly relevant information for the next review of PM for regulatory decisions.

RESEARCH TOPIC 10. ANALYSIS AND MEASUREMENT

To what extent does the choice of statistical methods in the analysis of data from epidemiological studies influence estimates of health risks from exposures to particulate matter? Can existing methods be improved? What is the effect of measurement error and misclassification on estimates of the association between air pollution and health?

The first report of this committee (NRC 1998) outlined several methodological issues that needed further study. These included the

choice of statistical methods for analyzing data obtained from other studies, especially epidemiologic studies. Because more than one method can be used to analyze data, it will be important to understand the extent to which alternative approaches can influence analytical results. In addition, new study designs will require new approaches to analyze the data. These include development of analytical methods to examine several constituents and fractions of PM in an effort to understand their associations with health end points and design of models and approaches to incorporate new biological insights. Specific attention was given to measurement error, an issue inherent in most epidemiological studies that use ambient-air data to characterize subjects' exposure. The committee's second report (NRC 1999) reiterated those needs and noted the existence of relevant research and papers nearing completion.

Review of scientific literature, meeting abstracts, and the HEI database identified extensive progress on several methodological subjects. The review was intended to evaluate the extent to which the research needs previously identified by the committee are being addressed and to stimulate further targeted research.

General Methodological Issues

Model Development and Evaluation

Over the last several years, there has been considerable development of time-series data-analysis methods, which have provided much of the evidence on the association between PM exposures and health effects. The methods assess the variation in day-to-day mortality or morbidity counts with variation in PM concentrations on the same or previous day. Although systematic and comprehensive comparisons of alternative methods have not been reported, limited comparisons have suggested that results are relatively robust to the statistical approach used. However, the choices of input variables and data have been shown occasionally to influence results (Lipfert et al. 2000). That is particularly true with respect to the choice of pollution variables in

the statistical models. The presence of other variables in the models can influence the association between health measures and particulate air pollution.

The application of the time-series studies has been facilitated by recent advances in hardware and software and by the development of statistical approaches that can appropriately account for the data structure of the daily time series. Time-series analyses were initially conducted on a single location that had been selected primarily on the basis of data availability, rather than representing selection from a defined sampling frame. Meta-analysis was then used to summarize the data and to gain a more precise estimate of the effect of PM on mortality or morbidity. Recently, studies of more-formal, multicity designs have been conducted. These approaches have a priori plans for selecting locations and have standardized statistical methods across locations. The European Air Pollution and Health: A European Approach (APHEA) project (Katsouyanni et al. 1995) is a pioneering effort that initially analyzed routinely collected data from 15 European cities in 10 countries with a common statistical protocol, examining mortality and emergency hospitalizations in some cities. In the United States, the HEI has funded the National Morbidity, Mortality and Air Pollution Study (NMMAPS) (Samet et al. 2000, 2001). The NMMAPS includes analyses of mortality and morbidity separately; a joint analysis of morbidity and mortality is planned. For the mortality analysis, the NMMAPS investigators used a sampling frame defined by U.S. counties. The 90 largest urban areas (by population) were selected, and the daily mortality data for 1987-1994 were analyzed to assess associations with PM and other pollutants.

The methods used in the APHEA project and the NMMAPS show the potential power of multicity approaches. The potential selection bias of only a single or a few locations is avoided. Combining information across locations, increases power and heterogeneity. In addition, health effects can be compared between regions that have similar air-pollution levels.

Other research efforts involving model development are the exploration of distributed-lag models (Schwartz 2000a; Zanobetti et al. 2000), efforts to understand the dose-response relationship between PM exposure and health effects (Schwartz 2000b; Smith et al. 2000;

Schwartz and Zanobetti 2000), and examination of alternative ways of analyzing the relationship between air-quality data and health end points (Beer and Ricci 1999; Sunyer at al. 2000; Tu and Piegorsch 2000; Zhang et al. 2000). Other research efforts have also aimed at combining results from several studies, including those by Stroup et al. (2000) and Sutton et al. (2000).

Measurement Error

The difference between actual exposures and measured ambient-air concentrations is termed measurement error. Measurement error can occur when measures of ambient air pollution are used as an index of personal exposure. For PM, the three sources of measurement error are instrument error (the accuracy and precision of the monitoring instrument), error resulting from the nonrepresentativeness of a monitoring site (reflected by the spatial variability of the pollutant measured), and differences between the average personal exposure to a pollutant and the monitored concentration (influenced by microenvironmental exposures).

With regard to assessing the impact of outdoor exposures, the most important source of measurement error is related to the representativeness of the placement of monitors. In acute studies, other sources of error will not vary substantially from day to day. But in chronic studies, the most important errors are those associated with microenvironmental exposures. The presence of indoor sources of PM and the influence of home characteristics on penetration of outdoor particles into the indoor environment can be a source of substantial exposure error. The influence of home characteristics is important because it varies with geographical location, climate, socioeconomic factors, and season. Because those factors could introduce systematic errors, they must be considered in the analysis and interpretation of results of chronic epidemiological studies. They are often taken into account by using not direct measures of exposure, but surrogate measures that would influence the exposures, such as smoking in the household, the presence of gas stoves, and air conditioning.

Measurement error is of particular concern in studies intended to

isolate the effects of particles from those of gases or to distinguish the effects of individual particle species or size fractions from each other. When several population variables are included in the same analyses and the different variables have different magnitudes and types of measurement error, the issue of estimating the associations between health responses and specific variables is even more complicated. A well-measured but benign substance might serve as the best empirical predictor of community health effects, rather than a poorly measured but toxic substance that is similarly distributed in the atmosphere. The problem is that most pollutants tend to be similarly distributed, so collocated time series of pollutant measurements tend to covary because all pollutants are modulated by synoptic meteorological conditions. Long-term averages of pollutant concentrations tend to covary across cities because the rates of many categories of emissions tend to increase roughly with population. Various methods are available to adjust statistical analyses for the effects of differential measurement error (Fuller 1987; Carroll et al. 1995).

Several statistical issues must be considered in addressing measurement error. A full discussion of these issues is found in Fuller (1987) and Carroll et al. (1995). The most important is the type of model in which the measurement error is imbedded. Generally, in linear models, measurement error can be understood if it is assumed that errors are independent of each other and of other variables in the model and that they follow the same statistical distribution. However, it is common for measurement-error distribution and properties not to be readily apparent, for example in ambient-air quality data, because “true” measurements of personal exposure have not been available. Recent studies have generated data that will provide a better understanding of the properties of measurement error. Until its specific properties are understood, its consequences will be unclear. For instance, Stefanski (1997) cites examples from a linear model in which the regression coefficient could be biased in either direction or unbiased, depending on the characteristics of the measurement error. The issues are increasingly complex as one moves to multiple-regression models (Carroll and Galindo, 1998) and then to nonlinear models.

Development of a framework or method will be useful in consider

ing the effects of measurement error on population-mortality relative risks (Zeger et al. 2000). The framework demonstrates that for a wide range of circumstances the impacts of measurement error will either lead to underestimates of association or have a negligible effect. Combined with some of the data now being generated, the framework promises considerable progress toward an understanding of measurement error.

Harvesting

Harvesting is an issue raised by time-series mortality studies. The term "harvesting" refers to the question of whether deaths from air pollution occur in people who are highly susceptible and near death (and die a few days earlier because of air pollution than they otherwise would have) or the air pollution leads to the death of people who are not otherwise near death.

Many studies have identified associations between daily mortality and air-quality variables measured at the same time or a few days before deaths, but none of them has been able to address fully the issue of harvesting, although several recent analyses (Zeger et al. 1999, Schwartz 2000c) suggest that the findings of daily time-series studies do not reflect mortality displacement alone. Several analytical approaches have been proposed to address harvesting, and they need to be tried on additional data sets and refined to quantify better the degree of life-shortening associated with PM and other pollutants. Four recent papers examine this issue from different perspectives (Smith et al. 1999; Zeger at al. 1999; Murray and Nelson 2000; Schwartz 2000c).

Spatial Analytical Methods

An important issue in the analysis of data from studies that examine the association between city-specific mortality and long-term average pollutant concentrations, is whether observations of individual subjects are independent or correlated. Spatial correlation in

mortality can result from common social and physical environments among residents of the same city. Air pollution can be spatially autocorrelated as a result of broad regional patterns stemming from source and dispersion patterns.

In a recent reanalysis of data from the study by Pope et al. (1995), which examined associations between mortality in 154 cities throughout the United States and fine-particle and sulfate concentrations, Krewski et al. (2000) developed and applied new methods to allow for the presence of spatial autocorrelation in the data. The methods included two-stage random-effects regression methods, which were used to account for spatial patterns in mortality data and between-and within-city specific-particle air pollution levels, and application of spatial filtering to remove regional patterns in the data. Taking spatial autocorrelation into account in this manner increased the estimate of the mortality ratios associated with exposure to PM and led to wider confidence limits than in the original analysis; it was assumed that all individuals in the study represented independent observations.

The initial work on the development of analytical methods for the analysis of community-level data that exhibit clear spatial patterns warrants further investigation. Failure to take such spatial patterns into account can lead to bias in the estimates of mortality associated with long-term exposure to fine particles and to inaccurate indications of statistical significance.

Adequacy of Current Research in Addressing Information Needs

The recent research appears to address the research gaps and needs addressed by the committee. That is especially true for the measurement-error and harvesting issues. Because this research is new, it needs to be digested and applied to several data sets to increase our understanding. Data that are available or being collected allow further testing of the applications and methods. However, several subjects for further research are: elucidation of the statistical properties of the new spatial approaches discussed, consideration of

alternative ways of addressing spatial autocorrelation in the data, and application of such spatial analytical methods to additional data sets.

Application of Evaluation Criteria

Scientific Value

The research has been well conducted with strong statistical tools. In addition, it has taken advantage of the existing literature and statistical tools while applying them to new subjects. However, the statistical tools have been applied to few data sets. The value of the research will increase as it is applied to more data sets and as approaches and results from the various studies are compared, synthesized, and reconciled.

Decisionmaking Value

The research can contribute substantially to decisionmaking. Understanding of potential influence of model approaches on results is key to adequate use of the research findings. Because measurement error can affect the results, insights into the influence of measurement error will assist in the interpretation of the results and ultimately increase their influence in decisionmaking. Understanding of harvesting will help to place estimates of effects on mortality in a public-health perspective.

Feasibility and Timing

Feasibility is not a deterrent to the research in this field. It appears that extensive results will be available within the timeframe laid out by this committee.

4

Overall Findings and Recommendations

In this chapter, the committee summarizes key findings and recommendations resulting from its evaluation of the progress made in research on particulate matter (PM). The chapter also addresses general issues related to the program's implementation, providing a brief case study in the U.S. Environmental Protection Agency (EPA) implementation of the speciation and supersites monitoring program. Because the PM research program and the monitoring program have been initiated only over the last several years, the committee's evaluation is an interim one and cannot yet determine the extent to which research goals are being met. The committee will conduct a fuller assessment of the PM research program in its next report, which is scheduled for completion at the end of 2002.

KEY FINDINGS AND RECOMMENDATIONS CONCERNING SCIENTIFIC VALUE, DECISIONMAKING VALUE, AND TIMING AND FEASIBILITY OF PARTICULATE-MATTER RESEARCH

In Chapter 3, the committee presented specific evaluations of the progress made in addressing each of 10 research topics. This section takes a disciplinary approach, looking across research topics to characterize important knowledge gaps. It also addresses other topics,

including susceptible subpopulations and several methodological issues concerning data analysis that need further study.

Exposure Assessment

Exposure assessment is of paramount importance in understanding the effects of ambient particles and developing cost-effective exposure-control strategies. As more is learned about the characteristics of particles that determine their toxicity, more information will be needed on exposures to particles considered to have toxic potential. The current studies will enable the scientists, policymakers, and other interested parties to understand better the factors that affect the relationship between personal exposure and outdoor concentrations of particles.

In its first report, the committee recommended the development of longitudinal studies in which groups of 10-40 persons would be evaluated at successive times to examine the relationship between their personal exposures to particles, as indexed by mass, and the corresponding outdoor concentrations. Those exposure investigations are intended to focus particularly on subpopulations that could be susceptible to the effects of PM exposures, such as the elderly, children, and people with respiratory or cardiovascular disease. The committee recommended that the exposure studies include measurements of $PM_{2.5}$, PM_{10}, and gaseous copollutants, if appropriate. The committee expected the investigations to quantify the contribution of outdoor sources to personal and indoor exposures.

It appears that the developed study designs (such as repeated measurements of a small number of people) can address the key scientific questions. The studies that have been completed have identified some factors that influence relationships between outdoor air and personal exposure.

The committee expects the current longitudinal panel studies to be completed without difficulty. Although more time has been taken than expected in launching some of the currently funded panel studies, abundant personal and microenvironmental measurements have

already been made. However, the adequacy of personal monitoring data for CO should be examined.

Reporting of results from studies related to this research topic began during the summer of 2000, and completion of those studies is expected in about 2 years—about a year later than originally planned. Even though the findings are likely to raise further questions, progress in addressing key uncertainties in research topic 1 and topic 2 is expected. The committee will address how much progress in its next report.

Characterization of Emission Sources

The committee gave a separate set of research recommendations that address measurement of the size distribution and chemical composition of PM source emissions. Characterization of the emission rates of reactive gases that can form new particles on reaction in the atmosphere was also emphasized, including the need to maintain emission data on ammonia, the oxides of nitrogen and sulfur, and volatile organic compounds.

There is great scientific value in the research under way to develop new source-test methods and to demonstrate their capabilities to quantify particle size and chemical composition and ammonia and semivolatile organic compound emission rates. This information is needed to guide exposure-assessment studies and to help toxicologists and epidemiologists form potential hypotheses about components of PM that could be hazardous to human health. Emission data are also needed to support tests of advanced air-quality models that seek to relate pollutant emissions to ambient-air quality.

Accurate emission inventories are fundamental to the integrity of the decisionmaking process and to the selection of control strategies. Although the scientific merit of current work to develop new source-test methods is high, the potentially greater benefits to decisionmaking will emerge from more-complete and more-accurate knowledge of particle emissions by size and composition. The needed data will be obtained only if EPA substantially expands its source-testing

program over the next several years. At the same time, EPA should develop a comprehensive plan for systematically translating the new source-testing methods into a comprehensive emission inventory for the nation based on contemporary source tests of comparable quality. There is still ample opportunity to plan and conduct such a source-testing program. The goal of a high-quality inventory for particle size and chemical composition is not far out of reach if a comprehensive plan is prepared to select the sources to be tested and to set priorities for the work to be done over the next 5 years. The results of such studies are important for the development of cost-effective programs for reducing PM exposures.

Air-Quality Model Development and Testing

Air-quality models (source-oriented and receptor-oriented) provide essential information for developing effective and efficient air-quality management strategies that will be used for preparing state implementation plans (SIPs) for areas that are in nonattainment of the PM National Ambient Air Quality Standards. In addition, improved models would provide critical exposure data that could be used in health studies to examine relationships between exposure and health effects.

Source-oriented models require improved understanding of the chemical and physical processes that determine the size distribution and chemical composition of ambient particles. There is substantial support of current studies that are expected to make substantial contributions to the understanding of those processes. However, research is needed to develop, test, and evaluate source-oriented and receptor-oriented predictive models that represent the linkages between emission sources and ambient concentrations of the biologically relevant components of PM. In general, there has not been a sufficient effort to test the models developed by EPA and others. Nor has there been a sufficient effort to make extensive intercomparisons with other models to ascertain the differences and similarities in their results. Such efforts are needed to refine the models and to increase confidence in decisions based on their results. At present, however,

there is inadequate attention to organizing and carrying out the field studies that would provide the data for thorough evaluation of existing models. And only a small effort is being made to leverage investments in the PM monitoring program to provide a data platform for model evaluation.

The deployment of the PM monitoring program provides a basis for obtaining data to use in testing the models. If emission-characterization research is appropriately implemented, the necessary source data and source-oriented models would be readily available to combine with PM data. The emission-source profiles developed will also provide critical inputs to receptor-oriented models. In addition, efforts are under way to link air-quality models with exposure models.

Dosimetry

The committee's research portfolio recommended studies to improve scientific understanding of the deposition, translocation, and clearance of particles in the respiratory tract. This information is important for understanding exposure-dose-response relationships and extrapolating them among different types of human subjects and between animals and humans.

To the extent that research needs are being addressed, the scientific value of the work is generally high. Nearly all the work described in this report builds on previous knowledge in an incremental way and will lead to a more integrated understanding of PM-related health effects. Considering the previous lack of any data on dosimetry in people who have respiratory abnormalities or in animal models of these conditions, the data now being developed are needed and have scientific value.

An understanding of the differences between the deposited doses received by normal people and those with respiratory abnormalities could have a direct role in estimating safe and hazardous PM exposures of susceptible persons, such as those with asthma or chronic obstructive pulmonary disease (COPD). Improved understanding of dosimetry in animal- susceptibility models will play a more indirect

role in decisionmaking by influencing the selection of appropriate models, the interpretation of results of the use of models, and the understanding of the role of dose variables in human susceptibility.

Toxicology

The committee's research portfolio outlined a research agenda designed to improve understanding of the role of specific PM physical characteristics (such as particle size distribution and shape) and chemical constituents in the health outcomes associated with PM exposures. Research was also needed to develop experimental models, or PM surrogates, for use in toxicity studies.

The scientific value of this research topic remains high. Clearly, understanding the role of PM physiochemical properties in eliciting health effects will assist in determining the mechanisms underlying toxicity. In addition, identification of characteristics that produce adverse responses in controlled studies will enable better comparisons of PM properties obtained from epidemiological evaluations and will thus provide important confirmation of the role of specific properties in adverse health outcomes. Fuller understanding of the biologically important PM characteristics will facilitate the identification of emission sources of the toxic components; this information is essential to guide risk-reduction strategies.

Animal models are being widely used to measure the effects of exposure to PM. However, many studies incorporate healthy normal animals rather than useful models of disease associated with human susceptibility. Timely research is needed to develop models that more closely elucidate the natural history of relevant human diseases.

Epidemiology

This research approach is expected to take on increasing importance in the committee's research portfolio because of the need to establish linkages from PM sources to health effects as a basis for

setting standards and implementing control strategies. The array of particle characteristics potentially relevant to health risks is large and possibly variable across a range of health effects.

A number of studies that are in progress should provide information on the risks posed by ultrafine particles. This topic and related hypotheses are the focus of the PM centers at the University of Rochester. Studies in Germany and Atlanta will be another key source of data for testing the ultrafine hypothesis, and EPA panel studies will contribute additional insights. A few studies are under way to examine other PM components.

Many studies that are in progress should provide relevant information on the modification of PM risks from other pollutants. However, consideration should be given to new population-based approaches that could be useful for hypothesis-testing and eventually for surveillance.

Susceptible Subpopulations

Several subpopulations have long been considered susceptible to air pollution in general and to PM specifically. Within these subpopulations, there is likely to be a range of susceptibility. Taken together, research efforts that are under way indicate that a rigorous evaluation of PM exposure risks to susceptible subpopulations with established diseases—such as asthma, COPD, coronary arterial disease, heart failure, and hypertension—can be expected. This evidence exists primarily in relation to PM mass as an exposure index. A complete understanding of risks in susceptible subpopulations will require research that cuts across several of the committee's topics, including exposure, dosimetry, toxicity mechanisms, and epidemiology.

Analysis and Measurement

The committee's first report outlined several methodological issues that needed further study. They included the choice of statistical

methods for analyzing data obtained from other studies, especially epidemiological studies. Because more than one method can be used to analyze data, it will be important to understand the extent to which alternative approaches can influence analytical results. In addition, new study designs will require new data-analysis techniques. There is a critical need for analytical methods that will aid in characterizing exposure-response relationships at low exposures, including ambient concentrations in the United States.

The research on this subject has been undertaken by groups using powerful statistical tools. The work has taken advantage of the existing literature and existing statistical techniques. The tools have been applied to a few of data sets. The value of the research will increase as it is applied to more, and in some cases better, data sets and when the various studies, methods, and results can be compared, synthesized, and reconciled.

IMPLEMENTATION OF SUPERSITE AND SPECIATION PROGRAMS: A CASE STUDY

Beginning with its first report, the committee has recommended that EPA investments in air-quality monitoring (mass-concentration network, chemical-speciation network, and supersites) be planned and implemented in a manner that addresses health, exposure, and atmospheric research needs at the earliest stages. The committee also recommended that planning and implementation seek to ensure the maximal knowledge return for the substantial public investment in air-quality measurement systems while providing critical data on compliance with the National Ambient Air Quality Standards (NAAQS). Such data are necessary for SIP development and testing of advanced monitoring instruments. There have been a number of efforts by EPA and others to follow those recommendations, and beneficial collaborations have resulted. But some needed attempts to coordinate these efforts over the long term have not been fully undertaken, so the full potential for lasting benefits and a better understanding of atmo

spheric processes, exposure, and health effects is at risk. This brief case study reviews progress made to date and identifies needs for continued attention and improvement.

The air-quality measurement system now being implemented includes several key elements:

- An extensive network of federal reference method (FRM) $PM_{2.5}$ monitors installed on a population-weighted basis, primarily to measure compliance of metropolitan areas with the 1997 NAAQS for $PM_{2.5}$.
- A much smaller number of continuous $PM_{2.5}$ monitors in key metropolitan areas only for air quality index (AQI) use.
- A network of speciation monitors to provide basic and comparable speciation of $PM_{2.5}$ samples on a daily, 3-day, or 6-day basis, depending on the site.
- The supersite program, which involves intensive shorter-term sampling efforts at selected sites around the country.

In addition to this committee's general recommendations for integrating that effort into a unified system, a special Technical Subcommittee on Fine Particle Monitoring of the Clean Air Scientific Advisory Committee (CASAC) has been providing detailed review of the implementation of the program.

In response to this committee's call for an integrated approach to implementing an air-quality measurement system, EPA and others have taken a number of valuable steps:

- In July 1998, EPA and the North American Research Strategy for Tropospheric Ozone (NARSTO) organized a multidisciplinary workshop to review the program; identify key health, exposure, and atmospheric research questions; and lay out key common elements that should be addressed by the measurement program (Albritton and Greenbaum 1998).
- NARSTO, in January 1999, launched an effort to conduct a multiparty assessment of PM research and atmospheric understanding and has striven to include health and exposure researchers in each step of the effort.

- During 1999, rapid implementation of the FRM monitoring network proceeded, and EPA and the states took initial steps to implement and site continuous and speciation monitors. The speciation-network deployment has moved slowly because of some initial difficulties with the sampling equipment, and a multistage evaluation program was implemented before full deployment of the network. The 54 trends-network sites operating every third day are to be operating by the end of 2000, and the remainder of the network is to be deployed in 2001. Because of the difficulty in meeting the equivalence requirements promulgated by EPA for continuous monitors, they are envisioned only as providing data for AQI calculations. This issue is being discussed with the CASAC PM monitoring subcommittee.
- In spring of 1999, EPA issued a request for proposals for the supersite program. In large measure, the request followed the ideas from the 1998 workshop (mentioned above) and specifically included opportunities and incentives for atmospheric scientists to work with health and exposure researchers in developing collaborations around the supersites. A special information session was held at the June 1999 PM colloquium, which included presentations from the principal investigators of the then-recently selected PM health and exposure research centers in an effort to facilitate collaboration.
- In January 2000, EPA announced the winning supersite proposals, all of which incorporated valuable plans for collaboration between health and atmospheric scientists. The program also established important common elements for sharing of all collected data.
- There have since been a variety of relatively informal efforts to bring together different parties to facilitate collaboration, including meetings of the PM research-center directors and meetings of the supersite directors. In addition, personnel from the supersites in the northeastern United States initiated efforts to bring together representatives of all the regional supersites, PM research centers, and EPA and state monitoring officials to discuss collaborative efforts linking supersites and

speciation measurements with current or planned health and other research efforts.

On balance, those efforts have resulted in improved efforts in multidisciplinary collaboration and integration of the monitoring systems into a more unified system of air-quality measurements. However, several key factors have limited the success of those efforts and, if not addressed, threaten to undermine the long-term benefits. Among the key challenges are the following:

- A need for a strong management system for PM programs in EPA's Office of Air and Radiation (OAR) that is comparable with that implemented in EPA's Office of Research and Development (ORD). Although there has been much good staff effort, adequate resources and top-level leadership must be provided to ensure that the system is developed in a sustainable fashion and carefully integrated with the ORD research efforts.
- A need to develop a clearer vision both in OAR and between EPA and the state air agencies of a unified system for speciation, supersite, and other measurements. A systematic approach will be essential for using this rich, new set of measurements to enhance the understanding of atmospheric processes on an appropriate scale (such as on the scale of the eastern United States). Achieving this vision will require substantial efforts to involve the states actively as partners and improved leadership from OAR working at top levels with counterparts at ORD.
- Beyond the larger management challenge, there is concern that the speciation network is not being developed with sufficient integration into the PM research program so that it can serve as a cornerstone of future efforts to conduct source apportionment and health research aimed at determining the relative toxicity of components of the PM mixture. There is also concern that the network is not being developed with systems in place to ensure its long-term sustainability.
- Finally, there are not well-developed plans to use the resulting

database in a comprehensive and prospective manner, nor the resources to support such an effort. Tens of millions of dollars is being spent to collect data and requests for applications for only relatively small projects to provide some data analysis among the supersites and to use the chemical-speciation and supersite data in health-effects research. A much more extensive effort is required to make use of the data resource that is being created. Such an effort will require planning, coordination, and resources—all of which are lacking.

OVERARCHING ISSUES RELATED TO IMPLEMENTATION OF PARTICULATE-MATTER RESEARCH PROGRAM

This section discusses overarching issues stemming from the committee's application of the three evaluation criteria for assessing the implementation of the PM research program: multidisciplinary interaction, integration and planning, and the accessibility of information.

Disincentives and Incentives for Multidisciplinary Interaction Among Particulate-Matter Researchers

Institutional and cultural obstacles often discourage attempts to perform research across disciplines, agencies, and institutions (including public, private, and nongovernmental organizations). Such obstacles tend to sustain historical tendencies to conduct research within particular disciplinary or organizational boundaries (for example, toxicology vs. epidemiology, EPA vs. the Department of Energy, and government vs. industry). For example, professional validation and advancement standards for individual researchers are usually set by technical societies that are organized along disciplinary lines. Simultaneously, a person's career advancement can require attention to institutional, rather than national, agendas. In addition, scientific journals often are reluctant to publish articles that incorporate findings and perspectives outside the scope of a particular field of inquiry

and thus unfamiliar to their reviewers. Professional societies and conferences tend to partition participants into parallel sessions on specific health, environmental, or engineering topics, thereby limiting opportunities for cross fertilization.

In viewing such disincentives as they apply to the interrelated tasks of conducting PM research, the committee recommends that a series of incentives be established, or in some cases continued, to orient professional and institutional policies, practices, and behavior in favor of joint planning and information exchange. These incentives should include the following:

- Encouraging federal-agency PM research programs to give greater priority to integrated, multidisciplinary projects.
- Developing a unified, cross-agency federal budget for key PM research initiatives (that is, a "virtual-agency or multi-agency budget" for PM research). The committee is aware that the Air Quality Research Subcommittee of CENR has undertaken such budgetary coordination for PM research. The subcommittee is encouraged to extend this coordination to the greatest extent practicable.
- Conducting regular and frequent multisponsor, multidisciplinary gatherings to build a common community of PM investigators with the goal of determining whether the research under development is being integrated for the purpose of achieving the principal goals of the PM research program. The PM colloquia on particulate air pollution and human health are examples of gatherings that bring together many disciplines and sponsored research activities.

Integration and Planning of Particulate-Matter Research Across Federal Agencies

How well are research planning, budgeting, and management integrated to optimize the use of financial resources, scientific talent, and infrastructure across government and private institutions? Since

the committee's second report, measurable progress has been made in several aspects of integrating and planning the conduct of the PM research program:

- Within EPA, the agency established a formal management structure, led by a top official of ORD and managed by a PM research program manager. This has enabled the initial development of multiyear research budgets (an important innovation) and regular reporting of budget priorities and progress toward addressing the committee's research portfolio. In addition, the assistant administrator for ORD had tasked ORD's Board of Scientific Counselors to review the management of the program in detail and provide specific recommendations on how to improve it.
- Across the federal government, the charter of the CENR Air Quality Research Subcommittee has been expanded, and efforts are under way to create a complete federal inventory of PM research and to make it available through the Particulate Matter Research Activities website (www.pmra.org). This is a critical first step in creating an integrated federal strategy. On the basis of the inventory, the Air Quality Research Subcommittee is developing a strategy for integrating PM research that is sponsored by federal agencies.
- There have been efforts (discussed below) to enhance accessibility of the data for scientists and others.

Those efforts have provided the PM research program with the potential to be integrated and well planned. Although it is too early to assess the effectiveness of current management efforts fully, several aspects of the current management structure pose potential challenges to successful implementation of the research program.

First, within EPA, although ORD has put in place a formal management structure that should help to ensure program success and there have been initial efforts to integrate health, exposure, and atmospheric research interests into the PM air-quality measurement system, OAR should strive to develop a strong management system for

PM programs that is comparable with that in ORD. An enhanced management structure in OAR will be essential to ensure full coordination with ORD, to catalyze active involvement of the state air agencies in developing and managing the speciation network (a key source of future data to support research), and to develop fully the source-emission inventories necessary to conduct future source apportionment accurately.

Next, the committee called in its second report for a federal effort to develop a coordinated interagency strategy, including a single process and budget to set priorities for research, specific methods to coordinate research, and strategies and mechanisms for leveraging funding in the federal, state, nonprofit, and private sectors. Although the expansion of the Air Quality Research Subcommittee and development of a Web-accessible inventory of federal research are important first steps, efforts to coordinate federal research have often found the attainment of this type of unified strategy difficult to accomplish. It will require sustained efforts on the part of the subcommittee to ensure that these next, more challenging steps are accomplished.

On balance, many of the elements for successful integration and planning of the PM research program have been put into place. Successful efforts to address the remaining planning and integration challenges are critical to ensure that the maximal research return is obtained from the sizable investments.

Connecting Research Management to Standard Implementation

The continuing process of planning and applying research in air-quality standard development is part of an established process linked to the preparation of the air-quality "criteria document" and the EPA "staff paper." Both documents undertake a synthesis of existing peer-reviewed scientific information and present its implications for standard-setting. The scientific community and the broader public have long maintained a participation in the process of reviewing the adequacy of scientific information and its application in the above documents.

At present, there is a lack of a sufficient understanding of the most toxic particle constituents, the toxicological mechanisms through which they act, and the actual exposures experienced by people. In the absence of such an understanding, a nationwide control strategy might reduce some kinds of PM exposures while failing to protect public health adequately, if the types of PM controlled are not the most important in causing adverse health effects. In other words, at the present time, there is uncertainty as to what specific types or components of PM need to be reduced to achieve substantial health-risk reduction cost effectively. It will also be important to obtain greater confidence about the shape of any dose-response relationship between PM concentrations and health outcomes.

Earlier discussions in this report concerning research topic 3 and topic 4 have indicated that efforts will be needed to develop and evaluate source-measurement techniques and air quality models. Such efforts will reduce scientific uncertainties associated with standards implementation, including application of air-quality models, controls for mitigating exposures, regional variations in air quality, and long-term changes in emission characteristics due to technological advances and changes in economic activities. Because of such critical information needs, research planning and management and scientific review should be extended into the standard-implementation process. Thus, the committee recommends that EPA develop a research-management strategy to address key uncertainties concerning implementation of air-quality standards for PM.

Accessibility of Information

The third criterion adopted by the committee for evaluating the implementation of the PM research program is related to the accessibility of information about the program. Specifically, the committee identified the need for the PM research program to provide information on its planning, budgets, progress, and results to parties that have an interest in PM research. Such parties could include other research organizations, public-health and environmental organiza

tions, industry groups, health professionals, the interested public, and the news media.

Information about PM research plans and results should be easily and effectively accessible. And, enhanced multidisciplinary efforts should be used to inform and engage interested parties in understanding research results.

As part of making PM research information accessible, the committee has found the inventory of research projects initiated by EPA and the Health Effects Institute (HEI) to be very useful for interested parties to maintain a capability of tracking research in progress. EPA and HEI have provided a valuable service that should be continued as the body of PM research continues to grow. Scientists in government, the private sector, and universities and the broader public can use the research inventory, and it represents a useful basis for identifying and planning future research.

Throughout the research program, progress has been made in enhancing accessibility to publicly funded data for scientists and others, as evidenced by the provisions of the supersite program and other elements of the air-quality measurement program for central archiving and public data access. In response to legislation, recent revisions to federal grant-making rules have broadened access to the data created by federally funded research. Because this legislation has just been implemented, its full impact, particularly with respect to decisionmaking value, is uncertain.

OVERALL EVALUATION OF PARTICULATE-MATTER RESEARCH PROGRESS

Although the initial phases of the nation's PM research program have shown promise and a substantial number of peer-reviewed publications are forthcoming, there is as yet insufficient evidence for the committee to predict the program's ultimate effectiveness. In general, the PM research program following on the committee's priorities is appropriately addressing many of the key uncertainties. However, as discussed in this report, there are a number of critical specific sub

jects that should be given greater attention. Because research results are being obtained more slowly than originally expected, managers of the research program might have to adjust the timing of future research activities.

EPA organizations and others have made progress in integrating the full range of research approaches into the implementation of the national PM air-quality measurement system. However, key shortcomings (such as inadequate efforts to provide for data analysis) have limited the agency's ability to plan for and take full advantage of the wealth of new data on air quality likely to emerge from the system. EPA and other organizations will need to support research to ensure that success is achieved.

WHAT IS SUCCESS?

As the committee continues its evaluation of PM research progress over the next 2 years, it will seek information to determine the extent to which the research program provides the following:

- Measurable growth in knowledge that is relevant to the policy-relevant issues that scientists and decisionmakers must resolve in reviewing the NAAQS for fine airborne PM.
- Full scope of research results obtained from the individual scientific disciplines in relation to the research priorities; its overall assessment will consider how understanding has been advanced in the committee's paradigm from sources of PM exposures to health effects.
- Degree of acceptance by public and private decisionmakers and other interested parties of the quality and relevance of the scientific information obtained and the process by which it was generated.

A key determinant will be the extent to which the research findings inform the setting of future NAAQS for PM, namely, identification of the indicator (such as $PM_{2.5}$), concentration of the indicator in air, time

over which measurements are made or averaged, statistical form of the standard used to determine the allowable number of exceedences, and the effective and efficient implementation of emission-control programs to achieve the NAAQS.

In the future, it will also be important to ask whether the PM research and this committee's role offer a model for conducting other major scientific investigations. Equally challenging and contentious scientific inquiries are under way for such issues as endocrine-disruption effects of chemicals and potential health impacts of genetically engineered organisms. Are there aspects of the way in which the PM research program is being planned, conducted, and overseen from which these other efforts could usefully draw? Among the key elements of the PM research example that might prove useful in other arenas are the development of a multidisciplinary research portfolio designed to address key public-policy questions, the laying out of a multiyear commitment to implementing the portfolio, the establishment of management mechanisms to ensure interagency and public-private coordination, the construction and continued use of a research-inventory database, and the continuing oversight and evaluation of the program by an outside, multidisciplinary committee. Of course, the evaluation of the success of the PM example will require others, outside this committee, to make fresh judgments as to which elements succeeded and which did not. However, some elements that succeeded might not be applicable to every other field of science. It is appropriate to begin documenting and evaluating key elements of the PM research example soon so that future observers can measure and learn from its success.

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Appendix A

Biographical Information on the Committee on Research Priorities for Airborne Particulate Matter

JONATHAN SAMET *(Chair)*, The Johns Hopkins University, Baltimore, Maryland.

Jonathan Samet is professor and chairman of the Department of Epidemiology at The Johns Hopkins University School of Hygiene and Public Health. Dr. Samet earned an M.D. from the University of Rochester School of Medicine and Dentistry and an M.S. in epidemiology from the Harvard School of Public Health. He is board-certified in internal medicine and the subspecialty of pulmonary disease. He was formerly professor and chief of the Pulmonary and Critical Care Division in the Department of Medicine at the University of New Mexico School of Medicine. He is past-president of the Society for Epidemiologic Research. He has served on EPA's Science Advisory Board. He is currently on the Board of Overseers and Board of Editors for the *American Journal of Epidemiology.* Dr. Samet was awarded the Surgeon General's Medallion in 1990. He was elected to the Institute of Medicine in 1997 and currently serves as chairman of the present committee. He also served recently as chairman of the NRC Committee on Health Risks of Exposure to Radon (BEIR VI), Phase II.

GLEN R. CASS, Georgia Institute of Technology, Atlanta, Georgia

Glen R. Cass is chairman and professor of the School of Earth and Atmospheric Sciences, and professor of civil and environmental engineering at the Georgia Institute of Technology. Previously, he was a professor of environmental engineering and mechanical engineering at the California Institute of Technology. He earned his Ph.D. in environmental engineering from the same institution. Research conducted by Professor Cass focuses on developing methods for identifying the least costly means of air pollution abatement in a complex regional setting. He is currently studying the formation and control of gaseous and fine-particle pollutants, control strategies for visibility improvement, indoor air quality, economic optimization of pollution control strategies, and strategies for protection of works of art from damage due to air pollution. He is a member of the research advisory committee for the Health Effects Institute, and a consultant to both government and industry on air pollution and its control. He previously served on the EPA Clean Air Scientific Advisory Committee and on EPA's FACA Subcommittee on Ozone, Fine Particles, and Regional Haze. Dr. Cass served on the NRC Committee on Haze in National Parks and Wilderness Areas and the Committee on Preserving Historical Documents.

JUDITH C. CHOW, Desert Research Institute, Reno, Nevada.

Dr. Judith C. Chow is a research professor at the Atmospheric Sciences Division, Desert Research Institute. She earned her Sc.D. in environmental science from Harvard University. She has been a major collaborator in more than 40 air quality studies and is currently co-principal investigator on several studies, including the evaluation of aerosol measurement methods, sampling strategies, and databases. She authored the Air & Waste Management Association's 1995 annual critical review on aerosol measurement methods and has over 100 peer-reviewed publications. She serves as chair of the Air & Waste Management Association's Measurement Division. She also serves as chair of the Metals 1 Subcommittee of the Intersociety Committee for Methods of Air Sampling and Analysis. Dr. Chow was technical program chair for the Air and Waste Management Association's International Symposium on $PM_{2.5}$: A Fine Particle Standard.

BART E. CROES, California Air Resources Board, Sacramento, California.

Bart E. Croes is the chief of the Research Division at the California Air Resources Board. He received his B.S. in chemical engineering from the California Institute of Technology and his M.S. in chemical engineering from the University of California at Santa Barbara. He was the program manager for the 1997 Southern California Ozone Study and Aerosol Program and former manager of atmospheric processes, particulate matter, and acid deposition research at the California Air Resources Board. He is on the Executive Steering Committee for the North American Research Strategy for Tropospheric Ozone (NARSTO) Program, has served on several EPA peer-review panels, and is a consultant to several Asian air pollution control agencies.

ROBERT E. FORSTER, The University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

Robert Forster is Isaac Ott Professor Emeritus in the Department of Physiology at the University of Pennsylvania School of Medicine. He received his M.D. from the University of Pennsylvania, is a former chairman of the Department of Physiology at the University of Pennsylvania, and is past-president of the American Physiological Society. He was awarded a Von Humboldt Prize in 1993. Dr. Forster was elected to the National Academy of Sciences in 1973 and has served as chair of NAS Section 23 (Physiology and Pharmacology) and as a member of several NRC committees. Dr. Forester's interests are in respiratory physiology, in particular on the kinetics of oxygen, carbon monoxide, and carbon dioxide processes in related exchanges.

DANIEL S. GREENBAUM, Health Effects Institute, Cambridge, Massachusetts.

Daniel S. Greenbaum is the president and chief executive officer of the Health Effects Institute, an independent research institute funded jointly by government and industry to provide impartial and relevant research on the health effects of air pollution. He earned his Masters of City Planning from the Massachusetts Institute of Technology. At the Health Effects Institute, Mr. Greenbaum has overseen the development and implementation of a research plan that focuses the institute's efforts on providing critical research and reanalysis on

particulate matter, air toxics, and alternative fuels. In 1999, he served as chair of the EPA Blue Ribbon Panel on Oxygenates in Gasoline, which made recommendations on how to preserve the air pollution benefits of reformulated gasoline while preventing water contamination from MTBE and other additives. Prior to joining the Health Effects Institute, he served as commissioner of the Massachusetts Department of Environmental Protection.

PHILIP K. HOPKE, Clarkson University, Potsdam, New York.

Philip Hopke is the Robert A. Plane Professor of Chemical Engineering and Chemistry at Clarkson University. He earned his Ph.D. in chemistry from Princeton University. Prior to joining Clarkson University, he was a professor of environmental chemistry at the University of Illinois at Urbana-Champaign. His research interests include chemical characterization of airborne particles. He currently serves on the EPA Clean Air Science Advisory Committee (CASAC). He is a former director of the American Association of Aerosol Research and editor-in-chief of its journal. He has served on six NRC committees, including the NRC Committee on Advances in Assessing Human Exposure to Airborne Pollutants. His most recent service has been on the NRC Committee on Health Risks of Exposure to Radon (BEIR VI), Phase II and the Committee on Risk Assessment of Exposure to Radon in Drinking Water.

PETROS KOUTRAKIS, Harvard School of Public Health, Boston, Massachusetts.

Petros Koutrakis is professor of environmental sciences and director of the Environmental Chemistry Laboratory at Harvard University. He received his Ph.D. in environmental chemistry from the University of Paris. His research interests include human exposure assessment, ambient and indoor air pollution, environmental analytical chemistry, and environmental management. Dr. Koutrakis has almost 100 peer-reviewed publications and seven patents. He is the director of the EPA/Harvard University Ambient Particle Center. He is the technical editor-in-chief of the *Journal of Air and Waste Management Association*, consultant to the EPA Science Advisory Board, chairman of the EPA speciation network, member of the American Chemistry Council Stra

tegic Science Team and consultant to the Chilean Environmental Agency.

DANIEL KREWSKI, University of Ottawa, Ontario, Canada.

Dr. Krewski is professor of medicine and of epidemiology and community medicine at the University of Ottawa and adjunct research professor of statistics at Carleton University. Previously, he served as director of risk management and as director of the Bureau of Chemical Hazards with Health Canada. He received his M.Sc. and Ph.D. in mathematics and statistics from Carleton University, and his M.H.A. from the University of Ottawa. Dr. Krewski is associate editor of *Risk Analysis and Journal of Epidemiology and Biostatistics.* He is currently a member of the NRC Board on Environmental Studies and Toxicology and its Committee on Toxicology. He recently chaired the NRC's Colloquium on Scientific Advances and the Future in Toxicologic Risk Assessment. Dr. Krewski has published more than 300 journal articles and book chapters in the areas of risk assessment, biostatistics, and epidemiology.

PAUL JAMES LIOY, University of Medicine and Dentistry–New Jersey, Piscataway, New Jersey.

Dr. Paul James Lioy is a professor of environmental and community medicine at UMDNJ–Robert Wood Johnson Medical School and deputy director at the jointly sponsored Environmental and Occupational Medicine (EOHSI) of Rutgers, the State University of New Jersey and University of Medicine and Dentistry of New Jersey. Dr. Lioy received his Ph.D. in environmental sciences from Rutgers University. He has over 150 peer-reviewed publications. His research interests include assessing human exposure to outdoor and indoor air pollutants, and techniques and field studies for characterizing atmospheric pollutants. He is a former chairman of the New Jersey Clean Air Council. He is a former member of the NRC's Board on Environmental Studies and Toxicology and five NRC committees. He served as chairman of the NRC Committee on Advances in Assessing Human Exposure to Air-borne Pollutants. Currently, he serves on the Science Advisory Board of the EPA and is chair of the Subcommittee on Health and Ecological

Effects Valuation. He is a member of the International Air Quality Board of the International Joint Commission of U.S./Canada.

J OE L. M AUDERLY , Lovelace Respiratory Research Institute, Albuquerque, New Mexico.

Dr. Joe L. Mauderly is a senior scientist and director of external affairs of the Lovelace Respiratory Research Institute and president of its subsidiary, the Lovelace Biomedical and Environmental Research Institute. Dr. Mauderly received his D.V.M. from Kansas State University and specialized in respiratory physiology and comparative pulmonary responses to inhaled toxicants. He is past director of the Inhalation Toxicology Research Institute. He is a past chairman of the Environmental and Occupational Health Assembly of the American Thoracic Society and a past president and councilor of the Inhalation Specialty Section of the Society of Toxicology. He is a former chairman of the Electric Power Research Institute's Air Pollution Health Studies Advisory Committee and a former member of the Health Effects Institute's Research Committee. He is a past chairman of EPA's Clean Air Scientific Advisory Committee. He serves on the editorial boards of *Inhalation Toxicology* and *Experimental Lung Research*, and is former associate editor of *Fundamental and Applied Toxicology.* He also served as a member of the NRC Subcommittee on Pulmonary Toxicology.

R OGER O. M CCLELLAN , Albuquerque, New Mexico and Emeritus, Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina.

Roger McClellan is president emeritus of the Chemical Industry Institute of Toxicology (CIIT) and adjunct professor of toxicology at Duke University, North Carolina State University, and University of North Carolina–Chapel Hill. He served as president of CIIT from 1988 to 1999. Dr. McClellan earned his D.V.M. from Washington State University and is a diplomate of the American Board of Veterinary Toxicology and the American Board of Toxicology. He is a former president and director of the Inhalation Toxicology Research Institute, Lovelace Biomedical and Environmental Research Institute. He has

served on numerous government advisory committees, including the NIH toxicology study section, NIEHS advisory council, EPA's science advisory board, and as chair of EPA's Clean Air Scientific Advisory Committee. He is a past president of the Society of Toxicology (SOT), the Inhalation Specialty Section of SOT, and the American Association for Aerosol Research and a fellow of the Society for Risk Analysis, the Health Physics Society, and the American Association for Advancement of Science. He serves or has served on various editorial boards, including *Journal of Fundamental and Applied Toxicology, Environmental Health Perspectives, Journal of Toxicology and Environmental Health*, and *Inhalation Toxicology*, and serves as editor of *Critical Reviews in Toxicology*. He has received special awards from the Society of Toxicology, Health Physics Society, the American Association for Aerosol Research, the International Society for Aerosols in Medicine, and the International Society of Regulatory Toxicology and Pharmacology. Dr. McClellan was elected to the Institute of Medicine in 1990. He is a former chair of the NRC's Committee on Toxicology and has served on several other NRC committees. He has a long-standing interest in the toxicology and assessment of human risks of airborne materials.

G ÜNTER O BERDÖRSTER , University of Rochester, Rochester, New York.

Günter Oberdörster is professor in the Department of Environmental Medicine and head of the Division of Respiratory Biology and Toxicology at the University of Rochester. He is internationally recognized for his research on the effects and underlying mechanisms of lung injury induced by inhaled nonfibrous and fibrous particles, including modeling and risk assessment. Dr. Oberdörster earned his D.V.M. and Ph.D. (med. vet.) from the University of Giessen in Germany. He is a past-president of the Society of Toxicology's Inhalation Toxicology Specialty Section (ISS), a consultant to EPA's Clean Air Science Advisory Committee, a former member of the EPA Science Advisory Board's Subcommittee on Heavy Metals, a former member of the International Agency for Research on Cancer Committee, and a former member of the Board of Scientific Counselors of the National Toxicology Program. Dr. Oberdörster is a recipient of the Joseph von Fraunhofer Prize (Germany), the Society of Toxicology's ISS Career Achievement Award, and the Society of Toxicology's ISS 1997 Paper of the

Year Award. He is on the editorial board of the *Journal of Aerosol Medicine* and *Inhalation Toxicology*. He is also currently a member of the NRC's Committee on Toxicology.

REBECCA PARKIN, George Washington University, Washington, D.C.

Dr. Rebecca Parkin is associate research professor at George Washington University School of Public Health and Health Services. Dr. Parkin earned her M.P.H. in environmental health and her Ph.D. in epidemiology from Yale University. She is a former director of scientific, professional, and section affairs at the American Public Health Association as well as assistant commissioner for the Division of Occupational and Environmental Health of the New Jersey Department of Health. She is a member of the NRC Water Science and Technology Board and has served on several NRC and IOM committees, including the Committee on Risk Assessment of Hazardous Air Pollutants. She is a liaison member of the U.S. Department of Health and Human Services' National Advisory Committee on Childhood Lead Poisoning Prevention. She has served as a member of study panels of the U.S. Agency for Toxic Substances and Disease Registry and continues to serve as a member on subcommittees of EPA's Science Advisory Board.

JOYCE PENNER, University of Michigan, Ann Arbor, Michigan.

Joyce Penner is a professor of atmospheric, oceanic, and space sciences at the University of Michigan-Ann Arbor. She earned her Ph.D. in applied mathematics from Harvard University. She is a former division leader of the Global Climate Research Division at the Lawrence Livermore National Laboratory. She is an associate editor for the *Journal of Geophysical Research* and the *Journal of Climate*. She was recently elected to the International Commission on Atmospheric Chemistry and Global Pollution. She is a member of the NRC Committee on Geophysical and Environmental Data and has served on the NRC Committee on Atmospheric Chemistry and the Panel on Aerosol Radiative Forcing and Climate Change.

RICHARD SCHLESINGER, New York University School of Medicine, Tuxedo, New York.

Dr. Richard Schlesinger is professor of environmental medicine at

New York University School of Medicine and is director of the Systemic Toxicology Program. He received his Ph.D. in biology from New York University and has held a number of research and academic appointments at the NYU Medical School since 1969. He was a recipient of a Research Career Development Award from NIEHS and the Kenneth Morgareidge Award from the International Life Sciences Institute for contributions to the field of inhalation toxicology. He is a past-president of the Inhalation Specialty Section of the Society of Toxicology and is recipient of the Career Achievement Award from the Specialty Section. He has served on EPA's Peer Review Panels for the Environmental Toxicology and Human Studies Divisions, and EPA's Expert Panel to Assess Needs for Ozone Research. Dr. Schlesinger is an associate editor of *Toxicology and Applied Pharmacology* and is on the editorial advisory board of *Inhalation Toxicology*. He has served on the NCRP Task Force for Dosimetry Modeling and on the NRC Subcommittee on Pulmonary Toxicology and is currently a member of the NRC Subcommittee on Acute Exposure Guideline Levels.

F RANK S PEIZER , Harvard Medical School, Boston, Massachusetts.

Frank Speizer is professor of medicine at the Harvard Medical School, professor of environmental science at the Harvard School of Public Health, and a senior physician at Brigham and Women's Hospital and Beth Israel Hospital. Dr. Speizer received his M.D. from Stanford University Medical School. He has held a number of academic appointments at the Harvard University Medical School and School of Public Health since 1968. He has served on the Scientific Advisory Board of the American Lung Association/American Thoracic Society, and was a councillor to the Board of the International Society for Environmental Epidemiology. He is currently associate editor for *Environmental Research.* Dr. Speizer was a member of the NRC Committee on an Assessment of a Study of Possible Occupational Health Effects on Ionizing Radiation Among Nuclear Utility Workers and a member of the NRC Subcommittee on Pulmonary Toxicology. He is a member of the Institute of Medicine.

M ARK U TELL , University of Rochester Medical Center, Rochester, New York.

Mark Utell is professor of medicine and environmental medicine at the University of Rochester School of Medicine. Dr. Utell earned his M.D. from Tufts University School of Medicine. He has been at the University of Rochester School of Medicine since 1975, holding a number of positions including director of the Pulmonary/ Critical Care and Occupational Medicine Divisions. Currently, he serves as the acting chairman of medicine. He has served on many national committees, including EPA's Science Advisory Board, EPA's Clean Air Science Advisory Committee, and NASA's Panel on Airborne Particulate Matter in Spacecraft. He is associate editor *of Environmental Research*, and a a recipient of the NIEHS Academic Award in Environmental and Occupational Medicine. Dr. Utell has served on several other NRC committees.

R ONALD H. W HITE , American Lung Association and National Osteoporosis Foundation, Washington, D.C.

Ronald H. White is formerly director of national programs at the American Lung Association and currently an advisor to the association. He is assistant executive director of education, research, and community affairs at the National Osteoporosis Foundation. He earned his Master of Science in environmental studies from Antioch University in 1978. Prior to joining the American Lung Association, he was a senior transportation/air quality planner and then a public participation coordinator with the Tri-State Regional Planning Commission in New York. He has served as a member of the Integrated Human Exposure Committee of the EPA Science Advisory Board, as well as of the EPA Blue Ribbon Panel to review the use of oxygenates in gasoline. Mr. White currently serves on the science advisory committees for several air pollution health effects research projects.

Warren H. White, Washington University, St. Louis, Missouri.

Warren H. White is a senior research associate at Washington University, St. Louis, Missouri. He received his Ph.D. in mathematics from the University of Wisconsin. Dr. White's research focuses on airborne particles and visibility impairment. He served on the review panel for the PM Criteria Document and is a former member of the EPA Clean Air Science Advisory Committee (CASAC) and its PM Moni

toring Subcommittee. He is on the NRC's Committee to Assess the North American Research Strategy for Tropospheric Ozone (NARSTO) Program and is a source of coordination with that committee, whose work is highly relevant to the present committee. He previously served as a member of the NRC Committee on Haze in National Parks and Wilderness Areas.

RONALD WYZGA, Electric Power Research Institute, Palo Alto, California.

Ronald Wyzga is technical executive of the Air Quality, Health, and Risk Area of EPRI (Electric Power Research Institute). He received his A.B. in mathematics from Harvard College, his M.S. in statistics from Florida State University, and his Sc.D. in biostatistics from Harvard School of Public Health. He has held various research and managerial positions within EPRI since 1975, including senior manager of air quality and risk. He has been involved in air quality research on particulate matter, ozone, air toxics, and visibility issues. He is a fellow of the American Statistical Association. He previously served with the Organization for Economic Cooperation and Development in Paris, where he coauthored a book on evaluation of environmental damage. He has served on several committees of the NRC and EPA's Science Advisory Board.

TERRY F. YOSIE, American Chemistry Council, Arlington, Virginia.

Terry Yosie is vice president of strategic communications at American Chemistry Council. He earned his doctorate from the College of Humanities and Social Sciences at Carnegie Mellon University. He has approximately 20 years of professional experience in managing and analyzing the use of scientific information in the setting of environmental standards. From 1978 to 1981, he was the first executive director of the Clean Air Scientific Advisory Committee (CASAC), which is responsible for reviewing the scientific basis of National Ambient Air Quality Standards. He served as director of EPA's Science Advisory Board (1981-1988) and as vice president for health and environment at the American Petroleum Institute (1988-1992). From 1992 to 1999, Dr. Yosie was executive vice president of Ruder Finn, Inc. where he was responsible for the firm's environmental management practice.

He was a member of the NRC Committee to Review the Structure and Performance of the Health Effects Institute and currently serves on the NRC's Board on Environmental Studies and Toxicology. He is also a consultant to EPA's Science Advisory Board.

Appendix B

The Committee's Statement of Task

The committee will assess research priorities, develop a conceptual research plan, and monitor research progress toward improved understanding of the relationships between airborne particulate matter (PM), its various sources, and its effects on public health. The study will focus on PM-related research being conducted, funded, or planned by the U.S. Environmental Protection Agency (EPA) in the context of PM-related research being conducted, funded, or planned by other agencies and organizations in the United States and abroad.

Four reports will be prepared. The first report, required by Congress within four months of project initiation, will identify the most important short-term and longer-term research priorities relevant to evaluating, setting, and implementing primary National Ambient Air Quality Standards (NAAQS) for particulate matter (PM). The second report will expand upon the assessment of research priorities and present conceptual plans for the monitoring and evaluation of research. Subsequent reports at the end of the third and fifth years will evaluate research progress and update the research priorities and plans as warranted.