Research Priorities for Airborne Particulate Matter: I. Immediate Priorities and a Long-Range Research Portfolio

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

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I

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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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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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PREFACE

New epidemiological evidence—largely obtained during the 1990s—renewed concerns about the health effects of particulate matter in ambient (outdoor) air, and ultimately led to new National Ambient Air Quality Standards for particulate matter that were issued in July 1997 by the administrator of the U.S. Environmental Protection Agency (EPA). Even as the standards were promulgated, scientists and policymakers recognized that further research on particulate matter was needed to address key uncertainties.

In the Fiscal 1998 appropriations to EPA, Congress directed the administrator to arrange for an independent study by the National Research Council (NRC) to identify the most important research priorities relevant to setting particulate matter standards, to develop a conceptual plan for particulate-matter research, and, over 5 years, to monitor research progress toward improved understanding of the relationship between particulate matter and public health.

The Committee on Research Priorities for Airborne Particulate Matter was established by the NRC in January 1998 in response to the request from Congress. The committee is charged with producing 4 reports over the 5 years 1998-2002.

This, our first report, offers a conceptual framework for an integrated national program of particulate-matter research, identifies the most-critical research needs linked to key policy-related scientific uncertainties, and describes the optimal short-term and long-term timing

and estimated costs of such research in an integrated research strategy, or "research investment portfolio." The committee was neither asked, nor did it attempt, to evaluate the scientific evidence on particulate matter and health in regard to the 1997 decision of the EPA administrator to issue new particulate-matter standards. The committee's identification of uncertainties and related research needs should not be interpreted as an evaluation of any specific point of evidence related to the new particulate matter standards. Rather, the committee identified uncertainties in the evidence base that should be addressed through a program of research. The findings of this research should strengthen the scientific foundation for policy decisions.

This report was produced in a 2-month period at the beginning of a 5-year study. The committee expects to gain a deepening understanding of research being conducted by EPA and others as it continues to do its work over the next 5 years, and recommendations made in this report will be refined and augmented in subsequent reports.

The committee has been generously assisted by many people, including those who presented valuable information and documents during the committee's public sessions at the National Academy of Sciences in Washington, D.C., on January 20-21 and February 18, 1998: Frank Cushing, U.S. House Appropriations Committee; William Farland, John Vandenberg, and John Bachmann, U.S. Environmental Protection Agency; Sheila Newton, National Institute of Environmental Health Sciences; David Hawkins, Natural Resources Defense Council; Carol Henry, American Petroleum Institute; Jane Warren, Health Effects Institute; Owen Moss, Chemical Industry Institute of Toxicology; George Hidy, University of Alabama; Gregory Wagner, National Institute for Occupational Safety and Health; and Robert Schnatter, American Industrial Health Council. Special thanks are due to Maria Costantini of the Health Effects Institute and John Vandenberg of the Environmental Protection Agency for preparing, at the committee's invitation, the Particulate Matter Research Inventory summary contained in Appendix B of this report.

This report was also improved by a separate group of expert reviewers, chosen by the NRC and anonymous to the committee members until public release of the report. The following persons provided prompt and insightful evaluations of the semifinal draft of this report:

Joan M. Daisey, Arthur B. DuBois, Clark W. Heath, Jr., Carol J. Henry, Morton Lippmann, Peter H. McMurry, Thomas W. Peterson, Robert F. Phalen, Joel Schwartz, John H. Seinfeld, and George T. Wolff.

The committee was ably assisted and deftly guided by staff of the NRC's Board on Environmental Studies and Toxicology, especially James J. Reisa, Kulbir Bakshi, Raymond Wassel, and Jamie Young. These staff members merit special recognition for their thoughtful contributions and extraordinary efforts in producing the report so rapidly, and for the many extra hours they worked to get the job done.

Finally, I would like to express my thanks and admiration to the members of the committee, who deserve to be remembered in NRC folklore for producing this report with extraordinary speed and thoughtfulness within 2 months of the committee's first meeting. Because of the urgent need of Congress and EPA for the committee's first report, the members of the committee, all serving *pro bono*, put in many long hours to prepare this report. The committee meetings lasted from early morning to late into the night, and the committee members followed through between meetings with draft report sections, countless revisions, and conference calls. In accepting service on this committee, every member voluntarily agreed not to seek or accept any air-pollution-related, noncompetitive research contracts or cooperative agreements over $10,000 from EPA during the 5-year duration of this NRC study. Without exception, the committee members have been knowledgeable, thoughtful, hardworking, and generous of their time. In spite of the pace, the committee and staff maintained a high level of cooperation and good humor.

The committee's collective response to our charge reflects our unified view of the potential significance of this report and the great responsibility given to this committee by Congress, EPA, and the NRC.

Jonathan Samet, *Chair*

March 1998

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RESEARCH PRIORITIES FOR AIRBORNE PARTICULATE MATTER: I. IMMEDIATE PRIORITIES AND A LONG-RANGE RESEARCH PORTFOLIO

EXECUTIVE SUMMARY

On July 18, 1997, the administrator of the U.S. Environmental Protection Agency (EPA) issued new National Ambient Air Quality Standards (NAAQS) for airborne particles smaller than 2.5 μm in diameter, called $PM_{2.5}$. Under the Clean Air Act, the administrator is required to set and to review at least every 5 years the health-based (primary) standards for several major air pollutants (so-called "criteria" pollutants), including particulate matter (PM). The standards are required to ensure the protection of public health, including potentially susceptible subpopulations, with "an adequate margin of safety." The process for setting the standards requires EPA to make both scientific assessments and policy decisions.

Airborne particulate matter is a generic term for a broad class of materials of varying chemical composition and sizes that are transported in the air as discrete solid particles or liquid droplets. Ambient (outdoor) particles originate from diverse natural processes and human activities, such as forest fires, wind erosion, agricultural practices, fossil fuel combustion, industrial manufacturing, and construction of buildings and roads. The particles can be emitted directly from such sources or formed in the atmosphere from gaseous precursors such as sulfur dioxide or nitrogen oxides. The particles can contain heavy metals, acids, biological or biogenic material, and a great variety of other organic and inorganic materials.

The new $PM_{2.5}$ standards were developed by EPA largely on the basis of evidence from epidemiological studies that found relatively consistent

associations between outdoor particulate-matter concentrations and various adverse health effects, including premature mortality, exacerbation of asthma and other respiratory-tract diseases, and decreased lung function. The biological basis of most of the associations is essentially unknown (at the ambient particulate levels at which the associations were observed). There is a great deal of uncertainty about the implications of the findings for risk management, due to the limited scientific information about the specific types of particles that might cause adverse health effects, the contributions of particles of outdoor origin to actual human exposures, the toxicological mechanisms by which the particles might cause adverse health effects, and other important questions. These questions are not presented here as a rationale for abandoning efforts to control public exposures to fine particulate matter and other pollutants, but they do indicate the critical need for better scientific knowledge to guide such efforts.

EPA has estimated that implementation of the new $PM_{2.5}$ standards will prevent approximately 15,000 premature deaths per year in the United States. By law, EPA cannot consider compliance costs when setting these standards. EPA has announced, along with its timetable for implementing the new $PM_{2.5}$ standards, that it contemplates no actual regulatory emission-control requirements to be implemented until well after the next scheduled review of the particulate-matter standards in the year 2002. In the meantime, Congress has mandated and has begun to fund a major program of research to reduce the key scientific uncertainties. In EPA's Fiscal 1998 appropriations, Congress provided $49.6 million for particulate-matter research—nearly twice the amount requested by EPA. Congress also directed the EPA administrator to arrange for this independent study by the National Research Council (NRC) to identify the most important research priorities relevant to setting NAAQS for particulate matter, to develop a conceptual plan for particulate-matter research, and, over the next 5 years, to monitor and evaluate research progress toward improved understanding of the relationship between particulate matter and its effects on public health.

In response to the request from Congress, the Committee on Research Priorities for Airborne Particulate Matter was established in

January 1998 by the National Research Council, the principal operating agency of the National Academy of Sciences and the National Academy of Engineering. The committee (see Appendix A for biographical information) consists of 20 experts, chosen by the NRC, in epidemiology, medicine, pulmonary physiology, toxicology, public health, exposure assessment, atmospheric chemistry and transport, air quality modeling, air monitoring techniques, biostatistics, risk assessment, research management, and regulatory policy. Its members come from universities and other organizations and perform this public service without financial compensation through the NRC. In forming the committee, the NRC deliberately sought a balance of candidates with differing views on relevant major issues. Committee members were asked to serve as individual experts, not as representatives of any organization.

The committee is charged to produce 4 reports between 1998 and 2002. To date, the committee has held two working meetings at the National Academy of Sciences in Washington, D.C., on January 20-21 and February 18-19, 1998. Those meetings included public sessions at which the committee heard presentations from representatives of the U.S. Environmental Protection Agency (EPA), EPA's Clean Air Scientific Advisory Committee (CASAC), the National Institute of Environmental Health Sciences (NIEHS), National Institute for Occupational Safety and Health (NIOSH), North American Research Strategy for Tropospheric Ozone (NARSTO), Health Effects Institute (HEI), Lovelace Respiratory Research Institute (LRRI), American Petroleum Institute (API), Chemical Industry Institute of Toxicology (CIIT), Electric Power Research Institute (EPRI), American Industrial Health Council (AIHC), and Natural Resources Defense Council (NRDC).

This report, the first of the 4 planned reports from this NRC committee, offers a conceptual framework for an integrated national program of particulate-matter research, identifies the 10 most critical research needs linked to key policy-related scientific uncertainties, and describes the recommended short-term and long-term timing and estimated costs of such research in an integrated research strategy, or "research investment portfolio." The committee has made no attempt to evaluate the adequacy of the current scientific basis for EPA's new $PM_{2.5}$ standards, and no evaluation should be inferred, because the process of setting

such standards also involves legal requirements and policy choices that the present committee was neither charged nor constituted to address.

The committee organized its evaluation of particulate-matter scientific uncertainties and research needs according to a simple, coherent, science-based conceptual framework (see Chapter 3), whose components are generally familiar to EPA and the environmental research community. The framework has 5 main components:

Sources—Outdoor sources of particulate matter (or gaseous precursors) that can adversely affect public health. Sources include motor vehicles; fossil-fueled electric power plants; industrial facilities; agricultural practices, consumer products; other human sources; and natural processes, such as forest fires or wind erosion. This element of the framework includes factors determining the release characteristics, dispersal, and transport of emissions that lead to atmospheric contamination.

Ambient Indicators—The mass concentration or other measures of indicators such as PM_{10} (airborne particles smaller than 10 μm diameter) or $PM_{2.5}$ in ambient air. Data for the indicators are collected at fixed outdoor monitoring sites to determine regulatory attainment of the NAAQS, or in some health studies, to represent particulate-matter exposure in a given area.

Exposure—The concentration of particulate-matter indicator actually coming into contact with an individual over a specified period. Actual exposure to humans is determined by ambient air concentrations, contributions from indoor sources, and human time-activity patterns. The relevant point of contact is the breathing zone of the individual. For EPA, the aspect of exposure most relevant to regulatory policy is the portion of total exposure that is attributable to outdoor air.

Dose—The amount and specific types of toxicants deposited in various parts of the respiratory tract and other sites within the body over a specified period. The dose of specific toxicants received by an individual is affected by factors such as retention and clearance of PM (or specific constituents of PM) from target tissues in the lung and respiratory tract. The dose delivered to specific tissues might result in injury and altered performance of repair mechanisms.

Response—Changes in specific human health parameters attributable to tissue doses resulting from inhaled particulate matter. These biological responses can be expressed in terms of molecular or cellular changes in the lung or other tissues, overall tissue damage, or ultimately, clinical signs of toxicity, such as illness or premature death.

In evaluating the key scientific uncertainties and assigning priorities to research needs on particulate matter, the committee used both strategic and practical criteria (see Chapter 3) organized in three categories: scientific value, the value of information for decisionmaking, and feasibility and timing considerations.

The committee judged the following 10 research topics (see Chapter 4) to warrant the highest priority. The order in which these research topics are presented does not represent relative ranking or sequence of the research topics recommended by the committee. All 10 topics met the committee's ranking criteria, and they are highly interdependent and interactive within the committee's research portfolio.

- Investigate quantitative relationships between particulate-matter concentrations measured at stationary outdoor monitoring sites and the actual breathing-zone exposures of individuals to particulate matter and gaseous copollutants, taking ambient outdoor and indoor pollutant sources and human time-activity patterns into account, especially for potentially susceptible subpopulations.

- Investigate exposures to the most biologically important constituents and characteristics of particulate matter that might adversely affect health, especially for potentially susceptible subpopulations.
- Develop advanced mathematical, modeling, and monitoring tools to represent the relationships between specific sources of particulate matter and human exposures.
- Apply modeling and other analytical tools to link sources of toxicologically important constituents and characteristics of particulate matter to exposed individuals and populations.
- Assess through toxicological and epidemiological studies the most biologically important physical and chemical characteristics and constituents of particulate matter that produce adverse health effects.
- Investigate the deposition patterns and fate of particles in the respiratory tract of individuals potentially susceptible to particulate matter.
- Investigate through toxicological and epidemiological studies the interactions between particulate matter and gaseous copollutants in producing harmful short-term and long-term exposures and resulting adverse health effects.
- Identify the human subpopulations that are potentially most susceptible to adverse health effects from particulate-matter exposures (e.g., children, the elderly, and people with chronic respiratory diseases, cardiopulmonary diseases, or compromised immune systems).
- Investigate the toxicological mechanisms by which particulate matter produces mortality and acute or chronic morbidity, using laboratory-animal models, human clinical studies, and *in vitro* test systems.

- Develop and apply advanced methods for statistical analysis of epidemiological studies and for dealing with measurement and misclassification errors in estimating adverse health effects of particulate matter.

For each of these research priorities, the committee presents in Chapter 4 of this report a description of the recommended research, comments on the potential scientific value of the research, comments on the potential value for decisionmaking, guidance as to feasibility and timing, and rough but informed collective-judgment cost estimates for the recommended research. In Chapter 5, the committee summarizes the above research recommendations in an integrated strategic plan (or research investment portfolio), designed for optimal sequencing of a goal-oriented, multidisciplinary research program on particulate matter. The portfolio is designed to maximize the growth of critical scientific knowledge about particulate matter expeditiously and cost-effectively through interactive components and iterative stages, providing a continuing stream of scientific evidence on continuously advancing topics. It spans 13 years, from 1998 to 2010—the estimated closure date for scientific input to EPA's anticipated 2012 review of particulate-matter standards. It is designed for the difficult goal of reconciling research and regulatory timetables to emphasize both early and longer-term research results to address key uncertainties about particulate matter and its health effects.

This portfolio, if aggressively and properly implemented by EPA, should result in substantial new information for the next scheduled EPA review of the particulate-matter standards in the year 2002. By that time, critical information would be expected regarding the most biologically important components and characteristics of particulate matter, the toxicological mechanisms through which they act, and how well the data from ambient air monitors represent the actual exposure of people to particulate matter, especially for the most potentially susceptible individuals. Later in the plan, the portfolio emphasizes epidemiological studies that will use the results of the earlier research activities to identify potentially susceptible human subpopulations, assess the effects of particulate-matter exposures on such subpopulations, and provide surveillance of the public-health consequences of implementing

the new $PM_{2.5}$ standards. The portfolio also places emphasis on research into combined exposures to particulate matter and gaseous copollutants. The development of advanced methods and models needed for research and assessment is also emphasized.

In Chapter 6, the committee compares its research recommendations with EPA's published statements of particulate-matter research needs and research-program strategy, and with EPA's current research activities and plans. Although the committee concludes at this early stage of its 5-year study that EPA's current and planned research activities generally appear to be reasonable and potentially useful, the committee disagrees with the early timing and funding of some elements of EPA's research plans, based on the briefings and documentation thus far provided by EPA staff. Most notably, the committee concludes that EPA should immediately devote more intramural as well as extramural resources to investigating the relationships between fixed-site outdoor monitoring data and actual human exposures to ambient particulate matter, and to identifying the most biologically important constituents and characteristics of particulate matter through toxicological studies. EPA's current plans appear to focus only about 4% of its intramural research resources on investigating ambient-versus personal-exposure relationships, and only about 3% of EPA's entire particulate-matter research budget appears to be focused on biologically important components of the particulate-matter mixture. This is crucially inadequate.

If the current mix of scientific expertise among the federal career staff of EPA's intramural laboratories is unable to respond expeditiously to this committee's recommendations, then EPA should look into the possibility of conducting this work extramurally. Moreover, because the competitively selected, university-based particulate-matter research centers requested by Congress will require time to develop before producing results, the committee recommends that some centers be initiated in 1998, instead of 1999 as currently planned. The competitively selected centers should be separate and in addition to the research funded through competitive, investigator-initiated research grants and cooperative agreements, because their role as multidisciplinary centers for integrated research should complement the more targeted research projects.

Independent of the research program, EPA's air regulatory office is initiating an extensive $PM_{2.5}$ NAAQS-attainment monitoring program to obtain data on $PM_{2.5}$ levels across the United States. The committee considered EPA's plans for this regulatory program and for the allocation of research resources to the development of new monitoring techniques (including new, more-sophisticated monitoring platforms). The committee recognizes that substantial resources must be applied to ambient monitoring to ascertain attainment of the standards in various geographic areas, but it is concerned that the monitoring program is moving forward rapidly with too narrow a focus on $PM_{2.5}$. The committee is concerned about the scientific value of the data to be collected in these efforts if such monitoring is fully planned and implemented before some of the immediate research priorities are addressed and data gaps are filled. Moreover, as a secondary but critical goal, such a monitoring program should also be designed to support relevant health-effects, exposure, and atmospheric-modeling research efforts, or else the costs of some important research will increase greatly because of the need for additional monitoring.

EPA cannot assume that the implementation of the national $PM_{2.5}$ monitoring network will provide useful data for improving research or risk assessments for particulate matter. Current plans (e.g., speciation of particulate matter at least every sixth day) are inadequate for this purpose. EPA's monitoring plans will undoubtedly provide substantial amounts of data useful for determining attainment of new $PM_{2.5}$ standards in various locations. However, these data will only be useful in research if monitoring-system design and site location lead to population-exposure measures of sufficient biological relevance and accuracy. Without this, the State Implementation Plans may miss important targets for control.

Based upon theoretical considerations, the Federal Reference Method (FRM) sampler to be used by EPA is expected to lose volatile material (e.g., some nitrates and organics) from particle samples in quantities that are likely to depend upon location and season. Ongoing experiments are attempting to quantify the extent of this loss, and some data showing the bias toward undersampling of organics and nitrates have been presented at several conferences during the past 12 months.

If those losses turn out to be substantial, then using the FRM would amount to quantifying only a fraction of the outdoor concentration, and that fraction would vary geographically and seasonally. Alternative technologies that overcome some of these biases are available and could instead be adopted.

EPA's planned $PM_{2.5}$ monitoring network appears to place great emphasis on site zones intended to represent the outdoor exposure of large communities. Greater use of continuous (hourly) monitors would help determine the times of day and the exposures of people who are commuting, working, or exercising outdoors. Such monitoring would facilitate time-series epidemiological studies. More chemical characterization of particulate matter would help to enable testing of more specific indicators than $PM_{2.5}$ mass alone.

The committee recommends that EPA re-evaluate its current plans for the $PM_{2.5}$ monitoring program in light of this report. The committee recommends that EPA consider more fully the possibility that future research results might indicate that the expensive monitoring program is not measuring the most biologically important aspects of particulate matter.

The plans for this program (e.g., number and location of monitors and specific objectives and operating conditions) should be thoroughly and independently peer-reviewed at an early date, while the opportunity still exists for such review to influence the monitoring-network design and operation. Changes could then be made to increase the scientific utility of EPA's monitoring data, while still meeting the need for assessing regulatory attainment of particulate-matter standards at selected sites. Included in the EPA monitoring program are plans for several "super" monitoring sites where more extensive monitoring efforts will take place. At these sites, ambient-concentration data will be collected for gaseous pollutants, as well as for several size and chemical fractions of particulate matter. The costs of these monitoring efforts will be considerable, but their utility for health-effects studies has not been adequately considered to date. EPA has proposed to spend more funds on the $PM_{2.5}$ monitoring network than on all particulate-matter-research activities combined. Therefore, it is essential to leverage both regulatory monitoring and research efforts together to

make the most effective use of resources to improve the scientific basis for decisionmaking.

Chapter 7 presents additional guidance for implementation of the committee's recommended research program. It discusses the need for a comprehensive, continually updated, on-line inventory of federal and nonfederal particulate-matter research activities; periodic reassessments of the focus, effectiveness, and accountability of ongoing research activities; a clear strategy for integrating extramural contributions with EPA's intramural research activities; and sustained funding for particulate-matter research.

The committee is encouraged by the leadership shown by Congress when it provided Fiscal 1998 funds for particulate-matter research well above the amounts requested by EPA, and recommends support of the highest-priority particulate-matter research at roughly similar levels for the next decade and beyond. Specifically, as detailed in Chapters 4 and 5, the committee estimates that the highest-priority particulate-matter research recommendations presented in this report will require the following funding over the next 13 years:

Fiscal Year	Estimated Cost ($ million, rounded)
1998	40
1999	46
2000	51
2001	57
2002	55
2003	46
2004	31
2005	31
2006	19
2007	19
2008	19
2009	15
2010	15

These cost estimates are not intended to represent the recommended total particulate-matter research budget for EPA or the nation.

Instead, they represent the estimated costs of the committee's recommended 10 highest-priority particulate-matter-research activities. Other particulate-matter-related research beyond that recommended in this report can be useful or even necessary. Examples of such additional research are the completion of worthwhile projects already under way, research that meets various technical information requirements of regulatory program offices, and the administrative and infrastructure costs of creating and operating the particulate-matter research centers mandated by Congress. These were not included in the committee's cost estimates.

The committee has not yet had time to evaluate in detail all of EPA's particulate-matter research plans and proposed budget allocations at this early stage of the 5-year study. More detailed assessments will be presented in the committee's second report in December 1998. The committee's cost estimates are probably more accurate for the early years than for later years in the portfolio plan, because results of early research will undoubtedly influence substantially the direction and costs of research in the later years.

The highest-priority research activities recommended in this report are critical to determining actual exposures of human subpopulations most susceptible to harm from the most hazardous constituents of particulate matter. Such research will be an investment in public health and a means to ensure that resources spent in the future on control technology and regulatory compliance will have a reasonable probability of success. The committee is convinced that success is achievable and that the research recommended in this report can help achieve better public-health protection and more effective regulatory efforts.

The potential cost of ignorance is by no means limited to wasting considerable dollars and effort, but, more important, failing to protect people from preventable harmful exposures. Failure to plan, implement, and sustain an integrated program of the highest-priority research activities could have undesirable consequences. If particular biologically important constitutents or characteristics of particulate matter exist and are not adequately identified, then fixed-site or personal monitors could fail to indicate the most serious particulate-matter risks to public health. Epidemiological and experimental studies

that rely upon such information could be impeded or misdirected. In addition, sources of the most toxic components of particulate matter could be misidentified, leading to ineffective air-pollution control strategies.

The research costs estimated by the committee can be viewed as investments in the scientific foundation upon which all particulate-matter regulatory activities—planning, implementation, monitoring, compliance, and enforcement—of EPA, state and local governments, and the private sector will be built. A solid scientific foundation can help ensure that all of these other investments will yield a sound return. An inadequate scientific foundation will lead to continued uncertainty, contentious debates, and potentially unwise regulatory efforts that fail to minimize the risks of particulate matter to public health.

The committee's second report is scheduled for completion in December 1998. It is expected to include more detailed assessments of the ongoing and planned particulate-matter research activities of EPA and other organizations, as well as expanded descriptions of the committee's research recommendations and long-range strategy for improving the scientific basis for particulate-matter decisionmaking. The committee's third and fourth reports, scheduled for completion in December 2000 and December 2002, respectively, will report upon the progress of particulate-matter-research activities of EPA and other agencies and organizations within and outside the United States.

1

INTRODUCTION

Section 109 of the Clean Air Act requires the administrator of the U.S. Environmental Protection Agency (EPA) to set National Ambient Air Quality Standards (NAAQS) for particulate matter (PM) and five other widespread air pollutants, the so-called "criteria" pollutants (carbon monoxide, ozone, sulfur dioxide, nitrogen dioxide, and lead). The primary NAAQS for each criteria pollutant must be set to protect public health "with an adequate margin of safety" for the general public and potentially susceptible subpopulations. That requires EPA to make both scientific assessments and policy decisions. EPA is further required to review periodically (at least every 5 years) the primary NAAQS for each pollutant and the scientific criteria upon which they are based, and to revise the standards as warranted.

Airborne PM is a generic term applied to a broad class of particles ranging in size from molecular clusters less than 0.001 μm to particles of more than 50 μm in diameter. The particles are composed of chemically diverse materials. They are transported in the air as solid particles or liquid droplets. Outdoor particles originate from varied natural processes and human activities, including forest fires, wind erosion, agricultural practices, fossil-fuel combustion, industrial manufacturing, and the construction and use of buildings and roads. The particles can be emitted directly from the sources or formed in the atmosphere from gaseous precursors, such as sulfur dioxide, nitrogen oxides, and hydrocarbon vapors. The variety of sources of particles and gases and the

transformations of particulate matter in the atmosphere produce airborne particles of different sizes and chemical composition. For example, the particles can contain heavy metals, acids, biological or biogenic material, or other organic and inorganic compounds.

Although particulate matter is regulated as a single pollutant by EPA, it consists of a mixture of materials that are far more complex than regulated gaseous pollutants, such as ozone or carbon monoxide. Particles that can be inhaled into the respiratory tract span a range of aerodynamic diameters from molecular clusters as small as 0.001 μm up to larger particles of 10 μm or more in diameter. The numbers of particles and their chemical composition can vary within specific particle size fractions from location to location and over time, depending on the types of source emissions and atmospheric conditions.

Concern about airborne particulate matter in recent years has been driven largely by epidemiological studies that have reported relatively consistent associations between outdoor particulate-matter levels and adverse health effects. However, assessing the specific health risks resulting from exposures to airborne particulate matter, and distinguishing these effects from those produced by gaseous copollutants, involves substantial scientific uncertainty about the influence of copollutants and weather, about whether some particulate-matter fractions (size or chemical) might be more highly associated with health risks, and about the nature of dose-response relationships between particulate matter and health. Many previous analyses have not considered the simultaneous presence of all of the gaseous criteria air pollutants (sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone) and potentially important weather factors in estimating the association between particulate matter and health, and the treatment of such factors has not been uniform across previous studies. It will be important to understand how these factors influence estimates of particulate-matter risks to health and to learn whether the relationships are consistent across study areas. There is limited information about the physical, chemical, or biological properties of particles that might cause the observed adverse health effects, and information is also limited on the mechanisms of toxicity and the locations, activities, and intensity of actual human exposures to such particles. To date, researchers have

not obtained a sufficient picture associating specific toxic constituents of airborne particles with health indicators, such as respiratory and cardiovascular ailments, nor have they found definitive toxicological evidence to suggest plausible biological mechanisms to explain the toxic effects attributed to particulate matter in epidemiological studies (Vedal 1997; EPA 1996a) or to determine the extent to which populations at risk are exposed to these constituents.

Without knowing the most toxic particle constituents, the toxicological mechanisms through which they act, or the actual exposures experienced by people, a nationwide control strategy might reduce some kinds of particulate-matter exposures while failing to protect public health adequately, if the types of particulate matter 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 particulate matter 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 particulate matter concentrations and health outcomes. Linear and nonlinear models both need to be considered, and the role of measurement error on estimated relationships needs to be investigated. These uncertainties are not presented here as a rationale for abandoning current or future efforts to control public exposures to particulate matter, but they do indicate the critical need for better scientific knowledge to guide such efforts.

The first NAAQS for particulate matter was set in 1971; it targeted total suspended particulate (TSP) mass per unit volume of air (Table 1.1), without regard to the chemical composition of the particles. In 1987, EPA revised the standard, changing the indicator from TSP to particles of 10 μm aerodynamic diameter or less, called PM_{10}.[1] PM_{10} was considered to be more important than TSP for protecting public

[1] PM_{10} refers to particulate mass 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. TSP was defined as the particulate 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.

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

Past Actions	
1971	EPA issues TSP NAAQS.
1979-1987	Review of criteria and standards
1987	EPA issues PM_{10} NAAQS
1994-1997	Review of criteria and standards
1997	EPA issues $PM_{2.5}$ and revised PM10 NAAQS
Planned Review and Implementation of $PM_{2.5}$ NAAQS	
1999	EPA will designate areas as "unclassifiable" for $PM_{2.5}$.
1998-2000	$PM_{2.5}$ monitors to be in place nationwide.
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 the $PM_{2.5}$ standard.
2012-2017	States will have up to 10 years to meet $PM_{2.5}$ standards plus two 1-year extensions.

health because it targets particles more likely to reach the bronchial tree and the gas exchange regions of the lung. (Figure 1.1 shows the distributions of airborne particle diameters as described by various metrics: particle number, particle surface area, and particle volume (or mass). The PM_{10} standard, like the TSP standard, was based on mass without regard to chemical composition.

The most recent particulate-matter criteria document (EPA 1996a) and the related EPA regulatory options document (EPA 1996b) were completed in 1996. They were reviewed by EPA's Clean Air Act Scientific Advisory Committee (CASAC). CASAC's evaluations (see Chapter 2) of the two documents were summarized in "closure" letters to the EPA administrator (CASAC 1996a, 1996b, 1996c).

In July 1997, the EPA administrator issued new particulate-matter standards that targeted $PM_{2.5}$ (also called fine particles) for the first time, again without regard to chemical composition (EPA 1997b). Two standards for $PM_{2.5}$ were promulgated: an annual standard of 15 $\mu g/m^3$ in air, with attainment based on the 3-year average of annual arithmetic mean $PM_{2.5}$ concentrations from single or multiple community-oriented monitors, and a 24-hour standard of 65 $\mu g/m^3$, with attainment based on the 3-year average of the 98th percentile of 24-hour $PM_{2.5}$ concentrations at each population-oriented monitoring site within an area. The previous 24-hour PM_{10} standard (150 $\mu g/m^3$) was revised to be based on the 99th percentile of 24-hour PM_{10} concentrations at each monitoring site within an area, while the averaging time and form of the annual PM_{10} standard (50 $\mu g/m^3$) was retained.

The new $PM_{2.5}$ standards were developed by EPA largely on the basis of epidemiological studies that found relatively consistent but poorly understood associations between ambient particulate-matter concentrations and various adverse health effects, including premature (excess) mortality, exacerbation of asthma and other respiratory-tract diseases, decreased lung function, and increased hospitalization for cardiopulmonary diseases. EPA has estimated that compliance with the new $PM_{2.5}$ standards will prevent approximately 15,000 premature deaths per year in the United States (EPA 1997a). The new standards have aroused substantial public debate, due largely to the current lack of knowledge of toxicological mechanisms and actual human exposures

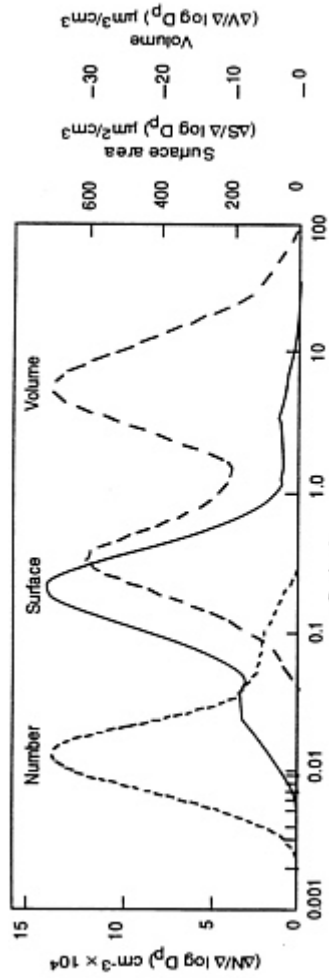

FIGURE 1.1 A hypothetical distribution of airborne particle diameters as described by particle number, particle surface area, and particle volume (or mass). D_p refers to the diameter of a particle. Particles with diameters less than approximately 0.1 μm are referred to as nucleation mode particles. Accumulation mode particles are those particles with diameters between the approximate range of 0.1 and 1.0 μm. Coarse particles have diameters greater than about 1 μm. Source: McClellan and Miller (1997) as adapted from Whitby (1978).

to outdoor $PM_{2.5}$, as well as uncertainties about the magnitude of estimated potential risk reduction and the potential costs of complying with the new standards. (By law, EPA cannot consider compliance and other costs when setting primary, health-based NAAQS.)

EPA has stated that the new particulate-matter standards will have no actual regulatory impact until well after the next scheduled review of the particulate-matter NAAQS, which is due to occur in July 2002 (see Table 1.1). Many experts believe that substantially more scientific information is needed to assess the standards, and Congress has directed and funded a major program of research. In EPA's Fiscal 1998 appropriations, Congress provided $49.6 million for particulate-matter research, nearly twice the EPA request, and substantial funding over the next several years is generally believed to be needed to reduce current scientific uncertainties. Congress also directed the EPA administrator to arrange for an independent study (the present study) by the National Research Council (NRC) to identify the most important research priorities relevant to setting and reviewing NAAQS for particulate matter, to develop a conceptual plan for particulate-matter research, and to monitor and report over 5 years on research progress toward improved understanding of the relationship between particulate matter and its effects upon public health.

In response to the request from Congress, the Committee on Research Priorities for Airborne Particulate Matter, which prepared this report, was established by the NRC in January 1998. The committee consists of experts, chosen by the NRC, in epidemiology, medicine, pulmonary physiology, toxicology, public health, exposure assessment, atmospheric chemistry and modeling, emission sources, air-monitoring techniques, biostatistics, risk assessment, research management, and regulatory policy. Its members come from universities and other organizations and serve *pro bono*. In forming the committee, the NRC deliberately sought a balance of candidates with differing views on the major issues. Committee members were asked to serve as individual experts, not as representatives of any organization.

The committee is charged to produce four reports over the 5 years 1998-2002. This is the committee's first report. To date, the committee has held two working meetings at the National Academy of Sciences

in Washington, D.C., on January 20-21 and February 18-19, 1998. Those meetings included public sessions at which the committee heard presentations from representatives of EPA, EPA's CASAC, the National Institute of Environmental Health Sciences (NIEHS), the National Institute for Occupational Safety and Health (NIOSH), the North American Research Strategy for Tropospheric Ozone (NARSTO), Health Effects Institute (HEI), the Lovelace Respiratory Research Institute (LRRI), the American Petroleum Institute (API), the Chemical Industry Institute of Toxicology (CIIT), the Electric Power Research Institute (EPRI), the American Industrial Health Council (AIHC), and the National Resources Defense Council (NRDC). In addition, the committee received valuable documents and other written material from most of the presenters.

In developing its research priorities, the committee has considered particulate matter not in isolation, but in the context of the mixture of air pollutants of which particulate matter is a part. Other air pollutants are also of public-health concern; they might have effects similar to particulate matter or might interact with it to cause adverse health effects. Although the principal focus of this report is on particulate matter, the committee also considered research that can simultaneously and cost-effectively address the health effects of the full mixture of air pollutants.

Faced with the challenge of reconciling research planning and regulatory decision-making schedules, the committee has developed an approach that articulates a long-range research strategy for particulate matter over the next 13 years and also seeks to deliver timely results on important policy-related scientific questions as early as possible. The committee recognizes that the regulatory timetable places difficult demands on the planning and implementation of research. However, by careful prioritization of research activities during the period leading up to 2002, the committee believes that additional scientific information will be forthcoming to enhance the scientific basis for decision-making in the next scheduled review of the particulate-matter NAAQS, subsequent reviews of particulate-matter standards by EPA, and the development of particulate-matter control strategies.

This report offers a general framework for a program of highest-priority research on particulate matter. It presents a conceptual framework

and criteria for determinating research priorities. It describes 10 recommended research topics linked to key scientific policy-relevant uncertainties and integrates the recommended research activities into a 13-year research investment portfolio. The estimated cost and timing of the recommended research activities are also presented in the committee's recommended research portfolio.

During the course of its review, the committee identified several key uncertainties and limitations in existing scientific information. No attempt was made to evaluate the scientific adequacy of existing particulate-matter standards, and none should be inferred. It is important to recognize that legal requirements and policy choices are important factors in setting such standards, and this committee was not constituted or charged to address legal and policy matters.

Given the potential magnitude of public-health consequences associated with exposures to particulate matter and the potential economic costs of implementing the new $PM_{2.5}$ standards, it is essential that policymakers and the American public have confidence that sufficient, high-quality scientific and technical information is available to reduce the risks effectively and efficiently. Proceeding in the absence of such information could lead policymakers to focus on standards and controls for particulate matter that are not of the highest public-health priority.

Failure to plan, implement, and sustain an integrated program of the highest-priority research activities could have undesirable consequences. If the most biologically important toxic components of particulate matter are not adequately identified, then fixed-site or personal monitors might fail to indicate the most serious particulate-matter risks to public health. Epidemiological and experimental studies that rely upon such information could be impeded, or worse, be misdirected. In addition, sources of emissions of the most toxic portions of particulate matter or their precursors could be misidentified, leading to ineffective air-pollution-control strategies.

The highest-priority research activities recommended in this report are critical to determining actual exposures to human subpopulations at the greatest risk of harm from the most hazardous components of particulate matter. The potential cost of ignorance is by no means

limited to wasting considerable dollars and effort, but, more important, failing to protect people from preventable public-health risks. Such research will be an investment in public health and a means to ensure that resources spent on control technology and regulatory compliance will have a reasonable probability of success. Given the extensive potential consequences of implementing the particulate-matter standards, only both kinds of success are acceptable. The committee is convinced that such success is achievable and that the recommended research can help guide public-health protection and cost-effective regulatory decisions.

It is also important that the scientific community speak with a clear voice in communicating research priorities for airborne particulate matter. Nonscientists in Congress, the Executive Branch, and the American public deserve to have a clear explanation of the state of scientific knowledge and uncertainty regarding particulate matter, what research is needed, and how more research could make a difference in guiding public-health decisions. Scientists have a responsibility to identify opportunities for clarifying the facts underlying important public-policy debates and to demonstrate that science can help resolve important issues that concern the public.

Chapter 2 of this report summarizes previous reviews of particulate-matter research needs and activities by EPA and other organizations. Chapter 3 presents the committee's conceptual framework and decision criteria for developing its research recommendations. The committee's highest-priority research recommendations are presented in Chapter 4. The recommended phasing and estimated costs of these research activities are integrated into a research investment portfolio in Chapter 5. In Chapter 6, the research priorities and strategies recommended by the committee are compared with those previously identified by EPA. Chapter 7 discusses additional aspects of implementing the committee's recommended research strategy.

2

PREVIOUS REVIEWS OF PARTICULATE-MATTER RESEARCH NEEDS

Unanswered questions about the relationships between airborne particulate matter and public health have stimulated several organizations, including EPA, to assess and recommend relevant research needs. The approaches taken in these efforts have varied among the groups, as has the basis for assigning priorities. Because the present NRC committee faced a similar challenge, several approaches taken previously by others are summarized in this chapter.

REPORT OF THE PARK CITY WORKSHOP ON PARTICULATE-MATTER RESEARCH STRATEGIES

A workshop sponsored by the U.S. Centers for Disease Control and Prevention was held in Park City, Utah, on April 29-30, 1996, in conjunction with the Second Colloquium on Particulate Air Pollution and Health, held May 1-3, 1996. The main objective of the workshop was to determine research needs related to health effects of the complex mixtures of particles and vapors commonly encountered in air. The starting point for identifying critical gaps and uncertainties was to synthesize the current knowledge of the nature, extent, and causes of health effects associated with general population exposures to such mixtures.

A published summary of the workshop (Lippmann et al. 1996) identified the following areas of research to be most useful with respect to health risk assessment for particulate matter:

- Study accumulation-mode aerosol with the objective of disentangling the roles of its chemical constituents, as well as their interactive effects, with each other and with coexisting gaseous criteria pollutants.
- Study the health effects of coarse-mode PM_{10} and the ultrafine particles in nuclei-mode aerosol.
- Study sensitive human subpopulations—infants, the elderly, and people with pre-existing cardiopulmonary diseases.
- Further develop and validate animal models for sensitive human groups. Validated animal models are needed for target (sensitive) human populations to investigate:

- the roles of specific constituents of particulate-matter mixtures
- the roles of exposure concentrations and durations of responses
- the risk factors that predispose individuals to be responsive to particulate-matter exposures
- physiological, biochemical, molecular, and pathological correlates of mortality, tissue and organ damage, and chronic disease development

EPA'S PARTICULATE-MATTER RESEARCH-NEEDS DOCUMENT

As part of each periodic review of NAAQS under the Clean Air Act, EPA prepares a so-called "criteria" document intended to describe the state of relevant scientific knowledge and important uncertainties in the existing evidence. In a separate document, EPA also identifies research needed to improve the scientific bases for future reviews of the NAAQS. Therefore, in 1996, when EPA prepared the revised criteria

document on particulate matter (EPA 1996a), it also prepared a draft research-needs document, *Particulate Matter Research Needs for Human Health Risk Assessment* (EPA 1996d). That document was reviewed by several outside groups and revised (EPA 1998) in response to comments obtained from EPA workshops held in 1996 and 1997 and from CASAC (summarized below). EPA's research-needs document does not present a research plan or program. Instead, its primary purpose is to provide guidance to EPA's national research laboratories and other organizations that undertake and support research as they develop and justify particulate-matter research plans and programs.

The particulate-matter-related research needs identified by EPA included research on health effects, toxicology, atmospheric science, monitoring, modeling, and human exposure. The research-needs document does not address research related to implementing particulate-matter air-quality standards, determining compliance, or determining effective control techniques to attain such standards.

The document identifies research needs to improve human-health risk assessment for particulate matter and to reduce uncertainties associated with particulate-matter standards. It emphasizes that the uncertainties associated with establishing standards for particulate matter are more difficult than those associated with standard-setting for other criteria pollutants, all of which target single pollutants. The key uncertainties identified by EPA are listed in Table 2.1. The research needs document recommends highest-priority needs and second-level (high) priority needs. The specific links between uncertainties and research needs generally are not made explicit in the EPA document.

EPA'S PARTICULATE-MATTER RESEARCH-STRATEGY DOCUMENT

Particulate Matter Research Program Strategy (EPA 1996c) described EPA's research strategy for particulate matter in the areas of health effects, exposure, risk assessment, and risk management. The document was intended to guide future particulate-matter research to be performed or funded by EPA's Office of Research and Development

TABLE 2.1 Uncertainties and Highest-Priority Research Needs Identified by EPA for Establishing Standards for Airborne Particulate Matter[a]

Key Uncertainties	Highest-Priority Research Needs	Second Highest-Priority Research Needs
• Lack of demonstrated mechanisms to explain mortality and morbidity associated with particulate matter at ambient levels • Measurement error and the inadequacies of ambient monitors • Particulate-matter population exposure estimates introduced by using central-site monitoring data • Confounding of particulate-matter effects by other pollutants • Specific components or physical properties of fine particles that are associated with the reported effects of particulate matter • Shape of the ambient concentration-response relationship • Unaddressed confounders and methodological uncertainties inherent in epidemiological studies of long-term particulate-matter exposures • Extent to which lifespans of individuals are being shortened, especially for sensitive human subpopulations • Annual and daily ambient background concentrations of particulate matter in outdoor air • Lack of animal, clinical, and community studies of the effects associated with exposure to coarse-fraction particles	• Effects of long-term exposure to particulate matter, such as life shortening, progressive disease, and increased susceptibility to acute effects • Susceptibility of subpopulations most at risk • Biological mechanisms for particulate-matter contribution to life shortening, daily mortality, and morbidity • Key components of particulate matter associated with different biological responses • Exposure relationships between monitored ambient concentrations and average personal exposures. Relationships between ambient particulate-matter concentrations, non-ambient sources, and health effects • Exposure-dose-response relationships for short- and long-term exposure, various health end points, various susceptible groups, and various aspects (size, composition, etc.) of particulate matter • New techniques and equipment to generate ambient or simulated ambient particles for laboratory exposure studies, diagnose the effects of exposure to air pollutants for toxicology and epidemiology, and for more precise and accurate measurements of particulate-matter mass, components, and parameters	• Determination of background concentrations • Effectiveness of mitigation approaches • Atmospheric modeling • Source characterization

[a]Uncertainties and research needs presented in the table are taken from the 1998 EPA research-needs document (EPA 1998).

(ORD). The particulate-matter research-strategy document was developed by a multidisciplinary group of EPA staff from several offices within ORD and the Office of Air and Radiation. The document emphasized research that pertains directly to EPA's responsibilities to establish and implement NAAQS. Thus, it did not cover all particulate-matter-related research topics identified in the EPA research-needs document summarized below.

EPA's 1996 research strategy document presented a two-step planning framework for setting research priorities:

- Assessment of current knowledge
- Identification of major knowledge gaps and key scientific questions

The EPA document proposed the following criteria for ranking particulate-matter research:

- *Risk-Based Planning*. The focus is on research to reduce uncertainties in the assessment of health risks from exposure to airborne particulate matter and to develop or assess technologies for reducing emissions, exposures, and, ultimately, risks.
- *Scientific Excellence*. Scientific quality is critical to development and testing of hypotheses, data collection and evaluation, and, ultimately, support of credible regulatory standards.
- *Policy Relevance*. Importance is placed on the expected utility of research products for addressing short-term and long-term regulatory issues.
- *Other Sources of Data/Information*. Research being conducted by organizations other than EPA is also considered in setting priorities and allocating resources for EPA research. Through venues such as the EPA Particulate Matter Research Needs Workshops (held in 1996 and 1997) and the interagency Committee on Environment and Natural Resources, which coordinates certain federal research activities, EPA seeks to be aware of the research activities of other organizations, such as the Health Effects Institute and the Electric Power Research Institute, as well as federal research organizations.

- *Capabilities and Capacities*. This criterion focused on research implementation issues, such as ensuring that EPA has the facilities and expertise to conduct or oversee the needed research. Inhouse expertise is necessary to oversee research, even if it is conducted by outside organizations through grants, cooperative agreements, or contracts. Capabilities of the extramural scientific community are tapped mostly through EPA's Science to Achieve Results (STAR) grants program, which is investigator-initiated, competitive, and peer-reviewed.
- *Sequence of Research*. The success of most research, no matter how important, usually depends on the results of previous studies. Research that depends on studies that have not yet begun or are only partially complete received lower immediate priority in the EPA strategy document, regardless of eventual importance.

EPA applied the above criteria to potential research activities and thereby identified an initial list of research priorities. The sequencing of research (i.e., the order in which research should be conducted) was an important consideration in the ranking. Another important consideration was that some research is needed in the near term to support the next review and subsequent implementation of the new particulate-matter NAAQS, while other research is needed in the longer term to support future NAAQS reviews.

Table 2.2 summarizes and links the key research questions and priorities identified by EPA in 1996 for FY 1997 through FY 1999. EPA stated that its proposed research will be conducted by intramural and extramural investigators, taking into consideration the capabilities and capacities of the investigators to conduct the needed research.

A 1997 progress report (EPA 1997a) on EPA's particulate-matter research strategy reported that various methods and models are being developed in human, animal, and *in vitro* systems to improve the basis for future evaluations of the particulate-matter NAAQS. EPA's 1997 progress report described research under way in problem characterization, dosimetry, mechanisms of toxicity, and host-susceptibility factors.

An inventory of current federal and nonfederal research activities on particulate matter, recently prepared through a joint effort by the Health Effects Institute and EPA's Office of Research and Development, is summarized in Appendix B.

TABLE 2.2. EPA's Particulate-Matter Research-Strategy Summary[a]

Risk Paradigm	Science Questions	FY97	FY98	FY99
Effects	What are the biological mechanisms of effect?	Investigate causal mechanisms and particle characteristics →→→→→→		
	Can improved methods address confounding and improve interpretation of epidemiologic observations?	Evaluate and test epidemiology observations →→→→→→→→→→→→→		
	What affects the dosimetry of PM?	Elaborate on dosimetry →→→→→→→→→→→→→→→→→→→→→→→→→→→		
	What are the shapes of the exposure-dose-response curves?			Improve understanding of exposure-dose-response relationships→→→→→→→→→→→→→→→
Exposure	What types and concentrations of particles are people exposed to? Where are they exposed?	Develop and evaluate particle measurement methods →→→→→→→→→		
		Develop atmospheric models →→→→→→→→→→→→→→→→→→→→→→→→→		
		Characterize ambient PM exposures→→→→→→→→→→→→→→→→→→→→→		
		Improve personal exposure assessment →→→→→→→→→→→→→→→→→→→		
Risk Assessment	What is the state of knowledge of PM exposure and effects?			Conduct scientific assessments →→→→→
Risk Reduction	What sources of particles need the most control to reduce risk?	Characterize source emissions→→→→→→→→→→→→→→→→→→→→→→→→→		
	What are the most cost-effective approaches to reducing fine particle exposure and risk?			Tools to support new market-based regulatory approaches →→→→→→→→→→→→→→→→→→→→
		Improve PM control technology →→→→→→→→→→→→→→→→→→→→→→→→→		

[a]Reproduced from EPA (1996c).

CASAC'S REVIEWS OF EPA'S PARTICULATE-MATTER RESEARCH-NEEDS AND RESEARCH-STRATEGY DOCUMENTS

CASAC is authorized by the Clean Air Act to review the scientific basis of EPA's NAAQS and to identify information needs associated with these standards. Supplemented by expert consultants (and collectively called the panel) (CASAC 1997), CASAC reviewed a previous draft (EPA 1996d) of *Particulate Matter Research Needs for Human Health Risk Assessment* at a public meeting in Chapel Hill, N.C., on November 18-19, 1996. The panel made numerous recommendations for improving the draft document.

CASAC's main criticism of EPA's 1996 draft research-needs document was that it failed to place particulate-matter research needs clearly in the context of the present large uncertainties in assessing the health risks from inhaled particulate matter. The panel expressed concern that EPA's 1996 research-needs draft did not reflect the uncertainties adequately and recommended that the nature and magnitude of present uncertainties should be better described.

The panel also noted that EPA's 1996 draft research-needs document conveyed the notion that direct causal links of particulate matter (and especially $PM_{2.5}$) with health effects, as observed in epidemiological studies, were already established. Although the CASAC panel agreed that the available evidence warranted investigation, and most panel members generally supported implementation of some type of fine particle standard, the panel recommended that the EPA document should clearly state that the causality of adverse health effects due to $PM_{2.5}$ had not been firmly established yet.

On particulate-matter research priorities, the CASAC panel recommended that "a useful approach would be to begin with a framework consisting of the key steps in health risk assessment and standard setting. The key uncertainties presently limiting analysis at each step could then be listed in summary form, and then summary statements of the information needed to reduce the key uncertainties could be listed. With this structure as a prologue, the most important research and the research approaches likely to be most productive could be described" (CASAC 1997).

The CASAC panel did not develop a detailed description of particulate-matter research needs, but it described the following general research areas to be of highest priority (CASAC 1997):

- Effects of long-term exposures and relative contributions of short-term peak and cumulative exposures to long-term health outcomes
- Mechanisms by which particulate matter could contribute to life shortening, daily mortality and morbidity
- Linkages between particulate-matter data from outdoor monitors and actual personal exposures
- Particulate-matter classes and physical-chemical characteristics associated with response pathways and potency
- Extent to which particulate matter causes health effects independent of other pollutants

No second rank of priorities was given by the CASAC panel. Several other research topics were mentioned, but there was no consensus on their priorities.

The panel also recommended the following important concepts:

- Interdisciplinary collaboration and integration of efforts
- Research training
- International cooperation

The CASAC panel also recommended that in determining research needs, EPA would benefit from more consideration of the technical feasibility and time requirements of conducting proposed research. Some of the research suggested in EPA's 1996 draft research-needs document was judged by CASAC as not feasible for technological reasons. The panel recommended that the time required to fill critical information gaps should be estimated, and that the research-needs document would benefit from the placement of research in a time context, with the 2002 review of the particulate-matter NAAQS as one benchmark.

3

THE COMMITTEE'S FRAMEWORK AND CRITERIA FOR EVALUATION

The committee developed a simple, coherent, science-based framework (Figure 3.1) for organizing its evaluation of particulate-matter research. This framework links the sources of emissions of particulate matter or its gaseous precursors with adverse health outcomes in exposed individuals or populations. This source-to-response framework provides a useful overall structure for identifying and organizing the critical scientific information and research topics that must be addressed to reduce uncertainties underlying the establishment and implementation of the NAAQS for particulate matter. The components of this framework are generally well known to EPA and the environmental research community but have not previously been developed in the integrated, iterative manner recommended in this report. At each step in the framework, various scientific uncertainties exist that decisionmakers must consider in making policy choices. Improved scientific information at each step could assist policymakers and the public to understand better the health risks associated with particulate matter and to develop cost-effective strategies to reduce such risks.

Key elements of the committee's framework include the following:

- ***Sources***—Motor vehicles, fossil-fueled electric power plants, industrial facilities, agricultural practices, consumer products, other human sources, and natural processes, such as forest fires or wind erosion, all

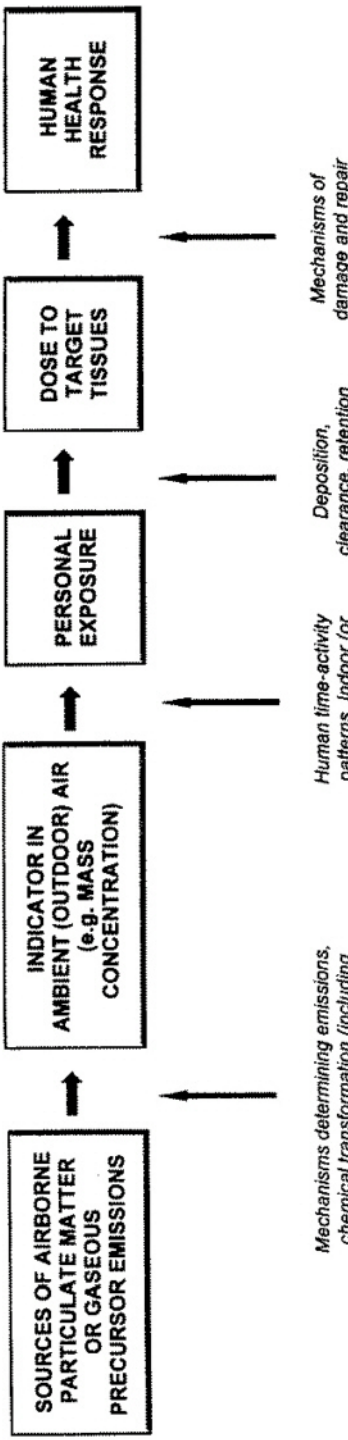

FIGURE 3.1 A general framework for integrating particulate-matter research.
Source: Modified from NRC (1983, 1994), Lioy (1990), and Sexton (1992).

release particulate matter (or precursors) that can adversely affect public health. This element of the framework includes factors determining the release rates, locations, chemical composition, particle size, deposition, transport, and transformation of emissions that lead to indoor and occupational atmospheric contamination.

- ***Ambient Indicators***—Mass or other measures, such as measures of size or composition of particles, per unit volume of ambient air. Data for specific pollutant indicators (e.g., $PM_{2.5}$ or PM_{10}) are typically collected at fixed outdoor community-monitoring sites to estimate local attainment of NAAQS.
- ***Personal Exposure***—The concentration of particulate-matter indicators with which an individual comes into contact over a specified period of time. Actual exposure of humans is determined by outdoor-air concentrations, indoor sources, and human time-activity patterns. The relevant point of contact is the breathing zone of the individual. The regulatory objective is to measure the amount or intensity of such exposures that are attributable to outdoor sources.
- ***Dose***—The amount and chemical species of toxicants that reach and remain in the lung and other sites within the body over a specified period. Dose is influenced by factors such as deposition, retention, deposition, and clearance of particulate matter and specific constitutents from target tissues. The dose delivered to specific tissues may result in injury and altered mechanisms of repair.
- ***Response***—Changes in specific health parameters attributable to tissue doses of inhaled particulate matter. These biological responses can be expressed in terms of molecular or cellular changes in the target tissue, overall tissue damage, or ultimately, clinical signs of pulmonary, cardiac, or other toxicity.

For particulate matter, current knowledge is incomplete for all steps in this framework (Table 3.1). There is limited evidence on the relationship between ambient concentration measures of particles and

TABLE 3.1 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 individuals 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

other pollutants in outdoor air, and the actual human exposures to those outdoor pollutants after time-activity patterns and indoor sources are taken into account, particularly for individuals within the populations considered most susceptible to air pollution. Doses of particles vary according to physical and chemical aspects of particles as well as physiological factors, such as human activity levels, breathing patterns, lung morphometry, and alterations of lung structure and function. Effects of particulate matter can vary with co-exposure to gaseous pollutants. Through the application of computer models of lung deposition, the relationship between exposure and dose can be estimated (empirical validation of the relationship is lacking at present). EPA currently assumes that the particles deposited in the lung elicit biological responses that result in adverse health effects in the respiratory tract and cardiovascular system. Although there is general understanding of how inhaled pollutants lead to respiratory and cardiovascular injury, that understanding does not extend to the low personal exposures and associated low doses at which effects of particulate matter have been observed in epidemiological studies. Toxicological mechanisms—how particles interact with target cells and subsequently elicit toxic responses—have been postulated, based on observations at higher levels of exposure and on toxicological models, but there is not yet a substantive body of human data on these relationships, and there is general uncertainty about toxicological mechanisms.

Epidemiological evidence, principally time-series studies, has indicated relatively consistent associations between measures of ambient concentrations of particulate matter and adverse health responses, but the evidence provides limited insight into the intervening steps of the committee's framework. The limited dose and mechanistic evidence contributes to uncertainty about the interpretation of epidemiological findings. The committee believes that evidence on toxicological mechanisms could significantly reduce many uncertainties about source-receptor relationships and strengthen the scientific knowledge base for risk assessment and risk-management decisions. Understanding such mechanisms could augment the credibility of the epidemiological evidence and provide a basis for guiding cost-effective control strategies for toxic particles. Another key uncertainty identified by the committee

is the relationship between outdoor particulate-matter concentration measurements and actual personal exposures and doses after indoor exposures, human time-activity patterns, and lung-clearance processes are taken into account. Tools are available for characterizing the relationship between ambient concentration and exposure and for exploring the association of exposure with dose. To date, however, only limited work has addressed those two important contributors to uncertainty.

The committee's highest-priority research recommendations and integrated research investment portfolio to address such uncertainties are presented in Chapter 4 and 5, respectively.

EVALUATION CRITERIA

The criteria chosen by the committee for assigning priorities to particulate-matter research needs are multidimensional, reflecting the complex physical and chemical processes and variety of biological effects associated with particulate-matter exposures, the varied information needs of decisionmakers for establishing and implementing the NAAQS, and the feasibility and timing of research activities.

In considering criteria to be used in establishing priorities for particulate-matter research, the committee was mindful of the need to integrate scientific and policy questions relevant to standard-setting and implementation. Each standard consists of four elements:

- *Indicator(s)*—the specific measurement (e.g., mass, chemical form, or size fraction, such as $PM_{2.5}$ or PM_{10}) of airborne particles that is important to control to protect public health.
- *Concentration*—the amount per unit volume of air
- *Averaging time(s)*—the period for which measurements are made or averaged (e.g., annual or 24-hour periods)
- *Form*—the statistical nature of the standard, used for determining the allowable number of exceedences per averaging time (e.g., 98th percentile).

The main overall categories of criteria chosen by the committee for identifying research priorities are scientific value and the value of research results to meet the information needs of decisionmakers. Research that would not ultimately have a potential effect on the standard-setting or implementation process was given low priority. Research directed at addressing key uncertainties and meeting key information needs within a risk assessment framework was ranked higher.

SCIENTIFIC VALUE

The committee believes that any research activities should be of significant scientific value. Such knowledge should pertain to one or more of the components of the committee's conceptual framework for reducing uncertainty (Figure 3.1), The scientific value of the information generated can be assessed in terms of its overall contribution to scientific knowledge about particulate matter and its health effects. Such knowledge will provide information on cause-and-effect relationships. It would be obtained through investigations that address testable hypotheses in a reproducible manner and provide results that can be generalized, to some degree, beyond the immediate study being performed.

Of particular value are innovative investigations that promise to fill important data gaps. Whereas confirmation of existing results is not always needed, studies designed to strengthen the basis for existing conclusions through new research results or replication of previous results, particularly those lacking a clear interpretation, are important. Studies that increase the ability to generalize upon previous findings are also valuable. Studies that contribute to the development of an integrated understanding of the health effects of particulate matter and gaseous copollutants are of particular value.

The committee also noted that some investigations can have side benefits in addition to knowledge generation *per se.* Specifically, new types of research might have the added benefit of building new research capacity and skills that might be valuable for addressing future questions about particulate matter and other air pollutants.

DECISIONMAKING VALUE

Research activities should contribute to reducing key uncertainties (Table 3-1) in standard-setting and risk-management decisions concerning particulate matter for the next scheduled review of the NAAQS in 2002 and in subsequent reviews.

Uncertainties exist at all stages of the committee's source-to-response framework (Figure 3.1). There are uncertainties about sources of particulate matter, biologically important particulate-matter constituents and mechanisms, ambient concentrations, levels of actual personal exposure, dose-response relationships, and the extent of short-term and long-term human health risk. Investigations that make a major contribution to particulate-matter risk assessment, through better characterization of particulate-matter risks, reduction in uncertainty about risks, or both, are of particular importance to policymaking.

FEASIBILITY AND TIMING

Research needs to be operationally, technically, and financially feasible. Operational factors include having sufficient research capacity and expertise available to successfully achieve the research objectives. The technical methods needed to conduct the research must also be available. Research objectives should be achievable within reasonable budgets, should make effective use of available financial and human resources, and where appropriate, should be leveraged with other scientific studies.

Particulate-matter-related research activities currently under way within EPA and other research organizations, as well as many of the research recommendations in this report, are largely directed toward the next review of the NAAQS for particulate matter in 2002. It is important that results be achieved in a timely manner. In addition, it is necessary to plan the overall research program in the context of a longer-range strategy and 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.

The committee understands that various decisionmakers will place different values on each type of information. Research results that can be *generalized* (i.e., extended generally to particulate matter or some fraction thereof or to other pollutants) are of enhanced value. *Leveraging* (the degree to which the results of a research activity can also increase the feasibility or value of other research results) also is valuable. And finally, the *cost of ignorance* (the potential health consequences and economic costs of proceeding inappropriately without the specified information) is a critical consideration.

The extent to which new research is needed to confirm previous findings was also considered. Based on the collective judgment of the committee, some research findings no longer need duplication (e.g., the now well-documented statistical association between daily mortality counts and various indicators of outdoor air pollution, including measures of particulate matter). On the other hand, some findings still need independent confirmation to be validated. For example, only a few studies contribute evidence on the long-term effects of particulate-matter exposures on morbidity and mortality. For these questions, the committee supported studies to provide independent confirmation. Furthermore, most currently available methods for toxicity testing for particulate matter can be used only for acute and subacute studies. Techniques are urgently needed for chronic or subchronic toxicity studies. Information is also severely lacking on the degree of actual human contact with $PM_{2.5}$ in populations at risk.

In establishing priorities for research on particulate matter, as for other areas of environmental research, practical considerations are also important. Feasibility, cost, timing, and the capacity of investigators to conduct the needed research are fundamental. Beyond the prerequisites, research that creates synergism by building on existing or new projects was given greater weight by the committee. For example, research that can be conducted by adding to existing population studies within a reasonable time was more highly rated, but only when it did not deviate from or adversely affect testing of key hypotheses. For specific steps within the framework, investigations that can be integrated with other research are also emphasized by this committee.

Improvements in particulate-matter measurement methods are also

needed to advance understanding of relationships between ambient concentrations of particulate matter and actual exposures of individuals at high risk of adverse health effects. Methods to perform continuous analyses of ambient concentrations or integral analyses over extended intervals would provide better real-time data for exposure assessment, compliance analyses, pollution-episode identification, and remedy selection. The data generated by improved measurement methods would also be useful for systematic studies of exposure misclassification and measurement error. These studies would enhance the analysis of population distributions of exposures and applications in epidemiological studies.

For each research activity recommended in Chapter 4, the committee provides rough but informed collective-judgment estimates of the cost of such research, based on the knowledge and experience of the committee members (see Appendix A).

4

THE COMMITTEE'S 10 HIGHEST-PRIORITY RESEARCH RECOMMENDATIONS

In this chapter, the committee identifies the 10 particulate-matter research needs that it judges to be of highest priority and describes general types of research that should be undertaken to address those needs. The research needs described herein are considered to be of equivalent importance. The committee evaluated approaches for obtaining such information within its framework linking source emissions to health responses (see Figure 3.1 in Chapter 3). The research priorities described below do not include the full universe of potentially useful research. Instead, in the committee's judgment, they are the 10 most critical scientific questions to be answered in pursuit of understanding the complex relationships that lead from particle sources (including formation of secondary particles from gaseous interactions) to ambient particulate-matter concentrations, actual human exposures, doses delivered to the lung, and, ultimately, to adverse health effects from the most biologically active constituents or characteristics of particulate matter.

The 10 particulate-matter research priorities identified in this chapter include some research activities that should be started immediately and others that should begin only after a better foundation is built from current or new research. Information obtained from approaches in one field can and should be used to advance methods and knowledge for other research needs. For example, epidemiological findings

that point to potentially susceptible subpopulations within the general population can be used as part of the basis to develop laboratory animal models and toxicological studies. Toxicological results, in turn, may help to identify biologically important constituents or characteristics of particulate matter or potentially susceptible subpopulations. This information can then be used to focus on human exposures to biologically important aspects of particulate matter. An iterative process involving interpretation of evidence from toxicological and exposure studies will lead to the selection of the metrics of exposure for designing future epidemiological studies on the health effects of particulate matter and other pollutants. The process should also lead to a better understanding of source-concentration-exposure-dose-response relationships through the application of successive generations of analytical tools for the most biologically important components or characteristics of particulate matter and gaseous copollutants. Although each of the research topics discussed below was evaluated individually, the committee recognized and addressed the fundamental interdependence of the individual elements. In the research investment portfolio presented in Chapter 5, the committee integrates these interdependent issues into a set of year-by-year timing recommendations and funding priorities for research. A truly integrated research strategy has rarely been used to investigate environmental problems, and it will require a major shift in current approaches to filling knowledge gaps and building toward a coherent understanding of the particulate-matter problem.

In addition to their scientific value, the research priorities described below are also expected to strengthen the basis of evidence for establishing allowable emission rates for the chemical components and precursors of particulate matter that are biologically important. This evidence base will be essential for designing and implementing effective control strategies for particulate matter in outdoor air through state implementation plans and for developing other mitigation approaches, including educational activities, voluntary emissions reductions, and product improvements for reducing indoor particulate-matter emissions that are not currently regulated.

Each research priority is presented with a description that includes

specific research tasks that are linked to individual steps and interactions among steps in the committee's framework. The value to scientific knowledge and the information needs of decisionmakers is also discussed. In addition, the feasibility, timing, and rough but informed collective-judgment estimates of the cost to conduct each recommended research task are discussed.

RESEARCH PRIORITIES

RESEARCH TOPIC 1 OUTDOOR MEASURES VS. 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 potentially susceptible subpopulations and individuals?

DESCRIPTION

Several studies have identified associations between measures of particulate-matter mass concentrations and health responses in ambient air (Dockery and Pope 1994; EPA 1996; Wilson and Spengler 1996; Vedal 1997). However, the currently available information is not sufficient for general characterization of the relationships of ambient air concentrations of particulate matter and gases to actual human exposures that include the indoor environments.

Personal exposures to certain air pollutants have consistently been found to differ from estimates based on corresponding outdoor concentrations. The differences are largely due to the variable contributions of outdoor air to indoor environments, the indoor fate of outdoor contaminants, and the substantial contribution of indoor sources and sinks to total personal exposures to particulate matter (Lioy et al. 1990). Most people spend the majority of their time indoors, exposed to a mixture of particles that penetrate from outdoors and those generated

indoors. Studies to date have found that a significant fraction (50-90%) of smaller indoor particles have outdoor origins (Koutrakis et al. 1992; Clayton et al. 1993; Thomas et al. 1993). Once indoors, particles may deposit on surfaces, or they can be altered through volatilization, as with ammonium nitrate, or through reactions with other pollutants present indoors, as with neutralization of sulfuric acid by ammonia. Indoor particles are further affected by the myriad of indoor particle sources, including cooking, resuspension, cleaning, tobacco smoking, pets, insects, and molds (lioy et al. 1990; Waldman et al. 1990; Koutrakis et al. 1992; Clayton et al. 1993; Thomas et al. 1993). The emission rates of most indoor-particle sources, however, have not been adequately quantified. Furthermore, factors that affect the contribution of outdoor particles to indoor concentrations have not been well characterized.

Information is especially lacking on the relationship between particulate matter in outdoor air and personal exposure to particulate matter for subpopulations that may be particularly susceptible to the effects of particulate-matter exposures, such as the elderly, individuals with respiratory or cardiovascular disease, and children. That gap in knowledge needs to be addressed immediately. Investigations must be designed specifically to test hypotheses related to actual human exposures. These studies should not be deferred while waiting for further health-effects studies. Hypothesis-driven exposure studies must be designed to provide fundamental information on actual human exposure to particulate matter and gaseous pollutants (NRC 1991). The recommended studies will be used to determine the exposure metrics that are most suitable for establishing exposure-response relationships. The following specific research tasks are needed to attain these goals:

- Field studies that differentiate the contributions to personal particulate matter and gas exposures made by ambient air and by the penetration of ambient air indoors. These studies will require coordination and temporal resolution among measures of personal exposure and ambient concentrations of particulate matter and gases.
- Longitudinal panel studies, in which a group of individuals is studied at successive points in time, to examine interpersonal and intrapersonal

variability, as well as seasonal and temporal variability in particulate-matter exposure. These studies should assess how such variability affects the relationship between personal exposures and ambient exposure estimates from measurements at central outdoor-monitoring sites. The studies should be extended later to characterize simultaneous personal exposures to particulate matter and pollutant gases.

- Analyses of information collected from the field studies and longitudinal studies described above to determine the contributions of outdoor versus indoor sources for each pollutant, and to examine the degree to which the use of more accurate exposure information would, or would not, alter the findings of the epidemiological time-series studies concerning particulate matter and adverse health effects.
- The sampling of particulate matter should include measurements of both $PM_{2.5}$ and PM_{10}.

SCIENTIFIC VALUE

Most epidemiological studies of particulate matter to date have been based on outdoor measurements. Therefore, the investigation of relationships between actual personal exposures and outdoor air-particle concentrations is crucial for validating and interpreting the results of epidemiological studies by providing better estimates of actual human exposure. Results from preliminary studies suggest significant intrapersonal and interpersonal variability in exposures to particles (Lioy et al. 1990). The recommended exposure-assessment studies will generate large data sets that will make it possible to assess factors influencing actual personal exposure. The results of these studies can also be used to design new prospective epidemiological and toxicological studies by establishing better metrics of exposure. Using the data base of exposure measurements for particles and gaseous pollutants, we will be able to provide better metrics of personal exposure in terms of concentrations of chemical species and of other covarying pollutants to be used in epidemiological investigations that focus on particulate matter while controlling confounding effects of gaseous pollutants. Differences between personal exposures and ambient measures can be

characterized and incorporated into subsequent analyses. (Also see section on measurement error.)

DECISIONMAKING VALUE

Pollutant concentrations in outdoor ambient air often are very different from actual personal exposures. Understanding the relationship between particulate-matter mass concentrations measured at fixed outdoor sites and actual human exposure to particulate matter will help guide and improve decisions about ambient pollution control strategies (NRC 1991). From a public-health perspective, it is very important to characterize actual exposures of particularly susceptible subpopulations to ambient particles and gaseous pollutants. Understanding the origin and composition of such exposures and their relationships to various human activities is of paramount importance for developing and implementing risk-reduction strategies for ambient sources and for nonregulatory (e.g., educational or product-improvement) strategies for indoor sources. That can be accomplished by determining the relative contributions of different sources to personal exposures, as well as by investigating how these contributions are influenced by patterns of personal activity.

FEASIBILITY AND TIMING

Many of the sampling and analysis techniques needed for this type of research have already been developed and field tested. Such methods can be used to measure 12-hour or 24-hour integrated personal exposures to particles and criteria gaseous pollutants (e.g., ozone, sulfur dioxide, nitrogen oxides, carbon monoxide). In addition, pilot exposure-assessment studies have already established the feasibility of conducting personal monitoring on presumed susceptible subpopulations, such as persons with chronic obstructive pulmonary disease (COPD), the elderly, and children. Continuous and semicontinuous personal

monitors are under development and will be available within the next couple of years.

The design and execution of a panel exposure-assessment study will take approximately 3 years. That includes subject recruitment, field measurements, collection of time-activity data, and data analysis. Therefore, it is feasible that panel exposure assessment studies be completed within a relative short period. Several such studies should be initiated almost immediately. These studies should examine different, potentially susceptible subpopulations in various geographical locations.

COST

A minimum of three studies in different parts of the United States will be needed to define ambient and personal exposures for populations at risk. Those studies should include at least one in the western United States, one in the northeast, and one in the southeast. The east-west differences will provide information on particulate-matter composition and variability, while the north-south studies will examine the effects of climate and living conditions. A possible design strategy might involve a study of 20 or more individuals for at least 15 days of sampling in the summer and winter. It would include members of presumed susceptible subpopulations, as well as representatives of the general population. Because of the complex aerometric measurements required, the three studies will require approximately $3.0 million per year for 3 years. Adding potentially susceptible subpopulations to such studies could increase that cost by a factor of 3 or more.

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?

DESCRIPTION

As the database on particulate-matter constituents that induce health effects enlarges, and as specific chemical constituents or particle-size fractions are indicated as plausible causal agents, exposures to those constituents of particulate matter need to be quantified for both the general public and susceptible subpopulations. The process will be iterative, with information developed from earlier studies guiding the planning of later studies. Population-based field studies will provide information on the distribution and intensity of exposure of the general population to experimentally defined components and size fractions. The studies should be conducted for statistically representative groups of the general population, with some oversampling for potentially susceptible subgroups. The studies could be coupled to health outcome investigations, but they should be designed to determine the extent to which members of the population contact these biologically important constituents and size fractions of concern in outdoor air, outdoor air that has penetrated indoors, and air pollutants generated indoors.

The following specific research tasks should be addressed after obtaining and interpreting results of studies and information from Research Topic 1:

- Measure population exposures to the most biologically important constituents and size fractions of particulate matter. These exposure studies should include members of the general population and potentially susceptible subgroups, using personal-monitoring studies and ambient stationary sites to examine the outdoor contributions to measurements of total personal exposure.
- Further refine the sampling and analysis tools developed in Research Topic 3 (below) to permit their routine application for the determination of biologically important chemical constituents and size ranges of particulate matter.

SCIENTIFIC VALUE

This information will be vitally important in designing exposure assessments for critical particulate components as part of the prospective long-term epidemiological studies that will provide the basis for more accurate risk assessments. It is important to investigate through population-based studies the distribution of ambient particulate-matter exposures and doses for different susceptible subpopulations and to identify the differences between distributions and the exposures experienced by the general population.

DECISIONMAKING VALUE

Because these studies will focus on examining the actual exposures of individuals to the most biologically important components or characteristics of particulate matter, the results can be critical to the choice of the measured indicators that would be specified in the NAAQS and to standard setting for these critical indicators. At the same time, the identification of critical indicator species will help in the implementation of cost-effective strategies to protect individuals at high risk, because control resources will be devoted more efficiently to the sources of the specific causal agents of the health effects.

FEASIBILITY AND TIMING

Some population-exposure studies could be initiated soon, but a more targeted set of studies should await a better understanding of the physical, chemical, and biological properties of airborne particles responsible for the reported mortality and morbidity outcomes. This research in exposure should then be conducted expeditiously to affect decisions on source-reduction strategies. Focusing on the specific causal attributes of particulate matter will be essential to make population-exposure studies cost-effective.

Sampling and analysis techniques similar to those that will be used

for the panel exposure-assessment studies could also be used for population-based studies. Additional techniques for measuring biologically important parameters, like the oxidative potential of particles, should be developed and tested before the initiation of the studies called for in Research Topic 3. Statistical analysis and participant recruitment methods developed over the past decade can be used to select cohorts that are representative of the total population. Finally, once sampling and analysis techniques are available, 3 to 5 years will be needed to complete these studies successfully.

COST

The committee estimates that at least five studies will be needed to cover the range of conditions that exist across the country. In the western United States, at least two cities should be studied. In the northeastern and southeastern United States, cities that represent climatic variations of the region will need to be studied. A city in the midwestern United States would provide geographical balance and establish exposure profiles for specific segments of the U.S. population. The studies would need to include at least 400 to 500 people per city. These studies are estimated to cost approximately $4.0 million per year for 5 years, depending on the indicators being measured.

RESEARCH TOPIC 3 SOURCE-RECEPTOR MEASUREMENT TOOLS

What are the advanced mathematical, modeling, and monitoring tools needed to represent source-response relationships more accurately?

DESCRIPTION

Determination of the constituents and characteristics of particulate matter that cause adverse human health effects will provide an opportunity

for more effective protection of public health by permitting the control of the most important aspects of particles that cause health effects. In order to be able to utilize that information in effective strategies for monitoring and source emission control, new tools that link sources with ambient air quality will be needed. For example, a detailed knowledge of the specific nature of emissions (gases and particles) from sources, and the chemical reactions that these materials undergo in the atmosphere, will provide an inventory of the sources of potentially hazardous, airborne chemical substances that might be present at locations where people are exposed to ambient air. Because the development of a general capability to relate particulate-matter sources to the responses will take time, such an effort must begin as soon as possible. However, the implementation of source-response investigations should not begin until most of the biologically important components of particulate matter are believed to be identified. If source-response investigations were undertaken with the current limited knowledge, significant resources might be wasted by studying biologically unimportant components of particulate matter. That could also lead to false expectations about air-quality improvements relevant to health risks from particulate matter.

Unlike other criteria pollutants that are completely defined by their chemical structure, particulate matter consists of a wide variety of chemical components and a wide range of particle sizes. Without knowledge of the biologically important components and particle sizes, it would be impracticable to apply source-receptor techniques to each of those components. Therefore, accurate and precise analyses are needed for representative samples from emissions and ambient air with respect to chemical compositions of particulate matter, especially $PM_{2.5}$, and gaseous pollutants. It is possible that the organic carbon fraction of particulate matter contains compounds that are biologically important or would provide useful marker compounds to characterize various source emissions. For example, wood smoke and motor vehicle emissions have been found to contribute to the mutagenic activity of particulate-matter extracts (Lewis et al., 1988). However, the capability currently exists only to separate, identify, and quantify a small fraction of the organic species associated with particulate matter.

Recently, new systems that can analyze size and composition on a particle-by-particle basis and in real time have been developed (Johnston and Wexler 1995; Gard et al. 1997; Murphy and Thompson 1997). Those systems permit the characterization of particles larger than about 0.2 to 0.3 μm in terms of aerodynamic diameter and their general chemical composition. The systems show real promise of providing real-time characterization of the ambient aerosol, but at this time, the particle compositional analyses are still qualitative, and their ability to accurately characterize the distribution of ambient aerosol properties is still uncertain.

The following specific research tasks should be undertaken to develop the capability to apply effective tools to understand the source-receptor relationships of biologically important particulate-matter components:

- Develop advanced modeling techniques for relating source emissions to ambient concentrations of particulate matter by more quantitatively incorporating atmospheric dynamics—including the effects of complex terrain, passages of frontal air masses, vertical mixing of air, and cloud and fog processes—into source-oriented models. The first generation of first-principle models is available. The models need to be tested operationally (i.e., with data) and mechanistically (i.e., to diagnose specific atmospheric processes). Then they need to be improved, assessed for reliability, and made more accessible. It will also be necessary to collect urban data to test and improve the models. The modeling of organic compounds will pose a particularly difficult challenge; laboratory data and theoretical constructs will also be needed.
- Develop better mathematical tools for assessing spatial and temporal variability in identifying and quantitatively apportioning particulate-matter properties, particularly for secondary particles (particles not directly emitted but formed in the atmosphere). These tools must deal with missing and below-detection-limit values and must impose appropriate constraints on the resulting solutions. Priority should also be placed on developing quantitative receptor models for secondary particulate matter. New models are needed for resolving the components of personal exposure incorporating ambient and indoor sources.

- Develop new personal-and ambient-monitoring techniques that have the capability of measuring chemical species and particle sizes associated with the inorganic and organic fractions of $PM_{2.5}$ and PM_{10}. The methods must be able to account for a substantial portion of organic carbon, as well as the inorganic components of indoor and outdoor particulate matter and their sources.
- Improve the ability of continuous particle-by-particle analysis systems to quantitatively determine the composition of individual particles and to quantitatively characterize their ambient distribution.

SCIENTIFIC VALUE

To advance exposure and risk assessment, it is necessary to be able to identify and quantify a much larger fraction of airborne particulate-matter mass in terms of specific biologically important compounds and to determine the intensity of the actual exposure of people to components of particulate matter that might produce adverse health effects. Carbonaceous particulate matter accounts for more than 30% of the $PM_{2.5}$ mass in many urban and nonurban areas in the United States (Malm et al. 1994). A current major problem is the speciation of the organic carbon associated with particles and the associated positive and negative sampling artifacts. Current methods are only able to identify and quantify about one tenth of the organic material associated with particles. Much of the mass of that material is highly polar in nature and not amenable to simple separation and identification methods. It is critical that a substantial majority of the organic carbon mass be separated and identified to provide the basis for toxicological and epidemiological studies. That will require sampling on various media, in addition to quartz fiber filters, to capture the gaseous and solid phase of carbon compounds. Thus, significant improvement in analytical methods that lead to routinely applicable techniques would represent a significant advance in analytical science and provide for major improvements in exposure and risk assessment.

Improved understanding of atmospheric processes, and the codification of that knowledge in the form of models that can predict the transport

of source emissions and their transformation in transit to materials that either form new particles (nucleate) or condense on the surface of existing particles, would represent a significant advancement. Such models will require new information, including the thermodynamics of condensible organics and mixtures of organic and inorganic compounds.

The development and use of advanced receptor models would help to improve understanding of source-receptor relationships and provide critical complementary information to the advanced source-oriented models.

DECISIONMAKING VALUE

The ability to relate emissions to ambient concentrations accurately is critical to the development of effective and efficient air-quality management strategies focused on biologically important particulate-matter components. Such analyses will help to identify the significance of specific particulate-matter components that might cause adverse health effects, as well as to evaluate effects of emissions reduction strategies. The development of mathematical tools is also needed for continued development of receptor-modeling methods for the quantitative apportionment of particulate-matter mass for secondary and reactive species, as well as for predictions of the intensity of human exposures in various settings. The methods would provide quantitative estimates of uncertainties for identified source categories.

FEASIBILITY AND TIMING

Improved computational power has made it practical to develop much more sophisticated models of particle formation and transport, and the tools are in place to move ahead to the next generation of such models. Similarly, improved numerical tools can now be used to improve the quality of receptor models and exposure models. Measurement of the critical organic fraction has improved in recent years with

improved liquid chromatographic methods along with better methods to transfer the analyze from the output of the chromatograph to the mass spectrometer, but these improvements have not been fully validated. The resolution and sensitivity of mass spectrometers have also improved so that the necessary basic tools are available.

The modeling of emissions, atmospheric transport, and transformations of particulate matter are important for designing control strategies. Because the attainment or nonattainment status of outdoor monitoring sites will not be determined until after the next NAAQS review cycle, the models will not be needed until that time. However, to have appropriate models in place by the time they are needed, the development effort should start soon. Models are needed both to relate source emissions to ambient concentrations (source-oriented models) and to relate observed concentrations to their human receptors (receptor-oriented models). The current status of both types of models for evaluating particulate-matter source/receptor relationships has been reviewed recently by Seigneur et al. (1997).

To develop, evaluate, and improve the models, appropriate air quality-data will be needed. A well-designed monitoring program could help facilitate this effort and could minimize the costs of collecting incremental data for modeling purposes. It is unclear how EPA's currently planned $PM_{2.5}$ monitoring program will adequately help the atmospheric-modeling community meet the needs of decisionmakers.

COST

The atmospheric modeling efforts, including the associated laboratory studies, are estimated to cost about $2.0 million per year for 6 years. The receptor modeling development will require about $1.0 million per year for 3 years. In addition, $1.0 million per year is needed in the first 3 years for the development of advanced exposure analytical methods for use in the epidemiology studies to be undertaken in year 4 and beyond. Advanced analytical methods for monitoring biological responses to toxic particulate-matter components will also be needed and are estimated to cost $1.5 million per year from years 4 through 6.

Data-collection efforts for model development and testing will require substantial additional resources if the data need to be collected independently of EPA's $PM_{2.5}$ monitoring program. The additional costs could be as high as $2.0 million to $10.0 million per urban area.

RESEARCH TOPIC 4 APPLICATION OF METHODS AND MODELS

After biologically important components of particulate matter are identified, how can the analytical tools developed in Research Topic 3 be applied to link those components to their sources to provide effective and efficient air-quality management to protect human health?

DESCRIPTION

Source-oriented (air dispersion) models relate emissions to ambient concentrations by using either Eulerian or Lagrangian methods (Seigneur et al 1997). The current models that can be considered useful for state implementation plan (SIP) development are three-dimensional Eulerian models that include a particulate-matter module. Lagrangian models, such as plume-trajectory models, are not considered to be as suitable for SIP development as the Eulerian models (Seigneur et al. 1997). The Eulerian models can be classified into two groups. In the first group are models that include detailed atmospheric chemistry but are generally limited in their application to simulations of a few days because of their computational costs. The second group includes simplified treatment of the chemistry, but can be applied for longer intervals. In both cases, improving computer capabilities will permit more-detailed chemistry to be incorporated into the models without computational problems. However, Eulerian models will reach the point at which they are limited by the lack of basic physical chemical information fairly quickly. There is insufficient current and accurate information on the thermodynamics of important particulate species particularly in mixed-composition systems. At present, phenomena such as

nucleation and surface adsorption on heterogenous or agglomerate particles are treated with simplifications because they are not fully understood. A much better understanding of the processes leading to secondary organic particle formation from gaseous precursors is also needed to resolve a number of questions regarding the nature of the important precursors as well as the overall importance of such particles in the ambient atmosphere.

Receptor models have been effectively used to identify local sources of particulate matter. Most applications of receptor modeling have been to airborne particulate matter. EPA has approved the use of one model, the chemical mass balance (CMB) model, as part of the SIP process (EPA 1987). That model assumes that the number of sources and their compositional profiles are known, and that the only remaining unknowns in the equation

$$C_{ik} = \sum_{j=1}^{J} F_{ij} S_{jk} \quad \text{for } j = 1 \text{ to } J$$

where:

C_{ik} = concentration of chemical species i for sample k

F_{ij} = source composition of species i in source j

S_{jk} = source contributions from the j^{th} source to k^{th} receptor

are the mass contribution of the sources to each sample. Such an approach works well for larger-sized particles (> 1 μm), where there are generally sufficient compositional differences between emissions from different sources to permit them to be distinguished from one another. The CMB model is a multiple-regression model. In the implementation prepared for EPA, the model incorporates the estimated uncertainties in the emitted source-material compositions, as well as the uncertainties in the measured elemental compositions of the particulate-matter samples (Watson et al. 1990). The effective variance least squares fitting procedure is used to solve the problem iteratively (Watson et al. 1984; Cheng et al. 1988). Source-apportionment studies have typically been carried out and reported for PM_{10} nonattainment areas, most of which are in the western United States.

Because of the separation of emitted primary particles from the secondary particle precursor gaseous emissions, some pollutants, such as oxides of sulfur, oxides of nitrogen, ammonia, and secondary organic particles, are not directly attributed to source categories. Those pollutants

will need to be controlled to meet a fine-particle standard. Thus, it is essential to be able to associate the observed concentrations of secondary species with specific source types, and potentially with specific source locations. Only then can an effective implementation plan be developed. Because the primary particle-source signatures are lost in transit, other kinds of information need to be included to identify and apportion sources of secondary particulate matter. Receptor models have considerable promise, but they require further development, testing, validation, and packaging for use by state and local air-quality managers. In addition, they must be linked to models that estimate population and individual exposures to particulate matter and gaseous pollutants.

The development of new personal-exposure samplers is critical to fulfilling the research needs discussed above. For investigations of the relationship between personal particulate exposures and outdoor concentrations, for example, new personal samplers for $PM_{2.5}$ and $PM_{1.0}$, that are sensitive enough to collect 12- and 24-hour integrated samples should be developed. Also, the samplers should be small, lightweight, inexpensive, and easy to operate, allowing them to be used in large-scale exposure studies. Because NAAQS have been issued for PM_{10} and $PM_{2.5}$, the samplers should also allow personal exposures to be measured for both particle sizes simultaneously. In addition, samplers that are able to measure personal particulate exposures continuously or semicontinuously are needed to investigate the temporal variability in particulate exposures. Currently available continuous personal-particulate monitors (most of which measure particle concentrations based on light scattering) were originally developed to measure occupational exposures and are unable to measure the lower ambient particle concentrations accurately. New methods that are able to measure currently observed ambient concentrations accurately need to be developed. Finally, personal-sampling techniques should be developed to provide information about the physical, chemical, or biological properties of particulate exposures, such as particle size distribution, chemical composition, and oxidative potential. This information is critical to investigating and estimating the origin and the toxicity of personal particulate exposures.

The further development and targeted application of improved

source-oriented models, receptor models, and supporting sampling and analytical methods will be critical to effective air-quality management. The following specific research tasks should be addressed after biologically important components of particulate matter have been identified:

- Enhance the modeling and measurement tools to provide estimates of emission sources of, and population and individual exposure to, biologically important particulate-matter components. This will require apportionment of exposure through source tests for biologically important components, inventories of appropriate sources, and development of the associated emission-source and emission-receptor models.
- Modify the models, sampling, and analysis so that they can be easily applied and thus be readily accessible to the state or local air-quality-management officials who will be required to develop implementation plans. These modifications include providing for the diverse geographical and temporal scales needed by different states and localities.

SCIENTIFIC VALUE

Meeting these needs will help to improve understanding of atmospheric chemistry and source-emission characteristics. It will improve source and receptor models and improve the linkage between biological data and human exposure and atmospheric concentrations of particulate matter.

DECISIONMAKING VALUE

This research is essential to developing control strategies targeted at the emission sources of the most biologically important particulate-matter components. It will also help integrate source-receptor modeling information with biological and health effects information to evaluate better the effectiveness of control strategies, and will enhance the

cost-effectiveness of multi-pollutant control strategies through the application of improved source-receptor modeling.

FEASIBILITY AND TIMING

This research will require a more advanced biological understanding of important agents as a result of toxicological, clinical, and epidemiological research. Thus, it must be staged to follow the first stages of dose-to-response research, which should begin immediately.

COST

Research to link biologically important particulate-matter components to their emission sources does not require significant resources for the first 3-year timeframe during which improved analytic tools will be developed in response to Research Topic 3. Based on previous efforts at developing analytical methods, modeling source receptors (e.g., Ozone Transport Assessment Group (OTAG) and Ozone Transport Commission (OTC)), and accounting for the increased complexity inherent in collecting data and implementing source and receptor modeling for a complex mixture like particulate matter, the committee estimates that a budget of $4.0 million per year beginning in year 3 and extending to year 8 will be necessary to accomplish these goals. In addition, $1.0 million per year is needed in the first 2 years for the development of advanced exposure-measurement technology for the epidemiological studies to begin in year 4. Advanced tools for monitoring biological responses to toxic components of particulate matter will also be needed.

RESEARCH TOPIC 5 ASSESS HAZARDOUS PARTICULATE-MATTER COMPONENTS

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

DESCRIPTION

There is insufficient understanding of the relationships between chemical composition, shape, and size of ambient particulates and resulting health effects. In fact, the results of epidemiological studies might be generally interpreted in two ways. On the one hand, general consistency among different studies performed in different areas with various populations might suggest that the responses are merely some function of the mass dose of the particle mixture common to many areas, rather than of specific chemical species within the mixture. Alternatively, variations among studies in the relative-risk estimates related to exposure suggest that toxicity might depend upon physicochemical characteristics of the particulate matter, which can differ among regions. The differences in the relative risk estimates may also reflect differences in designs, confounding effects, and other factors among studies. Moreover, present knowledge of the toxicity of various components of particulate matter strongly suggests that mass is not a sufficient metric for understanding health effects. Some of the uncertainty in epidemiological findings of adverse effects associated with particulate matter might be due to the possibility that mass concentration alone may not be sufficient to identify the putative portions of the particulate-matter fraction that produce mortality or morbidity. To explore adverse health effects of particulate matter requires coordinated efforts in epidemiological and controlled exposure studies that provide adequate exposure metrics that characterize size and chemistry. Thus, within this broad research area, several important points must be addressed, and studies should be designed such that results will provide input to the data base required to address these issues. The most relevant route of exposure is inhalation. Therefore, inhalation should be the route of choice.

Develop and use particulate matter surrogates for use in controlled exposure studies.

Ambient particulate matter is a complex mixture that includes material derived from natural and anthropogenic sources. The potential for

daily and seasonal changes in composition and for variability in particle composition between different regions limits the ability to describe a standard ambient aerosol or the ability to develop a reference ambient particulate-matter material. Thus, it is necessary to use surrogate particles for controlled exposure studies. Surrogates that have been employed include ambient particulate matter, which is resuspended for exposures; concentrated ambient particulate matter, which is directly delivered to an exposure system; and various potential components of ambient particulate matter, such as residual oil fly ash (ROFA), acidic sulfates, road dust, diesel soot, and carbon black. These atmospheres can be well defined and, with the exception of the concentrated ambient particulate matter, reproduced in the laboratory. Because of the exposure variability in studies using concentrated ambient particulate matter, these must include a careful characterization of particle composition (size and chemistry) and accompanying gaseous components. All surrogate atmospheres have advantages and disadvantages in terms of their usefulness in contributing to our knowledge of the toxicity of actual ambient particulate-matter exposure. Thus, efforts should be directed at determining the relevance of surrogate particles to ambient particulate matter and to determine which surrogates are most relevant. Within this effort, the potential role of biologically-derived particulate material must be considered.

Assess relevant dose metrics for particulate matter to explain adverse health outcomes.

Routine atmospheric sampling of particulate matter in recent years has typically produced data for PM_{10} and occasionally $PM_{2.5}$. Only rarely have measurements of particle numbers been made. However, it is not clear whether mass is the appropriate metric to explain dose-response relationships for adverse health effects of particulate matter noted in epidemiological studies.

Dose is traditionally expressed by mass delivered to the exposed person. However, experimental studies have shown that a given mass of the same particulate compound delivered as distinctly different particle sizes (e.g., 20 nm vs. 250 nm) can elicit significantly different

toxic responses. Thus, in some cases, particle mass might not be the best dose metric for comparison of responses, but particle surface area might be more appropriate. It is, therefore, possible that the best dose metric for ambient particulate matter might differ for different particle types, depending perhaps upon the physicochemical properties of the specific particulate-matter exposure atmospheres. Because ambient air-quality standards are based upon mass concentration, current estimates of exposure derived from atmospheric sampling networks will not relate meaningfully to response in cases where adverse biological effects are causally associated with a different particle metric for a specific particle type. Potential dose metrics can include, in addition to particle mass, particle number, particle surface area, and others related to chemical constituents (e.g., oxidant reactivity, metal content, and organic content). Furthermore, more than one metric might be needed to understand dose-response relationships for particles having different physicochemical properties. Such dose-response information is necessary to determine the nature of the model for particulate matter, i.e., linear or threshold, or perhaps both, depending upon the particulate-matter characteristics.

Evaluate the role of particle size (e.g., ultrafine versus fine versus coarse) in toxicological responses to particulate matter that relate to epidemiological health outcomes.

Ambient particulate matter generally consists of coarse and fine particles (see Figure 1.1). Within the fine-particle fraction, there are a nucleation mode (i.e., up to about 0.01 μm) and an accumulation mode (from about 0.01 μm to 1 μm), each containing particles having distinctly different size ranges. Because of limited monitoring data, only a few epidemiological studies have been able to consider alternative fractions of particulate matter. The results from the studies vary. Some of the studies suggest that adverse health outcomes are more highly associated with the concentration of the fine particle mode; other studies have not shared that finding. Furthermore, toxicological studies using model atmospheres have noted that within this mode, particles in the ultrafine size range seem to have greater inflammatory

potential per unit mass than do particles within the larger accumulation mode. Although differences in deposition efficiencies and ultimate disposition within the respiratory tract between different-sized particles might be important factors modulating toxicity, they cannot fully explain observed differences in biological responses. Research using controlled exposures in humans and animals as well as in vitro systems is needed to evaluate particle size-dependent toxicological responses and to evaluate any mechanistic differences related to size.

Determine the role of particulate-matter chemistry in toxicological responses to particulate matter that relate to epidemiological health outcomes.

Are relevant biological responses to particulate matter nonspecific, or do they depend upon specific chemical composition of the particulates? One of the major issues in assessing particulate-matter toxicity is the question of generic toxicity of particles versus toxicity due to the presence of specific chemical components within or on the particles. As noted above, generic toxicity due to an as-yet undetermined mechanism has been suggested for one size range of particulate matter, namely the ultrafines. On the other hand, experimental studies using various biological end points have suggested that certain chemical constituents of particulate matter might underlie toxicity. Based upon the available evidence, chemical components that might contribute to the biological activity of ambient particulate matter are acidity, certain metals, reactive organic components, and biological agents, such as bacterial toxins, spores and pollen. Particles do not have to be composed entirely of those chemicals, since active chemical species might exist as a surface layer on what otherwise would be a fairly chemically inert core material, such as carbon. In this regard, surface-absorbed, short-lived radicals, such as peroxides, have been suggested as potential contributors to the toxicity of ambient particulate matter, and primary reactive organics, as well as secondary organics derived from the oxidation of hydrocarbons in the atmosphere, should also be considered in this regard. Thus, there is a need to study biological responses to particles having specific chemical compositions, bearing in mind the relevance of this chemistry to actual constituents of ambient

particulate matter. Of the above chemical components of particulate matter, the greatest body of research has addressed acidity.

SCIENTIFIC VALUE

Better understanding of the role of particulate-matter physicochemical characteristics in eliciting adverse health effects should assist in determining the mechanisms underlying toxicity and the relationship between response and specific chemical composition and particle size.

Furthermore, identification of particle characteristics that affect responses of experimental animals and humans undergoing controlled exposure studies, followed by comparison to populations undergoing exposure in the ambient environment, would provide powerful confirmation of the role of specific physicochemical properties of particulate matter. The development of surrogates for ambient particulate matter for use in controlled exposure studies as an outcome of studies of physical and chemical characteristics would then allow for reproducible interlaboratory exposure testing using relevant materials and provide for a research model for controlled exposure studies. The proper design of controlled exposure studies to assess physicochemical properties analysis in relationship to response will also provide information on proper dose metrics. Furthermore, results of controlled exposure studies can provide epidemiological studies with information that will allow for refined exposure analysis. Thus, there must be close interaction between epidemiological and toxicological studies (animal and clinical) in this research area.

DECISIONMAKING VALUE

Once the biologically important particulate-matter characteristics have been identified, emission sources of the most important components of ambient particulate matter contributing to adverse effects could be identified, and appropriate risk-management strategies can be developed, including the control of specific particle components as air

toxics under a separate part of the Clean Air Act. Thus, obtaining this information can contribute substantially to public health protection, especially for susceptible individuals.

FEASIBILITY AND TIMING

Methods need to be developed and applied to identify physical properties of particulate matter, such as size, shape, or number, or toxic components such as acids, transition metals, peroxides, reactive organics, and secondary organics. The toxicological and clinical studies should begin immediately. The necessary expertise and technology are available. Major epidemiological studies should be delayed until the fourth year when information on personal exposure and toxicological mechanisms is expected to become available.

Some epidemiological researchers might believe that new epidemiological studies should begin immediately. However, this committee, which includes several epidemiologists, concludes that it may be more cost effective to delay certain epidemiological studies until further information on personal exposure and biologically important components of particulate matter becomes available. Without such information, the committee does not anticipate that epidemiological studies could be designed to identify the aspects of particulate matter most associated with adverse health effects, nor would they be likely to help resolve the currently divisive policy debates over particulate matter.

COST

The recommended laboratory animal and human clinical research on the toxic components of particulate matter using controlled exposure studies is estimated to cost $8.0 million a year for 5 years. This amount includes research to identify relevant dose metrics for particulate matter to assess epidemiological results. The recommended epidemiological research activity will require the development of more refined particulate monitoring and are estimated to cost $1.0 million in

the second and third years and $6.0 million per year from 2001 until 2010 to enable major field studies in each of three regions of the United States to assess potential differences due to particle composition.

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?

DESCRIPTION

Knowledge of the tissue-specific and cell-specific dose of particulate matter, and of particulate-matter constituents, is a critical link between individual exposures and health responses. The concept of dose includes the magnitude and rate of deposition on respiratory tract surfaces, the clearance, dissolution, and translocation of particulate matter from various sites, and the bioavailability of particulate-matter-borne toxic compounds. This information is not only critical to understanding exposure-dose-response relationships for health risks, but also to extrapolating these relationships between different types of subjects and between experimental animals and humans.

At a given airborne concentration in the breathing zone, the deposited dose of particulate matter depends on the amount inhaled (inhaled concentration × volume breathed), the breathing pattern, particle characteristics (e.g., aerodynamic diameter and diffusion diameter which is affected by size, shape, and density), hygroscopic changes in the aerodynamic behavior of the particles after inhalation, and the physical characteristics of the air passages.

Mathematical models have been constructed for predicting the regional deposition of particles in the respiratory tract. Although these models are available for making useful predictions of deposition of particles of most sizes in normal adult human airways, there is a basic

need for experimental measurements to refine them and to validate them through studies of deposition in living subjects.

Few data are available on the regional deposition of particulate matter in lungs of people with respiratory diseases and normal elderly individuals. Not only can the variations be observed between normal and diseased airways, but the airway surface morphology might also differ. Because the latter subjects are subpopulations presumed to be at special risk from particulate matter, it is important to acquire data on the geometry of the lungs of such individuals, to develop mathematical deposition models and to validate the models by studies of deposition in living subjects.

The fate of particles once they deposit in the lung is another crucial link in determining the relationship between exposure and response. Depending on size, shape, solubility, and other physicochemical characteristics, particles can have wide ranges of lifetimes, anatomical locations, rates of movement in the body, and susceptibilities to the body's defenses. A knowledge of the dose retained at the organ, tissue, and cellular levels is important for linking the deposited dose to the nature and mechanisms of effects.

For many types of particulate matter, there is a good understanding of the clearance rate of particles via different pathways, given the deposited dose and the physical and chemical characteristics. Scientists also have a good working knowledge of the movement of some types of particles and their solubilized components in the lung, and of the transfer of some solubilized components to other organs. However, it is essential to validate the translocation pathways and rate constants for all particulate-matter types in appropriately designed experiments.

Little is understood about the deposition and fate of ultrafine particles (under 0.10 μm) in the respiratory tract. The efficiency with which alveolar macrophages scavenge ultrafine particles is uncertain. There is sufficient evidence that ultrafine particles penetrate into and through the epithelial cell layer at a greater rate than larger particles, but there is yet little ability to predict transfer rates and either mass-based or number-based concentrations with time in different tissue compartments. There is also evidence that ultrafine particles of sufficiently low solubility can transfer from the lung to other organs, but there is no

ability at this time to predict the portion or size fraction of the ultrafine dose transported to other organs or to predict transfer rates or residence times. Moreover, there is no information on interspecies similarities and differences for any of the above phenomena.

The extent to which specific chemicals (organics, metals, salts, acids,) carried on particle surfaces are available to cells and tissues is only partially understood. There is information for only a limited number of compounds comparing the bioavailability and biopotency of the compound deposited either as a pure material or as a coating on particle surfaces. Factors affecting bioavailability include the form and the physical and chemical state of the compound, the nature of its bonding with the particle surface, the thickness of the coating, and the location of the particle (e.g., intracellular or extracellular). As different classes of compounds are shown to be important in particulate-matter health effects, some will require a better understanding of bioavailability if the linkage between deposited dose and effects is to be understood.

The following specific research tasks should be undertaken with respect to deposition patterns and fate of particles in the respiratory tract:

- Develop a quantitative description of representative lung morphometry and breathing patterns of potentially susceptible individuals (especially subjects with lung diseases, elderly subjects, and children).
- Obtain better understanding of particle deposition patterns within the respiratory tracts of susceptible subpopulations as a function of particle size, hygroscopicity, and breathing rate over the entire range of particle sizes.
- Develop and refine mathematical models for predicting the regional and local deposition in the respiratory tracts of subjects with lung diseases and elderly subjects for particles across the size ranges of interest, using deposition data collected experimentally to test the models to the extent possible.
- Enhance understanding of the clearance mechanisms and other particulate defense mechanisms (e.g., phagocyte function), translocation to tissue and extrapulmonary compartments, and the bioavailability

of particle-borne constituents over the full range of particle sizes in susceptible subpopulations and any differences between those individuals and the general population.

SCIENTIFIC VALUE

This research will advance basic understanding of the influence of disease and senescence on respiratory-tract structure and physiology. The resulting information will extend current understanding of diseased lungs and will also be very valuable to the growing field of drug delivery by inhalation. Also, it is central to defining critical dose terms and then estimating critical doses at the organ, tissue, and cellular levels for particulate matter and its associated compounds in susceptible populations.

DECISIONMAKING VALUE

This information will be critical to estimating the relative doses of particulate matter and biologically important constituents in normal and abnormal lungs, thus helping to determine the techniques needed to control the exposures of susceptible subpopulations.

FEASIBILITY AND TIMING

The skills and technology and some of the basic information needed for this research are available. Because the initial phases of this effort will involve developing basic data for abnormal lungs, it is not necessary to wait until the most biologically important types or constituents of particulate matter or the biological mechanisms are identified before initiating the work. Thus, this research should begin immediately and can provide a significant portion of the needed information before the next NAAQS review, although some of the work will need to extend beyond that time.

COST

Approximately $3.0 million will be needed in the first year and about $1.5 million per year will be needed for each of the next 3 years. The research will include detailed morphometric measurements on abnormal lungs, development of deposition models based on the morphometric measurements, and validation of the deposition models using in vivo studies of individuals with abnormal lungs.

RESEARCH TOPIC 7 COMBINED EFFECTS OF PARTICULATE MATTER AND GASEOUS COPOLLUTANTS

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?

DESCRIPTION

Particulate matter exists in outdoor air in a mixture that includes other pollutants resulting from natural processes and human activities. In typical urban environments, many of the same sources that give rise to primary and secondary particles also release gaseous pollutants, including sulfur oxides, oxides of nitrogen, carbon monoxide, and other organic compounds. Vehicles and other sources of hydrocarbons and oxides of nitrogen result in the formation of ozone, organic vapors and organic particles, particularly in regions or seasons where sunlight is abundant. Moreover, meteorological conditions can influence the concentrations of most air pollutants in similar ways, such that when levels of one pollutant are high, levels of other pollutants may also rise. To support standard-setting, researchers have attempted to identify the independent effects of particulate matter. That task is made difficult by the common sources of particulate matter and other pollutants, and correlations among their concentrations in ambient air.

7a. COPOLLUTANTS (TOXICOLOGY)

Toxicological studies have shown that interactions between particulate matter and gaseous pollutants are very complex. For example, even in a simplified situation where there is a combination of only two pollutants, the nature of any interaction (e.g., additivity, synergism, or antagonism) depends upon various factors, including exposure duration and the ratio of the concentrations of the two chemicals within the mixture. Gas-particle interactions of multiple chemicals present in ambient air are even more difficult to evaluate, making determination of the specific role of the particulate-matter component in causing adverse health effects associated with exposure quite difficult. An additional complication is the potential for ambient gases to alter lung ventilation, thus affecting deposition of inhaled particulate matter and the resultant dose to various tissues in the respiratory tract. In addition, gases might interact chemically with particulate matter, perhaps altering surface characteristics of the particles.

7b. COPOLLUTANTS AND EFFECTS OF LONG-TERM EXPOSURE (EPIDEMIOLOGICAL STUDIES)

Epidemiologists have generally followed two approaches to try to characterize the independent effects of particulate matter: using regression models for data analysis that includes pollutants other than particulate matter, and examining the effects of particulate matter across areas having differing levels of other pollutants. The great majority of studies that relate particulate matter to health have evaluated acute health measures (e.g., death, emergency room visits, or hospital admissions) with increments above previous daily averages of particulate matter. These studies demonstrate a consistent positive association between these two factors, but not all of them have considered confounding effects of copollutants.

Long term exposure to particulate matter has also been associated with mortality in two large-scale cohort studies, the Harvard Six-Cities Study and the American Cancer Society Study of 151 U.S. cities. The two studies had certain limitations, including limited consideration of gaseous pollutants, and are currently undergoing detailed reanalysis to

confirm the original findings and to evaluate the robustness of the conclusions. New epidemiological investigations of the effects of long-term exposure are needed and should be designed to address also the influence of copollutants on the association between chronic health effects and exposure to particulate matter.

Further studies to investigate the influence of copollutants on health responses to particulate matter are needed in controlled-experiment laboratory studies (animal and controlled clinical studies) as well as in epidemiology.

The following questions need to be addressed:

- Can effects of particulate matter or its components be identified among persons living in locations with unique particulate-matter sources or characteristics?
- Do natural experiments involving changing patterns of source operation indicate effects of particulate matter?
- Do parallel investigations of multiple locations with different pollution characteristics indicate an effect of particulate matter or its components?
- Does the consideration of other pollutants in models influence the estimates of the association between particulate matter and acute health responses?
- What is the contribution of long-term exposure to particulate matter (or its components) and other pollutants present in ambient air to morbidity and mortality in the general population?
- How does exposure to mixtures of particulate matter with ambient gases alter toxic responses compared with those observed with particulate matter alone?
- How does exposure to mixtures of particulate matter with ambient gases alter the deposition or retention of inhaled particulate matter compared with particulate matter alone and to predictions based upon biologically based deposition or retention models that do not consider effects of copollutants on disposition of particulate matter?

SCIENTIFIC VALUE

Investigation of the influence of copollutants will reduce uncertainty

in estimates of the association between particulate matter and health. The presence of copollutants could also alter the health response to particulate matter. Controlled experimental laboratory research can contribute needed information on the toxicology of these mixtures.

The development of new information on the health effects of long-term exposure to particulates and other copollutants would be of considerable scientific value. Such studies should focus on both morbidity and mortality attributable to long-term exposure to airborne particulates, adjusted for concomitant exposures to other pollutants. Since only two such studies have been conducted to date, additional long-term studies are needed to validate and extend the results of these initial findings. Long-term studies in which detailed information on the temporal patterns of exposure to airborne pollutants could also provide information on the critical exposure-time windows for particulate health effects. Long-term follow-up studies involving children could also be used to determine whether particulate-matter-related depression of pulmonary lung function in childhood persists into adolescence and adulthood. Although one such investigation is currently underway, it will be important to independently confirm the findings.

DECISIONMAKING VALUE

It is important to understand the relative importance of combinations of various pollutants to health responses so that relevant pollutants can be regulated appropriately. It is also critically important to understand better the nature and effects of long-term exposures to particulate matter and gaseous copollutants, so that the full public health effect of these combined exposures can be assessed.

FEASIBILITY AND TIMING

The feasibility and timing of studies addressing gaseous copollutants in analyses of epidemiological data depends upon the availability of measurements of these pollutants in areas where studies have been undertaken. If data have to be collected, only prospective epidemiological

studies are possible; those will require considerably more time and resources. Methods for experiments involving controlled exposures to mixed atmospheres are available.

COST

Controlled exposure studies of experimental animals and humans require from $200,000 to $5.0 million per study. The number of studies to be undertaken will depend upon the number of health end points to be examined and the number of mixed atmospheres to be evaluated. The committee estimates that controlled exposure studies will require $3.0 million per year for the first two years, $4.0 million per year for the third through sixth years, and $5.0 million per year for the remaining years.

The cost estimates for carrying out the recommended epidemiological analyses of routinely collected monitoring data, along with existing administratively collected health-record data (e.g., Medicare records and hospital admission computerized data) relate to the costs of reducing such data to analytical files and the cost of analytical support. Those costs are estimated at approximately $200,000 per separate analytical effort and could begin immediately with two to four studies per year. If additional data collection is required within a given region for either the aerometric data or the health-related data to supplement existing information from other administrative sources, the costs could easily double, simply from the need to validate that joining data from multiple sources has been accurately done. This represents an opportunity to use the EPA's planned $PM_{2.5}$ monitoring network to reduce additional costs. Such an effort will require coordinated input into the EPA monitoring-network design to assure its utility for providing input to epidemiological studies.

New data, both aerometric and health-related, need to be actually measured, and the committee estimates the cost would be approximately $1.0 million per year for each kind of data from each site studied. Four studies would be needed to cover the different regions in the United States.

In the short term, existing population cohorts could be used, along

with available monitoring data for other pollutants. These relatively inexpensive studies should cost approximately $50,000-100,000 per study to augment existing analyses of epidemiology data. In the longer term, new data will need to be collected, for air quality and population cohorts. Analytical costs need to be augmented by the costs of exposure assessment for a considerable period, depending upon study design and populations needing to be followed for extended periods. The committee has estimated the cost of obtaining new data for the short terms to be $1.0 million per year per study for the 13-year period. The committee expects the design and implementation of new long-term epidemiological studies to be a principal activity of the university-based research centers.

An important long-term objective is the conduct of a large-scale prospective epidemiological study of the public health impacts of exposure to particulate air pollution, including both morbidity and mortality. Such a study would serve to validate and extend the results of two existing studies, and provide more definitive information on the effects of long-term exposure to airborne particulates. The committee recommends that such a study might begin in year two, and estimates the cost at $3.0 million annually for 10 years.

The committee also recommends that a study be conducted of the persistence of pulmonary lung function decrement observed in children. Such a study could be initiated in year two using a cohort of children 7-10 years of age, and following them through to adolescence or adulthood. The cost of such a study is estimated at $1.0 million annually over a twelve year period.

RESEARCH TOPIC 8 SUSCEPTIBLE SUBPOPULATIONS

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

DESCRIPTION

Not all individuals in the population respond to particulate matter

in the same way or to the same degree (EPA 1996a). Individual levels of susceptibility are influenced by individual variations in physiology, behavior, exposure, biological mechanisms, host factors, exposure to copollutants, and the biologically effective dose. Toxicological, clinical, and epidemiological evidence suggests that asthmatics, school-aged children, elderly people, and individuals with pre-existing heart and respiratory conditions might be especially susceptible to particulate matter (Lebowitz et al. 1987; Stankus et al. 1988; Pope et al. 1991; Menon et al. 1992; Pope and Dockery 1992; Schwartz 1994; 1995; Schwartz et al. 1994). The possibility exists that important subgroups might also include infants, preschool children, and pregnant women (see Appendix B). Susceptible subpopulations and the personal and environmental factors that affect particulate-matter susceptibility are largely unknown or poorly characterized. Susceptible individuals might experience different levels and types of particulate-matter exposures and doses than the general population. Their behavior and activity patterns might bring them into contact with varying mixtures of ambient particulate matter at varying concentrations at different times. For example, the lung morphology and increased breathing rates of children could increase their particulate-matter doses and cause them to experience greater health effects. In addition, the size and composition of the particulate matter, the presence of individual variations in deposition, retention and clearance rates, and personal characteristics (e.g., age, sex, prior disease, airway geometry, inflammatory and neural responses, or infectivity) could alter their biologically available and effective doses and responses. Important environmental factors might include secondhand smoke, gas, or kerosene heating or cooking, chemical reactions in indoor air, workplace exposures, pollen, insects, microbes, dander, or other factors. At this time, the limited knowledge about these and related factors in susceptible subpopulations prevents the development and validation of effective models for exposure assessment or prediction of actual doses. Controlled human-exposure studies and the development of appropriate animal models (that mimic human respiratory and cardiac disease) are needed to obtain the essential data for exposure and dose modeling in the subgroups. Once refined dose estimates can be made,

epidemiological field studies can complete the framework for defining susceptible subpopulations.

Concerns about the nature and severity of chronic adverse health outcomes have not been adequately addressed. The importance of short-term, peak, cumulative, and long-term exposures for long-term health effects needs to be determined. Although more research has been conducted on acute responses (particularly exacerbation of asthma), very little is known about the chronic or life-shortening effects of particulate matter in susceptible subpopulations. Therefore, it is essential to identify who is dying due to acute particulate-matter exposure, and the extent to which the mortality is premature. More work on ill adults and pregnant women should be considered. Clinical and epidemiological studies are needed to increase knowledge about the types and severity of health responses in susceptible subgroups.

SCIENTIFIC VALUE

The scientific value of studying susceptible subpopulations is considerable, because little is known about the host and environmental characteristics that place individuals at increased risk from exposure to particulate matter. Studies to identify and characterize the factors that affect exposures and biologically effective doses for subpopulations are especially needed to reduce uncertainties in risk assessment.

DECISIONMAKING VALUE

The decisionmaking value of new knowledge about susceptible subgroups is directly related to policy choices mandated by the Clean Air Act. EPA is charged with protecting the health of all Americans and has placed children's health in particular as a key priority. Without knowledge of susceptible subpopulations, decisionmakers cannot be fully informed and will not be able to meet the health-protection objectives of the Clean Air Act.

FEASIBILITY AND TIMING

It might not be feasible or timely for EPA to develop by 2002 all of the data and models needed for susceptible subgroups. Limitations in research capacity, technical capabilities to measure individual characteristics and exposures, and capacity to model biologically effective doses are current concerns. The agency's financial and human resources appear to be most suited to advancing knowledge about exposures. EPA should seek to leverage its capabilities with those of other agencies and organizations. Population-based field studies that emphasize key subpopulations would be timely and could be strengthened through such collaboration. Identification and characterization of the important aspects of particulate matter, copollutants, and acute and chronic adverse health outcomes should be pursued.

COST

Recognizing that studies of some subgroups are under way and others are nearing completion (see Appendix B), the near-term studies needed to address additional subgroups and factors is estimated to require $2.0 million per year for the first 2 years. Long-term studies of chronic health outcomes will require more time and extensive resources. The cost is estimated to be $3.0 million per year for the third through the eighth years.

RESEARCH TOPIC 9 MECHANISMS OF INJURY

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

DESCRIPTION

The significance of results from epidemiological studies will be greatly

enhanced if results obtained in controlled exposure studies can contribute plausible explanations of underlying biological mechanisms for ambient particulate-matter-associated health effects. In this regard, there is a need to understand how inhalation of particulate matter can result in local pulmonary and systemic responses noted as health outcomes in epidemiological studies. Specific research recommendations related to mechanisms of injury are described below under subtopics 9a, b, and c.

SCIENTIFIC VALUE

Because mechanisms by which particulate matter in ambient air contribute to respiratory and cardiovascular diseases are largely unknown, elucidation of such mechanisms would fill an important scientific data gap. This will require carefully designed clinical studies, as well as *in vivo* and *in vitro* toxicological investigations. Controlled clinical studies afford an opportunity to examine the hypothesis that particulate matter exacerbates pre-existing cardiorespiratory conditions in susceptible subpopulations. Appropriately designed toxicological investigations would provide mechanistic information on particulate-matter-induced damage to pulmonary tissue and on the cellular and molecular events involved in the causal pathways responsible for cardiorespiratory morbidity and mortality.

DECISIONMAKING VALUE

Elucidation of the mechanisms by which particulate matter might lead to cardiorespiratory morbidity and mortality would be of great value in risk-management decisionmaking by adding to the weight of evidence for a causal relationship between particulate-matter exposure and adverse health outcomes. At present, the interpretation of observed epidemiological associations is hindered by the lack of well-established mechanistic pathways. A clearer understanding of the etiology of particulate-matter-related morbidity and mortality would

therefore enable decisionmakers to develop more targeted and cost-effective strategies for reducing particulate-matter-related risks.

FEASIBILITY AND TIMING

The scientific infrastructure needed to conduct clinical and toxicological investigations of mechanistic pathways of particulate-matter-related cardiorespiratory disease is well established. Because sufficient information exists to design studies that would be informative and relevant, such studies should be initiated immediately and carried out in parallel with other investigations.

Cost is discussed for each of the three approaches below.

9a. ANIMAL MODELS

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

DESCRIPTION

Associations between exposure to generally low ambient particulate-matter levels with morbidity and mortality have been observed in susceptible subpopulations, but it is not likely that low environmental concentrations of particulate matter will elicit acute health effects in healthy animals, which are the usual models in toxicological studies. Epidemiological data strongly suggest that the associations between particulate matter and mortality and morbidity are manifested in subpopulations having special susceptibility factors. Therefore, laboratory studies should focus primarily on the use of animal models of these susceptible populations. The data indicate that the mortality associated with short-term increases in particulate matter occurs primarily in subgroups with pre-existing susceptibility factors, such as old age and respiratory or cardiac disease. Morbidity from

short-term particulate-matter exposures has also been observed in susceptible subpopulations, primarily asthmatics of all ages and other individuals with respiratory disease. Similarly, chronic exposures appear to be associated with pulmonary diseases as well as lung cancer. Several animal models of human cardiorespiratory disease are in use, but all have serious limitations. First, it must be recognized that a good understanding does not exist of the precise human conditions that need to be modeled. Not all asthmatics or all elderly people are identically susceptible for the same reasons. Second, although all the animal models mimic some portion of the human condition, few, if any, can model all of the relevant features of the condition of interest. Third, all animal models present difficulties in extrapolation to humans, and validation of the degree to which an animal system models a human condition occurs far less frequently than needed.

There is a need to extend the range of human cardiorespiratory disorders modeled by animals or artificially induced animal preparations, and an equally important need to validate all animal models against their human counterparts. At present, we do not know whether the short-term or long-term associations between particulate matter and health will prove to be most important. Therefore, it appears that models of allergic and inflammatory respiratory disease, reduced defenses against infections, common forms of respiratory and cardiac insufficiency and failure, and lung cancer would all be useful models in studies of particulate-matter effects. At this point, it is difficult to prioritize among the conditions needed for laboratory modeling. Furthermore, particulate-matter inhalation studies should be designed at several exposure levels so that exposure-dose-response relationships can be established. Low exposure levels and relevant exposure routes and modes need to be emphasized. It is also necessary to assess deposition of particulate matter in different regions of the respiratory tract and to evaluate subsequent retention characteristics, which then can be correlated with specific biological responses and compared with results of exposure studies using healthy animals. Acute responses should be the initial focus, with effects caused by chronic exposure investigated later as more information is obtained on the significance of individual compounds or size fractions of particulate matter.

SCIENTIFIC VALUE

Animal models mimicking susceptible human subpopulations are a necessary prerequisite to studying effects of ambient or surrogate particulate matter. The models must be validated to reflect the human-disease state. Studies can be performed with these models that cannot be carried out in humans for ethical and technical reasons. In addition to particulate-matter-related research, they are also useful to investigate both the pathophysiology and treatment of human disease. The validated models provide insights into disease-oriented mechanisms of particulate matter, provided that physiological routes of exposure and relevant low doses are used. Furthermore, information on particulate-matter dosimetry in diseased lungs will be useful for purposes of extrapolation to humans. The ability to generate these validated models is of great value to developing a good data base by reducing variability in responses. Finally, the validated models form a valuable basis for developing clinical and appropriate in vitro mechanistic models.

DECISIONMAKING VALUE

Results from particulate-matter studies with validated animal models of human disease will provide information on pertinent particle characteristics for the purpose of particulate-matter standard setting. They will also provide valuable information for designing focused clinical and epidemiological studies that will contribute to the review of NAAQS for particulate matter. They will also contribute valuable information in guiding decisions on important policy issues such as the indicator for the standard and the amount of the margin of safety.

FEASIBILITY AND TIMING

An immediate, active program is required to develop new models and to validate existing animal models of human disease. The capacity and capability for this effort are available, but new research initiatives

are required to complete this important task successfully so that appropriate animal models are available within the next 2-3 years.

COST

The development and validation of these animal models is expected to cost approximately $3.0 million per year for the first 6 years.

9b. IN VITRO STUDIES

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

DESCRIPTION

In vitro studies with particulate matter have been performed to characterize specific cellular events and to determine underlying toxicological mechanisms. They are an important complement to studies in whole animals and humans. However, most in vitro studies have been executed without due consideration of doses administered to the cells. Therefore, it is important to use dose levels that are relevant to *in vivo* exposures. *In vitro* studies are useful to examine a specific hypothesis based upon results of *in vivo* studies and can be tested using target cells of the respiratory tract. However, the method of dosing has to be critically evaluated (e.g., via delivery of airborne particles or via particle suspension in the medium). Furthermore, the use of cell-lines versus primary cells or the use of cell co-cultures, as well as culture conditions, have to be carefully assessed. In general, *in vitro* studies should focus on specific mechanistic aspects of particulate-matter toxicity and might, therefore, be restricted to situations where results of *in vivo* studies indicate positive effects for a given particle type. Within this area, there is a need to test the usefulness of *in vitro* studies for investigating mechanistic events in cells that mimic those that occur in susceptible individuals (e.g., cells of old versus young organisms or sensitized cells).

SCIENTIFIC VALUE

In vitro models can be used to examine cellular and molecular mechanisms of toxicity due to particulate-matter exposure, including the role of specific tissues and cell types in the induction of toxic responses. To be of most value, it is essential to relate tissue doses to levels of exposure (i.e., *in vivo*) and to ambient levels and components of particulate matter. This will permit calibration of cellular and molecular events to ambient exposures, and will facilitate the use of such *in vitro* data for risk-assessment purposes. Positive results from such studies should be pursued by whole animal or clinical studies.

DECISIONMAKING VALUE

The use of appropriate *in vitro* models will provide valuable indirect information to support other investigations of the mechanisms of particulate-matter toxicity, which will assist in the interpretation of epidemiological data that show associations between particulate-matter exposure and cardiorespiratory disease. Specifically, disease-related mechanistic information at the cellular and molecular level could add significantly to the weight of evidence regarding a causal relationship between particulate-matter exposure and human morbidity. This information can also be helpful in interpreting the results of animal and clinical toxicity studies conducted in support of the development of the NAAQS.

FEASIBILITY AND TIMING

Several toxicology laboratories are well equipped to conduct mechanistic studies on the cellular and molecular events involved in particulate-matter toxicity. Such studies should be designed and conducted in conjunction with whole-animal and clinical toxicity studies.

COST

The cost of the recommended *in vitro* studies is estimated to be $3.0 million per year for the first 6 years.

9c. CLINICAL MODELS

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

DESCRIPTION

The association between particulate-matter exposure and adverse health effects reported from ecological epidemiology studies appears strongest for respiratory and cardiovascular deaths, especially in individuals 65-74 years of age and older. It is not clear if there are mortality effects in healthy individuals of any age, particularly those younger than 65 years of age. There is weak evidence for morbidity in children. Based upon epidemiological findings, the population subgroups potentially susceptible to particulate matter and, therefore, candidates for clinical studies, include the elderly with pre-existing respiratory conditions (e.g., COPD), the elderly with cardiovascular disease (e.g., previous myocardial infarction or arrhythmia), asthmatic children and adults, impaired and nonimpaired cigarette smokers, healthy children and healthy elderly (Utell and Drew 1998). Other aspects of life style (e.g., nutrition and activity) should also be considered in assessing potential susceptibility to particulate matter. Clearly, clinical models will focus on acute responses that often have implications for chronic effects.

SCIENTIFIC VALUE

Associations between exposure to generally low ambient particulate-matter levels and morbidity have been observed in susceptible

subpopulations. Controlled human studies provide an opportunity to examine responses to particulate matter in both healthy and susceptible subpopulations. Carefully designed clinical studies will provide information on symptomatic, physiological, and cellular responses in healthy and susceptible subpopulations, namely those with pre-existing cardiorespiratory conditions. Such studies can also provide much-needed information on particulate-matter uptake and retention in healthy and susceptible subpopulations. Preventive intervention trials within susceptible groups should be considered (e.g., an NIEHS trial).

DECISIONMAKING VALUE

Clinical studies have provided important information for other regulatory decisions. Elucidation of responses in humans is a key to defining critical effects levels and determining the nature of adverse health effects. Assessing acute responses in groups with chronic diseases will provide important leads on plausible mechanistic pathways. Moreover, it will provide crucially required information on relative differences in responsiveness between at-risk and healthy populations. Clinical research also aids decisionmaking on the complex issue of margin of safety.

FEASIBILITY AND TIMING

Research facilities exist for clinical studies that use environmental chambers and mouthpiece exposures. Studies could be initiated immediately and carried out in parallel with animal studies.

COST

The human studies are estimated to cost $3.5 million/year for six years due to the complexities and multidisciplinary teams required for the conduct of such studies.

RESEARCH TOPIC 10 ANALYSIS AND MEASUREMENT

Several methodological advances are needed to facilitate understanding of health effects related to particulate matter. These range from the development of appropriate models to estimate the fate and deposition of inhaled particulate matter, to improved monitoring methods, exposure methods, and statistical tools to analyze collected data.

10a. STATISTICAL ANALYSIS

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?

DESCRIPTION

The statistical analysis of epidemiological data on particulate matter and human health presents several difficult methodological issues. Time-series studies require consideration of the appropriate dose-response time lag and long-term and short-term trends in health and exposure data (due to factors such as seasonal and day-of-the-week effects). Since observations taken at different points might be correlated, the nature of the serial correlation in time-series studies needs to be characterized, and autocorrelation needs to be adjusted for in subsequent analyses.

Studies of long-term exposure require analyses of time-dependent exposure patterns to identify critical exposure-time windows. Identification of the unique effects of particulate matter or its constituents requires careful adjustment for simultaneous exposure to a complex mixture of copollutants. Extensive covariate adjustment is required to minimize the possibility of confounding factors. Exposure measurement error can have the effect of understating risk, as well as overstating the precision of risk estimates. Flexible exposure-response models including time-dependent covariates, are also needed to described accurately the nature of the exposure-response relationships observed in epidemiological studies of particulates.

Several analysis methods have been used to address these issues; to date there is no consensus about which method is preferable. Evaluation of alternative existing methods would be useful, along with the exploration of more innovative methods. The most important questions are

- What methods of removing the influence of long-term trends from parallel data on daily particulate-matter concentrations and population morbidity and mortality are most appropriate?
- Should time-series of health and/or environmental data be filtered before analysis? What filters are most appropriate for this type of data?
- What is the nature of the autocorrelation function in time-series studies? How should autocorrelation be taken into account in the analysis of time series data?
- How can the critical timing of exposure (e.g., frequency or duration) for particulate-matter-related morbidity and mortality be determined?
- How can the unique health effects of particulate matter and its biologically important constituents be determined in the presence of exposure to multiple copollutants?
- Are existing epidemiological data adequate to identify the most relevant timing characteristics of exposure?
- Is residual confounding a concern in particulate-matter epidemiological studies?
- What types of exposure-response models are most appropriate to describe the observed relationships between mortality and morbidity and exposure to ambient particulate matter?
- How can key covariates, including potential confounders and modifying factors, be best incorporated into risk models used to describe the effects of particulate matter on population health?
- How can the effects of long and short-term exposures to particulate matter on mortality, including reduction in life expectancy, best be estimated?
- Could the positive associations between particulate matter and adverse health outcomes, as observed in time-series studies, be false

positives resulting from multiple statistical tests using various regression models?

SCIENTIFIC VALUE

Analysis and evaluation of complex data on the health effects of particulate air pollution requires advanced statistical methods, including methods for the analysis of multivariate time series data. The application of such methods may involve a number of methodological choices during implementation, such as the method of detrending or filtering. With such complex analyses, it is important to ensure that the conclusions reached are not dependent on the choice of method used.

Validation of the statistical methods used in the analysis of epidemiological data on particulate air pollution will increase the level of confidence that can be attributed to conclusions drawn from such studies. The development of optimal methods of analysis may also lead to greater sensitivity in the detection of subtle health effects, and reduce the uncertainty associated with estimates of human-health risks due to exposure to particulate matter.

DECISIONMAKING VALUE

Given the potential public health impact of particulate air pollution, and the large costs associated with reducing pollution levels, it is critical that the scientific evidence on which air quality standards are based not be subject to uncertainty due to methods of data analysis and evaluation. Validation of analytic methods will not only enhance the scientific value of epidemiological findings, but will strengthen the basis on which future regulatory actions are taken.

FEASIBILITY AND TIMING

Although analytic methods for the evaluation of data from epidemiological studies of the health effects of particulate air pollution are relatively

well established, there exists considerable need for further methodological development. Given the existing knowledge base, such development is highly feasible. To be most effective, methodological research on the evaluation of epidemiological data on particulate health effects should be conducted in a multidisciplinary manner. The development of statistical methods of analysis should be undertaken in collaboration with scientists with expertise in biostatistics, epidemiology, and exposure assessment, and validated under conditions corresponding to those likely to be encountered in practice.

Methodological evaluation and development should be initiated immediately. This would enable the application of resulting methodological advances in the analysis of future epidemiological investigations initiated later, as well as in the reanalysis of previous epidemiological results.

COST

Methodological research is relatively inexpensive, compared to the costs of data acquisition. Methodological research could be established in the first year at a cost of $500,000. Subsequent development and application of methods could be undertaken by several multidisciplinary teams with an annual budget of $1 million per year for 6 years, including collection of data necessary to support this work. This program should include the conduct of focussed investigations designed to validate the methods used under conditions reflective of those encountered in practice.

10b. MEASUREMENT ERROR

What is the effect of measurement error and misclassification on estimates of the association between air pollution and health?

DESCRIPTION

Some of the studies undertaken to estimate the association between

particulate matter and human health relate population response to population exposures, whereas others are concerned with an individual's response to monitored particulate matter. To the extent that individual exposure measures are rarely available, most of the studies can be considered ecological in nature (Greenland and Robbins 1994; Kunzli and Tager 1997).

The response of a given individual to environmental agents such as particulate matter depends upon that individual's exposure to the agents. In the case of particulate matter, it is a complex mixture. Several differences between individual exposure to a pollutant and the monitored value of that pollutant must be considered in analyses of exposure and response. The components of this difference include errors in the accuracy and precision of the monitoring instrument; differences in exposure due to the placement of the ambient monitor (related to the zones of representation for a monitor or to the spatial homogeneity of the environmental agent measured); differences between ambient concentrations used to characterize a pollutant exposure and the average personal exposure to that pollutant or, for particulate matter, its mass or the size fractions and chemicals of biological significance; and the differences between average personal exposure levels and the exposure of a given individual.

Measurement error has several potential consequences. It can bias estimates of the association between a health end point and an environmental variable. (Usually the association is underestimated.) It can bias the estimated shape of any dose-response relationship between the health end point and environmental variable. Most often the bias is toward linearity; hence estimates of response thresholds can be obscured. In the context of a multivariate analysis, if the independent variables are correlated with each other and have relative differences in measurement error, then estimates of association can be biased. In general, associations between the health end point and those variables with smaller measurement error will be overestimated. The extent of the effect is determined very much by the type of analysis or statistical model used and by the nature of measurement error. For example, is the error linearly, nonlinearly, or multiplicatively related to the true measure? Is it systematic?

It is also possible for there to be misclassification error in the outcome variable. (For example, cause of death could be misclassified.) The effect of that type of misclassification will depend upon the nature of the misclassification and the statistical model used to analyze the data. For most of the models used to date, the effect of this error is not expected to be large. Other issues include

- How large are the various components of measurement error for each independent environmental variable (e.g., pollutants or weather)?
- How is the measurement error of one variable related to the measurement errors of other variables in the same model?
- What are the statistical distribution and types (e.g., Berkson or classical) of measurement error?
- What are the effects of measurement error on the estimated associations between particulate matter (or its size fractions and biologically important chemical constituents) and health?
- Does the presence of differential measurement errors in other variables in the model influence the estimate of association between a specific environmental agent and health?
- Is there any error or misclassification likely to be present in the outcome variable? Is that error likely to have any effect on the outcome of the statistical models used for analysis?
- Can methods of adjusting for the effects of exposure measurement error be used to mitigate the effect of exposure measurement error on risk estimates?
- Can spatial interpolation methods provide more accurate estimates of individual exposures to particulate air pollution?
- How would the use of measures of personal exposure improve estimates of the association between particulate matter and health?

SCIENTIFIC VALUE

Relatively little is known about the nature of exposure estimation error for the suite of criteria air pollutants. Effects of measurement error are known for a few classical situations when fixed assumptions

are made about the nature of these errors. The validity of these assumptions needs to be ascertained.

DECISIONMAKING VALUE

Until the effects of measurement error are understood and taken into account, the association between exposures to ambient particulate matter (or its size fractions and biologically significant chemical constituents) and health effects cannot be estimated without acknowledging the source of uncertainty and its potential effect on risk estimates or particulate-matter reduction strategies.

FEASIBILITY AND TIMING

Data need to be collected to ascertain the nature of measurement error. Once that is understood, the effects can be ascertained and methods can be applied to correct for error.

COST

Much of the data required to address the issue of exposure measurement error will be collected through personal exposure studies conducted as part of the enhanced exposure monitoring component of the overall particulate research program. Nonetheless, additional studies designed to characterize distribution measurement error distributions will be needed. Such studies will involve replicate measurements under the same conditions, and are estimated to cost approximately $1.0 million annually for the first, second, third, and fourth years. Methodological development of exposure measurement error methods is recommended on an overlapping time frame, beginning with a workshop to identify methodological approaches ($100,000 in year 1), and followed by a five year program of methodological development and application, costing $500,000 per year.

5

THE COMMITTEE'S RESEARCH INVESTMENT PORTFOLIO

In this chapter, the 10 highest-priority research recommendations, presented in Chapter 4, are integrated and summarized in a "research investment portfolio" developed by the committee. The analogy to an investment portfolio acknowledges that a research program has multiple goals that change over time, just as an individual financial investor might have a changing overall long-term investment strategy. A financial investment strategy must be responsive to external changes (e.g., changes in income streams, expenses, the stock and bond markets). Similarly, the committee's research investment portfolio relies on continuing responsiveness to new research findings, iterative transfers of knowledge across disciplines, investigative technology, the development of integrated interdisciplinary information, and changes in available resources.

In developing the research portfolio, the committee sought to integrate the scientific value, decisionmaking value, feasibility, sequencing, and rough but informed collective-judgment estimates of the costs of the recommended research activities. Within the portfolio, the 10 recommended research activities are not ranked by relative priority, and the numbers assigned to them are for identification purposes only. The 10 recommendations were judged to be interdependent, and all 10 are highly relevant to the reduction of policy-related uncertainties. All recommendations met the committee's criteria for research selection

(see Chapter 3). The portfolio is designed to maximize growth in critical knowledge as expeditiously and cost effectively as possible through interactive components and iterative stages, providing a continued stream of scientific evidence on a series of hierarchical topics to fill key gaps in the committee's overall research framework.

The committee's portfolio spans a 13-year horizon, from 1998 to 2010, the estimated closure date for scientific input to EPA's anticipated 2012 review of particulate-matter standards. This portfolio, if aggressively and properly implemented by EPA, should result in substantial new information for the next scheduled EPA review of the particulate-matter standards in the year 2002. By that time, critical information would be expected regarding the most biologically important components and characteristics of particulate matter, the toxicological mechanisms through which they act, and how well the data from ambient air monitors represent the actual exposure of people to particulate matter, especially for the most potentially susceptible subpopulations. It is noteworthy that EPA's current timetable (Table 1-1) for the implementation of the new $PM_{2.5}$ standards does not envision the implementation of actual control requirements until approximately 2012. The committee believes that the 1998-2010 time span is an interval over which a comprehensive research program could be reasonably anticipated to produce findings that would materially address key uncertainties in a deliberate plan that emphasizes both early and longer-term results. But the pace of research cannot always be adjusted to match the schedule of a regulatory decisionmaking process, which is determined mainly by law, policy, and administrative factors. Some of the committee's recommended research topics (e.g., effects of controlled exposures of susceptible subpopulations to particulate matter) can be quickly and efficiently addressed, with the possibility of definitive findings within a few years. Other research topics (e.g., long-term effects of air pollution on morbidity and mortality) will require substantially more time for resolution. Consequently, there needs to be a commitment to begin some research immediately, to sustain research on the longer-term questions, and to implement and maintain surveillance of the health effects of particulate matter as the new standards are implemented.

The committee's research investment portfolio is summarized in Table 5.1. It is based on the research recommendations presented in Chapter 4. It covers the committee's recommended timing and rough but informed collective-judgment estimates of research costs. The composition of the portfolio changes over time, initially emphasizing exposure assessment and toxicological investigations. Observational and experimental epidemiological studies are mostly deferred until later in the portfolio plan, pending the development of better methods to measure exposure and an enhanced understanding of the health-relevant characteristics of particles.

In Table 5.1, the committee's research plans for human exposure assessment appear first, front-loaded into the early years of the portfolio, because there is an urgent need to characterize actual exposures of potentially susceptible persons to particulate matter and to characterize the biological consequences of those exposures. Methods are already in hand to assess personal exposures to particulate matter and their outcomes, but little investigation has been done or is yet planned by EPA to investigate the particulate-matter exposures of susceptible persons, e.g., those with chronic obstructive pulmonary disease (COPD), asthma, and heart disease. There is also limited information on exposures of children to particulate matter. Further, there is a serious lack of understanding of the relationship of concentrations measured at fixed outdoor monitoring sites with the actual personal exposures of such individuals. Such gaps in knowledge should be addressed immediately in a 3-year program beginning in 1998.

Another phase of exposure assessment research will be needed, beginning in approximately 2001. This component of exposure assessment research should be initiated after the most biologically important constituents and characteristics of particulate matter have been identified through toxicological and clinical studies. Exposures of potentially susceptible subpopulations (as well as the general population) would again be assessed, but this time with emphasis on the components or aspects of particles judged to be most biologically important. At this stage, serious consideration can be given to the strategy of preventive intervention trials and the strategy for use of advanced techniques in new epidemiological studies.

New exposure-assessment tools will be needed, reflecting anticipated

TABLE 5.1 The Committee's Research Investment Portfolio: Timing and Estimated Costs* ($ million/year in 1998 dollars) or Recommended Research on Particulate Matter

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
SOURCE/CONCENTRATION/EXPOSURE													
1. Outdoor vs. human exposure	3.0	3.0	3.0										
2. Exposure to toxic PM components				4.0	4.0	4.0	4.0	4.0					
3. Source-receptor measurement tools													
3a. Atmospheric modelling	2.0	2.0	2.0	2.0	2.0	2.0							
3b. Receptor modelling	1.0	1.0	1.0										
3c. Analytical methods	1.0	1.0	1.0	1.5	1.5	1.5							
4. Application of methods and models	1.0	1.0	4.0	4.0	4.0	4.0	4.0	4.0					
EXPOSURE/DOSE-RESPONSE													
5. Assessment of hazardous PM components													
5a. Toxicological and clinical studies	8.0	8.0	8.0	8.0	8.0								
5b. Epidemiology		1.0	1.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0
6. Dosimetry	3.0	1.5	1.5	1.5									
7. Effects of PM and copollutants													
7a. Copollutants (toxicology)	3.0	3.0	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)	1.0	6.0	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	2.0	2.0	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	3.0	3.0							
9b. *In vitro* studies	3.0	3.0	3.0	3.0	3.0	3.0							
9c. Human clinical	3.5	3.5	3.5	3.5	3.5	3.5							
ANALYSIS AND MEASUREMENT													
10a. Statistical analysis	0.5	1.0	1.0	1.0	1.0	1.0							
10b. Measurement error	1.0	1.5	1.5	1.5	0.5	0.5							
SUBTOTALS ($ MILLION PER YEAR)	36.0	41.5	48.5	52.0	49.5	41.5	28.0	28.0	17.0	17.0	17.0	14.0	14.0
RESEARCH MANAGEMENT** (ESTIMATED AT 10%)	3.6	4.2	4.7	5.2	5.0	4.2	2.8	2.8	1.7	1.7	1.7	1.4	1.4
TOTALS ($ MILLION PER YEAR)	39.6	45.7	51.2	57.2	54.5	45.7	30.8	30.8	18.7	18.7	18.7	15.4	15.4

*The committee's rough but informed collective-judgment cost estimates for the highest-priority research activities recommended in this report. See Chapter 4 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 the report.

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

advances in knowledge about particulate-matter toxicity. Monitoring techniques and exposure models will be needed that are specific to those components or attributes of particulate matter that are determined to be most relevant to health (e.g., the metal content or acidity of particles). Monitors will be needed to characterize population exposures, but attention should be mainly directed at monitors and monitoring strategies to provide information beyond that gained from the current practice of placing monitors at fixed outdoor sites. Monitors will also be needed for use in epidemiological studies directed at particles (or their markers) that are found in the initial years of the research portfolio to be linked to toxicity.

The links between particle sources and receptors (i.e., people) need to be characterized more specifically to provide a much better basis for control strategies. Armed with knowledge of the determinants of particle toxicity, the sources of the toxicants need to be identified, and the relationships between sources and exposures must be described. Models to integrate these factors are a priority, because decisionmakers need them for risk management planning.

The committee also recommends (Table 5.1) extensive research on the exposure-dose-response continuum. One immediately addressable gap is the relationship between exposure and dose in persons with underlying lung disease, specifically COPD and asthma. A recent workshop on clinical studies and particulate matter (Utell and Drew 1998) identified candidate particles for clinical studies to include ultrafines, metals, and acid-coated particles, as well as concentrated ambient particles. The committee recommends a 4-year research program to address that gap. In addition, toxicological research efforts need to be directed at particle characteristics determining toxicity, the combined effects of particulate matter and other pollutants, and the toxicological mechanisms involved. The toxicological research recommended by this committee includes *in vitro* studies, animal studies, and human (clinical) studies. The committee's program initially emphasizes specific characteristics of particles but then shifts its emphasis to the combined effects of exposures to particulate matter with other pollutants. The changing balance reflects the anticipated gains in understanding of the determinants of particulate-matter toxicity in the initial years of the

portfolio, followed by a shift to research on how the most biologically important particles act in combination with other pollutants.

A 6-year program on mechanisms of particle toxicity that significantly increases current efforts is also included. This program would address more fundamental short-term and long-term mechanisms of injury by particles. The research would complement the more descriptive animal and clinical studies on particle characteristics and on the consequences of combined exposures.

The research portfolio also includes epidemiological studies needed to assess the effects of population exposures and to document any biological consequences of changing exposures. In the committee's proposed schedule, funding for major epidemiological studies is deferred until initial planning is accomplished and more information becomes available on exposure measurements for susceptible individuals and the most biologically important aspects of particles. It will be necessary to redirect current research efforts to fill gaps in knowledge of human exposure to ambient particulate matter and copollutants on a timely basis. However, the epidemiological studies can begin as soon as the information on exposures and biologically important particle constituents becomes known. Absent that vital information, epidemiological studies cannot be directly focused on the most relevant pollutants or subpopulations. The principal focus of future epidemiological investigations should be major population-based studies—both observational and intervention trials—directed at gaining an understanding of the health effects of particles, acting alone or in combination with other pollutants, that are found to determine toxicity in mechanistic experimental studies.

Some epidemiological researchers believe that new epidemiological studies should begin immediately. However, this committee, which includes several epidemiologists, concludes that it will be more productive and cost-effective to delay major epidemiological studies until further information on actual human exposure and the most biologically important components or characteristics of particulate matter becomes available. Without such information, the committee does not anticipate that epidemiological studies could be designed to provide much useful information beyond what is already known.

Some scientists have expressed concern that measurement error limits the interpretation of observational epidemiological studies, such as time-series studies and investigations like the Six Cities Study, that address the effects of particulate-matter exposures on individuals. Over the first 3 years in the committee's research portfolio, methodological research using improved exposure data developed in the program will begin to address this persistent concern.

The committee identified the need for support of a number of activities that underpin the development of new methods needed for the recommended research. There is an immediate need for well-characterized animal models of the chronic human diseases associated with susceptibility to particulate matter for future toxicological studies, as well as systems for studies of *in vitro* exposures to particulate matter and other pollutants. Better epidemiological methods are needed to increase the efficiency of studies of large populations using routinely collected data on health outcomes and air-pollutant concentrations and for using those data for surveillance of the health consequences of implementing air-pollution standards.

The cost estimates for the research portfolio are not based on a formal budgeting process, but drew on the extensive research and research-management experience and collective judgment of the members of this NRC committee (see Appendix A). The committee developed the estimates recognizing that any one research element might turn out to be somewhat more or less costly than estimated, but the overall estimates are based on informed collective judgments of the estimated levels of resources needed to reduce substantially the key uncertainties in regulatory decisionmaking for particulate matter. The committee will refine these estimates as it continues its work in this 5-year NRC study.

The research cost estimates summarized in Table 5.1 are by no means intended to represent the total particulate-matter research budget recommended for EPA or the nation. They reflect only the 10 research activities assigned highest priority by this committee. They do not represent all of the research that needs to be done on particulate matter. Other funding considerations might include the potential waste and undesirability of abruptly terminating lower-priority but

worthwhile and needed research activities that are already under way, the potential difficulty of changing research directions for some of the federal career research scientists in EPA's intramural laboratories, the technical information needs of EPA's regulatory offices, and the infrastructure costs of establishing and maintaining the research centers requested by Congress.

Over time, the research investment portfolio summarized in Table 5.1 would go a long way toward meeting the needs of decisionmakers, providing some answers for the next phase of decisionmaking and others later. The results of this recommended research would fill the key gaps in the committee's framework for establishing links between particulate-matter sources and health risks. Some questions (e.g., the long-term health effects of air pollution on public health) will require sustained investigation.

The research costs estimated by this committee can be viewed as investments in the scientific foundation upon which all particulate-matter regulatory activities of EPA, state and local governments, and the private sector —planning, implementation, monitoring, compliance, and enforcement—will be built. A solid scientific foundation can help ensure that the other investments yield a sound return. An inadequate foundation will lead to continued uncertainty, contentious debates, and potentially unwise investments that fail to minimize the risks of particulate matter to public health.

The committee realizes that questions undoubtedly will remain about some of the key areas of uncertainty, even after new scientific results have been obtained. Therefore, future judgments will need to be made on the adequacy of new scientific information to address those uncertainties and on the appropriateness of moving from one phase of the committee's recommended research strategy to another. Nevertheless, a coherent and effective particulate-matter research program will require a strongly iterative process that assimilates and uses the results of the multidisciplinary research recommended in this report.

6

COMPARING THE COMMITTEE'S RECOMMENDATIONS WITH EPA'S RESEARCH PLANS

To help ensure the adequacy of the scientific information used to establish NAAQS, EPA maintains active intramural and extramural research programs on ambient air quality and health. A major component of EPA's current air-pollution-related research program focuses on the health risks resulting from exposures to airborne particulate matter. The research funds being invested by EPA in particulate-matter exposure and health-effects research are by far the largest single commitment of public or private resources available to address key particulate-matter research questions related to protecting public health. Thus, the allocation of EPA's resources (intramural or extramural, alone or in leveraged partnerships) and the strategy by which they are invested will be important factors in determining whether the nation successfully addresses key particulate-matter research topics in a timely and effective manner. To that end, the present NRC committee has begun to assess the degree to which EPA's current overall research efforts and plans concur with or differ from the committee's recommendations for highest-priority research investments. In some important areas, it recommends the redirection of some of EPA's resources.

CURRENT EPA RESEARCH FUNDING

EPA's particulate-matter research budget for the 1998 federal fiscal

year is $49.6 million. During the past 2 months, the committee heard presentations and received background materials from EPA officials and scientists describing their overall plans for allocation of most of this budget. A categorized summary of the planned budget for Fiscal 1998, derived by the committee from EPA's materials, is presented in Table 6.1. Of the total EPA budget for particulate-matter research in 1998, approximately 50% is devoted to intramural research, 39% to extramural research; and the remaining 11% to interagency research activities.

The committee reviewed EPA's overall plans in comparison with the committee's source-concentration/indicator-exposure-dose-response framework presented in this report (Figure 3.1 in Chapter 3), and found that of the total available, more than half of EPA's particulate-matter research resources are directed at better understanding health responses, through mechanistic and long-term health-effects research. Nearly one-third of EPA's total particulate-matter research resources appear to be allocated toward efforts to identify the links between sources and ambient particulate-matter concentrations and to improve ambient monitoring. Only 4% of the intramural budget for particulate-matter research in EPA's laboratories is focused on better understanding of the relationship between actual personal exposure and the particulate-matter concentrations measured at outdoor, fixed-site monitors. This is a critical deficiency that requires immediate rectification. And by design, the agency is apparently not planning major research on dose-response questions until the year 2000.

COMPARING EPA'S RESEARCH ALLOCATIONS WITH THE COMMITTEE'S RECOMMENDED RESEARCH PORTFOLIO

After the committee developed its recommendations for a portfolio of highest-priority particulate-matter research investments (Chapters 4 and 5), it compared its recommended research investment priorities with EPA's current research-funding allocations and plans. The committee finds that all of the questions addressed in EPA's current research plans fit within the overall source-concentration/indicator-exposure-

TABLE 6.1 Estimated FY98 EPA Research Allocationsa

Category	Intramural (Laboratories)	Extramural (Grants, Centers, HEI)[b]	Interagency	Total
SOURCE				
Emissions Characterization	$2.9 (13%)	$0.3 (2%)	—	$3.2 (7%)
Atmospheric Chemistry/Modeling	$3.2 (14%)	$1.3 (7%)	—	$4.5 (10%)
CONCENTRATION				
Monitoring Methods/"Platforms"	$4.9 (22%)	$1.3 (7%)	—	$6.2 (14%)
EXPOSURE				
Exposure Relationships	$0.8 (4%)	$4.0 (23%)	—	$4.8 (11%)
DOSE				
Exposure-Dose-Response	—	—	—	—
RESPONSE				
Acute Health Effects[c]	$8.8 (40%)	$2.5 (14%)	$3.0	$14.3 (32%)
Long-Term Health Effects	$1.0 (5%)	$8.0 (46%)	$1.0	$10.0 (22%)
NEW TECHNIQUES	$0.5 (2%)	—	$1.0	$1.5 (3%)
TOTALS	$22.1 (100%)	$17.4 (100%)	$5.0	$44.5 (100%)

[a] In millions of dollars (Source: Letter from J. Vandenberg, EPA, to J. Samet, Feb. 15, 1998)

[b] Derived from relative estimates of allocations for centers

[c] Includes susceptibility ($7.4), mechanisms ($5.4), biologically important (or key) components ($1.5)

dose-response framework used by the committee. Given the short time (approximately 2 months) available for the committee's study and deliberations thus far in preparing this report, and the evolving nature of EPA's plans, the committee was not able to make precise determinations of all differences between its highest-priority research recommendations and EPA's particulate-matter research budget.

It is clear that many of EPA's particulate-matter research activities and plans are consistent with the committee's recommendations. However, several important overall differences in funding allocations and in timing of investments seemed apparent. The committee's recommended research portfolio differs from EPA's plans with respect to some priorities, cost allocations, timing of research investments, and, in some cases, the specific approaches to important questions.

RESEARCH TO ADDRESS THE COMMITTEE'S MOST-IMMEDIATE PRIORITIES

The committee has identified two critical areas that require immediate research attention and do not appear to be adequately addressed by EPA. Both are needed to inform near-term decisionmaking on the particulate-matter NAAQS and to provide a foundation for future health-effects and implementation-related research. These areas are:

- Developing a better understanding of the relationship between actual personal exposures and the ambient concentrations of particulate matter measured at stationary outdoor monitors to assess the validity and meaning of epidemiological studies and to build the base for future epidemiological studies and particulate-matter control strategies.
- Determining through controlled animal and human exposure experiments the most biologically important components or characteristics of particulate matter (e.g., particle size and chemical composition) to best target future source characterization, source-receptor model development, risk assessment, and implementation of any standard

in a cost-effective manner that targets control strategies at the most-important sources of the most-important particulate-matter constituents.

In contrast, EPA's 1998 allocation of resources appears to focus only about 4% of its intramural resources on investigating ambient-versuspersonal exposure relationships, and only about 3% of EPA's entire 1998 particulate-matter research budget appears to be focused on identifying the most hazardous components of the particulate-matter mixture. Merely measuring outdoor-air quality at stationary sites will be insufficient to help EPA meet the important goal of reducing the major gaps in knowledge about actual human exposures to biologically important components or characteristics of ambient particulate matter.

OTHER ELEMENTS OF EPA'S PARTICULATE-MATTER RESEARCH PROGRAM

The committee's recommendations also differ regarding three longer-range areas of EPA's program:

- ***Source-Concentration:*** Nearly one-third of EPA's particulate-matter research budget for 1998 appears to be directed at characterization of source emissions, atmospheric chemistry and modeling, and the development of new monitoring techniques and more sophisticated monitoring platforms. All of those components will eventually be needed in EPA's particulate-matter research and regulatory program, and this committee has recommended a smaller immediate commitment of resources (approximately 14%) to develop improved methods for the activities. However, the committee recommends that the largest EPA investments in these areas be deferred until a few years from now, when an improved understanding of the biologically important components and characteristics of particulate matter will allow more productive and cost-effective investment in measuring the important particle components in source emissions and ambient air. If EPA chooses to continue with earlier substantial efforts in this area (presumably in addition to the committee's recommended research activities), such efforts should be mainly devoted to advancing technology for sampling

and chemical speciation, especially for organic compounds, and to quantifying the composition and sizes of particulate matter that people breathe in outdoor and indoor air. Given the extended timetable for NAAQS implementation and state implementation plan (SIP) development over the next 15 years (Table 1-1), a major research investment in these areas at the turn of the century should provide ample time to develop these implementation tools.

- ***Exposure-Dose-Response:*** Although the committee believes that major investments in dose-response research will not be very useful until further information on toxicological mechanisms is available, it recommends that carefully designed efforts begin immediately to develop biologically based models for deposition and fate of particulate matter in the respiratory tract of human subjects, especially for susceptible subpopulations.
- ***Health Response:*** The committee notes that EPA has apparently proposed to make an appropriately large allocation of funds to research on health effects of exposure to particulate matter—more than 50% of the total particulate-matter research budget. However, the area of biologically important particulate-matter components and characteristics appears to be significantly underfunded, and the area of long-term effects, which is important and merits sustained investment over the longer term, is given too large an immediate allocation by EPA. The committee's second report, expected in December 1998, will investigate in greater detail the current EPA efforts and plans, and, if appropriate, will recommend more specific redirection in these important areas.

THE RELATIONSHIP OF RESEARCH TO MONITORING

Independent of the research program, EPA's air regulatory office is initiating an extensive $PM_{2.5}$ NAAQS-attainment monitoring program to obtain data on $PM_{2.5}$ levels across the United States. The committee considered EPA's plans for this regulatory-office program and for the allocation of research resources to the development of new monitoring techniques (including new, more-sophisticated monitoring platforms). The committee recognizes that substantial resources must be applied

to ambient monitoring to ascertain attainment of the standards in various geographic areas, but it is concerned that the monitoring program is moving forward rapidly with too narrow a focus on $PM_{2.5}$. The committee is concerned about the scientific value of the data to be collected in these efforts if such monitoring is fully planned and implemented before some of the immediate research priorities are addressed and data gaps are filled. Moreover, as a secondary but critical goal, such a monitoring program should also be designed to support relevant health-effects, exposure, and atmospheric-modeling research efforts, or else the costs of some important research will increase greatly because of the need for additional monitoring.

EPA cannot assume that the implementation of the national $PM_{2.5}$ monitoring network will provide useful data for improving research or risk assessments for particulate matter. Current plans (e.g., speciation of particulate matter at least every sixth day) are inadequate for this purpose. EPA's monitoring plans will undoubtedly provide substantial amounts of data useful for determining attainment of new $PM_{2.5}$ standards in various locations. However, these data will only be useful in research if monitoring-system design and site location lead to population-exposure measures of sufficient biological relevance and accuracy. Without this, the State Implementation Plans may miss important targets for control.

Based upon theoretical considerations, the Federal Reference Method (FRM) sampler to be used by EPA is expected to lose volatile material (e.g., some nitrates and organics) from particle samples in quantities that are likely to depend upon location and season. Ongoing experiments are attempting to quantify the extent of this loss, and some data showing the bias toward undersampling of organics and nitrates have been presented at several conferences during the past 12 months. If those losses turn out to be substantial, then using the FRM would amount to quantifying only a fraction of the outdoor concentration, and that fraction would vary geographically and seasonally. Alternative technologies that overcome some of these biases are available and could instead be adopted.

EPA's planned $PM_{2.5}$ monitoring network appears to place great emphasis on site zones intended to represent the outdoor exposure of

large communities. Greater use of continuous (hourly) monitors would help determine the times of day and the exposures of people who are commuting, working, or exercising outdoors (Watson et al. 1998). Such monitoring would facilitate time-series epidemiological studies. More chemical characterization of particulate matter would help to enable testing of more specific indicators than $PM_{2.5}$ mass alone.

The committee recommends that EPA re-evaluate its current plans for the $PM_{2.5}$ monitoring program in light of this report. The committee recommends that EPA consider more fully the possibility that future research results might indicate that the expensive monitoring program is not measuring the most biologically important aspects of particulate matter.

The plans for this program (e.g., number and location of monitors and specific objectives and operating conditions) should be thoroughly and independently peer-reviewed at an early date, while the opportunity still exists for such review to influence the monitoring-network design and operation. Changes could then be made to increase the scientific utility of EPA's monitoring data, while still meeting the need for assessing regulatory attainment of particulate-matter standards at selected sites. Included in the EPA monitoring program are plans for several "super" monitoring sites where more extensive monitoring efforts will take place. At these sites, ambient-concentration data will be collected for gaseous pollutants, as well as for several size and chemical fractions of particulate matter. The costs of these monitoring efforts will be considerable, but their utility for health-effects studies has not been adequately considered to date. EPA has proposed to spend more funds on the $PM_{2.5}$ monitoring network than on all particulate-matter research activities combined next year (Fiscal 1999). Therefore, it is essential to leverage both regulatory monitoring and research efforts together to make the most effective use of resources to improve the scientific basis for decisionmaking.

OVERALL RECOMMENDATIONS

The committee reviewed EPA's overall planned research funding allocations for Fiscal 1998 and compared EPA's plans with the committee's

highest-priority research recommendations presented in Chapters 4 and 5. The committee concludes that many of EPA's particulate-matter research activities and plans are consistent with the committee's recommendations. However, the current EPA allocations and plans for research funding, although generally addressing aspects of particulate-matter pollution that are important and warrant study, should be redirected in some areas to focus on the most immediately critical research questions. Specifically, the committee recommends that:

1. EPA should allocate its particulate-matter research funding priorities in accordance with the recommendations in this report, incorporating intramural, extramural, and interagency investment to implement the committee's portfolio, as well as tasks that the agency needs to accomplish in support of the regulatory program and to complete worthwhile studies already in progress. The committee expects its next (December 1998) report to examine EPA's particulate-matter research plans and approaches in greater detail and to offer more specific suggestions for investment of these funds.
2. This may require that EPA consider redirecting some of the funds planned for immediate work on source characterization and modeling by the agency's intramural laboratories and applying them instead to increased intramural research on the relationships between ambient monitoring results and actual personal exposures, particularly for potentially susceptible subpopulations. If the current mixture of expertise in EPA's intramural laboratories does not permit that change to be made expeditiously, then additional resources must be applied to support extramural research on the committee's recommended questions (although EPA also needs to build more inhouse capability in this area). At the same time, it is appropriate for EPA to continue to invest some funds in the development of tools for enhanced source characterization, atmospheric chemistry, and modeling.
3. EPA should reassess its current allocation of funds for research on toxicological mechanisms, susceptible populations, and long-term effects. This is necessary to ensure that more research is focused immediately on identifying the most biologically important components

and characteristics of the particulate-matter mixture and on identifying biological mechanisms that could link particulate matter more clearly to the health effects observed in the human population.

4. EPA should redirect sufficient resources to undertake immediately carefully designed efforts to develop a biologically based dose model for deposition and fate of particulate matter in the respiratory tract in normal and compromised subjects.
5. EPA should re-evaluate its current plans for the $PM_{2.5}$ monitoring program in light of this report. The agency should consider more fully the possibility that future research results might indicate that the expensive monitoring program is not measuring the most biologically important aspects of particulate matter. Such an inconsistency could undermine the credibility and effectiveness of future control strategies and could underprotect susceptible subpopulations.
6. EPA's currently planned, university-based centers of excellence for particulate-matter research will require time to develop before producing major results, so EPA should strive to initiate the competitive awards for more of these centers in Fiscal 1998 instead of Fiscal 1999, as currently planned. The centers should augment, not replace, specific investigator-initiated, competitive research grants or competitive cooperative agreements.
7. In addressing each of these recommendations, EPA should seek a mixture of extramural and intramural investigations that takes maximum advantage of the contributions that extramural scientists can offer, while enhancing the intramural capacity of EPA to address key questions about particulate matter in a timely and credible manner.

7

ADDITIONAL CONSIDERATIONS FOR IMPLEMENTING THE COMMITTEE'S RESEARCH STRATEGY

To reduce successfully the major uncertainties about health risks of exposure to particulate matter and other copollutants, EPA needs to ask the right research questions, have a clear strategy for planning and managing the research program, and apply resources appropriately matched to the questions being addressed. Earlier sections of this report have focused on the highest-priority research questions and the required resources and phasing of such research. This chapter discusses additional aspects of an appropriate management strategy to implement the committee's recommended research portfolio.

From the presentations provided to the committee in public sessions in January and February 1998, as well as from the knowledge and experience of its individual members (see Appendix A), the committee collectively has considerable awareness of federal and nonfederal particulate-matter-related research that has been conducted, research currently in progress, and planned research activities directed toward reducing uncertainties about the linkages between sources of particulate matter and health effects in people. Only 2 months into its 5-year NRC study at this stage, the committee has not yet had the opportunity to review all of EPA's current and planned research in detail, but it has gained sufficient insight to form the preliminary judgments described in Chapter 6, as well as additional conclusions about research-management aspects of the research effort on particulate matter being conducted

and planned by EPA, other agencies, and the nonfederal research community.

OVERALL COORDINATION

Nationwide, research on particulate matter is still largely uncoordinated and fragmented. Improvements in federal and nonfederal particulate-matter research coordination would enhance the likelihood of producing information that is useful in public-policy decisions and, ultimately, improves public health. The fragmented nature of the program is apparent even within EPA, with only loose connections established among programs oriented to monitoring for regulatory compliance, understanding the atmospheric transport and fate of particulate matter and related gaseous pollutants, and understanding the interaction of particulate matter with people and the development of particulate-matter-associated disease. One contributor to the lack of coordination might be the separate funding and implementation of these activities. But even within EPA, there is little evidence of an overall strategy for meaningfully coordinating the diverse array of intramural particulate-matter-related research activities under way with that conducted extramurally under EPA financial sponsorship.

Although many particulate-matter research activities have been under way for some time, and despite the worthwhile particulate-matter research workshops recently held by EPA, CDC, and HEI, the level of communication among the participants and with other stakeholders is mostly informal and insufficient. With the infusion of additional funds, recruitment of new participants, and initiation of new activities, communication among particulate-matter research investigators will need to improve. In particular, research scientists need to interact while research is being planned. It is not sufficient to hold workshops or symposia on the results of past research.

A comprehensive "evergreen" inventory is critically needed for particulate-matter-related research and monitoring projects, containing information on key participants, goals, hypotheses, research strategies, resource levels, anticipated deliverables, and schedules. The availability

of such information on-line and regularly updated would serve to stimulate interactions, identify gaps, improve the framing of research hypotheses, and avoid unnecessary duplication. The availability of such an inventory would also facilitate oversight of the particulate-matter research program. The inventories being prepared by EPA and HEI for federal and nonfederal particulate-matter research (see Appendix B) represent a good starting point and should continue.

The complexity of the issues being addressed, even in this era of modern communication technology, also requires regular face-to-face discussions among investigators. Interdisciplinary communication needs to be fostered to complement the already well-developed intradisciplinary communication forums, such as the American Thoracic Society, American Association for Aerosol Research, Society of Toxicology, International Society of Exposure Analysis, and International Society of Environmental Epidemiology. The travel budgets for EPA intramural and extramural researchers should be made adequate for this purpose.

PERIODIC REASSESSMENTS

Research activities, even those with a clear initial focus, require periodic reassessment to maintain focus, relevance, and accountability. This need is especially apparent for some of EPA's research activities that have been under way for a number of years. In some cases, these activities were initiated in the early 1990s, anticipating preparation of the most recent criteria document for particulate matter. It would be advantageous in such cases for individual EPA scientists and research-program managers, as well as outside scientists, to reassess periodically these research activities in light of current goals and new tools and knowledge. This is especially critical for intramural research activities in EPA's laboratories, as well as research supported by other funding sources. Ongoing activities need the same level of review and scrutiny as newly initiated activities to ensure maximum return on research investments.

INTRAMURAL AND EXTRAMURAL TALENT

The briefings provided by EPA to this committee in January and February 1998 provided a big-picture view of the agency's particulate-matter-related research and monitoring activities. It is anticipated that additional material and future briefings will provide more detailed information on individual projects. However, the briefings provided to date have not articulated a clear overall EPA strategy for coordinating intramural and extramural research activities and making complementary use of them to address particulate-matter issues.

Researchers with varied disciplinary backgrounds, both within and outside of EPA, can contribute a great deal to improving scientific knowledge on particulate matter and health. It is crucial that EPA develop a more proactive and clearer overall strategy for engaging outside talent and integrating their particulate-matter research contributions with the intramural research being conducted within EPA's laboratories. EPA has available for its use a number of administrative vehicles for supporting research outside the agency, including contracts for completion of specific tasks, cooperative agreements, competitive research grants, and grants to research centers. Each vehicle has advantages and limitations. The committee expects in its subsequent reviews to further examine the current use of these different vehicles by the agency, and to make recommendations on how to enhance their value.

SUSTAINING ADEQUATE RESEARCH SUPPORT

The uncertainties in scientific knowledge available today for regulatory decisionmaking on particulate matter have hampered efforts to set the NAAQS and to develop control strategies for achieving them. These uncertainties are largely the result of past inadequacies in support for research to understand the links between sources of particulate matter and related health responses. If substantial progress is to be made in resolving these uncertainties, there must be sustained support of both

goal-oriented research and investigator-driven research for a decade or more.

Current scientific knowledge of particulate-matter health effects has been developed by research projects conducted in government, academic, and private laboratories, with financial support from government and the private sector. Most of the research has been funded by EPA, the National Institutes of Health, the National Institute for Occupational Safety and Health, the Department of Energy, the National Science Foundation, the National Oceanic and Atmospheric Administration, and some state governments, notably California. Modest research resources have also been provided by the electric power industry (via the Electric Power Research Institute), the motor-vehicle industry (via the Health Effects Institute and others) and the chemical industry (via the Chemical Industry Institute of Toxicology and others).

The research agenda recommended by the committee in this report targets key uncertainties and information gaps, and, if followed, will lead to improved scientific knowledge on particulate matter and public health. The research agenda cannot be accomplished, however, without a sustained commitment to funding over the next decade or more. In the past, research funding for air pollution and other topics has too often been *ad hoc* and transient, following the schedule and demands of legislation, regulatory standard-setting, and administrative timetables, and not the feasible pace of research. The committee's recommended research agenda cannot be accomplished without commitment to funding research over a longer term, extending well beyond the year 2002, (the date for the completion of the next review cycle for particulate matter). The committee's research portfolio, presented in this report, extends through 2010. The committee has no doubt that the adverse effects of particulate matter will remain as a public-health concern until contemporary questions about the short-term and long-term effects of particulate matter are answered.

The President's request to Congress for Fiscal 1999 funding for particulate-matter research in EPA approximated the Fiscal 1997 funding level and was substantially less than the congressionally approved Fiscal 1998 budget. This committee believes that the President's Fiscal 1999 request is insufficient to support the particulate-matter research

agenda recommended in this report for addressing the highest-priority research needs. The committee recommends that Congress correct this by making an appropriate commitment to particulate-matter research that includes the levels recommended in this report, as well as other particulate-matter research and development activities required by EPA. Without this commitment, a successful research agenda can not be implemented and sustained. Major uncertainties will continue to plague the next review of the particulate-matter standards, as well as the development of control strategies, to the detriment of both public health and the nation's economy.

Multiple sources of funding need to be continued. However, a sustained high level of funding through a single federal agency such as EPA is needed if critical research is to resolve major uncertainties. The members of this committee were encouraged by the leadership recently shown by the U.S. Congress when it provided supplemental funding to EPA for an enhanced particulate-matter research program in Fiscal 1998, and we recommend support at the same level for the next several years.

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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 his 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 the 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 NAS Institute of Medicine in 1997 and currently serves as a member of the Commission on Life Sciences. He also served recently as chairman of the NRC Committee on Health Risks of Exposure to Radon (BEIR VI), Phase II.

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

Judith C. Chow is research professor at the Energy and Environmental

Engineering Center, 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 data bases. 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 EM-2 Receptor Source Apportionment Technical Committee and as vice-chair of that organization'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".

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, past-president of the American Physiological Society, and 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.

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

Daniel S. Greenbaum is 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. Prior to joining the Health Effects Institute, he served as Commissioner of the Massachusetts Department of Environmental Protection.

MAUREEN HENDERSON, University of Washington, Seattle, Washington.

Maureen Henderson is professor emeritus of epidemiology and medicine at the University of Washington; and Member of the Public Health Sciences Division at the Fred Hutchinson Cancer Research Center, and founder and former head of the Cancer Prevention Research Program. Dr. Henderson received her M.B.B.S. (M.D.) and D.P.H. from the University of Durham, England, School of Medicine. She has been a member of the U.S. National Committee for the International Union Against Cancer, the National Cancer Advisory Board, and the International Cancer Alliance. Dr. Henderson is a recipient of the Georgeana Seegar Jones Award for Lifetime Achievement in Women's Health Research and the John A. Snow Award (Epidemiology Section) from the American Public Health Association. She was elected to the NAS Institute of Medicine in 1974. She is a former member of the NRC Board on Radiation Effects Research, was chair of the Committee on the Epidemiologic Investigation of Air Pollutants, and has served on many other NRC committees.

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

Philip Hopke is the Robert A. Plane Professor of Chemistry and Dean of the Graduate School 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 Science Advisory Board and is past-chairman of the EPA's Scientific Review Panel for Air Chemistry and Physics. He is a former director of the American Association of Aerosol Research and editor-in-chief of their journal. He has served on six NRC committees, including the NRC

Committee on Advances in Assessing Human Exposure to Airborne Pollutants. Presently, he is serving 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. He is technical editor-in-chief of the *Journal of the Air and Waste Management Association*, consultant to the EPA Science Advisory Board, and an advisor to the International Monitoring of Protected Visual Environments (IMPROVE), Panamerican Health Organization (PAHO), World Health Organization (WHO), and the United Nations Environmental Program (UNEP). He has served on several EPA review panels and chaired the EPA Review Panel for Research Proposals on Ambient Particle Modeling.

DANIEL KREWSKI, Health Canada, Ottawa, Ontario, Canada.

Daniel Krewski is director of Risk Management, Health Canada, professor of epidemiology and biostatistics in the Department of Epidemiology and Community Medicine at the University of Ottawa, and adjunct research professor of statistics at Carleton University. Dr. Krewski earned his M.S. and Ph.D. in mathematics and statistics from Carleton University, and his M.H.A. from the University of Ottawa. He is associate editor of *Risk Analysis, the Journal of Epidemiology and Biostatistics*, and *Regulatory Toxicology and Pharmacology*. He is currently a member of the NRC Board on Environmental Studies and Toxicology and its Committee on Toxicology, and he recently chaired the NRC's Colloquium on Scientific Advances and the Future in Toxicologic Risk Assessment.

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

Paul James Lioy is currently professor of environmental and community medicine of 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 Airborne Pollutants. Currently, he serves on the Science Advisory Board of the U.S. 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.

JOE L. MAUDERLY, Lovelace Respiratory Research Institute, Albuquerque, New Mexico.

Joe L. Mauderly is 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 current 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.

ROGER O. McCLELLAN, Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina.

Roger McClellan is president 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. 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 and American Association for Aerosol Research and a fellow of the Society for Risk Analysis. 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, American Association for Aerosol Research and the International Society for Aerosols in Medicine. 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.

GÜNTER OBERDÖRSTER, 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 non-fibrous 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 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, American Public Health Association, Washington, D.C.

Rebecca Parkin is director of scientific, professional, and section affairs at the American Public Health Association. Dr. Parkin earned her M.P.H. in environmental health and her Ph.D. in epidemiology from Yale University. She is a former 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 committees, including the Committee on Risk Assessment of Hazardous Air Pollutants. She is a member of the Children's Environmental Health Network Policy Committee and a peer reviewer for the New Jersey Cancer Research Commission. She has served on the Modeling Studies Group of EPA's Science Advisory Board and was a member of the Multisite Epidemiologic Studies Panel of ATSDR.

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

Joyce Penner is 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.

Richard Schlesinger is professor of environmental medicine at New York University School of Medicine and is director of the Systemic Toxicology Program and the Laboratory for Pulmonary Biology and Toxicology. 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. 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.

FRANK SPEIZER, Harvard School of Public Health, 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.

MARK UTELL, 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. 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* . He is a recipient of the NIEHS Academic Award in Environmental and Occupational Medicine. Dr. Utell currently serves on the NRC Committee on the Evaluation of the Department of Defense Comprehensive Clinical Evaluation Protocol and has served on several other NRC committees.

RONALD H. WHITE, American Lung Association, Washington, DC.

Ronald H. White is deputy director of National Programs and Director of Tobacco Control and Environmental Health at the American Lung Association. 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 currently serves as a member of the Integrated Human Exposure Committee of the EPA Science Advisory Board.

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

Ronald Wyzga is technical executive of the Air Quality, Health, and Risk Environmental Group 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, Ruder Finn, Inc., Washington, D.C.

Terry Yosie is executive vice president of Ruder Finn, Inc. where he is responsible for the firm's environmental management practice. He earned his doctorate from Carnegie Mellon University. He has approximately twenty years of professional experience in managing and analyzing the use of scientific information in the setting of environmental standards. From 1978-1981, he was the first executive director of EPA's 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). 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

PARTICULATE-MATTER RESEARCH INVENTORY (IN PROGRESS)

Prepared by

Maria Costantini, Health Effects Institute

John Vandenberg, U.S. Environmental Protection Agency

CONTENTS

Particulate-Matter Research Inventory (in progress), March 16, 1998
Summaries of Studies in Each Category Organized by Funding Institution*

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms						
API (13)	Analyze uncertainties and statistical artifacts in PM epidemiologic studies to address issues of conflicting results, confounders, and measurement error (including using results of personal monitoring data); possibly reanalyze existing studies. (2-3)			Characterize the effect of inhaled PM (including role of soluble metals) on ECG changes in dogs (see Lovelace). Evaluate susceptibility to inhaled particles using animals with diseases (supported also by EPRI and AAMA). (2)		Determine degree of correlation among stationary, microenvironmental and personal measurements of PM10 and PM2.5 (and other pollutants) in a group of COPD patients in Boston and Nashville and in elderly individuals in Baltimore. Characterize morphology and size distribution and elemental composition of PM on filters collected in Nashville/ Boston. (3)		Refine and validate personal exposure models using mutlipollutant monitoring studies. Evaluate PM chemistry and air quality models (see CRC). (2)	Characterize PM10 and PM2.5 emissions from refinery sources after pilot study, from oil and gas production field combustion units, and from gasoline and diesel vehicles (including size distribution) (see CRC). (3)	

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms						
CARB (25)	Prospective study to evaluate hospital admissions and ER visits in cities a high PM area in CA in relation to PM10, PM2.5, ultrafine, and PM composition. (1)	Evaluate the impact of community air pollution (including PM10 and PM2.5) on lung growth and respiratory health in children. (1)	Evaluate the health impact of exposure to smoke (derived from agriculture and silviculture) and the toxicology of air pollutants (ozone, nitric acid, nitrates, and carbon. (3)	Effects of exposure to fine and ultrafine ammonium nitrate and carbon particles on cell function and cardio-pulmonary response in young and old rats. (1)		Determine the level of particles and vapor-phase organics inside cars. (1)		Determine spatial and temporal variability of California atmosphere (including field and laboratory studies to characterize gaseous precursors, organic, carbonaceous, and nitrate species. (12)	Evaluate stationary and mobile source emissions of PM -size distribution and chemistry-including effects of fuels and operating conditions. (6)	

Particulate-Matter Research Inventory (in progress), March 16, 1998
Summaries of Studies in Each Category Organized by Funding Institution *(Continued)*

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms						
CIIT (5)			Compare the proliferative and neoplastic response in rats, mice, and hamsters exposed to fine and ultrafine titanium dioxide and correlate responses with lung overload. (1)	Compare molecular and cellular end-points in vitro and in vivo (such as altered apoptosis and expression of adhesion molecules) after exposure to fibrous and non fibrous particles. (2)	Develop models for the deposition and clearance of particles in humans and animals, identify the factors influencing the delivered dose. Determine particle deposition efficiency in the rat nasal passage and the inhalability factor for particles as function of diameter. (2)					
CRC (5)							Determine contribution of vehicle emission to ambient carbonaceous PM and analyze PM in Denver. (2)	Study mechanisms of production of secondary organic aerosols. Review UAMAERO model. (2)	Characterize primary particle emissions from light-duty motor vehicles. (1)	

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)			Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms	Dosimetry					
DOE (5)						Research on ultrafine instrumentation nad aerosol optical properties. (1)	Research on global aerosol models and chemical dynamic processes governing aerosols. (4)			
DOE/ NREL (2)						Characterization and evolution of secondary aerosols during PM2.5 and PM10 episodes in the SoCAB. (Planned with CRC) (1)			Size distribution of in-use heavy-duty vehicle particulate emissions (1)	

Particulate-Matter Research Inventory (in progress), March 16, 1998
Summaries of Studies in Each Category Organized by Funding Institution *(Continued)*

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms						
EPRI (16+?)	Investigate possible statistical artifacts in time-series studies and determine influence of measurement error and alternative statistical approaches. Reanalyze Harvard 6-cities mortality data. Study the relationship between ambient monitoring for several PM fractions mortality and morbidity. Conduct a prospective study of mortality and morbidity. Study relationship between health parameters and air pollution in COPD patients. Study relationship between PM/ozone exposure and emergency room visits by asthmatics. (8)		Cardio-pulmonary effects of exposure to model particles in healthy and COPD adults and of heavy occupational exposures in workers. (2)	Review literature to identify plausible mechanisms. Investigate homeostasis disruption as possible mechanism. (2) Additional mechanistic studies planned.		Collect outdoor monitoring data for PM and other pollutants. Determine indoor/outdoor and personal exposure for a group of elderly individuals (2)		Develop and test plume and grid models, characterize total aerosol, define secondary organic formation (1)		Integrated risk management framework including regional source characterization, transfer module, cost components, and management options (1)

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms						
EMA (1)									Particle size distribution from modern diesel engine (1) Planned	
EPA/ NCEA, NERL, NHEERL, NRMR (55)	Develop and apply methods to assess PM2.5, PM10 and copollutant exposures and cardiac, pulmonary, and inflammatory effects in elderly population in Baltimore. Study effects of outdoor and indoor PM on children's lung function in China. Study daily mortality and morbidity associated with PM and copollutants. (6)	Collaborate with USC and CARB to assess morbidity and mortality effects of ozone and copollutants (including PM) in Seventh Day Adventist children and in other communities. (3)	Evaluate effects of PM and co-exposure (viral infection, allergens) on cardiopulmonary system, and evaluate physicochemical properties and toxicity of PM. (8)	In vivo and in vitro research to characterize potential cardiac, pulmonary inflammatory and neurogenic causal mechanisms. Identify key components (metals and organics) of PM in causing health effects. Develop and evaluate models of susceptibility (COPD, CVD, asthma). (10)	Apply serial bolus technique to measure dose of course, fine, and ultrafine PM in lung regions of normal and diseased humans. Model air flow dynamics and regional particle deposition. (6)	Develop/apply new semi-continuous personal PM monitor. Ambient, indoor, outdoor, personal monitoring and determination of air exchange rates in and around elderly residential facilities (Baltimore epi study), and homes of COPD patients in a second city. Study of PM and PAH source strength and decay rates in occupied homes. (5)	Develop PM Federal Reference and Equivalent Methods and advanced methods for particle speciation. Conduct intensive ambient PM monitoring, including size speciation, in three cities. Provide ambient particles for toxicology tests and reanalyze selected filter samples from the Harvard Six City Study. (4)	Establish the chemical and physical processes that control the organic and inorganic composition and size of fine particulate matter; incorporate these into the next generation, integrated air quality model (Model-3); evaluate the model's sensitivity against field data prior to application. (4)	Characterize primary fine PM emissions and their composition from stationary, fugitive, and mobile sources. Develop emission factors for emission inventory, develop receptor modeling tools and apply these in analysis of field data sets. (6)	Evaluate integrated controls for PM and toxic and acid gases. Analyze data on soiling of building materials from PM for cost analyses. Develop criteria document (3)

Particulate-Matter Research Inventory (in progress), March 16, 1998
Summaries of Studies in Each Category Organized by Funding Institution *(Continued)*

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EPA/ NCERQA (43)	Studies of daily mortality and acidic PM in 3 US cities, of respiratory health and ultrafine PM in children with respiratory symptoms, of hospital admission and air pollution. Evaluate confounders in time series studies of PM and mortality. Determine association between asthma indices and exposure to fine particles and formaldehyde and between transition metals and sources of fine particles on mortality. (6)		Compare pulmonary toxicity of PM and ozone in vivo and determine effects of PM on respiratory bronchioles. (2)	Pathophysiologic mechanisms associated with exposure to CAP in vivo. Inflammatory mediators production induced by PM in vitro. (4)			Measure and apportion to sources human exposure to air pollutants. Develop methods for measuring components of PM10 and PM2.5, including semi-volatile particulate species. Monitor particle composition, morphology, and size in ambient air. (18)	Atmospheric fate and deposition of soot using an isotopic tracer. Chemistry of secondary aerosol formation. and reactivity of aerosols. Develop and test a model for regional and urban photochemistry of PM. Develop population-based exposure models and source apportionment models. (12)		

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)			Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms	Dosimetry					
European Union (8 multicenter studies)	Investigate respiratory and cardiovascular deaths, including mortality displacement, in relation to air pollution (APHEA 2). Follow elderly persons with measurements of health indices (ULTRA II). Establish dose-response relationships for cancer risk from exposure to air pollutants. Assess risk of development of allergy, asthma, etc., in children in relation to exposure to air pollution. (4)					Measure personal and microenvironmental exposure to air pollutants and develop predictive exposure models (EXPOLIS). Compare particle counters and assess size and elemental composition of fine particles in cites. Conduct measurements of platinum, palladium, and rhodium in the environment. (3)	Determine soluble elements in PM10 within PEACE study framework. (1)			

Particulate-Matter Research Inventory (in progress), March 16, 1998
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	Acute effects	Long-term effects	Health effects	Mechanisms						
Health Canada (5)	Relation between hospital admission and indices of air pollution (including PM). (1)	Respiratory health of children and adolescents in relation to long-term exposure to acidic particulates in New Brunswick. Long-term follow-up to the 24-cities studies of students in grades 11 and 12 in British Columbia. (2)	Interactive effects of ozone and PM in vivo. (1)	Relationship between atmospheric aging of PM and their potency in vitro. (1)						

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
	Acute effects	Long-term effects	Health effects	Mechanisms						
HEI (16)	Identify people at risk, factors that increase risk of mortality, PM components more strongly associated with mortality increases. Relationship between PM exposure and sudden cardiac death. Relationship between air pollution and mortality/morbidity in a large number of US cities (NMMAPS). (5)	Reanalyze epidemiologic studies on effects of long-term exposure to PM. (1)	Compare effects of exposure to CAP or DE on production of inflammatory mediators in humans. (1)	Mechanisms of toxicity (inflammation, ECG changes, susceptibility to infections) of CAP and ultrafine particles in rodents and dogs with induced heart or lung disease. Reactivity of model particles and their components in causing cellular changes in rats. Role of particle aging and chemical form of iron on oxygen radical production and role of iron on production of inflammatory mediators in vitro. (8)	Role of particle binding on the dose of iron or benzo(a)pyrene in the blood of exposed dogs. (1)					

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Lovelace Respiratory Research Inst. (11)			Effects on airway inflammation and reactivity of combined exposure to cigarette smoke and other agents inflammation and reactivity in mice. (1)	Compare effects of different particles on production of inflammatory mediators and DNA changes in vitro and pulmonary responses in animals and humans. Study changes in cancer-related genes in PM-induced human and animal lung tumors. Study effects of PM on heart function in dogs. Review utility of animal models of disease. (6)	Distribution of particles in the lungs of humans, monkeys, and rats with light and heavy burdens of particles. Effect of particle size and flow rate on particle deposition in the upper airways. Interspecies comparison of particle retention in the lungs of rats, guinea pigs, and dogs. Bioavailability of particle-borne organics (4)				PM emissions from portable kerosene heaters to assess exposure of soldiers during gulf war. (1)	

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	Acute effects	Long-term effects	Health effects	Mechanisms						
Mickey Leland Natl Urban Air Toxics Res Ctr (2)						Determine personal exposure to VOC, aldehydes, PM2.5, and metals over time of students in NYC and LA and residents of CA, TX, and NJ and evaluate the contribution of outdoor sources to indoor concentration and personal exposure (2)				

Particulate-Matter Research Inventory (in progress), March 16, 1998
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NHLBI (5)			Correlate daily symptoms and expiratory flows with air pollution in asthmatic children. Develop magnetic resonance microscopy to measure structure and function changes after exposure to PM and quantify lung injury (using aerosol deposition and wash-out measures) in animals with emphysema. (3)		Modeling of aerosol deposition for PM applicable from birth to old age using aerosol deposition measures in hollow airway models . Mathematical analysis of aerosol behavior in the periphery of animal lungs. (2)					

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
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NIAID (7)		Inner city asthma study: Test efficacy and cost-effectiveness of a protocol designed to reduce exposure and sensitization to allergens. Cofunded by NIEHS and EPA (7 centers)								
NIEHS (24)	Relationship between air pollution (PM and acid aerosols) and cardiovascular morbidity and other effects in various subgroups of the population (infants and mothers, adolescents, elderly). (7)		Effects of PM and other air pollutants on lung function; studies of environmental justice related to asthma and air pollution. (7)	Cellular, biochemical, and immunologic mechanisms by which PM cause effects. (9)			Identity and sources of mutagens in ambient aerosols (1)			

Particulate-Matter Research Inventory (in progress), March 16, 1998
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NIOSH (31)		Relationship between lung cancer and diesel exhaust (2)	Responses and susceptibility of humans to particles; causes of occupational asthma and predictors of respiratory disease. (4)	Mechanisms, responses, and biomarkers after exposure to dusts (including metals) (13)	Analysis of tissues and particles (1)	Characterization of exposures to inorganic dusts (1)	Monitoring of dust exposures (6)	Characterization of particle surface chemistry (1)	Evaluation of diesel exhaust emission controls (1)	Control and reduction of occupational exposures. Risk analysis of emerging hazards (4)
NIPHE (NL) (15)	Cardiovascular effects in elderly people. (1)	Study in panels of children and asthmatics. (1)		Studies on the causality of PM health effects using inhaled CAP, fine and ultrafine particles, instilled PM10/PM2.5 in animals with diseases. In vitro studies using PM10 and PM2.5. (4)	Dosimetry modeling of PM in healthy and compromised airways. (1)		Ambient PM monitoring program. (2)	Modeling of emission inventories to determine levels of PM10, PM2.5, PM carbonaceous, PM secondary. (2)		Predict PM health effects in general population and specific subgroups and risk reduction based on emission and traffic reductions. Conduct cost-benefit analysis. (4)

Funding institution (no. of projects)	Epidemiology		Experimental (clinical, animal, in vitro)		Dosimetry	Exposure assessment and relationships	Aerosol methods and monitoring	Atmospheric chemistry and physics, meteorology, and modeling	Emission characterization and source apportionment	Risk assessment and management, cost-benefits
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UK Deptm. Health (14)	Effect of air pollution on daily mortality, hospital admission, and physician consultation and on cardiorespiratory health. Role of PM and other pollutants on prevalence and history of asthma and on respiratory function and symptoms in children. Relationship between PM exposure and blood coagulation factors. Effects of lowering traffic congestion on pollutant exposure and respiratory mortality. (6)	Role of indoor air pollution on chronic respiratory symptoms in adolescents. Effects of cumulative air pollution exposure on chronic respiratory effects in a national cohort. Effects of occupational exposure to coal dust on health (3)	Effect of PM exposure in patients with respiratory disease. Lung function and biochemical changes after acute exposure to DE in normal and asthmatic volunteers. Response to allergen challenge after exposure to fine and ultrafine particles in asthmatic volunteers. (3)							Assess the impact of health advice on respiratory health and the health-related cost of PM air pollution. (2)

Particulate-Matter Research Inventory (in progress), March 16, 1998
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University of Wageningen (NL) (3)	Relationship between highway traffic and respiratory health (1)	Long-term exposure to air pollution and mortality. Development of asthma and other chronic respiratory conditions in young children (2)								
VDA (2)				Comparative pulmonary response of humans and animals to dust exposures. (1)					Characterize particles from sources (1).	

*Prepared by Maria Costantini, Health Effects Institute, and John Vandenberg, U.S. Environmental Protection Agency.

PARTICULATE-MATTER RESEARCH INVENTORY

(In progress), March 18, 1998

Prepared by Maria Costantini (Health Effects Institute) and John Vandenberg (U.S. Environmental Protection Agency)

LIST OF RESEARCH PROJECTS FUNDED IN THE U.S. AND ABROAD (organized by institutions and categories)

AMERICAN PETROLEUM INSTITUTE

Epidemiology/acute effects

"Analysis of time-series PM data to assess uncertainties, Phase II".

Contractor: Fred Lipfert.

"Analysis of uncertainties and statistical artifacts in PM epidemiology studies".

Contractor: TBA

Experimental/mechanisms

"Impact of inhaled particles on canine electrocardiography-Examination of the role of soluble metals in the toxicity of particulate matter".

Contractor: Joe Mauderly, Lovelace Respiratory Research Institute.

"Impact of inhaled particles on canine electrocardiography" (cont.)

Contractor: Joe Mauderly, Lovelace Respiratory Research Institute.

"Use of compromised animal models to evaluate the susceptibility to inhaled PM".

Contractor: Joe Mauderly, Lovelace Respiratory Research. (Funded also by EPRI and AAMA)

Exposure assessment and relationships

"Personal, indoor, and outdoor particulate matter monitoring".

Contractor: Petros Koutrakis, Harvard School of Public Health.

"Microscopic analysis of filters from Nashville/Boston COPD study"

Contractor: Petros Koutrakis, Harvard School of Public Health.

"Measurement of personal exposure to multiple criteria and hazardous air pollutants".

Contractor: Petros Koutrakis, Harvard School of Public Health, and Ted Johnson, TRJ Environmental.

Atmospheric chemistry and physics, meteorology, and modeling

"Personal PM exposure model".

Contractor: TBA

Emission characterization and source apportionment

"Characterization of PM emissions from petroleum sources(refinery) sources. Phase I and II".

Contractor: EER.

Characterization of emissions from oil and gas production field combustion units".

Contractor: Radian Corporation.

"Measurement of exhaust PM emissions from various vehicles, under different driving conditions with various fuel specifications".

Contractor: CRC.

"Evaluation of PM chemistry and air quality models able to address PM standards".

Contractor: CRC.

CALIFORNIA AIR RESOURCES BOARD

Epidemiology/acute effects

Prospective study to evaluate hospital admissions and ER visits in cities a high PM area in CA in relation to PM10, PM2.5, ultrafine, and PM composition. (1)

Epidemiology/long-term effects

Evaluate the impact of community air pollution (including PM10 and PM2.5) on lung growth and respiratory health in children. (1)

Experimental/health effects

Evaluate the health impact of exposure to smoke (derived from agriculture and silviculture) and the toxicology of air pollutants (ozone, nitric acid, nitrates, and carbon. (3)

Experimental/mechanisms

"Effects of Exposure to Fine and Ultrafine Ammonium Nitrate and Carbon Particles on: Cytotoxicity, Cell Proliferation, Particle Clearance, Histopathology, Oxidative Stress, Macrophage Function, Production of NO, Cardio-Pulmonary Response, in Young, Adult, and Old Rats"

U CAL Davis and U CAL Irvine Collaborative PM Research

Exposure assessment and relationships

Determine the level of particles and vapor-phase organics inside cars. (1)

Atmospheric chemistry and physics, meteorology, and modeling

Determine spatial and temporal variability of California atmosphere (including field and laboratory studies to characterize gaseous precursors, organic, carbonaceous, and nitrate species. (12)

Emission characterization and source apportionment

Evaluate stationary and mobile source emissions of PM-size distribution and chemistry-including effects of fuels and operating conditions. (6)

CHEMICAL INDUSTRY INSTITUTE OF TOXICOLOGY

Experimental/mechanisms

Interspecies differences in proliferative and neoplastic response to insoluble particles (talc, diesel exhaust, titanium dioxide, carbon black) and correlation of these responses with lung overload.

Comparison of molecular and cellular end-points in vitro and in vivo (such as altered apoptosis and expression of adhesion molecules).

Dosimetry

Develop models for the deposition and clearance of particles in humans and animals, identify the factors influencing the delivered dose of particles, measure particle deposition efficiency in the nasal passage of rats.

Determine the inhalability factor for particles as a function of diameter, and evaluate endotracheal intubation of rats as a means of bypassing the nose.

COORDINATING RESEARCH COUNCIL

Aerosol methods and monitoring

"Contribution of Vehicle Emissions to Ambient Carbonaceous Particulate Matter"

"Carbon Isotopic Analyses for the Norther Front Range Air Quality Study's Summer and Winter 1966-1997 Program"

Atmospheric chemistry and physics, meteorology, and modeling

"Mechanisms for Production of Secondary Organic Aerosols and Their Representation in Atmospheric Models"

"Review of the UAM-AERO Model"

Emission characterization and source apportionment

"Primary Particle Emissions from Light-Duty Motor Vehicles"

Atmospheric chemistry and physics, meteorology, and modeling

Research on global aerosol models and chemical dynamic processes governing aerosols. (3)

DEPARTMENT OF ENERGY

Aerosol methods and monitoring

Research on freshly nucleated ultrafine particles and the development of instrumentation to measure down to 3mm-10mm diameter.

Atmospheric chemistry and physics, meteorology, and modeling

Evaluation of global aerosol models and satellite-and surface-based aerosol optical deposition data and surface concentration data to estimate the direct radiative forcing by anthropogenic aerosols.

Research on the optical properties of aerosols and lab studies of carbonaceous aerosols.

Development of global sulfate aerosol models utilizing surface meteorological data as input

Research on the chemical and dynamic processes governing atmospheric aerosols.

DEPARTMENT OF ENERGY (NATIONAL RENEWABLE ENERGY LABORATORY)

Aerosol methods and monitoring

"Characterization and evolution of secondary aerosols during PM2.5

and PM10 episodes in the South Coast Air Basin (SoCAB)" (Planned with CRC)

Principal investigators: Glen Cass and Suzanne Herring

Emission characterization and source apportionment

"Size distribution of in-use heavy-duty vehicle particulate emissions" Contract under negotiation

ELECTRIC POWER RESEARCH INSTITUTE

Epidemiology/acute effects

Investigation of artifact-analyses of data sets to rule out the existence of an artifact in statistical analyses of time series data; review of econometric issues in data analysis.

Contractor: Fred Lipfert (parts jointly funded with API)

Determination of influence of alternative statistical approaches to analyze time series data analyses of daily mortality air quality data for Harvard six-cities using a wide variety of statistical approaches in order to investigate robustness of results.

Contractor: Klemm Analysis Group

Determine influence of measurement error in statistical analyses; statistical analyses of alternative error structures on alternative data sets.

Contractor: Fred Lipfert.

Reanalysis of Harvard six-cities mortality air quality data (analyses to consider gaseous pollutant data as well as alternative methodologic approaches).

Contractors: Klemm Analysis Group, Harvard School of Public Health.

Acute mortality/morbidity analyses using air quality data from data collected at outdoor monitoring sites, for several PM fractions and

gaseous pollutants (health data to be collected from cities where monitoring was undertaken).

Contractor: TBA.

Prospective cohort study (using data from a cohort for which detailed individual data are available, mortality/morbidity rates will be related to ambient air quality data in the cities where cohort members reside).

Contractors: TBA

A panel of COPD patients has been observed for an extended period of time; various cardio-pulmonary health parameters were collected for this population on a daily basis and will be compared to ambient and indoors air quality.

Contractor: Henry Gong, Rancho Los Amigos.

Study of asthmatic response to PM/ozone exposure: daily emergency room visits by asthmatics in Atlanta are to be related to daily ozone, PM exposures (analyses will consider weather, socioeconomic factors).

Experimental/health effects

Chamber studies of healthy adults, COPD, and asthma patients. (Subjects will be exposed to clean air and fixed concentrations of ammonium nitrate and oxalic acid (cardio-pulmonary responses associated with exposures will be examined).

Contractor: Henry Gong, Rancho Los Amigos

Investigation of a heavily-exposed occupational group: personal exposures measurements and pre-and post-exposure measures of ACG and lung function were made for a groups of workers who cleaned out boiler interiors of a coal-fired power plant. (Particulate exposures over 2000 $\mu g/m^3$ were recorded. Health exposure data have been collected, but analyses are not complete.)

Contractor: J. Hicks, Geomatrix.

Experimental/mechanisms

Review of epidemiology/mechanisms literature. (Review of literature to understand how epidemiology literature relates to what is known about potential mechanism.)

Contractor: Robert Frank, Johns Hopkins University.

Investigation of disruption of homeostasis as a mechanism to explain mortality response to air pollution; development of an appropriate animal model, testing of the animal model with alternative exposures to PM and other environmental factors.

Contractor: C. Tankersley, Johns Hopkins University

Additional studies of mechanisms planned:

a. to understand alternative toxicological models
b. to investigate influence of alternative pollutants, PM fractions.

Contractors; TBA

Exposure assessment and relationships

Determination of outdoor/indoor/personal air quality measures for a suite of pollutants for a group of senior citizens in two seasons.

Contractors: Harvard School of Public Health; TRJ Consultants (jointly funded with API)

Collection of extensive daily outdoor monitoring data for criteria pollutants and PM10/PM2.5 fractions at several monitoring site (initial sites are near final selection, and monitoring will begin Jan 1998).

Contractors: TBA

Atmospheric chemistry and physics, meteorology, and modeling

Develop and test plume and grid models, characterize total aerosol, define secondary organic formation

Contractors: TBA

Risk assessment and management/cost benefit

Integrated risk management framework including regional source

characterization, transfer module, cost components, and management options

Contractors: TBA

ENGINE MANUFACTURERS ASSOCIATION

Emission characterization and source apportionment

Determination of the particle-size distribution of the exhaust emissions of a modern diesel engine. (Research under planning.)

ENVIRONMENTAL PROTECTION AGENCY-NATIONAL CENTER FOR ENVIRONMENTAL ASSESSMENT

Epidemiology/acute effects

Relative effects of $PM_{2.5}$ versus $PM_{(1.0-2.5)}$ on respiratory health indicators.

Principal investigator: Douglas Dockery, Harvard School of Public Health

Analysis of daily mortality in Dublin, Ireland, in relation to particulate air pollution control.

Principal investigator: Douglas Dockery, Harvard School of Public Health

Respiratory health in relation to outdoor and indoor PM exposure in Chinese cities.

Robert Chapman and William Wilson

Experimental/health effects

Study of occupational silica exposure and its relationship to pulmonary fibrosis.

Jeffrey Gift

Dosimetry

Upgrade of RDDR particle dosimetry model: Clearance, hygroscopicity and human ventilation activity patterns.

Principal investigator: Anthony James, ACI Associates

Revision of regional respiratory tract deposition model for laboratory animal species.

Principal investigator: Anthony James, ACI Associates

Exposure assessment and relationships

Mean group $PM_{2.5}$ exposure in an asthmatic panel.

Principal investigator: Thomas Stock, University of Texas School of Public Health

Risk assessment and management, cost-benefits

Soiling of building materials from exposure to particulate matter.

Principal investigator: Ray Fornes, North Carolina State University

ENVIRONMENTAL PROTECTION AGENCY-NATIONAL EXPOSURE RESEARCH LABORATORY

Exposure assessment and relationships

Collaborative exposure/epidemiological study.

Relationship of personal exposure of high risk sub-populations to ambient concentrations of fine particles.

Use of innovative monitoring techniques to estimate source strengths and decay rates for several important sources of fine particles.

Aerosol methods and monitoring

Regulatory methods and quality assurance.

PM research methods.

PM Environmental Characterization: Baltimore, Phoenix, Fresno.

Atmospheric chemistry, physics, meteorology and modeling

Chemistry and physics of atmospheric aerosols.

Chemical and physical process and mechanism modeling.

Community multiscale air quality modeling system.

Model evaluation/testing and application.

Emissions characterization and source apportionment

Pm source apportionment and receptor modeling.

ENVIRONMENTAL PROTECTION AGENCY-NATIONAL HEALTH AND ENVIRONMENTAL EFFECTS RESEARCH LABORATORY

Epidemiology/acute effects

Cardiopulmonary responses in elderly persons exposed to ambient particulate air pollution.

Principal investigator: John Creason

Air pollution and morbidity and mortality among California Kaiser Permanente members.

Principal investigator: Steven VanDenEeden, Kaiser Foundation Research Institute

Epidemiologic studies of criteria pollutant particles and gases.

Principal investigator: Diane Gold, Brigham and Women's Hospital

Epidemiology/long-term effects

Respiratory health in non-smoking California residents with differing long-term ambient ozone levels.

Principal investigator: David Abbey, Loma Linda University

Short-term and long-term exposure to ozone and particulate air pollution and respiratory health in Southern California children.

Principal investigator: Ed Avol, University of Southern California

Epidemiologic investigation to identify chronic health effects of ambient air pollutants in Southern California

Principal investigator: Helene Margolis, California Air Resources Board

Experimental/health effects

Particulate matter effects on animal models of asthma.

Principal investigator: Steve Gavett

Combined effects of particle exposure, dust mite allergy, and viral infection in the Brown Norway rat.

Principal investigator: Ian Gilmour

Changes in electrocardiographic waveform parameters after exposure to residual oil fly ash in cold-acclimated and cardiovascular-compromised rats.

Principal investigator: Matthew Campen and Penn Watkinson

In vivo toxicity of emission and ambient air particles in animal models of cardiopulmonary disease.

Principal investigator: Sarah Gardner and Urmila Kodavanti

Effect of particles on innate immune responses to infection: Antimicrobial peptide gene expression and cytokine production by lung cells exposed to endotoxin and particles in vitro.

Principal investigator: Lisa Ryan

Physicochemical properties and pulmonary toxicity of air particulate matter.

Principal investigator: Kevin Dreher

Lung cell injury induced by diesel exhaust particles in vivo and in vitro.

Principal investigator: Michael Madden

Experimental/Mechanisms

Pulmonary toxicity of Utah Valley PM: Are empirical indices of adverse health effects coherent with epidemiology?

Principal investigators: Robert Devlin and Dan Costa

Oxidant generation and pulmonary inflammation induced by iron-containing particles.

Principal investigators: John Lay and Andrew Ghio

Role of biogenic material and transition metals in particle-induced activation of human alveolar macrophages in vitro.

Principal investigator: Susanne Becker

Transition metal components of fine particulate air pollutants: Evaluation of airway epithelial cell response.

Principal investigators: William Reed and James Samet

Activation of intracellular signaling pathways in human bronchial epithelial cells exposed to combustion-derived metallic particles.

Principal investigator: James Samet

The role of neuropeptides in particulate (PM_{10}/$PM_{2.5}$) induced airway inflammation

Principal investigators: Bellina Veronesi and Susanne Becker

Effect of air particulate matter exposure on the cardiovascular compromised host.

Principal investigators: Kevin Dreher and Penn Watkinson

Reactive oxygen species mediate induction of cytotoxicity and cytokine gene expression in airway epithelial cells exposed to residual oil fly ash.

Principal investigator: Ian Dye

Chronic obstructive pulmonary disease: What can a rat model tell us

about the mechanism of PM-associated mortality and morbidity?

Principal investigator: Urmila Kodavanti

Role of matrix metalloproteinase in emission and ambient air PM-induced lung injury?

Principal investigators: Kevin Dreher and Wei Yi Su

Dosimetry

Fine-mode aerosol deposition in human and rat lungs.

Principal investigator: Ted Martonen

Assessment of regional deposition dose of inhaled ultrafine, fine, and coarse particles in humans.

Principal investigator: Chong Kim

Particle deposition characterization in bifurcating airway models.

Principal investigator: Chong Kim

Effect of age on lung deposition dose of inhaled fine particles: Comparison between children, young and old adults.

Principal investigators: William Bennett and Chong Kim

ENVIRONMENTAL PROTECTION AGENCY-NATIONAL RISK MANAGEMENT RESEARCH LABORATORY

Exposure assessment and relationships

Determine the relationship between indoor and outdoor particle size distribution and concentrations and the mechanisms of penetration through building shells which influence this relationship.

Principal investigator: Ronald Mosley

Aerosol methods and monitoring

Comparison of sampling devices used to measure the size of particles from fugitive sources.

Principal investigator: Bruce Harris

Emission characterization and source apportionment

Fine PM emissions from residential wood combustion.

Principal investigator: Robert McCrillis (Co-funded by AWMA)

Chemical and physical characteristics of fine pm emissions from combustion sources.

Principal investigator: William Linak and Andy Miller (Coordinated with NHEERL)

Fine particle emissions from on-road heavy duty diesel trucks.

Principal investigator: Bruce Harris

Fugitive particle emissions from construction sites.

Principal investigator: Charles Masser

Ammonia emissions from animal waste

Principal investigator: Bruce Harris

Risk assessment and management, cost-benefits

Determine performance of upgraded fine PM control technologies.

Principal investigator: Charles Sedman (Cooperative agreement with Southern Research Institute)

Characterize technical issues associated with management of $PM_{2.5}$ emissions and develop tool to evaluate fine PM management options.

Principal investigator: Charles A. Miller

ENVIRONMENTAL PROTECTION AGENCY-NATIONAL CENTER FOR ENVIRONMENTAL RESEARCH AND QUALITY ASSURANCE

Epidemiology/short-term effects

"The Reactive Associations of Transition Metals and Sources of Fine Particulate Matter to Increased Daily Mortality" (R82-6245) (FY 97)

Principal Investigator: Lucas M. Neas, Harvard University ($211,733 - total)

"Acidic Particulate Matter and Daily Human Mortality in Three U.S. Cities" (FY 96)

Principal Investigator: George D. Thurston, New York University Medical Center. ($383,000 - total)

"Ultrafine Particle in Urban Air and Respiratory Health Among Children with Respiratory Symptoms". (FY 96)

Principal Investigator: Joel Schwartz, Harvard School of Public Health. ($196,000 - total)

"Air Pollution and Hospital Admissions in Washington State". (FY 96)

Principal Investigator: Suresh H. Moolgavkar, Fred Hutchinson Cancer Research Center. ($420,000 - total)

"An Evaluation of Confounders in PM_{10}/Mortality Associations". (FY 96)

Principal Investigator: Kazuhiko Ito, New York University Medical Center. ($363,000 - total)

"Asthma Indices Associated with Ambient Submicron Particles and Formaldehyde in Ambient Air Pollution". (FY 96)

Principal Investigator: Kevin P. Fennelly, National Jewish Center for Immunology and Respiratory Medicine. ($179,000 - total)

Experimental/health effects

"Particle Toxicity and the Respiratory Bronchiole" (R82-6246) (FY 97)

Principal Investigator: Kent E. Pinkerton, University of California at Davis ($525,000 - total)

"Pulmonary Toxicity of Particulate Matter and Ozone". (FY 96)

Principal Investigator: Lung Chi Chen, New York University Medical Center. ($172,000 - total)

Experimental/mechanisms

"Mechanism of PM Induced Acute Health Effects" (R82-6244) (FY 97)

Principal Investigator: Terry Gordon, New York University Medical Center ($600,799 - total)

"Mechanisms of Particulate-Induced Mediator Expression Human Airway Epithelial Cells" (R82-6270) (FY 97)

Principal Investigator: William Reed, University of North Carolina at Chapel Hill ($374,174 - total)

"Pathophysiologic Mechanisms of Mortality Associated with Exposure to Concentrated Particulate Urban Air Toxics". (FY 96)

Principal Investigator: John Godleski, Harvard School of Public Health. ($521,000 - total)

"Cellular Mechanisms of Pulmonary Inflammation by Environmental Particles" (FY 95)

Principal Investigator: Lester Kobzik, Harvard School of Public Health. ($547,000 - total)

Aerosol methods and monitoring

"Morphological and Chemical Characteristics of the Submicron Atmospheric Aerosol: Implication for Standards" (R82-6232) (FY 97)

Principal Investigator: Sheldon K. Friedlander, University of California at Los Angeles ($ 345,247 - total)

"The Contribution of Biomass Combustion to Ambient Fine Particle Concentrations in the United States" (R82-6233) (FY 97)

Principal Investigator: Glen R. Cass, California Institute of Technology ($532,642 - total)

"Real-Time Measurement of the Size and Composition of Atmospheric Particulate Matter" (R82-6234) (FY 97)

Principal Investigator: Anthony S. Wexler, University of Delaware ($374,833 - total)

"Real-Time Monitoring of Individual Atmospheric Aerosol Particles: Establishing Correlations between Particle Size and Chemical Speciation" (R82-6240) (FY 97)

Principal Investigator: Kimberly A. Prather, University of California at Riverside ($547,000 - total)

"Research Consortium on Ozone and Fine Particulate Formation in California and the Northeastern United States" (FY 97)

Principal Investigator: TBA ($1,500,000 - total)

"Southern Center for the Integrated Study of Secondary Air Pollutants" (FY 97)

Principal Investigator: TBA ($1,500,000 - total)

"Investigations of Factors Determining the Occurrence of Ozone and Fine Particles in Northeastern USA" (FY 97)

Principal Investigator: TBA ($1,500,000 - total)

"Field-Useable Compact Capillary Based Ion/Liquid Chromatography. Real Time Gas/Aerosol Analyzers" (R82-5344) (FY 96)

Principal Investigator: Purnendu Dasgupta, Texas Technology University ($333,141 - total)

"Measurement and Source Apportionment of Human Exposures to Toxic Air Pollutants in the Minneapolis-St. Paul Metropolitan Area". (FY 96)

Principal Investigator: Gregory C. Pratt, Minnesota Pollution Control Agency, MN. ($554,000 - total)

"Development of a Semi-continuous Monitor for Determination of Trace Elements and Heavy Metals in Ambient Aerosol Particles". (FY 96)

Principal Investigator: John M. Ondov, University of Maryland. ($396,000 - total)

"Real-Time Analysis of PAY Bound to Size-Resolved Atmospheric Particles by Tandem Time of Flight Mass Spectrometers" (R82-5391) (FY 96)

Principal Investigator: Kenneth Smith, Massachusetts Institute of Technology ($375,000 - total)

"Development and Evaluation of a Novel Sampling Method to

Determine the Phase Partitioning of Semi-volatile Organic Compounds". (FY 96)

Principal Investigator: Petros Koutrakis, Harvard School of Public Health. ($410,000 - total)

"Development of a Continuous Monitoring System for PM_{10} and Components of $PM_{2.5}$" (FY 96)

Principal Investigator: Morton Lippmann, New York University Medical Center. ($436,000 - total)

"Continuous Measurement of $PM_{2.5}$ and Associated Semi-volatile Particulate Species". (FY 96)

Principal Investigator: Delbert J. Eatough, Brigham Young University. ($353,000 - total)

"Development and Validation of a Novel Technique to Measure Ambient Particle Properties: Bound Water, Mass Density and Mean Diameter". (FY 96)

Principal Investigator: Petros Koutrakis, Harvard School of Public Health. ($380,000 - total)

"Distribution of H+ and Trace Metals in Ultrafine Ambient Aerosol". (FY 96)

Principal Investigator: Beverly S. Cohen, New York University Medical Center. ($590,000 - total)

"Speciation of Volatile and Reacting Compounds in Particulate Matter" (R82-3980) (FY 95)

Principal Investigator: Murray Johnston, University of Delaware ($334,445 - total)

"Determination of Trace Atmospheric Gases by Capillary Electrophoresis (CE). Size-Selective Sampling and Analysis of Atmospheric Particles by CE-based Analyzer" (R82-1117) (FY 95)

Principal Investigator: Purnendu Dasgupta, Texas Technological University ($353,188 - total)

Atmospheric chemistry and physics, meteorology, and modeling

"Investigations of the Chemistry of Secondary Aerosol Formation Using Thermal Desorption Particle Beam Mass Spectrometry" (R82-6235) (FY 97)

Principal Investigator: Paul J. Ziemann, University of California at Riverside ($294,762 - total)

"Development of Population-Based Particle Exposure Models for Human Health Risk Assessment". (FY 96)

Principal Investigator: Halak Ozkaynak, Harvard School of Public Health. ($500,000 - total)

"Atmospheric Fate and Dry Deposition of Urban Soot to Great Waters Using a Novel, State-of-the-Art Isotopic Particulate Tracer". (FY 96)

Principal Investigator: John Ondov, University of Maryland ($455,000 - total)

"Development and Testing of a State-of-the-Art PMx Particulate Module for Regional and Urban Photochemical Models". (FY 95)

Principal Investigator: Spyros N. Pandis, Carnegie Mellon University. ($412,000 - total)

"Product Formation and Identification in the Photo Degradation of PAY in Models of Atmospheric Particulate: Effects of the Surface Physical and Chemical Properties" (R82-3328) (FY 95)

Principal Investigator: Rafael Arce, University of Puerto Rico, Rio-Piedras ($254,723 - total)

"Tracer Studies of SO_2 in Clouds (R82-3422) (FY 95)

Principal Investigator: Liquat Husain, New York State Department of Health ($335,659 - total)

"Formation and Physical Properties of Secondary Organic Aerosol" (R82-3514) (FY 95)

Principal Investigator: Spyros Pandis, Carnegie Mellon University ($382,668 - total)

"Effects of Non-Uniform Cloud Drop Composition on Pollutant Transformation and Removal In Winter Clouds" (R82-3979) (FY 95)

Principal Investigator: Jeffrey Collett, Colorado State University ($339,273 - total)

"Applications of Receptor Modeling to Time Series Data for Aerosol Chemical Components" (R82-1288) (FY 95)

Principal Investigator: Sheldon Friedlander, University of California at Los Angeles ($287,900 - total)

"A Study of Absorptive Gas/Particle Partitioning to Ambient Aerosol Organic Material" (R82-2312) (FY 95)

Principal Investigator: James Pankow, Oregon Graduate Institute of Science and Technology ($305,433 - total)

"Influence of Organic Films on Reactivity and Hygroscopicity of Sulfuric Acid Aerosol" (R82-2476) (FY 95)

Principal Investigator: Morton Lippmann, New York University Medical Center ($387,276 - total)

"Development of Multivariate Receptor Models for the Determination of the Sources of Airborne Pollutants" (R82-2482) (FY 95)

Principal Investigator: Philip Hopke, Clarkson University ($349,359 - total)

EUROPEAN UNION/DG XI

Epidemiology/acute effects

APHEA 2. "Short-term effects of air pollution on health: A European approach to methodology, dose-response assessment, and evaluation of public health significance" (32 European cities, 20 centers)

Coordinator: Klea Katsouyanni, University of Athens, Athens

ULTRA II. "Exposure and risk assessment for fine and ultrafine particles in ambient air" (3 centers)

Coordinator: J. Pekkanen, National Public Health Institute, Helsinki

"Biomarkers of genotoxicity of urban air pollution: A dose-response study" (8 centers)

Coordinator: S. Kyrtopoulos, National Hellenic Research Foundation, Athens.

"Risk assessment for exposure to traffic-related air pollution and the development of inhalant allergy, asthma, and other chronic respiratory conditions in children"

Coordiantor: B. Brunekreef, Landbouwuniversiteit Wageningen, Wageningen

Exposure assessment and relationships

EXPOLIS. "Air pollution exposure distribution of adult urban populations in Europe" (8 centers)

Coordinator: M Jantunen, National Public Health Institute, Finland

ULTRA I. "Exposure and risk assessment for fine and ultrafine particles in ambient air" (3 centers)

Coordinator: J. Pekkanen, National Public Health Institute, Helsinki

CAPLACA. "Assessment of environmental contamination risk by platinum, rhodium, and palladium from automobile catalyst" (12 centers)

Coordinator: A. Palacios, Universidad Complutense de Madrid

Aerosol methods and monitoring

"Elemental composition of airborne particulate matter (PM10) sampled in European countries within the framework of the PEACE study" (2 centers)

Coordinator: A. Schutz, Lunds Universitet, Lund

HEALTH CANADA

Epidemiology/acute effects

Relation between hospital admission and indices of air pollution (including PM).

Epidemiology/long-term effects

Study of the respiratory health of children and adolescents in relation to long-term exposure to acidic particulates in New Brunswick.

Long-term follow-up to the 24-cities studies of students in grades 11 and 12 in British Columbia.

Experimental/health effects

Interactive effects of ozone and PM in vivo.

Experimental/mechanism

Relationship between atmospheric aging of PM and their potency in vitro.

HEALTH EFFECTS INSTITUTE

Epidemiology/acute effects

"Particulate air pollution and daily mortality in Montreal, Quebec, 1984-1993"

Principal investigator: John Bailar, McGill University (RFA 94-2)

"A case-crossover study of fine particulate air pollution and sudden cardiac arrest"

Principal investigator: Harvey Checkoway, University of Washington (RFPA 96-2)

"Association of PM components with daily mortality and morbidity in urban populations" Principal investigator: Mort Lippmann, New York University Medical Center (RFPA 94-3)

"Particulate air pollution and daily mortality in Erfurt (East Germany)"

Principal investigator: H.-Erich Wichmann, GSF-Forschungszentrum für Umwelt und Gesundheit, Germany (RFA 94-2)

"National Morbidity, Mortality, and Air Pollution Study"

Principal investigator: Jon Samet, Johns Hopkins University (RFQ 94)

Epidemiology/long-term effects

"Reanalysis of cohort studies of long-term mortality and particulate air pollutants"

Principal investigator: Daniel Krewski, University of Ottawa (RFQ 97)

Experimental/health effects

"Inflammatory mechanisms with exposure to air pollution particles"

Principal investigator: Stephen Holgate, University of Southampton (RFA 96-1)

Experimental/mechanisms

"Mechanisms of morbidity and mortality from exposure to ambient air particles"

Principal investigator: John Godleski, Harvard School of Public Health (RFA 94-2)

"Adverse health effects of ambient PM_{10} in compromised animal models"

Principal investigator: Terry Gordon, New York University Medical Center (RFA 94-2)

"Ultrafine particles as inducers of acute lung injury: Mechanisms and correlation with age and disease"

Principal investigator: Günter Oberdörster Oberdörster, University of Rochester (RFA 94-2)

"Immunomodulation as a mechanism for PM_{10}-induced effects upon host mortality"

Principal investigator: Judith Zelikoff, New York University Medical Center (RFPA 94-3)

"Particle characteristics responsible for effects on human lung epithelial cells"

Principal investigator: Ann Aust, Utah State University (RFA 96-1)

"The effects of atmospheric gases/reductants and sunlight on the liability and hydroxyl-radical generating capability of iron in particulate matter from different sources"

Principal investigator: Bruce Faust, University of California at Los Angeles (RFA 96-1)

"Role of peroxides and macrophages in fine particulate matter toxicity"

Principal investigator: Debra Laskin, Rutgers University (RFA 96-1)

"Mechanisms of particle toxicity in the respiratory system"

Principal investigator: Kent Pinkerton, University of California at Davis (RFA 96-1)

Dosimetry

"Epithelial penetration and clearance of particle-borne compounds"

Principal investigator: Alan Dahl, Lovelace Respiratory Research Institute (RFA 96-1)

LOVELACE RESPIRATORY RESEARCH INSTITUTE

Experimental/health effects

Study of the effects of combined exposures to cigarette smoke and other noxious agents on the induction of adverse health effects

Experimental/mechanisms

Standardization of an in vitro screening test for the toxicity of particles using cultured cells, co-cultured cells, and lung slices

Study of the effect of particle size on toxicity in vivo

Study of electrocardiographic changes in dogs exposed to noxious aerosols

Study of the comparative pulmonary responses of humans and animals with known heavy exposures to inhaled particles (diesel soot, carbon black, coal dust, silicates) deriving information from animal and human pathology material.

Study to determine the changes in protein expression that occur in response to DNA damage from air pollutants, including particles, in vitro

Review utility of animal models for research on mechanisms, susceptibility, and risk.

Dosimetry

Study the kinetics of inhaled ultrafine particles administered by various routes in rats and monkeys.

Quantify the distribution of particles in the lungs of humans, monkeys, and rats with light and heavy burden of particles.

Study of the deposition of ultrafine particles in the upper tracheobronchial airway to determine effects of particle size and flow rate on the differential deposition of ultrafine particles.

Study of interspecies comparison of particle retention in the lung of rats, guinea pigs and dogs.

Emission characterization and source apportionment

PM emissions from portable kerosene heaters to assess exposure of soldiers during gulf war.

MICKEY LELAND NATIONAL URBAN AIR TOXICS RESEARCH CENTER

Exposure assessment and relationships

"Urban air toxic exposures of high school students".

Patrick Kinney, Columbia School of Public Health

"Contribution of outdoor sources to indoor concentrations and personal exposure to air toxics"

Clifford Weisel, EOHSI, Robert Wood Johnson Medical School

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Experimental/health effects

"Ancillary study to Childhood Asthma Management Program (CAMP): Air quality and asthma symptoms in childhood asthma"

Shapiro Gail and Jane Koenig, University of Washington (add-on to a 8-canter study of the long-term effects of asthma treatments on lung growth and physical and psychosocial development)

"In vivo MR microscopy of environmental lung disease"

Johnson Allan, Duke University Medical Center

"Aerosol probes of lung injury in a chronic disease model"

Rosenthal Frank, Purdue University

Dosimetry

"Age and body size factors in inhaled particle deposition"

Phalen Robert, University of California at Irvine

"Chaotic mixing of aerosol in rhytmically expanding lung"

Tsuda Akira, Harvard School of Public Health

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Epidemiology/Long-term effects

National Cooperative Inner-City Asthma Study (1996-2000) (Co-funded by NIEHS and EPA)

"National cooperative inner city asthma study" 1-U01-AI-39761-01, Shapiro Gail, University of Washington ($280,001 - FY 96)

"Trial of interventions to reduce asthma morbidity"

1-U01-AI-39769-01, O'Connor George, Boston University School of Medicine ($279,876 - FY 96)

"Targeting the environment and asthma management"

1-U01-AI-39900-01, Crain Ellen, Albert Einstein College of Medicine ($280,979 - FY 96)

"National asthma inner city study-Tucson field center"

1-U01-AI-39785-02, Morgan Wayne, University of Arizona ($259,188 - FY 96)

"National cooperative inner city asthma study"

1-U01-AI-39901-02, Kattan Meyer, Mount Sinai School of Medicine ($321,909 - FY 96)

"Chicago inner city asthma study"

1-U01-AI-39902-02, Evans, Richard, III, Children's Memorial Hospital ($280,435 - FY 96)

"Data Coordinating Center for NCIASII"

1-U01-AI-39776-02, Mitchell Herman, New England Research Institutes, Inc. ($431,228 - FY 96)

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Epidemiology/acute effects

"Ambient Air Pollution and Cardiovascular Morbidity"

I-R29-ES-0724-03, Morris Robert, Tufts University ($94,544 - FY 96)

"Air Pollution Health Effects in a U.S. Population Sample"

5-R01-ES-07410-02, Schwartz Joel. Harvard University ($128,569 - FY 96)

"Effects of Acid Aerosols and Ozone on Urban Populations"

5-R01-ES-06239-05, Dockery, Douglas, Harvard University ($810,499 - FY 96)

"Health Effects of Particulate Acids in Late Adolescence"
1-R01-ES-08391-01, Speizer, Frank, Harvard University ($326,346 - FY 96)

"Air Pollution and Hospital Admissions of the Elderly"
1-R01-ES-07937-01A1, Schwartz Joel, Harvard University ($148,910 - FY 96)

"Environmental Agents-Asthma Development and Severity"
5-R01-ES-07456-03, Leaderer Brian, John B. Pierce Lab, Inc. ($676,567 - FY 96) (Co-funded by NIAID)

"Acid Aerosol-Respiratory Effects in Infants and Mothers"
5-R01-ES-05410-08, Leaderer Brian, John B. Pierce Lab, Inc. ($566,577 - FY 96)

Experimental/health effects

"Toxic Effects of Particles and Oxidants on Lung Function"
5-R01-ES-02679-17, Utell Mark, University of Rochester ($434,702 - FY 96)

"Effects of Environmental Pollutants on Human Lung Function"
5-P30-ES-02147-23 (S-0064), Utell Mark, University of Rochester ($785,069 - FY 96)

"Mechanisms of morbidity/mortality due to air particles"
5-P01-ES-8129, John Godleski, Harvard School of Public Health ($1,041,583 - FY 96)

"Baltimore Environmental Justice Project"
R25-ES-07734, Dr. Sattler, University of Maryland ($165,000 - FY 96)

"Community-Based Asthma Intervention in Pregnant Women"
R21-ES-08716, Dr. Persky, University of Illinois-Chicago ($356,000 - FY 96)

"Lower Price Hill Environmental Leadership Coalition"
R21-ES-07717, Dr. Hansel, University of Cincinnati ($154,000 - FY 96)

"Case Management and Environmental Control in Asthma"
R21-ES-08711, Dr. Fisher, Washington University ($366,000 - FY 96)

Experimental/mechanisms

"Mechanisms of Air Pollutant-Induced Airway Permeability"
5-R01-ES-03251-12, Bhalla Deepak, Wayne State University ($235,328 - FY 96)

"Inhaled Pollutants-Mechanisms of Injury and Adaptation"
5-K04-ES-00256-05, Gordon Terry, New York University Medical Center ($69,174 - FY 96)

"Mechanisms of Particle Induced Lung Injury"
5-R01-ES-04872-09, Oberdorster Gunther, University of Rochester ($347,565 - FY 96)

"Biological Determinants of Environmental Airway Injury"
5-R01-ES-07498-03, Schwartz David, University of Iowa ($221,179 - FY 96)

"Epigenetic Mechanisms of Toxicity of Environmental Metal"
5-R01-ES-0543-09, Chou, lih-Nan, Boston University ($209,286 - FY 96)

"Mechanisms of Particulate Chromate Carcinogenesis"
5-R01-ES-05304-07, Patierno Steven, George Washington University ($241,000 - FY 96)

"Role of Ozone in Modulating Chromium-Induced Lung Immunotoxicity"
5-R01-ES-06783-03, Schlesinger Richard, New York University Medical Center ($301,000 - FY 96)

"Grain Dust, Endotoxin and Air Flow Obstruction"
5-R01-ES-06537-04, Schwartz David, University of Iowa ($256,000 - FY 96)

"Cellular and Biochemical Mechanisms of Particle-Induced Lung Disease"

Z01-ES-25030-10, Bonner JC, Intramural, NIEHS

Aerosol methods and monitoring

"Mutagens in Ambient Airborne Organic Aerosols-Identity and Sources"

3-P01-ES-07168-03S1, Sarofim Adel, Massachusetts Institute of Technology

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

Epidemiology/Long-term effects

Mortality Follow-up of Diesel Exposed Miners

Cohort and Case Control Study of Lung Cancer and Diesel Exhaust

Experimental/Health Effects

Cough Sounds and Aerosols as a Predictors of Respiratory Disease

Occupational Asthma: High and Low Molecular Weight Asthmagens VAG909

Pulmonary Responses to Occupational Dusts VAG913

Identification of Sub-populations Susceptible to Particle Exposure

Experimental/Mechanisms

Identification of Sub-populations Susceptible to Particle Exposure VAGN31

Biomarkers of Occupational Disease Risk: Role in Human Carcinogenesis

Investigation of Occupational Diseases Caused by Metals

Metals: Asthma and Hard Metal Disease

Toxic Respirable Particle Biological Surface Interactions
Molecular Mechanisms of Metal Carcinogenesis
Pulmonary Responses to Occupational Dusts
Occupational Asthma Disease Models
Susceptibility of Workers to Lung Infection After Exposure to Different Occupational Dusts and Fibers
Role of Adhesion Molecules in the Pathogenesis of Lung Disease
Asphalt Fumes: Inflammatory Effects and Pulmonary Injury
South African Biomarker Study
Role of dextran powder in latex hypersensitivity VGN 33

Dosimetry

Particulate and Tissue Analysis Research and Service VOT387

Exposure assessment and relationships

Characterization of Inorganic Dust Exposures VAGN12

Aerosol methods and monitoring

Respirable Dust Measurement and Analysis (Instrumentation) VRE015
Development of a Portable XRF Unit for Air Sample Screening VAG830
Evaluation of LIF Technology for Bioaerosol Screening
Development of a Portable XRF Unit for Air Sample Screening
Improved Application and Monitoring of Dust Control Parameters
Monitoring Cristalline Silica Dust

Atmospheric chemistry and physics, meteorology, and modeling

Surface Chemistry Characterization of Respirable Particles

Emission characterization and source apportionment

Evaluation of Diesel Exhaust Emission Controls VQCN14

Risk assessment and management, cost-benefits

Risk from Emerging Hazards: Asphalt Fumes, Coal Dust, Diesel Exhaust

Control of Silica Dust Exposures in Underground Coal Mining

IEQ Intervention Study

Prevention of Silicosis in Surface Miners

NATIONAL INSTITUTE OF PUBLIC HEALTH AND THE ENVIRONMENT, BILTHOVEN (NL)

Epidemiology/acute effects

Study of cardiovascular effects in elderly people.

Epidemiology/long-term effects

Study in panels of children and asthmatics.

Experimental/mechanisms

Studies on the causality of PM health effects using inhaled CAP, fine and ultrafine particles, instilled PM10/PM2.5 in animals with asthma, heart failure, pulmonary hypertension. In vitro studies using PM10 and PM2.5. (4)

Dosimetry

Dosimetry modeling of PM in healthy and compromised airways.

Aerosol methods and monitoring

Long-term air quality monitoring programme though the Dutch air monitoring network

Specific monitoring campaigns for urban sites and smog episodes.

Atmospheric chemistry and physics, meteorology, and modeling

Modeling of emission inventory to determine levels of PM10, PM2.5, PM carbonaceous, PM secondary.

Source apportionment program

Risk assessment and management/cost-benefits

Integrating exposure and exposure-effect models to predict effects in the (Dutch) general populations and specific risk groups.

Development of cost-benefit analysis techniques.

Risk reduction predictions based on emission/concentration reduction scenario's.

Importance of traffic emissions and reductions measures during wintertime smog episodes.

UNITED KINGDOM DEPARTMENT OF HEALTH

Epidemiology/acute effects

"Effects of Air Pollution on Daily Mortality, Admissions, and General Practitioner Consultations in London"

Principal Investigator: Ross Anderson, St. George's Hospital Medical School

"The Relationship Between Urban Pollution and Cardiorespiratory Health"

Principal Investigator: Raymond Agius, University of Edinburgh

"Study of the Aetiological Effect of Vehicle Traffic Pollution in the Prevalence and Natural History of Asthma in Norttingham School children"

Principal Investigator: John Britton, Nottingham City Hospital

"Effect of Fine Particulate Air Pollution and Acid Aerosols on Respiratory Function and Symptoms in Schoolchildren"

Principal Investigator: S. Walters, University of Birmingham

"Air Pollution and Cardiovascular disease: An Investigation of the Relationship Between Particulate Air Pollution and Blood Coagulation Factors"

Principal Investigator: A. Seaton, University of Aberdeen

"The Effects of Relieving Traffic Congestion on Pollutant Exposure and Respiratory Morbidity".

Principal Investigator: Michael Burr, University of Wales

"The Acute Effects of Particulate Air Pollution in Patients with Respiratory Disease"

Principal Investigator: C. Luczynska, McAughey, et al

Epidemiology/long-term effects

"Chronic Respiratory Health Effects of Cumulative Air Pollution Exposure: A National Birth Cohort Study"

Principal Investigator: David Strachan, St. George's Hospital Medical School.

"Indoor Air Pollution as a Risk Factor for Chronic Respiratory Symptoms in Adolescents"

Principal Investigator: Joanne Clough, Southampton General Hospital

"Do Particulates from Opencast Coal Mining Impair Health?"

Principal Investigator: T. Pless-Mulloli, D. Howel, J. Tate, University of Newcastle upon Tyne

Experimental/health effects

"Study of Lung Function and Biochemical and Cellular Consequences of Acute Exposure to Diesel Exhaust in Normal and Asthmatic Subjects"

Principal Investigator: A. Frew, T. Sandstrom, S. Holgate, Southampton General Hospital

"To Assess the Effect of Challenge with Fine and Ultra-Fine Particles

on Airway Diameter and on Subsequent Response to Allergen Challenge in Patients with Asthma"

Principal Investigator: J Ayres, Birmingham Heartlands Hospital

Risk assessment and management/cost-benefits

"Public Awareness of Air Quality and Respiratory Health: Assessing the Impact of Health Advice"

Principal Investigators: Suzanne Moffatt, Christine Dunn, University off Newcastle upon Tyne

"Towards Assessing and Costing the Health Impacts of Ambient Particulate Air Pollution in the UK"

Principal Investigator: J. Hurley Institute of Occupational Medicine

UNIVERSITY OF WAGENINGEN (NL)

Epidemiology/Short-term

"Highway traffic and respiratory health"

Epidemiology/Long-term

"Long-term exposure to air pollution and mortality"

"Development of asthma and other chronic respiratory conditions in young children"

VERBANDES DER AUTOMOBILINDUSTRIE (D)

Experimental/mechanisms

"Comparative Pulmonary Response of Humans and Animals to Dust Exposures"

Principal investigator: Fletcher Hahn/ITRI/Albuquerque

Emission characterization and source apportionment

"Quellen der Partikelimmission in der Atemluft des Menschen (Sources of Particles)"

Principal Investigators: R. Niener, University of Munich, U. Heinrich, ITA, Hanover (supported in cooperation with "Forschungsvereinigung Verbrennungsmotore", Frankfurt/Main.)