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## **1.1 Center Mission and Quality Policy**

The researchers operating under the umbrella of the EPA-HSPH Center For Ambient Particle Health Effects (The Center) are strongly committed to good science and aggressive quality management (QM) practices. Our commitment is documented by developing integrated quality management practices for our monitoring and measurement activities, collection of health response data, statistical analysis and mathematical modeling within our purview. These QM practices are specifically designed to generate and process data of known and appropriate quality in a cost-effective manner. The purpose of this document is to define and describe the QM, Quality Assurance (QA), and Quality Control (QC) policies and responsibilities required by The Center. This document is intended to assist Center researchers in the uniform implementation of QM, QA, and QC requirements.

It is the policy of Center that there shall be sufficient Quality Management (QM) activities conducted within the Center to ensure that all environmental data generated and processed shall be: scientifically valid, of adequate statistical quantity, of known precision and accuracy, of acceptable completeness, representativeness, and comparability, and where appropriate, legally defensible. This goal can be achieved by ensuring that adequate QM steps and procedures are used throughout the entire scientific process (from initial study planning through data usage).

## **1.2 Center Overview**

### **1.2.1 Center Objective**

The objective of the EPA-HSPH Center For Ambient Particle Health Effects is to address key scientific issues regarding the health effects of ambient particles using our rich foundation of ongoing research and expertise. The specific aims of the Center reflect the National Research Council's research priorities for ambient particle research (NRC, 1998). To address these aims, our Center is focussing upon three research themes: (I) Exposure, (II) Susceptibility, and (III) Biological Mechanisms/Dosimetry. Each theme encompasses a series of highly integrated and interdisciplinary research projects. The research is performed by a group of scientists which has worked together for many years and has expertise in a variety of fields, including particle chemistry, exposure and risk assessment, environmental epidemiology, cardiac and pulmonary health, toxicology, physiology, biostatistics, dosimetry, public policy, indoor air pollution and air microbiology.

### 1.2.2 Center Themes

Theme I investigates human exposures to particles and gaseous co-pollutants in order to differentiate the health effects of particles from outdoor and indoor sources. This theme also quantifies the effect of exposure error for fine particles and their co-pollutants on risk estimates from epidemiological studies. Theme II identifies individuals who are sensitive to the effects of air pollution and measures the effect of chronic exposure on the development of chronic diseases. Theme III identifies the particulate characteristics and gaseous air pollutants that trigger adverse health effects and defines the biological mechanisms that may lead to fatal outcomes.

### 1.2.3 Center Projects

Theme I includes three projects that are based on data from our previous and ongoing exposure studies conducted in a variety of U.S. cities (Boston, Atlanta, Baltimore, Steubenville, and Los Angeles). Project Ia is intended to characterize the particulate and gaseous exposures of healthy and susceptible cohorts as a function of climate, cohort, home characteristics, and activity patterns. It also identifies factors affecting the relationship between personal exposures and outdoor concentrations. Project Ib quantifies the effect of measurement error for fine particles and their co-pollutants (coarse mass and the criteria gases) on risk estimates from epidemiological studies. Project Ic differentiates the health effects of particles from indoor and outdoor sources.

Theme II includes four projects which are based on data and methods from our ongoing epidemiological studies. Project IIa is a prospective cohort study that uses the Medicare database and the National Death Index to identify populations which are susceptible to particulate and gaseous air pollutants. The cities included in the initial phase of this study are: Boston, New Haven, Chicago, Utah County, Salt Lake, Minneapolis-St. Paul, and Spokane. Project IIb uses innovative analytical methods to examine whether particles advance mortality by a few days (harvesting) or have a more profound impact on public health. Project IIc assesses the chronic effects of air pollution exposure by extending follow up of adults in the Six Cities Study up to twenty-four years. Project IId assesses the chemical characteristics of particles associated with respiratory illness and lower lung function in children in 29 North American Cities.

Theme III includes three projects which aim to identify the particulate and gaseous air pollutants responsible for increased cardiac vulnerability as an adverse health effect and to define the biological mechanisms that lead to this outcome. Using our dog model of coronary occlusion with exposures to concentrated ambient particles, Project IIIa explores the role of particle size (coarse, fine, and ultrafine), particle composition (metals, ions, and carbon), and criteria gases (O<sub>3</sub>, NO<sub>2</sub>, CO, and SO<sub>2</sub>) on cardiac and respiratory health (Project IIIa). Project IIIa also uses pharmacological intervention to explore biological mechanisms by which particles accelerate and

increase sensitivity to the ischemic response, examining both autonomic nervous system and inflammatory mechanisms (Project IIIa). Project IIIb determines *in situ* particle doses during the inhalation studies using online measurements of particle number and size in the inhaled and exhaled air. This enables us to provide a better interpretation of the observed outcomes and to examine the role of particle composition, gaseous co-pollutants, and susceptibility on particle deposition. Project IIIc, a human panel study, is performed concurrent with these animal inhalation projects. It investigates the effects of particle mass, composition, and gaseous co-pollutants on blood viscosity, other clotting parameters, and cardiac health of individuals living in the Boston Metropolitan area. Results from this project will be integrated with results from laboratory studies to better our understanding of the role of particle composition and gaseous co-pollutants and biological mechanisms.

Collectively, these projects address eight out of the ten research priorities included in the NRC report. Our research agenda may be redirected to respond to future research needs by refocusing existing or developing new projects. This is accomplished by using a multi-step process described in the Research Coordination and Integration Core. Finally, the Center has a Technology Core that focuses on the development and transfer of technologies, such as particle generation systems for inhalation studies, personal exposure monitors, statistical tools to analyze data from particle epidemiological studies, and software to process cardiac function data. One of the objectives of the Center is to coordinate research activities and to exchange methods and technologies with the other particle Centers. Existing data and resources is utilized in order to obtain the most relevant and essential scientific information. Since each of the Center's projects leverage existing research conducted by Center investigators, the projects will be comprehensive, cost-effective, and innovative. The inter-disciplinary nature of the Center will enable us to integrate findings from a variety of studies as they emerge and, combined with structured methods to evaluate research needs and priorities, will allow the Center to remain flexible and at the forefront of the health effects research on particles. Findings from the Center will have important ramifications to environmental policy and control. Our findings will improve our ability to set appropriate and effective air quality standards for particulate matter. It will help us determine the relevant particle parameter and the appropriate level to regulate. These gains will, in turn, allow effective particle control strategies to be determined and will ensure the protection of public health from particle exposures.

#### 1.2.4 Center Cores

##### 1.2.4.1 Administrative Core

The Administrative Core is responsible for the overall coordination of the Center. This core includes administrative support, core secretarial support, fiscal management, central data management, quality assurance, internal Executive and External Advisory Committee meeting schedules, meeting organization, report preparation, and communication with EPA. Dr. Petros Koutrakis oversees all administrative and fiscal issues for the Center. He is assisted by Alice Smythe, the Center Administrator. All fiscal and administrative duties are directed by Linda Fox, Administrator of the Environmental Science and Engineering Program. She provides

quarterly budget summaries and projected expenditures. Ms. Fox is assisted by Gail Wainer, her financial administrative assistant, and also by Brenda Barrett, administrator of the Environmental Epidemiology. The research staff at Harvard University has considerable experience working with large exposure, epidemiological, and toxicological data sets. While the principal investigators have responsibility for processing and analyzing data for their individual projects, data from each of the projects also is stored and managed centrally, with Dr. Helen Suh overseeing the data management and supervising the data manager. We plan to hire a data manager. Finally, Jose Vallarino is the Center QA Officer. He has considerable experience in quality control procedures.

#### 1.2.4.2 Research Coordination Core

The Research Coordination Core is responsible for defining, coordinating, and integrating all research conducted as part of the Center and is led by Dr. Dockery. A key aspect of the Center is its intention to have an ongoing and continual evaluation of research needs and priorities. To achieve this goal, the Center includes a rigorous and multi-phased research coordination and evaluation process, which has been developed based on our experience from over twenty years of multi-disciplinary collaborations in air pollution health effects. This coordination and evaluation process draws from experts from a wide range of disciplines at the Harvard School of Public Health and the Medical School, as well as from experts from outside agencies, universities, and other organizations to provide focused and timely responses to current and evolving questions about airborne particulate matter. Specifically, experts from six internal and external groups contribute to the research coordination and evaluation process and determine the direction and coordination of PM research that is conducted at the Center. These groups include: the National Research Council, the External Science Advisory Committee, the consortium of EPA Airborne Particulate Matter Centers, the Working Group on PM Exposures and Health Effects, the Working Group on Research Strategy Evaluation, and the Harvard Center Steering Committee. Their contribution to the research coordination and evaluation process are described below.

##### 1.2.4.2.1 National Research Council.

The National Research Council panel on Research Priorities for Airborne Particulate Matter is and will continue to be an important source of direction for the Center. In fact, the Center's proposed ten initial projects were developed to address the immediate research priorities listed in NRC's report entitled "Immediate Priorities and Long-Range Research Portfolio." The Center is fortunate to have two investigators, Drs. Koutrakis and Speizer, as members of the NRC Expert panel. As a result, direct and immediate access to panel deliberations will be available to Center investigators and can be used to decide the Center's future research priorities and directions.

##### 1.2.4.2.2 External Advisory Committee

A multi-disciplinary External Advisory Committee of distinguished scientists provides input into both ongoing and future research directions. The Advisory Committee is comprised of experts in a range of disciplines, including atmospheric chemistry, exposure and risk assessment, policy, biostatistics, epidemiology, and toxicology. Some committee members are recruited from other PM Centers to foster and facilitate exchange and collaborations, including experts from the fields of Exposure and Risk Assessment, Atmospheric Chemistry, Epidemiology, Toxicology, Biostatistics, Cardiac and Respiratory Health, and Public Policy. The Committee meets annually to formally review the Center activities. The first meeting day will be devoted to the traditional presentation of study designs and results, and will be followed by a structured workshop on the second day to define research needs and priorities. This workshop would include both the Committee members and the Center investigators. The members of this advisory committee are listed at the end of this document.

#### 1.2.4.2.3 Consortium of EPA Airborne Particulate Matter Centers.

As one of EPA's PM Centers, we have formed a consortium of PM Centers. The specific aims of this Consortium is to ensure that research in each Center is coordinated with, complementary to, and not redundant with that of other EPA PM Centers, and to facilitate rapid dissemination of research findings and other information between Centers, the EPA, the rest of the scientific community, and the lay public. To achieve these specific aims, the Consortium organizes an annual colloquium to review particulate matter research. As part of this colloquium, representatives from each of the EPA-sponsored Centers participate in a structured meeting to plan and coordinate research activities. Through the Consortium, the EPA Centers establishes linked sites on the Web to provide descriptions of current research programs, downloadable copies of research reports and publications, and access to extended summaries and original data.

#### 1.2.4.2.4 Harvard Working Group on PM Health Effects.

A previously-established Working Group on PM Health Effects continues to meet bi-weekly to encourage informal interactions between the Center investigators. This Working Group, which was formed several years ago, includes experts in exposure and risk assessment, epidemiology, toxicology, clinical medicine, and physiology. The Harvard PM Center establishes a formal structure for this Working group and provides core support for its activities. Activities include a monthly series of informal Work-in-Progress seminars by Center investigators and formal presentations by local and invited experts.

#### 1.2.4.2.5 Working Group on Evaluation of Research Strategies

We use a formal decision and value of information analysis of particulate matter control and research to guide our decisions about future research activities. This analysis is based on the concept of the value of information (i.e., the expected value of the likely consequences of

suboptimal decisions) as a measure of the costs of current levels of uncertainty. To implement our research evaluation process, we characterize quantitatively the current risk uncertainties and develop estimates of the informativeness and cost of alternative research strategies. Uncertainty in risk estimates are examined based on two broad uncertainty sources: parameter and model uncertainty. Parameter uncertainty, of which the slope of the dose-response function of particle exposure and mortality is an example, is determined based on well-developed and widely accepted approaches.

Most of these approaches are based on frequentist notions of probability and standard approaches for analysis of the propagation of uncertainty (e.g., Gauss' law, lognormal error analysis, or Monte Carlo simulation). Model uncertainty is determined through the use of formally elicited expert judgment. These methods are first applied within our Working Group on Particle Health Effects to identify the specific areas which should be targeted as research priorities. Subsequently, they are being applied to the External Advisory Committee in a workshop following their initial meeting and also to the Consortium of EPA-sponsored PM Centers. In each case, the traditional assessment and the structure assessment of the Evaluation of Research Strategies Working Group is made available to the Steering Committee.

The Evaluation of Research Strategies Working Group is directed by Dr. Evans.

#### 1.2.4.2.6 Harvard PM Center Steering Committee.

The Harvard PM Center is directed by a Steering Committee consisting of the Center Director, the two Co-Directors, and the Principal Investigators of the research projects and cores. Dr. Koutrakis, the Principal Investigator, chairs the Steering Committee. The Steering Committee will be responsible for the overall direction, coordination, and integration of the research conducted by the Center. It establishes research priorities and directions based on recommendations from external groups, including the National Research Council, the External Advisory Committee, the Consortium of PM Centers, the Harvard Working Groups on Particle Health Effects and Evaluation of Research Strategies. The Steering Committee meets at least quarterly to monitor progress, identify new research initiatives, and coordinate research with other Centers.

#### 1.2.4.3 Analytical and Facilities Core

This core will be led by Dr. Godleski. The purpose of this core is to coordinate and facilitate the assessment of health response measurements. These include pulmonary, cardiovascular as well as other systemic responses. Most of the research is centered at the Harvard School of Public Health, located in the Longwood Medical Area of Boston. A portion of the work is carried out at the Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Veterans Hospital, and the Harvard Medical School. All medical area resources, including those of Harvard Medical School, Children's, Dana-Farber Hospital, Beth Israel Deaconess Medical Center, and Countway Library are available to investigators involved in this Center.

#### 1.2.4.4 Technology Development and Transfer Core

The Technology Core is led by Dr. Koutrakis, who has been involved in the development of many particle instruments and holds several patents. This Core encompasses the development and transfer of technologies and methods in three areas: particle measurement and generation, statistical methods, and cardiovascular measurement methods: *(i) Particle Measurement and Generation Methods*. The core supports the exposure assessment studies through the development and provision of state-of-the-art personal, micro-environmental, and outdoor particulate and gaseous samplers. Also, this core support toxicological studies by operating and servicing the concentrator and by developing new concentrator technologies. This core develops particle samplers and generating systems. As they are developed, they are made available to other Centers and research groups.

### 1.3 Quality Management Policies, Responsibilities and Requirements

#### 1.3.1 Center Quality Management Policies

1. Each Research Project that generates environmental and/or health response data shall develop and implement a Project Plan (PP) addressing the major elements contained in Section 2.1, and shall ensure that adequate resources (both monetary and staff) are provided to support the QM, QA, QC objectives of the PP. The project plan should specify the detailed procedures required to assure the generation of quality data. All project plans must be approved prior to data collection. All Center Laboratories analyzing research samples must have a written Quality Assurance Program or Laboratory Standard Operating Procedures addressing the major elements contained in Section 2.3 and 2.4.
2. All environmental and/or health response data generated shall be of known and acceptable quality. The data quality information developed with all environmental data shall be documented and available.
3. The intended use(s) of the data shall be defined before the data collection effort begins, so that appropriate QM measures may be applied to ensure a level of data quality commensurate with the monitoring objectives. The determination of this level of data quality shall also consider the prospective data needs of secondary users. Data Quality Objectives (DQOs) shall be established to ensure the utility of data for its intended use and as guidance for preparation of project plans. The Research Project Co-PI shall be responsible for determining the appropriate QM practices, using the DQO process for each PP. The intended data uses, level of quality, specific QM activities, and data acceptance criteria needed to meet the data quality needs of these uses shall be described in each monitoring activity's project plan.

4. Quality assurance activities shall be designed in the most cost effective fashion possible, without compromising data quality objectives.
5. The Center Quality Assurance Manager shall submit an annual Center QM Report and Work/Audit Plan, to the Center Principal Investigator for review and approval
6. The Center QM Program Plan shall be reviewed at least annually, by the Center Quality Assurance Manager and updated as required.

### 1.3.2 Center Quality Management Responsibilities

The Center Director has the overall responsibility for the development, implementation, and continued operation of the Center QM Program. The authority and responsibility for managing the QM activities within the Center shall be assigned to the Center Core Leaders for all research activities in their respective core. The Center Quality Assurance Manager will ensure that the Center's QM policy is uniformly applied to the generation and processing of all environmental and/or health response data. The Center Quality Assurance Manager shall function as a central quality Assurance authority organizationally independent of the programs supported, i.e., environmental and/or health response data generators and users. Each Research Project PI shall designate a Project Quality Control Program Manager, that will document and oversee the implementation and documentation of all quality control activities outlined in the PP.

### 1.3.3 Research Project's Quality Management Responsibilities

The Quality Management Program for each research project shall meet the following requirements:

1. Researchers in each group shall inform the Research Project's Quality Control Program Manager of activities relating to QM within their specific monitoring and research programs and facilitate development and implementation of Project Plans.
2. Facilities, equipment and services that, directly or indirectly, have an impact on data quality or integrity shall be routinely inspected and maintained.
3. Data processing shall be documented, reviewed, and revised as required by the Project Plan. Data shall be validated according to specific pre-stated criteria.
4. When data falls outside acceptable limits, the appropriate researcher shall, with the assistance of the Research Project's Quality Control Program Manager and the Center Quality Program Manager, develop and implement a mechanism for corrective action. This will assure that any deficiencies in data generation activities, detected by the QM program, can be corrected in a timely manner.

#### 1.3.4 Research Project's Principal Investigator's Responsibilities

Project PI's are responsible for specific research projects, and shall be held accountable for the management of the project and its ultimate data products. Therefore, Project PI's have the principal responsibility for ensuring that project data quality objectives are met. Some of the key responsibilities of Project PI's are:

1. Coordinate the preparation of a Project Plan for applicable environmental data generation activities and ensure that the Project Plan has received an appropriate technical review. Provide the final approval of the Project Plan prior to the commencement of data collection. Final approval authority of Project Plans resides with the Center Principal Investigator.
2. Prepare data quality objectives, specifications, and acceptance criteria for the project.
3. Review/evaluate data quality generated from projects.
4. Participate in conducting QA system/performance audits of projects.
5. Coordinate project oversight through the use of QA system/performance audits of project QA activities.
6. Take corrective action that may be required by audit findings.
7. Report QM/QA problems to the Core Leader.

#### 1.4 Center Themes and Projects

- |         |             |   |
|---------|-------------|---|
| 1.4.1   | Theme 1     | Assessing Particle Exposures For Health Effects Studies   |
| 1.4.1.1 | Project 1.a | Assessing Human Exposures to Particulate and Gaseous air Pollution  |
| 1.4.1.2 | Project 1.b | Quantifying Exposure Error and its Effect on Epidemiological Studies  |
| 1.4.1.3 | Project 1.c | Assessing Human Exposures to Particulate and Gaseous air Pollution  |
| 1.4.2   | Theme 2     | Identifying Populations Susceptible to the Health Effects of Particulate Air Pollution                        |
| 1.4.2.1 | Project 2.a | Examining Conditions in the Elderly which Predispose Towards an Acute Adverse Effect of Particulate Exposures |
| 1.4.2.2 | Project 2.b | Assessing Life Shortening Associated with Exposure to Particulate Matter                                      |
| 1.4.2.3 | Project 2.c | Investigating Chronic Effects of Exposure to Particulate Matter   |

- 1.4.2.4 Project 2.d Determining the Effects of Particle Characteristics on Respiratory Health of Children
- 1.4.3 Theme 3 Biological Mechanisms/Dosimetry
  - 1.4.3.1 Project 3.a Differentiating the Roles of Particle Size, Composition, and Gaseous Co-pollutants on Cardiac Ischemia.
  - 1.4.3.2 Project 3.b Assessing Deposition of Ambient Particles in the Lung
  - 1.4.3.3 Project 3.c Relating Changes in Blood Viscosity, Other Clotting Parameters, Heart Rate and Heart rate Variability to Particulate and Criteria Gas Exposures.

## 1.5. Center Key Personnel

Dr. Petros Koutrakis (Center Director): Dr. Koutrakis is a Professor of Environmental Sciences and the Director of the Environmental Chemistry Laboratory. Dr. Koutrakis is involved in most of the projects and responsible for all of the scientific issues mentioned above and, as such, will be responsible for the overall administration and coordination of the Center. In addition, he is Principal Investigator of Project Ia and, along with Dr. Helen Suh, will coordinate the exposure-related projects. He also works closely with Dr. Godleski on the generation and characterization of CAPs. Lastly, he is the Director of the Technology Development and Transfer Core.

Dr. John Godleski (Center Co-Director): Dr. Godleski is an Associate Professor of Pathology with expertise in physiology and toxicology. As one of the two Co-Directors, he works closely with Dr. Koutrakis on the administration and coordination of the Center. Because of his expertise in pathology, toxicology, and inhalation studies, Dr. Godleski is responsible for all Center activities that relate to animal exposures and cardio-respiratory health effects. Also, he is the Principal Investigator of Project IIIa and is responsible for the overall coordination of the biological mechanisms theme. Lastly, he is be the Director of the Analytical and Facilities Core.

Dr. Joel Schwartz (Center Co-Director): Dr. Schwartz is an Associate Professor of Environmental Epidemiology. As one of the two Co-Directors, Dr. Schwartz works closely with Dr. Koutrakis on the administration and coordination of the Center. Because of his expertise in air pollution epidemiology and biostatistics, he is responsible for all Center activities that relate to epidemiological studies and data analysis. He also is the Principal Investigator of Projects IIa and b.

Dr. Douglas Dockery (Director of the Research Coordination Core): Dr. Dockery is a Professor of Environmental Epidemiology who is an established investigator in air pollution research. He works closely with researchers from all particle Centers, and with the Center Directors on the coordination and integration of the research to be conducted by the Harvard Center. Dr. Dockery is the Principal Investigator of Projects IIc and d.

Dr. Helen Suh (Principal Investigator of Project Ib): Dr. Suh is an Assistant Professor of Exposure Assessment. She is an expert in particle exposure assessment and she is responsible

for the coordination of the exposure-related activities of the Center. She is the Principal Investigator of Project Ib.

Dr. Frank Speizer (Principal Investigator of Project IIIc): Dr. Speizer is a Professor of Environmental Science and Medicine and Director of the Channing Laboratories. He has over thirty years of experience in the field of air quality health effects, including both laboratory-based physiological studies and epidemiological field studies using physiologic tools in community settings. He is responsible for the overall direction of the project in terms of identifying subjects, monitoring the completeness of data collection, and supervising the technician who will work on this project.

Dr. Richard Verrier: Dr. Verrier is an Associate Professor of Medicine and a cardiovascular physiologist with more than twenty years of experience in sudden cardiac death. He has been instrumental in recognizing the importance of T-wave alternans as an index of vulnerability to lethal cardiac arrhythmias. He oversees the accurate execution of the cardiovascular methodologies and cardiovascular interpretation, and contributes to the planning and execution of the pharmacological studies.

Dr. Diane Gold (Principal Investigator of Project Ic): Dr. Gold is an Assistant Professor of Environmental Health at HSPH and an Assistant Professor of Medicine at HMS. She is an epidemiologist and board-certified physician in Critical Care and Pulmonary Medicine, with a primary interest in the health effects of air pollution and the physiological mechanisms through which these health effects occur. She is responsible for the overall coordination of Project Ic, and will oversee all cardiac measurements and data analysis. She will participate in ECG screening and administration of the Holter protocol to assure quality and continuity at all times.

Dr. Akira Tsuda: (Principal Investigator of Project IIIb). Dr. Tsuda is a Senior Research Scientist. He is an expert in particle transport and deposition of fine particles in the respiratory tract, particularly in the lung periphery. He is responsible for all aspects of the particle deposition.

Dr. Paul Catalano: Dr. Catalano is an Assistant Professor of Biostatistics. Currently, he is involved in the data analysis of animal inhalation and exposure assessment studies carried out by the research groups of Drs. Godleski and Koutrakis. He provides statistical support, collaboration, and data analysis for the Center. Dr. Catalano will collaborate with the Center researchers and will work closely with the design of the different studies.

Dr. Lester Kobzik: Dr. Kobzik is an Associate Professor of Pathology who uses *in vitro* methodology to define responses to airborne particulates. In this project, he carries out *in vitro* analyses of ambient particulate as a means to test their intrinsic toxicity in relationship to the results of the animal studies. He works closely with Dr. Godleski.

Dr. John Evans: Dr. Evans is a Senior Lecturer of Risk Assessment at HSPH. He is responsible for the Value of Information analysis. He also is a Co-Director of the Research Coordination and Integration Core and works closely with Dr. Dockery on research prioritization issues.

Dr. Peter Stone: Dr. Stone is the Co-Director of the Cardiac Unit, Director of the Cardiovascular Division and Clinical Trials Center at the Brigham and Women's Hospital which is a Harvard affiliate. He contributes his vast experience in clinical cardiology and cardiology research study design to the formulation and implementation of the study protocols for Project Ic. Also, he works closely with Dr. Gold and reviews the analytic approaches to the computerized reading of the Holter data.

Dr. James Butler: Dr. Butler is a Senior Lecturer in Physiology. He has more than 20 years of extensive experience in virtually all aspects of pulmonary physiology, including mechanics and aerosol transport, and is widely published. He brings essential knowledge of physiologic implications to the critical question of the particle deposition site within the lung, particularly with respect to exposure/dose relationship. He, together with Dr. Tsuda, conceived the novel idea of the "stretch and fold" mechanism as the origin of significant transport of fine and ultrafine particles deep in the lung periphery. He collaborates closely with Dr. Tsuda throughout the particle deposition studies.

Dr. Eric Lovett: Dr. Lovett is a Research Associate and bio-engineer. He has made major contributions to our signal processing and analytical capabilities in the area of cardiovascular response to particles. He works closely with Dr. Verrier, and his responsibilities will include the collection of ECG data and the interpretation of cardiovascular response.

Dr. Gopala Gazula: Dr. Gazula is a Research Associate and the Director of the inhalation facilities. He has over ten years of experience in inhalation toxicological research. Dr. Gazula oversees the inhalation equipment and animal exposure, which includes physiological monitoring of the respiratory parameters, as well as analyses of measurements derived from the Buxco system, a system which monitors breathing during the entire episode of exposure. He works under the direction of Dr. Godleski.

Dr. Mike Wolfson: Dr. Wolfson is a Research Associate with over twenty-five years of experience in the sampling and analysis of particulate and gaseous air pollutants. He is responsible for the physical and chemical characterization of human and animal exposures. He works under the direction of Dr. Koutrakis.

Dr. Joy Lawrence: Dr. Lawrence is a Research Associate with over fifteen years of experience in the field of analytical chemistry and physico-chemical characterization of ambient particulate matter. She conducts most of the particle chemical analysis, including measurements of carbonaceous aerosols, trace metals, and gaseous pollutants. She works under the direction of Dr. Koutrakis.

Mr. George Allen: Mr. Allen is an Engineering Supervisor with over twenty years of experience in the field of air quality monitoring. He has extensive experience preparing Quality Assurance Plans and supervising QC and data processing operations. Mr. Allen is responsible for overseeing all environmental measurements and the integrity of the collected data. He works under the direction of Dr. Koutrakis.

Mr. Stephen Ferguson: Mr. Ferguson is an Engineer who has designed and constructed many sampling and particle generation devices, including the Harvard Particle Concentrator. He is responsible for the maintenance of the fine concentrator and the construction of the coarse and ultrafine concentrators, as well as other particle devices. He works under the direction of Dr. Koutrakis.

Mr. Marshall Katler: Mr. Katler is a Senior Technician with experience in molecular biological methods, cell culture techniques, animal exposure techniques, animal dissection, and biochemical laboratory procedures. He is responsible for the day-to-day animal exposures to CAPs and criteria gases. He works under the direction of Dr. Godleski.

To be named (Data Manager): This position is crucial to the Center because it involves the responsibility of processing and managing the biological, aerometric, and epidemiological data from all Projects. The data manager will work under the supervision of Dr. Suh.

To be named (Project Coordinator/Field Technician): This individual in this position will work on Project Ic and will be responsible for Holter monitoring, questionnaire administration, data entry and equipment related issues. He/she will be supervised by Dr. Gold. This individual will be responsible for conducting the cardiac measurements for Project Ic and for tabulating the data (provided by the VA Hospital) for Project IIIc. (This individual's primary appointment is with the Channing Laboratory of the Harvard Medical School thus his/her salary compensation is listed in the Brigham and Women's Hospital subcontract.)

Ms. Diane Sredl: Ms. Sredl is a programmer analyst. She is responsible for the data management of the human subject health measurements Projects Ic and IIIc. She works under Drs Gold and Speizer.]

Mr. James Sullivan: Mr. Sullivan is a laboratory technician who has experience in operating the ambient particle concentrator and conducting sampling during the inhalation studies. He performs these activities for the inhalation studies. He is supervised by Dr. Wolfson.

Ms. Merin Brodsky: Ms. Brodsky is a laboratory technician who has experience in chemical analysis of air samples. She conducts all chemical analysis of the ambient and concentrated particle samples. She is supervised by Dr. Lawrence.

Graduate Student in Exposure Assessment: This student will be in the Environmental Science and Engineering Program at HSPH who will specialize in exposure assessment. He/she will perform the analyses of the exposure data and will work closely with Drs. Suh (Project Ib) and Koutrakis (Project Ia).

Graduate Student in Environmental Epidemiology: This student will originate from the Environmental Epidemiology Program at HSPH which specializes in particle health effects. He/she will perform the analyses of the mortality and morbidity data sets (Projects IIa,b,c and d). This student will work under the supervision of Drs. Schwartz and Dockery.

Graduate Student in Risk Assessment: This student will be in the Environmental Science and Risk Management Program at HSPH which specializes in the Value of Information method. This student will work under the supervision of Dr. Evans on the prioritization of research activities.

Ms. Alice Smythe: Ms. Smythe will be the Center Administrator and works closely with Drs. Koutrakis, Godleski, and Schwartz. She is be responsible for all of the administrative aspects of the Center, including organizing the Advisory Committee meetings and other Center meetings, assisting the Center Directors in coordination efforts with the EPA and other Centers, and, coordinating activities among the different research groups.

Ms. Gail Wainer: Ms Wainer is the Assistant Financial Administrator of the Environmental Science and Engineering Program at HSPH. She will be responsible for all financial aspects of the Center. Her responsibilities will include preparation of the budgets and financial reports. She reports to the Program Administrator, Ms. Linda Fox.

Mr. Jose Vallarino. Mr Vallarino is the center's Quality Assurance Manager. He reviews center research activities for compliance with protocols, documentation requirements and quality control activities stated in project plans. Mr. Vallarino also coordinates QA round robin samples for gravimetric and IC analysis with other laboratories. Mr. Vallarino works under the direction of Dr. John D. Spengler and is independent of all research activities of the Center.

## **2.1 Project Plan Contents**

The Project Plan documents the data quality objectives (DQOs) (acceptance criteria) for a project; identifies the critical measurements to be performed; and discusses the QA activities to be conducted during the sampling, analytical, and validation phases of the project. The Project Plan shall contain the following types of information:

1. Title Page, with provision for approval signatures
2. Table of Contents (more than 5 pages)
3. Project Description
4. Project Organization and Responsibilities
5. Objectives for Measurement Data
6. Sampling Procedures
7. Sample Custody and Documentation
8. Calibration Procedures and Frequency; and Preventive Maintenance
9. Analytical Procedures
10. Data Reduction, Validation, and Reporting
11. Internal Quality Control Checks
12. Performance and System Audits

13. Specific Routine Procedures Used to Assess Data Precision, Accuracy, Completeness, Representativeness, and Comparability.
14. Corrective Action
15. Quality Assurance Reports to Management
16. Safety (if applicable)

## **2.2 Data Quality Objectives**

Data Quality Objectives (DQOs) are comprised of qualitative and quantitative statements developed to ensure that data of known and appropriate quality are obtained, to support specific decisions or regulatory actions. The DQO process requires an up-front planning with the project decision makers and data users. The DQO process is comprised of the following steps:

- Clarify the study objective;
- Define the most appropriate type of data to collect;
- Determine the most appropriate conditions from which to collect the data; and
- Specify tolerable limits on decision error (determining an acceptable level of both false positive and false negative error rates for sample design, collection and analysis) which will be used as the basis for establishing the quantity and quality of data needed to support the decision.

## **2.3 Laboratory Quality Assurance Plan Contents**

The Laboratory QA Plan shall contain the following types of information:

1. Title Page
2. Table of Contents
3. Quality Assurance Policy Statement
4. Ethics Policy on Waste, Fraud, and Abuse
5. Quality Assurance Management
6. Administrative Organization
7. Personnel Qualifications
8. Facility Description and Capital Equipment
9. Preventive Maintenance
10. Corrective Action
11. Laboratory Evaluation and Audits
12. Quality Assurance Reports to Management
13. Lab Documentation and Forms
14. Sub-Contracting of Services
15. Standard Operating Procedures

16. Laboratory Personnel Training Record

**2.4 Standard Operating Procedures**

Standard Operating Procedures (SOPS) are documented methods for performing certain routine or repetitive tasks. These tasks frequently involve such operations as sampling, sample tracking, analysis, instrument or method calibrations, preventive and corrective maintenance, internal quality control, and data reduction and analysis. The SOPs shall be prepared in document control format by the user, as required, and shall be maintained on permanent file by the SOP user and the Center Quality Program Manager. The following are considerations involved in the development and utilization of Standard Operating Procedures.

A. Standard Operating Procedures Objectives

1. Adequate to establish traceability to standards, instrumentation, samples, and environmental data.
2. Simple, so a user with basic education, experience, and/or training can properly use them.
3. Complete enough so the user/reader can follow the directions in a step-wise manner through the sampling, analysis, and data-handling processes.
4. Consistent with sound scientific/engineering principles.
5. Consistent with current EPA regulations and guidelines.
6. Consistent with the instrument manufacturers' specific instruction manuals.

B. Benefits of Standard Operating Procedures

1. Record the performance of all tasks and their results.
2. Explain the cause for missing data.
3. Demonstrate the validation of data each time they are recorded, calculated, or transcribed.

C. Items to be Addressed in Standard Operating Procedures

1. General network or experimental design.
2. Specific sampling-site selection and health outcomes selection.
3. Sampling and analytical methodology.
4. Probes, collection devices, media or storage containers, and sample additives, such as preservatives.
5. Special precautions, such as holding times and protection from heat, light, reactivity, and combustibility.
6. Federal reference, equivalent, and alternate test procedures.
7. Instrumentation selection and use.
8. Calibration and standardization.
9. Preventive and remedial maintenance.
10. Duplicate, spiked, blank samples and analysis and biologic control as well as blinded analysis.

11. Quality control procedures such as inter-, and intra-field laboratory activities.
12. Documentation, sample custody, transportation, and handling procedures.
13. Safety.
14. Data handling and assessment procedures.
15. Precision, accuracy, completeness, representativeness, and comparability.
16. Service contracts.
17. Document control.

The degree of adherence to the approved SOPs shall be determined during the systems audits. SOPs shall be revised by the user and approved by the user's supervisor. As appropriate, these SOPs may be reviewed by the Center Quality Assurance Program Manager. In addition, our documentation, data and laboratories have been evaluated and are available for evaluation by outside independent auditor's, if request by the project sponsor. Outside audits involve protocol as SOP audits, facilities audits and data management audits.

## **2.5 Data Processing and Verification**

Data processing includes collection, validation, storage, transfers, and reduction. Precautions shall be taken each time the data are reduced, recorded, calculated, and transcribed to prevent the introduction of errors and the loss of information. As our reliance on computers increases, consideration should be given to the transmittal and storage of data in an electronic (digital) format. Most data systems and users have specific electronic data format requirements. Because of this variability, electronic transmittal and storage of data will have to be addressed on a project or program specific basis, which is beyond the scope of this document. The data processing requirements are detailed as follows:

- A. Collection - Each Project Plan shall address the checks which must be used to avoid errors in the data collection process.
- B. Validation - Data validation is defined as, "the process by which data are accepted or rejected based on a set of criteria." Since this aspect of QA may include various forms of manual or computerized checks, criteria for data validation shall be specified in each Project Plan.
- C. Storage - Each Project Plan shall indicate how specific types of data will be stored.
- D. Transfers - Each Project Plan shall describe procedures which will be used to ensure that data transfers are error-free, and that no information is lost in the transfer. Data transfer steps contained in each Project Plan shall be kept to a minimum.
- E. Reduction - Each Project Plan shall contain procedures for ensuring the correctness of data reduction processes. Data reduction includes, all processes which change either the form of expression or quantity of data items. It is distinct from data transfer in that it entails a reduction in the size (or dimensionality) of the data set. The Project Plan must identify the processes used to obtain the reduced data set. Each Project Plan shall describe procedures for verifying the accuracy of the data reduction process.

## 2.6 Data Quality Assessment

The quality of all environmental and/or health response data generated and processed shall be assessed for: accuracy, precision, completeness, comparability and representativeness, based upon the Project Plans. The data assessment requirements are detailed as follows:

### 2.6.1. Accuracy

Each QA Project Plan shall contain a mechanism which will demonstrate that the reported data are favorably comparable to the true value(s). Examples of activities to assess accuracy are:

1. Traceability of Instrumentation - Each measurement device shall be assigned a unique identification number. Documentation shall identify the specific measurement device; where and when used; maintenance performed; and the equipment and standards used for calibration.
2. Traceability of Standards - Each standard and each measurement device shall be compared against a standard of known and higher accuracy (where possible). All calibration standards shall be traceable to available National Institute of Standards and Technology (NIST). If NIST standards are not available, other documented primary standards shall be used.
3. Traceability of Samples - Each sample shall be assigned a unique identification number (laboratory No.). Documentation should identify sampling time, place, samplers name and action taken on each sample.
4. Traceability of Data - Data shall be documented to allow complete reconstruction, from initial field records through data storage system retrieval.
5. Methodology - If available, Federal reference, equivalent, or approved alternate test methods of known accuracy shall be used.
6. Reference or Spiked Samples - Recoveries shall be within predetermined acceptance limits.

### 2.6.2. Precision

Each Project Plan shall contain a mechanism which will demonstrate the reproducibility of the measurement process. Examples of such mechanisms are:

1. Replicate Samples - Replicate sample data shall be within predetermined acceptance limits.
2. Collocated Samples - Sample data from collocated sampling points or monitors shall be within predetermined acceptance limits.

3. Biologic health endpoint assessments. Positive and negative controls are included in the experimental design where appropriate.
4. Inter-/Intra-Laboratory Testing - Sample data from independent studies shall be within predetermined acceptance limits.
5. Instrumental Checks - Each measurement device shall have routine checks performed to demonstrate that variables are within predetermined limits. Examples of these include:
  - Zero and span Flow rate
  - Noise levels Pressure rate
  - Drift Linearity

#### 2.6.3. Completeness

Each Project Plan shall identify the quantity of data needed to support a planning or enforcement action. Completeness shall take into consideration the potential for environmental change with respect to time and timing.

#### 2.6.4. Comparability

Each Project plan shall contain procedures to assure the comparability of data. Examples are:

1. Consistency of reporting units.
2. Standardized siting, sampling, and analysis.
3. Standardized data format.

#### 2.6.5. Representativeness

Each Project Plan shall contain procedures to ensure that all samples collected, are as accurate and precise as possible and represent the media sampled.

Examples of activities to assess representativeness are:

1. Site Purpose - Each sampling site (environmental or health) shall have a preidentified and documented purpose.
2. Site Description - Each sampling site shall be specifically identified by location and by suitability to meet the pre-identified purpose.
3. Site Photo Documentation - Each environmental sampling site should be photographed from each of the four major compass directions when possible.
4. Sampling Conditions - The conditions under which each environmental sample was collected shall be described. Conditions include such items as: Stream flow and homogeneity Temperature, Wind speed and direction Barometric pressure. For health data, associated conditions medication records and a link to exposure data shall be recorded.

## **2.7 Corrective Action**

Each Project Plan shall include, provisions for written requirements establishing and maintaining QM reporting or feedback channels to the management responsible, to ensure that early and effective corrective action can be taken when data quality falls outside established data quality objectives (acceptance criteria). Each Project Plan shall also include, provisions to keep responsible management informed of then performance of all data collection systems. Each Project Plan shall describe the mechanism(s) to be used when corrective actions are necessary. Corrective action shall relate to the overall QA management scheme: who is responsible for taking corrective actions; when are corrective actions to be taken; and who follows-up to see that corrective actions have been taken and that they have produced the desired results?

## **2.8 Training**

Each research Project Principal Investigator shall ensure that all personnel performing tasks and functions related to data quality shall have the needed education, training, and experience. This includes laboratory technicians, analysts, maintenance technicians, supervisors, principal investigators, statisticians, project managers, and staff. Training needs shall be identified during performance evaluations and through career development plans. Training needs are not static, but are a dynamic function of program requirements.

## **2.9 Records Management of QM/QA Documents**

Official file copies of approved QM/QA Program Plans, Project Plans, SOPs and applicable Program or Project Specific QM/QA documents related to all environmental monitoring programs within Center shall be maintained by each Core Director. The Core Directors track and maintain documents related to the status of environmental data collection and research projects.

## **2.10 Computer Hardware and Software**

Each research group under the center is responsible for monitoring software licenses, and upgrading computer hardware.

## **2.11 Communication/Reporting/Work Plan**

The purpose of communications is to ensure that staff personnel in different monitoring programs can effectively develop and implement programs; perform activities; and resolve problems. One responsibility, of the QM Program, is to facilitate communications through the establishment of guidance documents and the issuance of procedures.

## **2.12 Center Organizational Chart**

**2.13 Center Science Advisory Committee**