

**A REQUEST FOR QUALIFICATIONS:
Epidemiologists and Statisticians to Participate in a Reanalysis of Cohort Studies
of Long-term Mortality and Particulate Air Pollution**

July 25, 1997

The Health Effects Institute (HEI), a non-profit research organization funded jointly by the U.S. EPA and industry, is sponsoring a reanalysis of cohort studies of particulate air pollution and long-term mortality. HEI is seeking a team of epidemiologists and biostatisticians to design and conduct this analysis.

Background and objectives of the project.

A body of epidemiologic work conducted over several decades, and reviewed recently by the U.S. EPA ¹, suggests that long-term exposure of U.S. urban populations to particulate air pollution may cause increased mortality from respiratory and cardiovascular disease. Two recent prospective cohort studies, the American Cancer Society (ACS) Study² and the Six Cities Study³ have reported estimated increases in annual average total mortality associated with fine particles (PM_{2.5}). A third prospective cohort study, the Seventh Day Adventist Health Study⁴ found evidence of increased respiratory disease morbidity, but not mortality, associated with exposure to total suspended particles and respirable particles (PM₁₀). The findings of these studies are controversial; the possibility that the magnitude of the observed associations may have been estimated inaccurately due to uncontrolled confounding and/or errors in the measurement of exposure remains a persistent concern. Some have suggested that the effects of factors such as sedentary

-
- ¹ U.S. Environmental Protection Agency. Air Quality Criteria for Particulate Matter. Vol III. EPA/600/p-95/0016F, 1996.
 - ² Pope CA III, Thun M, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Heath CW Jr. Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults. *Am J Resp Crit Care Med* 1995;151:669-674.
 - ³ Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr., Speizer FE. An Association Between Air Pollution and Mortality in Six U.S. Cities. *N Engl J Med* 1993;329(24):1753-1759.
 - ⁴ Abbey DE, Mills PK, Petersen FF, Beeson WL. Long-Term Ambient Concentrations of Total Suspended Particulates and Oxidants As Related to Incidence of Chronic Disease in California Seventh-Day Adventists. *Env Hlth Persp* 1991;94:43-50.

lifestyle and active⁵ or passive cigarette smoking⁶ might have been inadequately controlled in the Six-Cities and ACS studies, perhaps resulting in overestimates of the magnitude of the mortality risk due to particulate air pollution. Still others have suggested that these studies did not adequately characterize the long-term exposure of study subjects, and that this precludes firm conclusions with respect to the existence of effects of long-term exposure on chronic disease occurrence and mortality⁷. Such potential sources of error notwithstanding, the Six-Cities and ACS studies currently provide some of the most comprehensive data available with which to estimate the long-term risk of mortality due to exposure to particulate air pollution.

The U.S. EPA has relied, in part, on the results of the Six-Cities and American Cancer Society studies to support a new, more stringent, air quality standard for fine particles. Although these studies were reviewed by the EPA's Clean Air Scientific Advisory Committee (CASAC) as part of the PM Criteria Document process which preceded the promulgation of the new fine particle standard, representatives of industry, members of Congress, and other scientists have urged Harvard University, the American Cancer Society, and the EPA to make the original data from these studies available to other analysts. In response, Harvard University requested that HEI organize an independent reanalysis of these studies, and has agreed to provide a team of analysts, selected by HEI, with access to the data for the purposes of conducting a reanalysis. Recently, the American Cancer Society initiated a similar request which the HEI is reviewing currently.

Objectives and Scope

The overall objective of the project is to conduct a rigorous and independent assessment of the findings of the Six-Cities and ACS studies of air pollution and mortality.

The project has two main tasks:

- 1) Attempt to validate and replicate the published results by:
 - conducting a quality assurance audit on a sample of the original data;
 - attempting to reproduce the original numerical results.
- 2) Conduct sensitivity analyses to test the robustness of the original findings and interpretations to alternative analytic approaches.

⁵ Moolgavkar SH, Luebeck EG. A Critical Review of the Evidence on Particulate Air Pollution and Mortality. *Epidemiology* 1996;7:420-428.

⁶ U.S. Environmental Protection Agency. Air Quality Criteria for Particulate Matter. Vol III. EPA/600/p-95/0016F, 1996.

⁷ Vedal S. Ambient Particles and Health: Lines that Divide. *J Air & Waste Manage. Assoc.* 1997;47:551-581.

As part of this effort, HEI also hopes to identify analyses of these, and perhaps other, data sets, that can extend the previous observations, e.g., by adding data on additional variables or time periods, and which might be carried out as part of a separate, broader future effort.

Project structure and role of the Analytic Team.

Project oversight will be provided by an 8-member Expert Panel, chaired by Dr. Arthur Upton (Robert Wood Johnson Medical School) and comprising leading scientists with expertise in relevant scientific, technical, and clinical areas (see attached roster of Expert Panel members). The Expert Panel will select an Analytic Team from among the respondents to this Request for Qualifications. Throughout the project, the Expert Panel will monitor and review the progress and intermediate results.

The Analytic Team will design and conduct the reanalysis. Specifically, they will:

- develop an analytic plan to be reviewed and approved by the Expert Panel. This plan will address the objectives listed above, and will include both replicability of the original results, and a comprehensive set of sensitivity analyses;
- interact with the investigators who conducted the original studies (Original Investigators), who have agreed to provide the Analytic Team with access to the data and other documentation, and will be available to consult with them throughout the course of the project. The details and logistics of data access will be negotiated after the Analytic Team has been selected;
- carry out all analyses proposed in the analytic plan. (As noted above, a quality assurance (QA) audit of the original data will be conducted as part of the project. The Analytic Team and Expert Panel may decide that this component would be best conducted by a separate QA contractor under the Expert Panel's direction, in consultation with the Analytic Team.);
- work with the Expert Panel to develop ideas and approaches for future, more extensive, analyses of these, and perhaps other, data sets;
- prepare a comprehensive final report to HEI.

HEI's Health Review Committee will organize an independent peer-review of the final report, and will publish the final report and a commentary by the peer-reviewers as an HEI Special Report.

In order to provide the opportunity for input from a broad range of views, HEI will organize an Advisory Board composed of representatives of government, private industry, and public health and environmental organizations, which will be asked to provide comments to the Expert Panel at major project milestones.

Statement of qualifications of the Analytic Team.

HEI is seeking applications representing teams consisting of 2-4 epidemiologists, statisticians and air pollution exposure experts, one of whom should be designated as the principal investigator. HEI encourages the development of teams with a broad range of skills and perspectives. Members of a team need not be from the same institution. The following information should be provided in the Statement of Qualifications:

- 1) Names of the principal investigator and other members of the Analytic Team. Description of the role of each person on the team and of any previous collaborations among team members.
- 2) Description of the experience of the Analytic Team with respect to:
 - a) the design and conduct of epidemiologic studies of the health effects of air pollution and of cardiovascular and respiratory disease;
 - b) application of statistical methods for longitudinal data analysis in epidemiology, with particular reference to cohort studies of chronic diseases;
 - c) data reanalysis, pooling, or meta-analytic projects, including working with data developed by other research groups;
 - d) the critical review of epidemiologic studies of the health effects of air pollution and of cardiovascular and respiratory disease;
- 3) Information on current research and/or consulting activities, particularly those related to the health effects of air pollution, including any analyses of recent particulate epidemiology data, indicating the nature and extent of the work and sources of financial support.
- 4) Any other relevant information.

The statement of qualifications should document that adequate support personnel and other resources will be available to perform the required analyses, and that team members are able to commit adequate levels of effort to this project in order to complete it within the designated time frame. The principal investigator should submit the application according to the process described below.

Project schedule and management.

The expected period of performance will be from October 1997 through June 1999.

HEI expects to contract for this work in two phases:

- Phase 1 (October 1997 - December 31, 1997) Development of the Analytic Plan;
- Phase 2 (January 1, 1998 - June 30, 1999) Execution of Analytic Plan and Report Preparation and Review.

Because it will not be possible to develop a budget for this project until the scope of work is completed, HEI contemplates contracting for Phase 1 and Phase 2 separately, with the same Analytic Team. The compensation for Phase 1 will cover the time and travel expenses of the selected team for the scoping activities described in this request and detailed further in discussions with the team, subject to the limitations described below. Phase 2 compensation will be established by a project budget, to be developed as the part of the Analytic Plan, and reviewed and approved by the Expert Panel and HEI's Board of Directors.

HEI's research agreements are cost-reimbursement contracts, subject to federal regulations that apply to EPA funding, since HEI anticipates partially funding this work with EPA funds. HEI assumes that the home institution of the principal investigator will be the prime contractor for this work, for both phases, and that the work of other members of the team will be handled through a subcontract(s) with the prime contractor, if necessary. It is important that applicants and their institutions are aware that HEI's Board of Directors has established a policy that indirect costs on all HEI research contracts be limited to a maximum of 30% of direct costs, excluding equipment charges.

Application and decision process.

Applicants should submit an application consisting of a statement of qualifications not to exceed 5 pages in length, and the resumes of all prospective team members. Please do not send additional materials. Fifteen copies of the complete application should be provided. **The application should arrive at HEI no later than Friday, September 19, 1997. Applications arriving after that date will not be considered.**

The applications will be reviewed by the HEI Expert Panel, which will recommend selection of an Analytic Team to the HEI Board of Directors based on:

- experience of the team with the epidemiologic, statistical, and subject matter questions involved;
- ability of the team to bring an independent, critical perspective to the project;
- demonstrated ability to deliver similar projects in a timely fashion;
- consideration of any possible conflicts of interest.

Selection of the team is expected by the end of October 1997.

Please send all applications and address all inquiries to:

Aaron J. Cohen, M.P.H., D.Sc.
Health Effects Institute
955 Massachusetts Avenue
Cambridge, MA 02139

Telephone: (617) 876-6700
FAX: (617) 876-6709
Email: acohen@healtheffects.org

**HEI COHORT STUDIES REANALYSIS PROJECT
EXPERT PANEL**

Arthur C. Upton (Chairman)
Robert Wood Johnson Medical School
Piscataway, NJ

Steve Colome
Integrated Environmental Services (Irvine, CA)
UCLA School of Public Health
Los Angeles, CA

Leon Gordis
The Johns Hopkins University School of Hygiene
and Public Health
Baltimore, MD

Geoffrey Howe
Columbia University School of Public Health
New York, NY

David Jacobs
University of Minnesota
Minneapolis, MN

Suresh H. Moolgavkar
Fred Hutchinson Cancer Research Center
Seattle, WA

Sverre Vedal
University of British Columbia
Vancouver, BC

Clarice Weinberg
National Institute of Environmental Health Sciences (NIEHS)
Research Triangle Park, NC

Bernard D. Goldstein (ex-officio)
Environmental and Occupational Health Sciences Institute
University of Medicine and Dentistry of New Jersey
Piscataway, NJ