INSTRUCTIONS FOR COMPLETING THE APPLICATION

GENERAL INFORMATION

Applications must be submitted on the *HEI Application for Research Agreement* (forms F-1 to F-12). Applications should be typed single-spaced, within the margin limitations indicated on the forms (1 inch minimum), and using a minimum font size of 11 pt. Interactive forms can be downloaded from our website at www.healtheffects.org/research/funding/application-instructions.

Any contract awarded under this Request for Applications is expected to be funded in part by a grant from the U.S. Environmental Protection Agency. This award process will be subject to regulations contained in 40 CFR Subchapter B, and particularly Part 30 thereof. Neither the United States nor the U.S. Environmental Protection Agency is nor will be a party to this Request for Applications or to any resulting agreement.

HEI and its funded institutions are subject to the Office of Management and Budget and EPA accounting regulations. NEW: Please provide a DUNS number for your institution.

BUDGET (FORMS F-4 AND F-5)

Cost or Pricing Data: Provide adequate data and analysis to assure HEI that the proposed costs are necessary and reasonable and that adequate accounting procedures will be used. For RFA 17-3, the *Walter A. Rosenblith New Investigator Award*, the budget cap is $150,000 per year for 3 years at a total of $450,000 per study, including indirect costs. For applications responding to RFA 17-3, the budget should be prepared assuming a project start date of October 1, 2018.

The total budget should include funds and an appropriate percent effort from key personnel for writing the final report in the final year of the study. Investigators should also be aware that additional time effort is expected at a later time to address requests for revisions and answering editorial queries. Please refer to the *Final Report* section in *HEI Project Negotiation, Management, and Investigator Commitments* (see separate document) for details.

PERSONNEL

List the names and positions of all applicant organization personnel involved in the project, both professional and nonprofessional, whether or not salaries are requested. Estimate the percentage of time or effort, or hours per week, on the project for professional personnel in relation to the total professional activity commitment to the applicant organization; estimate the hours per week on the project for nonprofessional personnel. List the dollar amounts separately for each individual for salary and fringe benefits. Fringe benefits may be requested to the extent that they are treated consistently by the applying organization as a direct cost to all sponsoring agencies.

The amount to be reimbursed to each individual, when added to his or her compensation for all other full-time duties, should not exceed the individual's base salary. In computing estimated salary changes, an individual's base salary represents the total authorized annual compensation that an applicant organization would be prepared to pay for a specific work period whether an individual's time is spent on sponsored research, teaching, or other activities. The base salary for the purposes of computing charges to an HEI Research Agreement excludes income that an individual may be permitted to earn outside of full-time duties to the applicant organization.

Where appropriate, indicate whether the amounts requested for the principal investigator and other professional personnel are for summer salaries or academic-year salaries and indicate the formulas for calculating summer salaries.

Indicate whether current rates or escalated rates are used. If escalation is included, state the degree (percent) and methodology, e.g., annual flat rate applied to base rate as of a specific date or a mid-point rate for the period of performance.

Note that under the Walter A. Rosenblith New Investigator Award, senior personnel and mentors cannot be included for salary support.

HEI requires the involvement of a (bio)statistician in the study design, selecting appropriate statistical approaches, and the final data analysis and interpretation. Statisticians can be included under the main study personnel or as consultants. If the investigator's Institution provides core statistical services, this should be indicated; in this case, a particular statistician should be identified by name. Exemption from this requirement can be obtained only if the Principal Investigators or other key personnel have appropriate expertise in this area, evidence of which should be submitted as part of the application. The statistician's involvement should be evident in the application, for example by including a letter from the statistician indicating that they have read the application and approve the study design and statistical approaches. (See also *Additional Submissions* below).

CONSULTANT COSTS

Consultant service should be explained by indicating the specific area in which such service is to be used. Identify the contemplated consultants. State the number of days of such services estimated to be required and the consultant's quoted rate per day, and indicate the number of hours per day in which work will be performed. The maximum consultant rate is $600/8-hr day. HEI's participation in consultant costs is subject to limits set by federal regulations. (See also *Additional Submissions* below).

SUPPLIES AND OTHER EXPENSES

All supplies and other expenses should be itemized in sufficient detail to allow reviewers to understand the major categories of expenditures (i.e., glassware, media, chemicals, animal purchase and housing, as well as publication costs, page charges, and books, listed by category and unit cost). Itemize and justify such items as patient compensation, travel, and per diem costs, rentals, leases, and computer costs. Unusually expensive items for special processes should be separately identified by quantity and price and the use or application thoroughly explained in the project plan. Each individual expense item must be categorized as supplies or other expenses according to the practices of the accounting office of your institution. Items that cost more than $5,000 should be listed under equipment (see below).

The costs of construction per se are not permissible charges. If the costs of essential alterations of facilities, including repairs, painting, removal or installation of partitions, shielding, or air conditioning, are requested, itemize them by category and justify them fully. When applicable, indicate the square footage involved, giving the basis for the costs, such as an architect's or applicant's detailed estimate. When possible, submit a line drawing of the alterations being proposed.

TRAVEL EXPENSES

Limit travel to one scientific meeting per year. Do not include the travel to the HEI Annual Conference within the budget, since HEI will cover these costs directly. If travel is required for other purposes, such as meetings with collaborators, indicate the estimated number of trips, destination, reason for travel, and cost. Identify and support any other special transportation costs attributable to the performance of this project. HEI pays for foreign travel only if it is approved in advance of the trip.

INDIRECT COSTS

Indirect costs are limited to a maximum of 30% of direct costs excluding equipment charges and subcontracts. Indirect costs cannot be greater than the government-negotiated rate for your institution. Expenses normally included in the calculation of the indirect cost rate may not be itemized as direct expenses. Please attach a copy of your institution's most recent approved indirect cost rate. Budget review will be delayed if the indirect cost rate certification is not attached.

The HEI Board of Directors has approved a very limited exception to this cap on indirect costs for organizations that can meet both of the following conditions: (1) the research institution provides a unique capability for a project essential to HEI's mission, and (2) the institution is prohibited by the U.S. Government from accepting less than full cost recovery.

EQUIPMENT

Provide an itemization and justification of all equipment to be purchased or fabricated for use in this study. Please note that HEI reimburses institutions only for those equipment items explicitly listed in the Approved Budget or subsequently authorized in writing by HEI's Director of Science or Director of Finance & Administration. The equipment budget is not subject to indirect cost charges.

SUBCONTRACTS

Itemize and enter a total for these costs. Describe and justify all appropriate costs for services purchased for, or associated with, third parties, including applicable indirect costs. These costs may include, but are not necessarily limited to, consortium agreements or formalized collaborative agreements. Indirect costs for subcontracts are also subject to HEI's 30% cap (see above). Develop separate budgets for the initial and future budget periods for each organization involved in consortium arrangements or formalized collaborative agreements, and submit them using the appropriate budget form (F-4b and F-5b). Subcontract budgets are not subject to indirect cost charges by the principal investigator's institution.

PROJECT PLAN (FORM F-6)

The Project Plan should include all the sections listed below. Include sufficient information in the Project Plan and in any appendix to facilitate an effective review. Be specific and informative and avoid redundancies. Sections A, B, and C together should total no more than four single-spaced pages. The Institute reserves the right not to consider proposals that exceed this limit. Appendices may be provided as supplementary information, but review will be based mainly on the information provided in the Project Plan. Section D should be concise but adequately detailed to permit critical evaluation. Sections D and E combined should not exceed 15 pages (excluding references). **Please use an 11-point font size or larger and 1-inch margins**.

A. Objectives

State concisely and realistically what the research described in this application is intended to accomplish and/or what hypothesis is to be tested.

B. Anticipated Results and Significance

Briefly sketch the background to the present proposal, critically evaluate existing knowledge, and specifically identify the gaps that the project is intended to fill. State concisely the importance of the research described in this application by relating the specific aims to the stated objectives of HEI and explain the regulatory significance.

C. Related Previous Studies

Provide an account of, and references to, the principal investigator's previous studies pertinent to the application and/or any other information, including preliminary findings, that will help to establish the experience and competency of the investigator to pursue the proposed project. The appendix can be used for published references or details of available pilot studies.

D. Experimental Plan and Methods

Discuss in detail the experimental design and the procedures to be used to accomplish the specific aims of the project.

Define your study sample (such as cell type, animal strain, or subject population) and explain the rationale for choosing it. If the study involves human participants, describe how they will be selected, and the informed consent procedure. (See *Additional Submissions* below).

HEI is committed to research that can lead to a better understanding of health responses of all members of the general population, particularly the most sensitive. Accordingly, consider the composition of the study population, including gender, racial/ethnic composition, and other aspects that might affect response, and provide a rationale for the choice of composition.

Provide sufficient details of the experimental design and study protocol so that it can be understood clearly by the reviewers. Applicants should provide details of exposure systems for specific pollutants (and the rationale for their selection), randomization procedures, methods used for any blinding of observations, and

the proposed number of observations (including number of animals or participants and exposure groups). Describe any new methodology and its advantage over existing methodologies.

Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims.

Where appropriate, describe the procedures to be used to ensure that the quality of the data is adequate in view of the objectives of the study (see *Quality Assurance and Quality Control* in *HEI Project Negotiations, Management, and Investigator Commitments*). However, detailed QA information should not be submitted with the original application but will be requested for successfully funded studies that meet the above criteria.

E. Statistical Design, Analysis Plans, and Access to Data

Provide calculation of statistical power, and a justification of the proposed numbers of animals/participants/samples. Include a description of the statistical methods to be used for analysis and interpretation of the data. Describe the proposed statistical procedures with sufficient detail to allow evaluation by a biostatistical reviewer. Please note that in addition to reviews by experts in the subject matter, HEI often asks statisticians to review the statistical design of studies.

NEW: include a plan for data sharing and data accessibility at the end of the study. Please see HEI's *Policy on Data Access*.

F. Milestones and Timeline (NEW)

Please include a list of milestones to be met during the project, with a timeline. Please use this template and fill in the cells to indicate when a specific aim or task will be ongoing and completed.

Milestone Chart

Year	Year 1				(etc)
Quarter	Q1	Q2	Q3	Q4	(etc)
Specific Aim 1: (add text)					
Task 1: (add text)					
Task 2: (add text)					
(etc)					

G. Literature Cited

References in the text should consist of author and year. Provide complete citations in alphabetical order at the end of the Project Plan.

OTHER SUPPORT (FORM F-7)

Describe current and pending grants or contracts from which the investigators included in the proposed project are now drawing or anticipate drawing support. Identify program by title, agency, or organization supporting such work, and level of financial support given, and the percentage of time spent on each project. Briefly describe the contents of each. If any of these overlap, duplicate, or are being replaced or supplemented by the present application, justify and delineate the nature and extent of the scientific and budgetary overlaps or boundaries.

RESOURCES AND ENVIRONMENT (FORM F-8)

Describe all the facilities to be used and, in the space provided, indicate their capacities, pertinent capabilities, relative proximity and extent of availability to the project. List the most important equipment items available for this project, noting the location, and pertinent capabilities of each.

BIOGRAPHICAL SKETCHES (FORM F-9)

Provide information on the education and research and/or professional experience for professional personnel and consultants beginning with the Principal Investigator. Do not exceed 2 pages per individual.

ADDITIONAL SUBMISSIONS (FORM F-10)

Human Participants

If Item 6 on the Title Page (Form F-1) of the application has been marked "YES," submit OMB form No. 0990-0263 (page F-11 of HEI application forms).

Safeguarding the rights and welfare of human participants in projects supported by EPA grants is the responsibility of the institution, which receives or is accountable to EPA for the funds awarded for the support of the project. The EPA regulations require applicant institutions to comply with the Department of Health and Human Services (DHHS) guidelines for human participants as well as additional requirements specified by the EPA. HEI is responsible for ensuring that these guidelines are followed by all Institutions and investigators receiving HEI funds.

The Institution must submit to HEI, for review, approval, and official acceptance, a written assurance of its compliance with guidelines established by the Department of Health and Human Services concerning protection of human participants. However, institutions that have submitted and have had accepted general assurance to DHHS under these guidelines will be considered as being in compliance with this requirement (as documented by form F-11). The DHHS's regulation, 45 CFR 46, is available from the Office for Protection from Research Risks, National Institutes of Health, Bethesda, MD 20892, or from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20420, USA (or see *http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html*). Institutions outside the U.S. that have not obtained assurance of compliance to DHHS will need to provide assurance of compliance to the World Health Organization/Council for International Organizations of Medical Sciences (WHO/CIOMS), national agencies, or United Nations agencies.

If the application involves human participants, the application should include the following information on Form F-10:

- Identify the sources of the potential participants, derived materials, or data. Describe the characteristics of the participant population, such as their anticipated number, age, gender, ethnic background, and state of health. Identify the criteria for inclusion or exclusion. Explain the rationale for research involving fetuses, in vitro fertilization, pregnant women, children, institutionalized mentally disabled participants, prisoners, or other participants, especially those whose ability to give voluntary informed consent may be in question.
- Describe the recruitment and consent procedures to be followed, including the circumstances under which consent will be solicited and obtained, who will seek it, the nature of information to be provided to prospective participants, and the methods of documenting consent. Include the consent form to be used.
- Describe potential risks to the participants — physical, psychological, social, legal, or other — and assess their likelihood and seriousness. Describe alternative methods, if any, that were considered and why they will not be used.
- Describe the procedures for protecting against or minimizing potential risks and include an assessment of their likely effectiveness. Include a discussion of confidentiality safeguards, where relevant, and arrangements for providing medical treatment if needed.
- Describe and assess the potential benefits to be gained by the participants, as well as the benefits that may accrue to society in general as a result of the planned work.
- Discuss the risks in relation to the anticipated benefits to the participant and to society.

If HEI decides to fund a study involving human participants, the investigator will be asked to submit a detailed protocol before starting the study and to comply with HEI's special QA/QC procedures (see *HEI Project Negotiation, Project Management, and Investigator Commitment*, and *Appendix C*). Approval of the

study by the Institutional Review Board (IRB) at the investigator's institution is required before starting a study with human participants. In addition, HEI will need to obtain approval from EPA before signing the contract, as described under *HEI Project Negotiation, Project Management, and Investigator Commitment*. Documentation submitted to HEI should include (1) the complete application to the IRB; (2) consent forms, if applicable; and (3) a signed letter from the IRB indicating that the study has been approved or exempted.

Laboratory Animals The applicant shall provide with the application written assurance that any use of laboratory animals will comply with the provisions of the Animal Welfare Act (7 U.S.C. S 2131 et. seq.) and the guidelines set forth in the Guide for the Care and Use of Laboratory Animals. These documents are available from the Office for the Protection from Research Risks, National Institutes of Health, Bethesda, MD 20892. When laboratory animals are to be used in the proposed studies, state the species, strains, ages, and numbers of the animals involved and the methods to be used to comply with the above-mentioned guidelines. If approval from the Institutional Animal Care and Use Committee has been obtained, the approval letter should be included with the application. Investigators are also encouraged to read the *Animal Research: Reporting of In Vivo Experiments (ARRIVE) Guidelines* (see http://www.nc3rs.org.uk/page.asp?id=1357). Although these guidelines pertain to reporting of research, HEI urges investigators to plan animal experiments being cognizant of the ARRIVE recommendations.

Recombinant DNA Applicants proposing work with recombinant DNA should adhere to the current *NIH Guidelines for Research Involving Recombinant DNA Molecules*. A copy of the Guidelines is available from the Office of Recombinant DNA Activities, National Institutes of Health, Bethesda, MD 20892.

Sponsor Participation If "YES" has been marked under sponsor participation (i.e. any of the organizations funding HEI) on page F-8 of the application form (Other Support), please explain on a separate sheet the nature of sponsor participation. Identify and explain the role of any individual employed by EPA or industry sponsors of HEI (see www.healtheffects.org/about/sponsors) who is involved with any aspect of the proposed study. Also, list any resources provided by sponsors, including animals, equipment, and facilities. Please note that employees of organizations funding HEI cannot receive funds from HEI for salary or any other costs.

Consultants Consultant arrangements and proposed collaborations with investigators at other institutions must be confirmed in writing. Attach appropriate letters from each individual, confirming his or her role in the project.

Statistician The assigned (bio)statistician needs to provide written confirmation that s/he (1) has reviewed and approved the study design and statistical approaches, and (2) will be actively involved in data analysis and interpretation.

Additional Materials (Rosenblith Award only) Applications to the Walter A. Rosenblith New Investigator Award should include a cover letter, two letters of reference, a letter indicating institutional support, a mentoring plan with letters from each mentor, three recent publications and a list of all publications by the candidate. Please refer to the RFA for details and use the designated set of application forms to assemble the materials in the order requested.

Quality Assurance All applicants should provide a quality assurance plan that includes a list of standard operation procedures, qualifications of personnel, and other measures in place to assure the quality of the research and resulting data. In addition, HEI applies special QA procedures to all approved research projects that are anticipated to produce data of regulatory significance. This includes all human studies, as well as certain designated animal studies. Those studies will undergo an external audit, and the final report will include a QA Statement from the auditor(s). See *Quality Assurance and Quality Control* in *HEI Project Negotiations, Management, and Investigator Commitments* and *Appendix C* for more details.

Personal Data **(Form F-12 — OPTIONAL)** HEI has a continuing commitment to monitoring the operation of its review and award process to detect, and deal appropriately with, real or imagined inequities with respect to age, ethnicity, race, or gender of the proposed principal investigator. To provide HEI with the information needed to fulfill this commitment, we request that each applicant complete the optional personal data form (Form F-12) and attach it as the last page of the signed original application. Upon receipt at the HEI office, this form will be separated from the application and used only for internal HEI monitoring procedures (please send this form as a separate PDF). **If you do not wish to provide this information, or do not complete the form, it will in no way affect consideration of your application.**