Theme One: Health and Exposure

Theme Lead: Bob Devlin

By 1996, considerable evidence had accumulated suggesting that exposures to ambient particulate matter (PM) at or near the level of the then current National Ambient Air Quality Standard (NAAQS) were eliciting significant human health effects in the U.S. population. This evidence led to the promulgation of a new PM NAAQS in 1997, including a standard for PM smaller than 2.5 μm in aerodynamic diameter ($PM_{2.5}$). The revised standard, coupled with continuing concerns and uncertainties regarding PM health effects, prompted Congress to augment the President's recommended U.S. Environmental Protection Agency (EPA) budget and charge EPA with accelerating investigations of the role of PM in air pollution-associated health outcomes and implementing health risk reductions via scientifically defensible regulatory actions. A comprehensive national research endeavor was initiated by EPA in 1998 and currently involves the coordinated efforts of intramural and EPA-funded extramural investigators, partners, and other Federal organizations that function within a scientific framework of research needs developed by an independent National Academy of Sciences National Research Council (NRC) committee of experts.

Six years of intensive research activity have now passed and these studies have resulted in significant advances in health and exposure research. Some of the areas where significant progress has been made are: (1) understanding the relationship between community monitoring and individual exposures; (2) identification of PM components responsible for adverse health effects; (3) identification of the people most susceptible to PM; and (4) characterization of the mechanisms by which PM causes adverse health effects;. Yet, while much has been learned in this timeframe there remains considerable uncertainty regarding PM-associated health effects. For example, the research concerning the components and attributes of PM has raised several hypotheses that cannot be excluded from the assessment of causality and thus require further investigation. The ability to link adverse health effects to specific source emissions rather than PM mass would allow emission reductions to be targeted at those source types. A much better understanding of the factors and mechanisms which underlie susceptibility is needed. Clearly, additional effort is needed to advance this knowledge base and make it useful in NAAQS development. The goal of these efforts, of course, is to provide health and exposure data appropriate to the review of the NAAQS and to ultimately assist the Agency in setting PM standards most protective of human health.

This session is intended to summarize and highlight the salient ORD-sponsored scientific advances in PM health and exposure since 1997. The session is framed according to the priority research needs noted in the three NRC reports published to date and in the context of the programmatic and regulatory needs of EPA's Office of Air and Radiation (OAR). In addition the envisioned future directions and goals for the specific research topic area research efforts are also discussed.

Research Topic 1. Outdoor Measures Versus Actual Human Exposures

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

The epidemiological studies that provided much of the scientific basis for the PM NAAQS of 1997 indicated that increased risks of mortality and morbidity are associated with ambient PM across a

wide range of concentrations. A remarkable feature of these studies is the strength of the concentration-response relationship between data from community monitors and a human population that spends most of its time indoors. It is almost counterintuitive that monitors representing the widely distributed PM mass within a given airshed could serve as a surrogate for individual human exposures given the diversity of lifestyles and activities. Indeed, those found to be most at risk, including the elderly and individuals with coronary or respiratory disease, are least likely to be outdoors and exposed to PM as measured by ambient monitors. Additionally, data from early studies suggested that personal PM exposures may differ substantially from outdoor concentrations due to contributions from indoor sources. Finally, there was little information about the ability of outdoor PM to penetrate indoors.

Consequently, understanding the source-to-personal exposure component of the risk paradigm became a primary concern of ORD's PM Research Program. Specifically, understanding the relationship between PM measured at community monitors and local outdoor, indoor, and personal exposure concentrations was considered essential to understanding risks. Likewise, the effect of human activities and other factors on these relationships required investigation. Field studies, laboratory studies, and model-development research have been combined to quantify important relationships and to understand how subpopulations, regions, seasons, housing type, and human activities affect these relationships.

The poster presented by Williams summarizes some of the studies that characterize inter-personal and intra-personal variability in exposure to PM mass and describe the relationship between personal exposures and ambient exposure estimates based on central-site monitoring. They take into account differences in housing stock air conditioning use, and other factors. In addition the **poster presented by Kim** demonstrates that potential differences in behavior patterns among susceptible subpopulations do not appear to alter their personal exposure to PM, compared with healthy individuals.

What Remains to Be Done

These studies have defined relationships between PM mass measured at a community based monitor and exposure to individuals within that community. Additional work is needed to improve models that can predict individual exposure based on these measurements, together with factors such as housing ventilation, and use of air conditioners. Although these measurements and models may be able to predict personal exposure based on PM mass measurements, there is also a need to understand the homogeneity in distribution and penetrance indoors of individual PM components. If, in fact, the toxicity of PM resides in its matrix or constituents (e.g., metals, organics, or other components), it will be important to ascertain whether the PM components follow the mass spatial distribution in evaluating PM health effects. **The poster presented by Vette** in Session 3 includes a study which is designed to look at the relationship between various PM components, and the sources from which they arise, on the basis of both community and personal exposure monitoring.

Research Topic 5. Assessment of Hazardous Particulate-Matter Components

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

The justification for the 1997 PM NAAQS was primarily based on a large epidemiological database showing associations between ambient PM mass and excess mortality and morbidity. These associations are somewhat counter-intuitive, since PM pollution is a complex mixture of organic and

inorganic constituents whose composition can vary widely depending on the time of year and geographical location. It exists over a wide range of sizes and geometries and contains several different classes of components comprised of hundreds of individual compounds. In order for the EPA to reduce the risk associated with PM exposure, it is critical to understand the contribution of various PM components (and the sources from which they arise) to the observed adverse health effects. Assessment of the toxic nature of PM must build upon a fundamental understanding that exposure to PM constitutes exposure to a complex mixture of PM of differing size and composition that may or may not be chemically or toxicologically altered by the various gaseous co-pollutants that coexist in an airshed. There was very little information six years ago as to which components may contribute to PM-induced health effects, though there several hypothesis had been proposed. ORD sponsored research has primarily focused to date on the following properties or classes of components of PM:

- Particle size
- Metals
- Organics
- Biologics

Particle Size – Ultrafine PM

The physical attributes of PM - size, surface area and number - are interrelated descriptive metrics of PM. These properties influence PM deposition, penetration, and persistence in the lung, as well as the potential for systemic transport and the inherent toxicity of the particle itself. Ultrafine particles (UFP) have a very high specific surface area, which can in principal make them more reactive chemically and biologically compared to larger-sized particles. Moreover, the larger surface area can function as a carrier for gaseous and semi-volatile co-pollutants. The chemical composition of ambient UFP includes elemental and organic carbon compounds, heavy metals and inorganic compounds, with the smaller UFP (<~20 nm) having higher amounts of organics. Furthermore, because of their small size, UFP have the potential to distribute to target sites outside the respiratory tract, including the cardiovascular system and the central nervous system (CNS).

While a few epidemiological studies show correlations between health outcomes and ultrafine (<100 nm) ambient PM, the bulk of the information regarding the toxic potential of ultrafine particulates and the role of surface area as an alternate health-related PM metric has derived from controlled exposure or in vitro studies of surrogate insoluble particles (e.g., TiO_2 and carbon black). More recently toxicology studies have begun to directly compare the potency of ambient air collected in different size ranges. **The poster presented by Oberdorster** shows representative studies from ORD's PM program which confirm that UFP can induce biological effects (oxidative stress; inflammation) in the respiratory tract as well as other organ systems including the cardiovascular system and the central nervous system (CNS).

Particle Size - Coarse PM and Biologics

As opposed to the ultrafine PM, less attention was initially paid to coarse PM ($PM_{2.5-10}$), primarily because the association between mortality and PM was much stronger for fine PM ($PM_{2.5}$) than coarse PM. Coarse PM originates from abrasive practices such as milling and sand-blasting, re-dispersion of crustal and biogenic material, and natural processes like sea spray and pollen release. It makes up 30 – 50% of PM mass depending on the geographical local. Elemental analysis shows enrichment in crustal metals such as aluminum silicates and lower amounts of combustion byproducts such as organic and elemental carbon and sulfates. Recent questions about whether health effects associated with coarse PM are substantial enough to warrant a coarse PM standard, especially in some Western states, has elevated the issue of coarse PM to a high priority for the Office of Air and

Radiation (OAR). **The poster presented by Gilmour** shows some of ORD's research on health effects associated with coarse PM, with a special emphasis on bioaerosols, which are preferentially present in this size fraction. These studies show that coarse PM from some areas can actually cause more lung inflammation than either fine or ultrafine PM. This appears to be driven, at least in part, by biological components, which can make up 10-20% of coarse PM by mass. This fraction may be of special concern to asthmatics since they are sensitive to many of the bioaerosols found in coarse PM.

Metals

Since 1997, ORD sponsored in vivo and in vitro studies using emission particles enriched for metals such as ROFA, or soluble metal salts, have contributed substantial new information concerning the health effects of PM-associated bioavailable metals. The metals of most interest are the transition metals of iron, vanadium, copper, nickel, chromium, cadmium, zinc, and arsenic. These metals are ubiquitous constituents of PM derived from anthropogenic fossil fuel emissions and exposure to metals seems to be widespread. Those chemical properties which allow transition metals to function as catalysts in the reactions of molecular oxygen inside the body also make them a threat to health via the generation of O_2 based free radicals.

To date, far more effort has been spent studying the effects of metals than any other PM component. Representative examples of this research are shown in the **poster presented by Ghio**. A number of publications have shown an association between the amount of bioavailable metal present in ambient PM and cardiopulmonary effects, as well as significant health effects in animals and humans following exposure to metal-enriched PM from specific sources. These studies have been replicated in vitro and cutting edge molecular techniques used to better understand the mechanisms by which metals cause adverse health effects. Some of these mechanisms are outlined in **posters presented by Ghio, Samet, and Froines.** The Froines poster is particularly noteworthy because it presents data showing the both metals and organic compounds may cause adverse effects by the same mechanism.

Perhaps the best example of the health effects induced by metals is described in the **poster presented by Dye** in Session 3. PM collected in the Utah Valley before, during, and after the shutdown of a steel mill was instilled into human volunteers and animals. Material collected when the mill was operational was highly enriched in transition metals and caused significant lung inflammation and damage, compared with an equal mass of PM collected when the mill was on strike. These studies showed remarkable coherence with epidemiological studies of hospitalization and mortality that were done at the same time.

The poster presented by Godleski in Session 3 describes a recent efforts in which animals or humans were exposed to ambient PM and statistical approaches used to associate PM components with health end points. Some of these studies have shown linkage between metals found in ambient air and health effects in both humans and animals.

Organic Constituents

Organic components of PM have not been as extensively studied as metals or particle size, with the exception of those components emitted in diesel exhaust, primarily because of the difficulty in accurately characterizing in detail the classes of organic compounds present in ambient PM samples. ORD sponsored health effects research on diesel emissions is **presented by Madden** in Session 3. Like metals, organics are common constituents of combustion-generated PM and are found in ambient PM samples over a wide geographical range. Organic carbon (OC) constituents comprise a substantial portion of the mass of ambient PM (10 to 60% of the total dry mass), with the highest ratio being in

UFP. Frequently, the organic fraction of PM is designated simply as OC versus EC in health studies due to its complexity and the cost to analyze and speciate it. However, more recently ORD has begun to place a larger emphasis on understanding the contribution of organic compounds to PM-induced adverse health effects, including both particle bound as well as vapor phase organics. This has been driven in part by the realization that PM omitted from mobile sources, which is enriched in organic components, appears particularly potent in causing health effects. An example of this type of approach is shown in the **poster presented by Froines** in Session 3 which describes research done near LA freeways, which are a potent source of UFP enriched in organic compounds.

What Remains to Be Done?

Although numerous studies have examined a wide range of PM chemical and size characteristics, the results of these studies have not always been consistent. Furthermore, they have not yet been able to narrow down the list of potential PM properties to bring greater focus to research on PM components. Continuation of research using statistical approaches to link health effects with specific components or physical properties in ambient PM will be important in future studies, not only because of their potential to identify relevant components, but also because of their potential to link health effects with specific sources of PM. Additional mechanistic studies are also critical; if several components exert their effects by the same or similar mechanisms (as appears increasingly to be the case), this information would have important implications for control strategies. **The poster presented by Froines** shows an example of this approach.

Epidemiological studies have been substantially hampered by the lack of air quality monitoring data that characterize particles using parameters other than mass. However, the Speciation Trends Network have begun to provide these types of measurements, which should serve as a platform for future epidemiology studies directed at assessing particle characteristics and public health. It will also be important to conduct toxicology studies in conjunction with these epidemiology studies. When information from toxicology, epidemiology, and panel studies conducted in the same areas can be integrated, it will offer a new opportunity to investigate coherence across disciplines. When interwoven, these approaches should provide considerable insight into the components and sources that can be linked to PM-associated heath outcomes.

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

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

The 1996 PM Air Quality Criteria Document concluded that PM, alone or in combination with other pollutants, was associated with a range of adverse health effects. A key uncertainty concerned the relationship between PM and co-pollutants in these adverse effects, especially where PM and the co-pollutants were related to the same sources. In addition, several other issues remained unresolved, including linearity of the response curve (threshold) and harvesting (are the people dying so sick they would have died in a few days anyway). The poster presented by Schwartz describes ORD sponsored research that has reduced much of the uncertainty associated with the times series epidemiology studies.

Our current knowledge of long-term PM effects is based on a handful of longitudinal epidemiological studies that compare differences in the survival or other health effects of well-characterized cohorts of human subjects with air pollution levels in their cities of residence. However,

the two largest such studies, the ACS and the Harvard Six Cities Study, were not originally designed to monitor health effects associated with PM exposure and thus there are methodological issues which limit the usefulness of these studies. Despite these limitations, the 1997 PM annual NAAQS relied heavily upon evidence from both of these studies that annual cardiopulmonary mortality rates were significantly associated with long-term average PM concentrations. Because of the importance of these studies, the ORD sponsored an extensive reanalyses of the data available on these cohorts, which is summarized in the **poster presented by Lippmann**. This poster also describes results from the Children's Health Study in 12 California communities which found that lung function growth was significantly depressed in relation to long-term average concentrations of PM2.5, NO2, and acid vapor, and that proximity to high traffic density is associated with asthma onset, asthma-related school absence, and impair lung development. The Lippmann poster also describes the only ORD sponsored chronic animal exposure study, in which rats were exposed to ambient PM for several months and a number of health end points assessed.

In a recent evaluation of research concerning PM exposure and health effects, the NRC highlighted a critical need for additional studies of the long-term health effects of particulate matter. The NRC recommended that studies evaluate alternative particulate matter exposure metrics, the effect of particles in combination with gaseous co-pollutants, and effects in potentially susceptible groups. This information is needed to more fully characterize the health risks posed by air pollution in regions where different pollutant sources predominate and where intra-urban concentration gradients exist.

ORD has recently funded several studies to address the uncertainties regarding the health effects of chronic PM exposure. These studies are outlined in the **poster presented by Kaufman**. Five of the studies are developing a retrospective exposure assessment of long-term PM_{10}, $PM_{2.5}$ and other pollutants using currently available information on health and air quality exposure. ORD also recently funded a study of $PM_{2.5}$ exposure in association with indicators of the progression of cardiovascular disease and cause-specific hospital admissions and mortality. This ten-year study will use state-of-the-art methods to evaluate the extent of atherosclerosis and severity of underlying systemic inflammation, oxidative stress, and other adverse responses. Together these studies will provide new and critically important information to understand the relation between long-term exposure to ambient air pollution and morbidity and mortality in susceptible populations. The results will provide greater insight on the effect of PM, especially $PM_{2.5}$, and gaseous copollutants pertaining to several aspects of the continuum from sources to exposure to disease and mortality. These data will provide a basis for refinement of air quality regulations by the EPA or state authorities and will provide an opportunity to investigate the extent of risk reduction that is anticipated from specific recently enacted regulatory actions.

What Remains to Be Done

Multi-city studies have been a corner stone of air pollution epidemiology for many years particularly in the characterizing regional differences, including PM and other air pollutants (e.g. gaseous pollutants, air toxics) from a variety of sources. Multi-city multi-pollutant analyses need to be conducted to address remaining areas of uncertainty about PM derived from various sources and potential interactions between PM and other pollutants. **The poster presented by Neas** in Session 3 describes such an approach. In addition, controlled exposure studies can directly test relationships between PM and other pollutants, including confounding and synergy. Finally, studies are needed to develop smog chambers in which various atmospheres can be created under controlled conditions in which interactions between various air pollutants can be studied and linked to health effects by placing animals in the chambers. This type of approach is described in the **poster presented by Kleindienst**.

Research Topic 8. Susceptible Subpopulations

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

An understanding of susceptibility is critical to achieving the public health protection called for by the 1990 Amendments of the Clean Air Act, which extended protection against adverse health effects beyond the general population to especially susceptible subpopulations. The population as a whole is heterogeneous in its susceptibility to particles. However, diverse characteristics that may increase susceptibility to adverse health effects from inhaled PM include age (infants and older adults), the presence of underlying disease (chronic heart and lung diseases), altered deposition and clearance (morphological and physiological changes in the respiratory tract), activities that increase lung dose (e.g. work).

Initial time-series epidemiological studies associating mortality and hospital admissions with daily ambient PM concentrations indicated that elderly people with cardiopulmonary disease (e.g. COPD, severe cardiovascular disease) were at the greatest risk. These initial studies have been confirmed by additional epidemiology studies. In addition a number of panel, controlled human, and controlled animal studies have studied the effects of PM on exacerbation of cardiopulmonary disease. **The poster by Cascio** describes some of these studies and shows data that elderly and people with cardiovascular disease have greater PM-induced cardiovascular changes than young healthy people. **The posters presented by Watkinson, Kodavanti, and Frampton** also describe cardiovascular effects induced by PM.

Other epidemiology studies have linked PM levels with increased use of medications, doctor visits, and hospital visits in individuals with pulmonary disease such as asthma. Asthmatics, especially children, also have been identified as a potential susceptible subpopulation based on their diary records, hospitalization, school absenteeism, and use-frequency of bronchodilators in association with ambient PM levels. **The poster presented by Peden** describes ORD sponsored panel studies and toxicology studies showing that PM is able to exacerbate lung inflammation and symptoms in asthmatics.

It is assumed that the disease state of the individuals with pulmonary disease weakens their ability to return to a normal homeostatic state following PM exposure. However, it is also possible that pre-existing pulmonary disease may affect the amount of inhaled PM that is retained in the lungs, as well as its distribution within the lung. **The poster presented by Kim** shows evidence that people with lung disease, and even smokers with no overt clinical signs of lung disease, retain increased levels of particles within their lungs. Furthermore, the deposition of the particles is altered in such a way as to be more concentrated at the site of disease.

There is growing recognition that the subpopulations who are most susceptible to PM exposures and the factors related to increased health risks are more numerous and diverse than once thought. Part of this realization is based on recent studies which have shown that soluble components of PM or ultrafine particles can exit the lung and travel through the blood stream to other organ systems. **The poster presented by Dreher** discusses emerging evidence that PM may affect other populations besides those with pulmonary or cardiac disease. The poster presents evidence that diabetics are especially susceptible to PM. It also shows preliminary evidence indicating that pollution may affect birth weights and intrauterine processes in pregnant women. **The poster presented by Oberdorster** shows that PM may translocate to the brain and cause inflammation in key regions associated with Alzheimer's disease.

What Remains to Be Done?

Despite recent advances, substantial uncertainties about susceptible populations still need to be addressed. Most of the current studies have focused on identification of susceptible populations, but little information is available about the factors which render these populations susceptible. Thus, while the first step is to identify susceptible groups within the general population for inclusion into the overall risk assessment paradigm, characterizing the risk factors that underlie susceptibility may be the most fruitful revelation in the long run by virtue of its predictive power.

Research on other pollutants and tobacco smoking suggest that certain people should respond with greater than normal intensity to PM because of genetic makeup. The recent revolution in "omics" technology has provided the tools that can be used to address this question. Identification of biomarkers which can predict susceptibility to PM in an ostensibly health individual would provide critical information that allow potentially susceptible individuals to take protective actions against PM exposure before the pollutant could cause overt clinical disease. **The poster presented by Huang** describes some of the strategies that could be used to identify genes responsible for susceptibility.

Research Topic 9: Mechanisms of Injury

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

The recommendations for changes in the 1997 PM_{10} and $PM_{2.5}$ NAAQS were primarily based on a large and coherent epidemiological database of significant associations between ambient air PM concentrations and excess mortality and morbidity. However, at that time there was little information from human or animal toxicology studies that addressed the biological plausibility of how exposure to quite small levels of PM (less than $1/20^{th}$ of what would be inhaled from a single cigarette) can lead to death within hours. In addition, almost nothing was understood about the cellular or molecular mechanisms that underlie the presumed pathophysiological processes responsible for adverse health effects. One of the major advances in PM research over the past seven years has been the identification of several plausible biological mechanisms that are consistent with the epidemiology studies.

The primary portal of entry for PM air pollution is the lung, and PM interactions with respiratory epithelium and alveolar macrophages likely mediate a wide range of pulmonary effects. **The poster presented by Gavett** describes studies in which PM has been shown to cause lung injury and inflammation, as well as changes in lung function, in healthy and susceptible populations. PM has been shown to increase susceptibility to infection and exacerbate some lung diseases such as asthma. Long term exposure to PM has also been shown to impair lung growth in growing children.

There are several mechanisms by which PM may directly or indirectly affect the cardiovascular system. Potential neural mechanisms involve the autonomic nervous system (ANS) via direct pulmonary irritant reflexes or reflexes activated during pulmonary inflammation that would ultimately influence cardiac function. Ultrafine particles or soluble PM components may enter pulmonary capillary blood and be rapidly transported to extrapulmonary tissues, such as heart, liver, and bone marrow tissues, with either direct or indirect effects on organ function. Some of these effects could

include changes in ion channel function in myocardial cells, ischemic responses of the myocardium, or systemic responses including inflammation which can trigger endothelial cell dysfunction, and triggering thrombosis via alterations in the coagulation and clotting cascade. **The posters presented by Watkinson and Cascio** summarize studies which demonstrate that PM exposure can affect autonomic control of heart rhythm in both animals and humans. Studies are presented which show that PM can cause severe arrhythmias in animals and damage to cardiac cells.

Acute coronary events frequently occur as a result of thrombus formation in the site of a ruptured atherosclerotic plaque. Increased levels of clotting and coagulation factors, platelet aggregability, and blood viscosity, together with reduced fibrinolytic activity (ability to dissolve clots) and endothelial cell dysfunction, can promote a pro-coagulant state which could potentially contribute to thrombus formation. **The poster presented by Frampton** summarizes several studies which show that PM can damage endothelial cells that line blood vessels, and that it can lead to increased levels of inflammatory markers in the blood such as C reactive protein, increased levels of acute phase proteins such as fibrinogen, and changes in clotting/coagulation pathway proteins to creating a potentially more pro-thrombogenic environment. The poster also shows that animals exposed to PM for many weeks have increased atherosclerotic lesions.

In addition to understanding biological mechanisms at an organ or tissue level, it is also important to define the molecular, biochemical, and cellular mechanisms which control the pathophysiological responses to PM. **The poster presented by Samet** exemplifies this type of cutting-edge research, which seeks to understand what happens from the time a particle touches the outer surface of a cell until a battery of genes is activated which will trigger a cascade of events leading to an adverse health response. This approach can also lead to the identification of mechanisms that may be responsible for several pathophysiological responses, as well as characterize different PM components by how they damage tissues. **The poster presented by Froines** presents work focused on oxidative stress as an underlying mechanism that might explain pulmonary, vascular, and cardiac effects caused by PM. It also shows that two very different PM components, metals and organic compounds, may both cause adverse effects by inducing oxidative stress.

What Remains to Be Done

Seven years ago, a description of PM health effects would typically include a caveat that the underlying biological mechanisms were largely unknown. The work captured in the posters described above shows that considerable progress has been made in understanding some of the patho-physiological mechanisms that underlie PM effects. However, research is still far from being able to clearly explain the pathways by which very small concentrations of inhaled ambient PM can produce the cardiovascular and pulmonary changes that can contribute to increased mortality/morbidity. Many of these studies have yet to be repeated enough to instill confidence in their results. Furthermore, as new potentially susceptible populations are identified (e.g. pregnant women) and new target organ systems identified (e.g. the nervous system), additional mechanistic research will be necessary to fully explain the effects of PM in humans. Since PM levels have been declining in many parts of the U.S., there is an opportunity to test whether there are less adverse health outcomes in areas with decreased PM; i.e. have decreased PM emissions actually resulted in an improvement in public health?

Conclusions

Seven years ago the PM NAAQS rested primarily on a group of time series epidemiology studies which, though they were coherent with one another and compelling, were nonetheless viewed

as insufficient by some to warrant strengthening the PM standard. There was only rudimentary understanding of how a person inhaling a very small amount of particles could die within hours. There was incomplete knowledge of which subpopulations might be susceptible to PM. There was no confidence that PM measurements taken at a fixed site community monitor accurately represented what people who spend much of their time indoors were actually exposed to. Finally, there was no agreement on whether individual PM components had different toxicities or whether PM emitted from various sources was equally toxic. The work shown in the posters in this session clearly demonstrate that PM research in the areas of Health and Exposure has made tremendous progress since 1997. Although there is still work to be done, these results have already been used by the EPA. **The poster presented by Ross** describes the process by which ORD sponsored research is used to recommend to the EPA Administrator whether the PM standard should be altered or not. Much of the research described in this session will play a key part in formulating that recommendation. Additionally, the Office of Air and Radiation has used ORD sponsored research in various ways to better inform the public about the threat of air pollution and protective measures that can be taken. Some of these efforts are described in the **poster presented by Stone**.