REQUEST FOR APPLICATIONS 17-2:
HEALTH EFFECTS OF AIR POLLUTION

INTRODUCTION
This Request for Applications (RFA) provides a mechanism for investigators whose area of interest falls outside of current RFAs, but is compatible with the HEI research program and mission, to apply for HEI funds. HEI is interested in receiving applications for research on novel and important aspects of the health effects of air pollutants, particularly those derived from motor vehicle emissions. Applicants will be asked to submit a preliminary application. Full applications will be by invitation only.

STUDY DURATION AND BUDGET GUIDELINES FOR RFA 17-2
HEI encourages interested applicants to submit preliminary applications for projects of up to 2 or 2.5 years in duration. The HEI Research Committee will generally not consider studies of longer duration. Preparation of the final report should be included in the budget and timeline of the final year of the study. The funding cap for each study will be $400,000 (total budget) and HEI expects to fund two studies from this RFA.

THE HEI RESEARCH PROGRAM AND RESEARCH PRIORITIES
Since the early 1980s, HEI’s research has addressed a broad range of questions about the health effects of air pollutants derived from motor vehicles emissions, including, carbon monoxide, nitrogen oxides, ozone, particulate matter — including diesel particles and associated compounds — methanol, and air toxics. Several studies have addressed the effects of exposure to more than one pollutant. In considering potential research topics, applicants should be aware of HEI’s current areas of interest, as described in the HEI Strategic Plan for the Health Effects of Air Pollution 2015-2020.

The Plan focuses on four key areas: (1) addressing the challenges of multi-pollutant science, (2) improving science for decisions: accountability and transparency, (3) addressing emerging fuels and technologies, and (4) addressing global health science. Appendix A includes sections of the Strategic Plan that describe HEI’s current research priorities and plans for implementing them. Appendix B provides a listing of HEI studies and reports, which gives information on the pollutants and issues in which HEI has been interested over recent years.

HEI studies have covered a wide range of designs: modeling, methods development, experiments with cell cultures, animal studies, controlled human exposure studies, and epidemiology investigations. In all studies, accurate characterization of exposure and appropriate statistical analyses are important. HEI’s ultimate goal is to provide data that can be used in regulatory decisions or provide better information for risk assessment; thus, human studies and studies to improve extrapolation from animals to humans are an important part of HEI’s program.

In addition, there are several crosscutting issues that the HEI Research Committee would like to emphasize in HEI-funded studies: development, application, and testing of multipollutant statistical models and methods; identification and integration of at-risk populations into HEI studies;

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1 Available at www.healtheffects.org/about/strategic-plan
2 All information and forms referred to in this RFA are available at www.healtheffects.org/research/funding
enhanced exposure assessment; consideration of climate change and health; application of new biologic techniques in air pollution health research; evaluation of other health outcomes and modifying factors; and capacity building, particularly support of early-career investigators.

OBJECTIVES

While we believe that an understanding of HEI's research priorities, as described in the HEI Strategic Plan, is important; another important goal of this RFA is to provide a means for investigators to suggest new areas of research. Thus, applications will be considered not only on issues raised in the discussion above and in HEI's Strategic Plan, but also on other issues related to improving our understanding and assessment of the health risks of exposure to motor vehicle emissions, secondary pollutants derived from them, and the whole air pollution mixture to which they contribute.

In general, applications should include studies at concentrations that occur in the environment. Initial experiments using either new techniques or investigating mechanisms of health effects may need to start at pollutant concentrations higher than ambient levels, but will only be considered if there is a real likelihood that the effects studied will be relevant to understanding effects at environmentally relevant concentrations. Although HEI is interested in both in vivo and in vitro methods, for the latter studies it will be important to explain the relationship of the assay system to the in vivo situation being modeled. Methods using isolated tissues, cells, or subcellular fractions should be appropriate for the physical characteristics of the inhaled chemicals and the metabolic transformations that may occur in vivo before target tissues are exposed. The respiratory, cardiovascular, reproductive/developmental, and central nervous systems are clearly important target sites, although other organ systems may also be appropriate for study if a strong rationale links them to possible toxic effects of air pollutants. HEI will not fund studies that employ diesel engines without diesel particulate filters.
The application process consists of two stages. The first stage involves the submission of a preliminary application, which is reviewed by the Research Committee. If the Research Committee has an interest in the study, then the investigator will be invited to prepare a full application. Invited full applications will be sent out for peer review and discussed by the Research Committee at a subsequent meeting.

**PRELIMINARY APPLICATION**

Applicants should submit a brief Preliminary Application that provides the following information: title, scientific rationale, a brief description of the study aims, design and methods, statistical methods, and anticipated results. An estimated total budget and study duration (up to 2 or 2.5 years) should be provided. In addition, brief biosketches (maximum 2 pages per person) of the principal investigator and any co-investigator(s) should be provided.

Investigators should use the Preliminary Application Form to submit the preliminary application. The preliminary application must be no more than 4 pages in length (using 11-point font size and 1-inch margins, single-spaced; including the cover page, but excluding references and biosketches); longer applications will be rejected. For the CVs, applicants can use HEI form F-8 or another format, as long as each biosketch is no longer than 2 pages. For details please visit [www.healtheffects.org/research/funding/application-instructions](http://www.healtheffects.org/research/funding/application-instructions). The application forms should be turned into a combined PDF with appropriate bookmarks before submitting.

**Deadline for Preliminary Applications**

Preliminary applications should be submitted by e-mail in PDF format to funding@healtheffects.org (subject line: [PI last name] RFA 17-2 Preliminary application) no later than **JUNE 30, 2017**, with a copy to Ms. Sharman Andersen (sanderson@healtheffects.org). HEI will acknowledge receipt of the application.

**Preliminary Application Evaluation Process**

Preliminary applications will be reviewed by the Research Committee and based on relevance of the proposed research to HEI's mission as well as scientific merit of the preliminary application, a limited number will be invited for a full application. Applicants will be informed whether or not to submit a full application by late August. For questions contact: Dr. Katy Walker (kwalker@healtheffects.org; +1-617-488-2310).

**FULL APPLICATION**

Full applications without pre-submission of a preliminary application and invitation from the Research Committee will not be considered. A full application will provide, in detail, the study aims, design, rationale, methods, and statistical analyses. If data from other studies are going to be used, information on the type of data available (including the period, location, and frequency of when the measurements were taken) and quality assurance should be included. Investigators should also discuss whether they will need to obtain IRB approval. A letter from the investigator who owns the data should be submitted, stating his or her willingness to share the data with the applicant and
with HEI, if requested (see HEI Policy on the Provision of Access to Data Underlying HEI-funded Studies).

Investigators invited to submit a full application should use forms F-1 to F-12 and consult the Instructions for Completing the Application. Please note that the required font size is 11 point with 1-inch margins. The application forms should be turned into a combined PDF with appropriate bookmarks before submitting. For details and forms please visit www.healtheffects.org/research/funding.

Deadline for Full Applications

Invited Full Applications for RFA 17-2 should be submitted to funding@healtheffects.org (subject line: [PI last name] RFA 17-2 Full application) no later than December 15, 2017. The application should be in PDF format with a maximum file size of 20 MB.

After submission, please notify Ms. Sharman Andersen (sandersen@healtheffects.org; +1-617-488-2345) of your submission; do not attach the PDF documents to this email. HEI will acknowledge receipt of the application. Applicants will be notified about the funding decision by late March, 2018.

Full Application Evaluation Process

Full applications will be evaluated in two phases. First, external scientists selected for their relevant expertise will evaluate the applications according to the following criteria:

- Relevance of the proposed research to HEI’s goals.
- Scientific merit of the proposed study design, approaches, methodology, analytic methods, and statistical procedures.
- Personnel and facilities, including:
  - Experience and competence of the principal investigator and scientific staff,
  - Adequacy of effort on the project by scientific and technical staff,
  - Adequacy of facilities.
- Reasonableness of the proposed cost and appropriateness of the allocation of the requested funds.

Second, the Research Committee will evaluate the full applications with consideration of the reviewers’ comments and of the ways the proposed research might improve the understanding of the specific problem under investigation. The Research Committee’s recommendation about funding will also consider whether studies are relevant to HEI’s Strategic Plan and how they would complement HEI’s ongoing research program, keeping in mind available resources. The Research Committee makes final recommendations regarding funding of studies to the Institute’s Board of Directors, which makes the final funding decision.

CONFLICTS OF INTEREST

HEI’s procedures for conflicts of interest are similar to the guidelines set forth by NIH. Members of HEI’s sponsor community are excluded from participating in RFA development, applying for support, application review, and funding decisions.

HEI invites external reviewers (or in the case of a major RFA, Review Panel members) who are unlikely to have a conflict of interest with the proposal(s) they are asked to review. A conflict occurs when the reviewer is named on the application in a major professional role; the reviewer (or close family member) would receive a direct financial benefit if the application is funded; the PI or
others on the application with a major role are from the reviewer’s institution or institutional component (e.g., department); during the past three years the reviewer has been a collaborator or has had other professional relationships (e.g., served as a mentor) with any person on the application who has a major role; the application includes a letter of support or reference letter from the reviewer; or the reviewer is identified as having an advisory role for the project under review. In addition, HEI Staff screen external reviewers for potential conflicts of interest with other applicants who have submitted a proposal under the same RFA.

For Review Panel members and Research Committee members, in some situations it may not be possible to avoid all possible conflicts of interest as outlined above. In such cases, Review Panel and Research Committee members who have a conflict of interest will not be assigned to review the application(s) in question and will be asked to leave the room during the discussion of those application(s). They will also not score or vote on the application(s) at issue and refrain from commenting on them during the overall discussion, and in the case of the Research Committee, from all deliberations regarding recommendation of applications for funding. If several Research Committee members are recused from the overall discussion of applications for such reasons, HEI will invite external consultants to join the Committee to fill in the missing expertise.

This peer review system relies on the professionalism of each reviewer, Review Panel member, and Research Committee member to declare to HEI the existence of any real or apparent conflict of interest. If a reviewer feels unable to provide objective advice for any other reason, he/she is expected to recuse him/herself from the review of the application(s) at issue.

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