The Health Effects of Fine Particles: Key Questions and the 2003 Review

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The Health Effects of Fine Particles:
Key Questions and the 2003 Review

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I. INTRODUCTORY MATERIAL

INTRODUCTION
EXECUTIVE SUMMARY
AGENDA
As part of its ongoing work to protect health and the environment, Directorate General XI (DG XI) of the European Commission (EC) is charged with proposing legislation to control potentially harmful effects from pollutants. The Commission increasingly has moved to carry out this responsibility by seeking to involve a broad range of stakeholders at different stages of the process.

The Health Effects Institute (HEI) is an independent research organization jointly and equally funded by industry and government to provide independent science on the health effects of air pollution to inform potential regulation.

The materials that follow are the proceedings from a workshop entitled *The Health Effects of Fine Particles: Key Questions and the 2003 Review* held in Brussels, Belgium, on 14–15 January 1999. This was the second in a series of collaborative efforts between the Directorate General XI and the Health Effects Institute. The workshop brought together leading European and U.S. researchers funded by Directorate General XII, HEI, and others, with representatives of the European Parliament, the World Health Organization, the European Science Foundation, the U.S. Environmental Protection Agency, member states, local authorities, industry, nongovernmental organizations, and multiple directorates within the Commission in an open and transparent dialogue to examine underlying science relevant to potential regulation.

Particulate matter was selected as the subject of this workshop in part in response to broad interest among policy makers in the current state of scientific knowledge about particles and their effect. Primarily, however, the workshop was designed to review key outstanding questions and identify research needs that are important to address as the Commission plans for its 2003 review of the Particulate Matter Limit Value, as called for in the Daughter Directive.

In planning the workshop, emphasis was placed on differentiating among scientific questions that have the potential of being addressed effectively prior to the 2003 review and those that will require a longer time to pursue. It is hoped that this meeting was an important step in identifying the scientific questions that are most relevant to risk assessment and future European regulatory needs.

Because particle research is an active and dynamic field, the meeting also included a poster session and short presentations of results of new studies in epidemiology and toxicology, and exposure assessment, expected to be of consequence in advancing the understanding of fine particles. In addition to materials presented at the workshop, this Communication includes the full text of the final PM directive (the Council Directive) in the appendix.

HEI wishes to thank the many diverse interests from within and outside government and the scientific community who contributed to this effort.
EXECUTIVE SUMMARY

BACKGROUND AND REGULATORY CONTEXT

Particulate matter (PM) is the term used to define a complex mixture of anthropogenic and naturally occurring airborne particles. These particles, which can be directly emitted by transport or stationary sources (i.e., primary particles) or created as a product of atmospheric transformation (i.e., secondary particles) are of concern to environmental regulators because of a body of epidemiology studies that link exposure to PM with excess mortality and morbidity in human populations. The most common size descriptor of particles is the aerodynamic diameter, which provides an indication of the particle size. Based on this parameter, ambient particles fall into three size classes or modes: ultrafine, or nuclei mode, particles (less than 0.1 \( \mu m \) in diameter); fine, or accumulation mode, particles (between 0.1 \( \mu m \) and 2.5 \( \mu m \) in diameter); and coarse particles (larger than 2.5 \( \mu m \) in diameter).

In the European Union, emerging concern about the health effects of PM led the European Commission’s Directorate General XI (DG XI) to propose under the terms of the Air Quality Framework Directive 96/62/EC a Daughter Directive establishing limit values for PM (as well as for \( SO_2 \), \( NO_2 \), and lead) in ambient air. In proposing the new limit values, the Commission relied on input from a range of experts and organizations. The input included the World Health Organization (WHO) Guidelines as well as recommendations presented in a 1997 White Paper by DG XI’s Working Group on PM. This group was chaired by member states and was composed of experts from member states, nongovernmental organizations, industry, WHO, the European Environment Agency, and the Commission.

The Daughter Directive put forward by the Commission proposed new limit values for PM measured as \( PM_{10} \) of 50 \( \mu g/m^3 \) (24 hours) and 20 \( \mu g/m^3 \) (annual), to be met by 1 January 2010. \( PM_{40} \) refers to the fraction of particles with an aerodynamic diameter of 10 \( \mu m \) or less.) The proposed Daughter Directives have recently been adopted as final in Council Directive 1999/30/EC, which is included at the end of this Communication.

In proposing a limit value for \( PM_{40} \), the Commission expressed interest in establishing a limit value for fractions smaller than \( PM_{10} \), and noted also the emerging evidence of stronger associations with health effects at smaller fractions. The Commission was, however, constrained by the absence of uniquely European studies or data demonstrating effects at smaller fractions. The Directive dealt with this limitation in part by proposing a review of new scientific information about the effects of particles, particularly the fraction below \( PM_{10} \), in 2003, to help inform consideration of whether a limit value should be established for this size. Key aspects of the 2003 review include achieving a more complete understanding of the 1) health effects of fine particles, including effects of particle size, number, composition, and other characteristics; 2) sources, both transportation and stationary and primary and secondary; 3) chemistry and transport; including local and transboundary; and 4) measurement, including technology and methodology. It is expected that the 2003 review would consider PM in the context of other pollutants and be undertaken in cooperation with a range of stakeholders.

In the United States, the Environmental Protection Agency (EPA) is required by the National Clean Air Act to review the health and environmental effects of the criteria pollutants (\( SO_2 \), \( NO_2 \), PM, CO, and ozone) every five years in consultation with its Clean Air Scientific Advisory Committee (CASAC). The CASAC is a group of experts from a range of relevant scientific disciplines who are charged with advising the EPA Administrator about the current state of the science to be used as the basis for establishing national ambient air quality standards (NAAQS). In its review, the EPA establishes a primary standard designed to protect public health with an adequate margin of safety, and a secondary standard, designed to protect public welfare and the environment. The two primary products of a CASAC review are a Criteria Document, which documents the universe of scientific studies upon which a standard may be based and a Staff Paper, in which the EPA in consultation with CASAC interprets the science and recommends a standard to the Administrator. The entire CASAC process is open to public involvement and comment.

Based on a comprehensive assessment of the science, in 1997 the EPA established a slightly modified \( PM_{10} \) standard of 50 \( \mu g/m^3 \) (annual) and 150 \( \mu g/m^3 \) (24 hour) and also established a new \( PM_{2.5} \) standard of 15 \( \mu g/m^3 \) (annual) and 65 \( \mu g/m^3 \) (24 hour). (\( PM_{2.5} \) refers to the fraction of particles with an aerodynamic diameter of 2.5 \( \mu m \) or less.) The EPA’s decision on the fine particle standard...
Characterization and Measurement

As mentioned earlier, ambient particles fall into a tri-modal size distribution: ultrafine (or nuclei mode), fine (or accumulation mode), and coarse. Ultrafine particles derive primarily from combustion processes and tend to grow into fine particles either by agglomeration or from condensation of volatile material on them. Fine and ultrafine particles are dominated by emissions from combustion processes, and coarse particles are mostly generated by mechanical processes from a variety of noncombustion sources.

Generally, the ultrafine and fine fractions are composed of carbonaceous material, metals, sulfate, nitrate and ammonium. The coarse fraction is composed mostly of particles mechanically generated and consists of insoluble minerals (wind-blown dusts) and biologic aerosols, with smaller contributions from primary and secondary aerosols and sea salts. Understanding how different sources contribute to the atmospheric particle levels is important for designing a rational control strategy.

In response to concerns expressed about uncertainties in the underlying science, a Presidential Executive Order accompanied the release of the new PM standard that underscored the importance of the next CASAC review of the science. That review is currently required to be completed by 2002, prior to actual implementation of the new standards. In 1998, major points from the Executive Order were adopted as law.

The current EU directive requirement for a review of the science of fine particles in 2003 and the US requirement to review the NAAQS in 2002 has resulted in extensive new research in both the European Union and the United States that can be expected to inform these upcoming regulatory efforts.

**PARTICLE CHARACTERIZATION, SOURCE APPORTIONMENT, AND EXPOSURE**

Particles in ambient air originate from a variety of sources and differ in size, composition, and other physical, chemical, and biological properties and in the processes they undergo in the atmosphere. Some are solid and some are liquid. Emissions from stationary fuel combustion sources combine in the atmosphere with the emissions from motor vehicles. A large fraction of emissions are from non-industrial sources. As the emissions from these sources mix in the atmosphere and are transported downwind, atmospheric chemical reactions take place and secondary particles are formed (for example, sulfate and nitrate are formed from the oxidation of $\text{SO}_2$ and $\text{NO}_2$, respectively).

**Characterization and Measurement**

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Generally, the ultrafine and fine fractions are composed of carbonaceous material, metals, sulfate, nitrate and ammonium. The coarse fraction is composed mostly of particles mechanically generated and consists of insoluble minerals (wind-blown dusts) and biologic aerosols, with smaller contributions from primary and secondary aerosols and sea salts. Understanding how different sources contribute to the atmospheric particle levels is important for designing a rational control strategy.

The measurement of ambient particulate matter is challenging because particle composition and size distribution vary from one location to another and from one time to another in the same location. There is an ongoing discussion over the most appropriate metric for particle measurement and for ambient standards. In addition to particle mass (which is currently the parameter by which particle levels are regulated), particle number or surface area may be relevant metrics for particulate matter. Depending on the parameter chosen, different parts of the size distribution are measured. The number concentration is carried by the nuclei mode particles; the surface area information is carried by the accumulation mode particles (both primary and secondary). The mass information is carried by both the accumulation and the coarse mode particles.

At this time it is unclear whether certain characteristics of particles are more closely associated with health effects than others, and regulatory action has focused on controlling the particle mass (both in emissions and in the ambient air). In order to develop air quality regulations, standard reference methods are needed for measuring particles of different sizes. The indicators that are currently being used to measure PM levels are $\text{PM}_{10}$ and $\text{PM}_{2.5}$.

The methods available for collecting and measuring the mass of $\text{PM}_{10}$ and $\text{PM}_{2.5}$ generally consist of drawing the ambient particles through a size-selective inlet onto one or more filters over a given period (generally 24 hours) and measuring the mass on the filter by weighing it. There are some performance concerns associated with the methods for collecting $\text{PM}_{2.5}$. Current samplers have limited sampling efficiency and are affected by humidity, temperature, and loss of volatile material. All available PM samplers are currently being tested at several sites in Europe with the goal of solving many issues regarding their performance and developing a sampling strategy (for example, frequency and duration of the measurements and location of the samplers).
Source Apportionment
Ongoing efforts are also being made to determine how the various emission sources contribute to ambient particle levels. These efforts will assist in the formulation of regional plans for the control of atmospheric particulate matter concentrations. Various approaches are being used toward this goal. A recent study by the TNO group (a Dutch research organization) estimated emissions of primary aerosols from stationary combustion, industrial process emissions, transport, agricultural practices, and waste incineration by applying emission factors for a certain activity rate for the individual source groups for individual European countries. These emission estimates were then integrated across the countries studied to estimate the contribution of various sources to the ambient particulate levels for Europe. From these inventories, predictions for future years can be made assuming different extents of emission reductions and other factors. Some approaches for apportioning particles to sources consist of combining emission data (including size distribution and chemical composition) from various sources with atmospheric transport models. These models simulate atmospheric transport and chemical reactions of the particles from their sources to the air quality monitoring sites. Another approach uses organic chemical tracers techniques. The latter method relies on the identification of organic molecular tracers that are unique to a given source. The results of the various modeling efforts need to be validated by comparing them with measured ambient concentrations. Generally, source apportionment studies have shown that stationary sources (primarily coal-fired power generators), road dust, and other dusts are the major contributors to particles in the range of 2.5 to 10 μm, and mobile sources are the major contributors to ultrafine and fine PM.

Exposure
The great majority of epidemiology studies investigating the association between exposure to particulate matter and mortality and morbidity have used ambient particle concentrations as a surrogate for personal exposure. The assumption that ambient exposure data are an adequate surrogate for personal exposure to PM has not yet been validated, however. To do so, we must understand better how the data for ambient levels relate to personal exposure, which involves varying amounts of time spent outdoors for individual members of the population. The studies conducted so far provide some insights about this relationship, but they also point to the need for additional research. Major information gleaned from these studies includes:

- Fine particles and the components associated with them penetrate indoors more readily than coarse particles.
- PM$_{2.5}$ outside the home is very similar to that measured at the stationary monitoring sites.
- The association between personal exposure and outdoor concentrations vary with both the size fraction and the season and, in general, is better for PM$_{2.5}$ than for PM$_{10}$. The correlation is low when the results are analyzed across individuals on a given day because of interpersonal variability, but improves when repeated longitudinal measurements are used.
- Personal exposure to PM for nonsmokers is generally higher than either indoor or outdoor concentrations during the day.

Some information about ambient particle concentration in Europe will be obtained as a result of the recent air quality Daughter Directive requiring member states to make measurements of both PM$_{10}$ and PM$_{2.5}$. Information on chemical composition by size fraction and measurements of number and size distribution are also needed to apportion particles to their sources better. More data on primary emissions from new technologies and fuels, the chemical process forming secondary aerosols, and the dynamics of ultrafine particles are also needed.

Information on personal exposure is being obtained from a number of studies sponsored by the European Commission in Europe as well as studies ongoing in the United States. Future research needs include obtaining repeated measurements in different subgroups of the population (especially those considered more susceptible) and examining temporal variations in personal exposure.

HEALTH EFFECTS OF PARTICULATE MATTER
European and US regulatory agencies are considering, or have recently promulgated, more stringent air quality standards for airborne PM. The scientific basis for these actions rests largely on the results of a large body of epidemiology research, which has found associations between increases in daily and longer-term rates of mortality and morbidity from respiratory and cardiovascular diseases and ambient concentrations of PM currently prevalent in Western industrialized countries. Although the epidemiology evidence is extensive, aspects of the epidemiology of PM
that could help guide regulatory action are not well understood. Even less well understood are the pathophysiological processes that might underlie these associations, though much current research is aimed at elucidating them.

**The Epidemiology Evidence**

Short-term exposure to PM has been associated with increased daily rates of cardiorespiratory morbidity and mortality in a large number of studies in the United States, Europe, and other locations worldwide. Associations between inhalable particles (PM$_{10}$) and daily mortality have been consistently observed, and the effects of the fine particle fraction (PM$_{2.5}$) appear in some studies to be greater than the effects of the coarse fraction (i.e., those with diameters between 2.5 and 10 microns). Far fewer studies have estimated the association of long-term exposure to PM with either the development of chronic cardiorespiratory disease or longer-term average mortality.

Most studies in the United States and Europe have observed increased rates of mortality from all natural causes, and from cardiovascular and respiratory diseases in particular, associated with various indices of particulate air pollution, but also with several gaseous air pollutants generated by the same sources, chiefly the combustion of fossil fuels. The APHEA (Air Pollution and Health: A European Approach) study of 15 European cities found associations of daily mortality with PM$_{10}$, but also with other indices of air pollution, such as sulfur dioxide (SO$_2$), ozone (O$_3$), and Black Smoke (BS, or soot). Air pollution-associated mortality varied by season, with larger relative increases observed in warmer weather.

Over the past decade, US epidemiologists have made extensive use of a nationwide network of PM$_{10}$ monitors, supported by the US EPA since 1987, and to more periodic and less extensive data bases on PM$_{2.5}$ and sulfates. Such resources have not been widely available in Europe, but several recent studies have examined the effects of PM components and gaseous pollutants on mortality. For example, a study in the Netherlands examined the relation of PM$_{10}$, sulfates, nitrates, and various gaseous pollutants with daily mortality over a three-year period, and found effects for both gaseous pollutants and PM. Ozone had the strongest association. Indices of fine PM (sulfate and nitrate) were more strongly associated with mortality than was PM$_{10}$. A recent German study made use of a sophisticated mobile monitoring system to collect data on both mass and number concentrations of PM in the city of Erfurt. Investigators observed a stronger association between the number concentration of ultrafine particles and the frequency of respiratory symptoms than between respiratory symptoms and fine particle mass concentration.

Daily mortality rates are strongly influenced by weather conditions, which also help determine ambient air pollution concentrations. For this reason, epidemiologists have gone to considerable lengths to ensure that the effects of weather have been adequately taken into account, and have not been mis-attributed to air pollution. Two US studies carefully explored a variety of statistical methods to account for the effects of weather and concluded that the associations of particulate air pollution with daily mortality could not be explained by the effects of weather. Studies of hospital admissions for respiratory and cardiovascular diseases in both Europe and North America have consistently observed associations with air pollution, including various PM indices, and gaseous pollutants such as ozone, CO, and NO$_2$.

Although the association between daily variations in air pollution, including PM, and daily mortality is relatively well established, the evidence for long-term exposure to PM on mortality is weaker. Over the past decade, two US studies have found that low levels of PM$_{2.5}$ or sulfate were associated with reduced survival among residents of more polluted areas, due to increases in mortality from cardiovascular and respiratory disease, including lung cancer. More recently, a third US study observed similar associations, though with notable differences such as lower relative rates for all-cause mortality and higher relative rates for lung cancer.

**The Prevailing Uncertainties in the Epidemiology Evidence**

Despite the relative wealth of epidemiology data on PM and health, there are aspects of the problem that are still not understood. Exposure assessment, the effects of multiple pollutants, and the impact of long-term exposure to PM are important areas where scientific uncertainties exist. These uncertainties affect the interpretation of the available evidence, and limit, to varying degrees, its use in policy making.

Most epidemiology studies have used routinely collected data on ambient air pollution to characterize the exposure of study subjects. As noted earlier, the extent and quality of these data are variable, and data on PM components, such as PM$_{2.5}$, may not be available or may be quite limited. Even when such data are extensive, they have usually been obtained from a single, fixed
monitoring site and may not accurately reflect the personal exposure of individuals to either PM or gaseous co-pollutants, though the extent of the difference is likely to vary among pollutants. Correlations over time between personal measurements and central monitor values are stronger for PM$_{2.5}$ than for PM$_{10}$. The measurement error that may result can produce inaccurate estimates of the health effects associated with air pollution. Research on the effect of measurement error suggests that under most conditions it will result in underestimates of the actual effects associated with air pollution, though complex correlations between the measurement errors for multiple pollutants may produce errors in either direction.

Risk factors for morbidity or mortality that are also associated with exposure to PM may create bias in epidemiology studies and distort estimates of the effects of PM. This bias is termed confounding. In time-series analyses of daily variation in PM and health effects, time-varying factors such as seasonal patterns, weather factors, and other temporally varying events affecting health may produce confounding. Modern statistical approaches, however, enable investigators to address these problems effectively.

Control of confounding is a more serious problem in studies of long-term exposure to PM and chronic disease because it is difficult to measure accurately long-term exposure to other risk factors such as smoking, diet, and occupational history, and to correctly specify their effects in statistical models. The effectiveness of control for confounding can be explored with sensitivity analyses; this is being done in reanalyses of the two major US studies of long-term exposure to PM and mortality.

Particulate air pollution is always present as part of a mixture of air pollutants, and PM levels are often highly correlated in time and space with levels of gaseous pollutants such as ozone, SO$_2$, and NO$_2$. Identification of the independent effects of PM is therefore difficult. Statistical models that include multiple pollutants can be helpful in this regard, particularly if the correlation between PM and other pollutants is relatively low. The examination of PM effect estimates among geographical areas that differ widely with respect to levels of other pollutants is a particularly effective analytic tool; the observation of relatively consistent associations with PM across diverse climate and air pollution conditions would argue for an independent effect of PM.

If the results of the few studies of mortality and long-term exposure to PM are valid, then they imply that PM at low ambient levels is responsible for life-span reductions on the order of years. The public health significance of the better-documented association of daily variations in PM with daily mortality is less clear, however. If the loss of life associated with these deaths was on the order of days—that is, if PM affected only those in whom death was already imminent (often indelicately the "harvesting effect"), then the public health impact might not be great. Research is currently underway to determine whether or not the associations of PM with daily mortality are largely the result of such a harvesting effect.

The current epidemiologic data do not indicate an ambient concentration of PM below which no effects are found, a so-called threshold. Whether this reflects a linear exposure-response relation, or simply the limitations of epidemiologic methods, is unclear. Some argue that the concept of a "threshold" has no meaning at the population level. As a practical matter, the size required for a study that could measure accurately the shape of the exposure-response relation at low levels of exposure and small relative effects might well render it infeasible.

The association of short-term exposure to PM with acute cardiopulmonary effects has been replicated in studies of diverse populations worldwide. This gives some confidence that these results may be broadly applied to other populations that may not have been studied, even without a detailed knowledge of the underlying biologic mechanisms. The same cannot be said for our current knowledge of the effects of long-term exposure to PM on mortality, which is based on limited observations in the United States.

**The Current Understanding of Pathophysiologic Mechanisms**

It is by no means clear how exposure to low ambient mass concentrations of PM might produce the health effects observed in epidemiology studies and whether certain attributes of PM may be more closely associated with these effects. The leading hypotheses regarding the role of particle characteristics that are being investigated include metal content, particle size, and particles as carriers of other toxic compounds (such as gases or biological toxins from bacteria and pollen, etc.). Transition metals (such as Fe, Cu, Ni, Co, Mn, etc.) have been hypothesized to be associated with effects because they can cause the production of hydroxyl radicals, which are considered to be toxic to the cells. Another hypothesis is that ultrafine particles are more toxic than larger particles because they deposit efficiently in the alveolar region and can
penetrate the lung epithelium. Last, it is possible that particles may carry potentially toxic gases or toxins into the deep lung, thus increasing the risk of cellular damage.

Epidemiology has helped focus toxicology research on several groups that may be at increased risk of adverse effects of exposure to particulate air pollution. These include persons with severe heart and lung diseases, individuals with asthma, and perhaps (more generally) the elderly and children. Together these groups would comprise a large pool of susceptible people in most developed Western societies.

The mechanisms by which low levels of PM might cause death or exacerbate disease in those with cardiovascular or respiratory illness have not been determined, but several have been hypothesized. One general mechanism is production of inflammatory mediators that could cause a cascade of physiologic reactions that, directly or indirectly, precipitate cardiopulmonary effects. For example, these mediators could exacerbate pre-existing lung disease (by impairing gas exchange), or increase plasma viscosity and the coagulability of the blood (by increasing fibrinogen, Factor VII, and plasminogen activator inhibitor). This could in turn trigger changes in the electrical activity of the heart, resulting in altered cardiac rhythm and/or repolarization and possibly leading to heart attacks, arrhythmias, or other coronary events. Particles may also directly or indirectly affect the nerves involved in regulating the heart and thus alter cardiac function. Other models for pulmonary effects of PM exposure include increased susceptibility to infection via effects on the lung's mucociliary clearance mechanism, by increasing adhesion of bacteria to epithelial cells, by impairing the activity of pulmonary macrophages, or by impairing specific or non-specific immune function. Although a number of studies are investigating different mechanistic hypotheses, thus far there is insufficient information pointing to a specific mechanism of action of PM.

ONGOING RESEARCH

Much research is being carried out both in Europe and the United States to address some of the needs regarding particulate matter. Several exposure assessment studies are being conducted in different locations with the goal of characterizing the personal exposure of potentially susceptible groups of the populations. A number of experimental and epidemiology studies are measuring health effects in potentially susceptible groups and the mechanisms by which particles may cause the effects observed in the earlier epidemiologic studies. Experimental studies (both in animals and in humans) are also investigating the role of different particle characteristics (such as the role of metals, acidity, and size) in causing effects. Results of some of these studies are available; others are likely to be available in the next few years. An important feature of some of the epidemiology and exposure assessment studies is that they are multicenter studies that allow the investigators to take advantage of differences in pollutants mix and socioeconomic conditions in different locations. The universe of PM studies is being inventoried and tracked on an internet web site maintained by HEI.

OUTSTANDING QUESTIONS AND GAPS FOR 2003 AND BEYOND

As described above, recent actions by both the European Union and the United States to tighten the regulation of emissions of particulate matter have increased the need for scientific information to improve decisions as efforts move forward to control emissions. Information is needed in a number of areas, including atmospheric concentrations, population exposure, effects of different components of the PM mixture, and the magnitude of life-shortening and other potential public health implications of exposure to PM.

A number of national and international agencies have been identifying and undertaking research to fill key data gaps for PM in order to meet both near-term (2003) and longer-term needs of decision makers for information. In Europe, the European Union is working in concert with the member states and the Joint Research Centre to establish a common European monitoring system to monitor population exposure to PM_{10} and PM_{2.5} for the purposes of measuring compliance with EU limit values, improving the database for source apportionment (and action plans), and assessing exposure for health effects research. Although this will provide some important pieces of information for compliance assessment and source apportionment, there are challenges for conducting full-source apportionment, including identifying and understanding secondary sources, and for conducting monitoring that is directly useful to health effects research (for example, monitoring for particle sizes smaller than PM_{2.5}).

In both the United States and Europe, efforts are underway to set priorities for PM research.
The National Academy of Sciences in the United States has established a Committee for Research Priorities on Airborne Particulate Matter that is charged to establish research priorities for PM for the near term and long term, and to oversee and advise on the conduct of that research for five years. In its initial report, the Committee identified 10 highest priority research areas and a portfolio of research investments to be made over the next 14 years to answer key questions on:

1. Outdoor measures of air pollution versus actual human exposure
2. Exposure of susceptible populations to toxic PM subcomponents
3. Source-receptor measurements
4. Application of methods and models
5. Assessment of hazardous PM components
6. Dosimetry: deposition and fate of particles in the respiratory tract
7. Combined and long-term effects of PM and gaseous co-pollutants
8. Susceptible subpopulations
9. Mechanisms of injury
10. Analysis and measurement

In Europe, the European Science Foundation Programme on Environment and Health (ENHE) through an initiative with WHO, the European Commission, and National Research Organizations has identified eight high-priority areas for research:

1. Source apportionment of PM in indoor and outdoor air
2. Characterization of European air quality and of personal exposure
3. Toxicological and clinical studies of acute and chronic respiratory and cardiovascular responses to PM
4. Epidemiology studies on the effects of long-term exposure
5. Formulation of a set of policy scenarios for PM and its public health impact
6. Formulation of a meaningful set of health impact indicators for PM
7. Evaluation of efficacy of previous and current regulatory approaches
8. Evaluation of risk management in different economic growth scenarios

To address these important research priorities, research programs are underway on both sides of the Atlantic. The European Commission Fifth Framework Programme is moving ahead with a substantial investment in its Environment and Health Key Action within the Quality of Life Program (160 million Euros over five years) as well as related research in the Environment and Sustainable Development Key Action of the Energy, Environment, and Sustainable Development Growth Programme. Portions of these funds are likely to be awarded, through competitive processes, to fund important research on PM. In the United States, the US Environmental Protection Agency is investing $45 to $50 million per year (45 to 50 million Euros) on PM research. There are also opportunities for public-private partnerships to fund high-priority research.

**SUMMARY**

As a result of air pollution policy debates and regulatory action in both the European Union and the United States, there is growing international interest in and attention to the health effects of particulate matter. Although there are many diverse parties with interest in these questions, it is apparent that they share a common interest in pursuing certain key questions about PM:

**Exposure**

- Improving monitoring of PM$_{10}$ and PM$_{2.5}$ for both compliance monitoring and health research purposes
- Better understanding the relationship of outdoor PM to personal exposure
- Enhanced tools for source apportionment of both primary and secondary PM

**Health Effects**

- Understanding the comparative toxicity of different components of the PM mixture (ultrafines, metals, etc.)
- Investigating the biological mechanisms that might cause effects
- Identifying sensitive subpopulations (children, elderly, etc.)

**Risk Management**

- Better tools for assessing the magnitude of life-shortening and other measures of public health impact
- Consistent methods for evaluating and applying results from one country in other countries

The conference presented in this Communication started the process of bringing all parties together to understand the extent of our current knowledge on the health effects of PM.
and to identify directions for future research. As part of the European Commission DG XI Clean Air for Europe Programme, this dialogue will continue in the fall of 1999 with an additional workshop on the sources and control technologies for PM, and with subsequent workshops in 2000 and beyond to bring all parties together regularly to hear and assess the latest information on health effects and other aspects of PM.
AGENDA

Joint Meeting of the EC and HEI

The Health Effects of Fine Particles:
Key Questions and the 2003 Review

Brussels, 14–15 January 1999

FINAL PROGRAMME

THURSDAY 14 JANUARY

9:30 Registration

Opening session

Chair: Prudencio Perera, European Commission, DG XI

10:00 Opening comments and welcome from the European Parliament

Prudencio Perera, European Commission, DG XI; Daniel Greenbaum, Health Effects Institute; and Christian Farrar-Hockley, Assistant to Anita Pollack, Member of European Parliament (United Kingdom)

10:20 European Union and US regulatory contexts

Lynne Edwards, European Commission, DG XI, and William Harnett, Environmental Protection Agency, United States

Overview of the current European PM Daughter Directive and US PM Ambient Air Quality Standards, the scientific basis for the different regulatory decisions, future regulatory time lines, and key policy questions.

11:00 Particle formation and characterization

Martin Williams, Department of Environment, United Kingdom

Overview of particle formation, characteristics, and size distribution (both primary and secondary); and particle levels, trends, and transport in Europe.

What are people exposed to and where do particles come from?

Chairs: Giovanni Angeletti, European Commission, DG XII; and Robert Sawyer, University of California at Berkeley, United States, and University College of London, United Kingdom

11:50 Relationship between personal exposure measurement and ambient concentrations

Petros Koutrakis, Harvard School of Public Health, United States

An overview of the current understanding of the relationship between ambient concentration and personal exposure. This information is important to understand the results of the epidemiology studies, which have relied on data on ambient PM concentrations collected at central monitoring sites as surrogates for personal exposure.

12:15 Capabilities and limitations of available particle measurement technologies

Emile De Saeger, Joint Research Center ISPRA, Italy

A discussion of the technologies available for characterizing particles in ambient air in terms of size and composition. Issues to be addressed include effects of cold temperatures, nitrate loss, black smoke versus PM, network consistency, health versus compliance issues, and US and European reference methods for PM$_{10}$ and PM$_{2.5}$. 
12:40 Discussion
13:00 Lunch
14:30 Apportioning particles to their sources
   Information on the results of ongoing efforts to develop and validate models to
   apportion primary and secondary particles (and their major constituents) to specific
   transport, stationary and other sources.
   Particulate matter emission estimates for several European countries
     Jan Berdowski, TNO Institute, The Netherlands
   Characterization and source apportionment of airborne particles
     Glen Cass, California Institute of Technology, United States
15:10 Discussion

What is known about the health effects of PM?

Chair: Ross Anderson, St. George’s Hospital Medical School, United Kingdom
15:30 Summary of the results of the epidemiology studies of acute and long-term effects
   Bert Brunekreef, University of Wageningen, The Netherlands
   An overview of the epidemiology studies that have found an association between
   exposure to ambient particulate matter and increases in mortality and morbidity,
   including a discussion of differences in findings between European and US results.
16:00 Gaps and uncertainties in the epidemiology studies
   Michal Krzyzanowski, World Health Organization Bilthoven, The Netherlands
   A discussion of the major issues that affect the interpretation of the epidemiologic
   results to date, including major outstanding confounding variables, the role of other
   pollutants present in the atmosphere, the impact of exposure measurement errors,
   and the extent of reduction in life span.
16:20 Discussion of the epidemiology studies
16:45 Current state of knowledge about how particles might cause health effects
   Mark Utell, University of Rochester, United States
   A discussion of the current mechanistic hypotheses that might explain the
   epidemiology findings.
17:15 Summary and introduction to poster session
17:30 Reception and poster session New PM research results from Europe and the USA
19:00 Adjourn

FRIDAY 15 JANUARY

What new research results are emerging?

The goal of this session is to present recent results of PM studies and to discuss the role of multi-
center studies in air pollution research. The topics highlighted are susceptible populations and
particle characteristics because an understanding of these issues will affect future regulations.

Chairs: Robert Maynard, Department of Health, United Kingdom; and Bernd Seifert,
Umweltbundesamt, Germany
9:00 Which groups of the general population may be at increased risk of exposure to PM?
   Bert Brunekreef, University of Wageningen, The Netherlands [children]
   Frank Speizer, Harvard School of Public Health, United States [people with cardiac
disease]
9:50 Which are the characteristics of particulate matter that are important to human health?
Leendert van Bree, Rijksinstituut voor Volksgezondheid en Milieu, The Netherlands
[primary versus secondary particles]
H-Erich Wichmann, GSF - Forschungszentrum fur Umwelt und Gesundheit, Germany
[role of ultrafine particles]

10:40 Break

11:00 The role of multicenter studies in air pollution research
Klea Katsouyanni, University of Athens, Greece [APHEA 2]
Jonathan Samet, Johns Hopkins University, United States [NMMAPS]
Matti Fantunen, National Public Health Institute, Finland [EXPOLIS]

12:15 Concluding remarks

12:30 Lunch

Outstanding questions and gaps for 2003 and beyond

The goals of this session are to discuss key research planning efforts undertaken to date, incorporating aspects of presentations made previously as appropriate, and encourage a dialogue on the key outstanding questions about fine particles in Europe that are expected to be most relevant to the 2003 review and those that should be addressed in the longer term.

Chairs: Daniel Greenbaum, Health Effects Institute, United States, and Rolaf van Leeuwen, World Health Organization Bilthoven, The Netherlands

14:00 National Academy of Sciences (US) PM research recommendations
Jonathan Samet, Johns Hopkins University, United States; (NAS Committee chair)

14:25 Setting up a monitoring network in Europe: Anticipating key needs for PM characterization and source apportionment
Peter Bruckmann, Landesumweltamt, Germany

14:45 The European Science Foundation Programme on Environment and Health (ENHE)
Charlotte Braun-Fahrlander, University of Basel, Switzerland

15:10 The European Commission Fifth Framework Programme
Kirsli Haavisto, European Commission, DG XII

15:30 Invited comments: What are the priority research questions relative to public health and regulation? What can be accomplished in time to inform the 2003 review?
Frazer Goodwin, European Federation for Transport and Environment, Belgium
Michael Spallek, Volkswagen AG, Germany
Wim Tordoiz, CONCAWE, Belgium

15:50 Open discussion with the audience

16:30 Summary: Needed research to inform regulations

16:45 Closing remarks: Where does the Commission go from here?
Lynne Edwards, European Commission, DG XI

17:00 Adjourn
LIST OF POSTER PRESENTERS

Exposure assessment studies

Celine Boudet, University of Grenoble, Grenoble, France
Matti Jantunen, National Public Health Institute, Kuopio, Finland
Peter Rombout, Rijksinstituut voor Volksgezondheid en Milieu, Bilthoven, The Netherlands
Juhua Pekkanen, National Public Health Institute, Kuopio, Finland
Xavier Querol, Consejo Superior de Investigaciones Cientificas, Barcelona, Spain
Andrejs Schütz, Lunds Universitet, Lund, Sweden

Epidemiology studies

Ursula Ackermann-Liebrich, University of Basel, Basel, Switzerland
Bert Brunekreef, University of Wageningen, Wageningen, The Netherlands
Anthony Fletcher, London School of Hygiene and Tropical Medicine, London, United Kingdom
Klea Katsouyanni, University of Athens Medical School, Athens -Goudi, Greece
Göran Pershagen, Karolinska Institutet, Stockholm, Sweden
Jonathan M. Samet, Johns Hopkins University, Baltimore, MD, USA
Frank Speizer, Harvard School of Public Health, Boston, MA, USA
Radim Šram, Institute of Experimental Medicine, Prague, Czech Republic
Jordi Sunyer, Instituto Municipal d'Investigacion Medica, Barcelona, Spain
H.-Erich Wichmann, GSF-Forschungszentrum für Umwelt und Gesundheit, Neuherberg, Germany

Toxicology studies

Daniel L. Costa, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA
Kenneth Donaldson, Napier University, Edinburgh, Scotland, United Kingdom
Joachim Heyder, GSF - Forschungszentrum für Umwelt und Gesundheit, Neuherberg, Germany
Günter Oberdörster, University of Rochester, Rochester, NY, USA
Thomas Sandström, University Hospital of Umeå, Umeå, Sweden
Leendert van Bree, Rijksinstituut voor Volksgezondheid en Milieu, Bilthoven, The Netherlands