

## HEALTH EFFECTS INSTITUTE

### REQUEST FOR QUALIFICATIONS AND PROPOSAL FOR QUALITY ASSURANCE OVERSIGHT

FEBRUARY 2022

#### SUMMARY

**The Health Effects Institute (HEI) is seeking qualified contractors to provide quality assurance services for eleven research studies on air pollution and health.**

#### BACKGROUND

The mission of HEI is to provide high-quality, impartial, relevant scientific information on the health effects of air pollution. As accurate scientific conclusions depend on the validity of the underlying data and the precision with which it is reported, HEI uses third-party quality assurance (QA) oversight for most research projects that involve human subjects and other projects with a high potential for use in regulatory decisions. These procedures augment the general QA/QC procedures applied to all HEI studies (through staff and Committee oversight) and provide assurance that data are collected under defined conditions and are reliable and traceable from collection through final analyses and reporting. Unless otherwise specified, the HEI special QA oversight entails two audits:

1. During the course of the study. Generally, the 1-2 day QA audit during the course of the study is conducted on-site (although exceptions are made, for example, because of travel restrictions).
2. At the end of the study with review of the data presented by the investigator in the HEI Final Report. The QA audit of the final report is conducted remotely.

A description of HEI Research and Review Processes and Quality Assurance / Quality Control procedures for HEI studies are enclosed (see Attachments 1 and 2).

#### DESCRIPTION OF STUDIES NEEDING QA OVERSIGHT

Brief descriptions of the individual studies including their current status and QA needs are described below. More details about the studies and the composition of each study team can be found at <https://www.healtheffects.org/research/ongoing-research>.

#### *RFA 19-2 and RFA 20-2, "Walter A. Rosenblith New Investigator Award"*

HEI has established the Walter A. Rosenblith New Investigator Award to provide funding for outstanding investigators who are beginning independent research. By providing financial support for investigators at this early point in their careers, HEI hopes to encourage highly qualified individuals to undertake research on the health effects of air pollution. The four Rosenblith studies are described below (studies 1-4).

#### **Study # 1: COUPH: Copenhagen Ultrafine Particles and Health**

Sparse epidemiological evidence suggests associations between exposure to ultrafine particles (UFPs) and cardiovascular disease (CVD), yet no previous studies have adjusted for road traffic noise. The overall objective of this project is to examine the association between long-term

exposure to UFPs and mortality and morbidity in a large, population-based cohort study in Copenhagen, Denmark, using recent Google Air View car high resolution measurements of UFPs in 2018-2020. The Specific Aims of the study are (1) to determine if long-term exposure to UFPs is associated with total natural and cause specific mortality (due to cardiovascular disease (CVD), respiratory disease, diabetes, and dementia), independently of particulate matter (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), black carbon (BC), and road traffic noise; (2) to determine if long-term exposure to UFPs is associated with incidence of CVD, chronic respiratory disease (including lung cancer), diabetes, and dementia, independently of PM<sub>2.5</sub>, NO<sub>2</sub>, BC, and road traffic noise; and (3) to validate Google Air View model predictions for UFPs, the main exposure used in the health studies in Specific Aims 1 and 2. The Investigators will define a new, population-based cohort by including people who were residing in the Copenhagen area defined by the Google Air View car routes measurement campaign from 2018-2020, and who were 30 years or older in 2010. The main source for exposure will be Google Air View data where exposure to UFPs, NO<sub>2</sub>, and BC will be estimated at subjects' addresses in 2010 by land-use regression models. PM<sub>2.5</sub> will be estimated from the European-wide hybrid LUR model. They will use Cox proportional hazard models to examine the associations between long-term exposure to UFPs and other pollutants with mortality and morbidity. To estimate the independent effects of UFPs, they will apply Bayesian kernel machine regression approach to identify the individual components of the mixture responsible for health effects.

Location: Copenhagen, Denmark

Duration: 3 years

Start date and anticipated end date: 5/1/2020 to 4/30/2023

Status: beginning of year 1

QA needs: On-site audit during study and off-site audit of the final report

Note: Preference for the same auditor for this study and Study #8 because they use overlapping datasets.

## **Study # 2: Robust statistical approaches to understanding the causal effect of air pollution mixtures**

Dr. Antonelli and his team propose to develop statistical methods for analyzing air pollution mixtures, with a focus on causal inference approaches. First, they will define policy-relevant causal estimands for air pollutant mixtures, while developing methods to increase the power to detect the typically small effect sizes in air pollution epidemiology (Aim 1). Next, they will characterize population heterogeneity in causal effects of pollution mixtures and identify vulnerable subgroups (Aim 2). To improve exposure assessment beyond assigning exposure based on a single location, the investigators will then develop methods to handle spatial interference, or exposure 'spillover', of pollutant mixtures (Aim 3). Finally, they will develop sensitivity analyses to assess bias from unmeasured confounding in the air pollution mixtures context (Aim 4). Methods will be applied to study air pollutant mixtures (including PM<sub>2.5</sub>, sulfates, nitrates, ammonium, organic matter, BC, mineral dust, and sea salt) and adverse health outcomes among a national cohort of Medicare (e.g., U.S. health program for adults ages 65+) recipients for years 1999-2016.

Location: United States  
Duration: 3 years  
Start date and anticipated end date: 5/1/2021 to 4/30/2024  
Status: middle of year 1  
QA needs: Off-site audit of the final report

**Study #3 Urban air and noise pollution in sub-Saharan Africa in sub-Saharan Africa: a study of prenatal exposures, birth outcomes and sleep disturbance in infants**

This study seeks to examine associations between long-term maternal exposures to PM<sub>2.5</sub>, NO<sub>2</sub>, and environmental noise pollution and adverse birth outcomes in Accra, Ghana. The study also seeks to determine the effect of these exposures on sleep disruption in infants and toddlers and on risk of lower respiratory infections in infants. The study population will be pregnant women (N=1,320) and infants or toddlers (N=200). Health outcomes to be assessed are preterm birth, term birthweight, term low birthweight, respiratory infections, and sleep disturbance in infants, toddlers. Exposures will be assessed by land-use regression models and personal and household monitoring (N=200).

Location: Accra, Ghana  
Duration: 3 years  
Start date and anticipated end date: 1/1/2022 to 12/31/2025  
Status: starting up  
QA needs: On-site audit during study and off-site audit of the final report

**Study #4 Air Pollution Source Impacts at Fine Scales for Long-term Regulatory Accountability and Environmental Justice**

The investigators will develop national, fine-scale, daily PM<sub>2.5</sub> source impact exposure estimates. They will first apportion daily PM<sub>2.5</sub> concentrations using data from U.S. monitors and receptor modeling. To simulate source impacts, they will use chemical-transport modeling. They will then use an ensemble machine learning model to predict daily PM<sub>2.5</sub> source impacts and estimate uncertainties. They will quantify the extent that exposure changes have occurred equitably across population groups.

Location: United States, national  
Duration: 3 years  
Start date and anticipated end date: September 1, 2022 and August 31, 2023  
Status: Not started  
QA needs: On-site audit during study and off-site of final report

*RFA 20-1A, "Assessing Improved Air Quality and Health from National, Regional, and Local Air Quality Actions"*

Studies 5-7 were funded under RFA 20-1A, which provides a mechanism for investigators whose area of interest falls outside of current RFAs but is compatible with the HEI research program

and mission. The funded studies included two studies on health effects of wildfires and one study on accountability of air quality regulations. These three studies are summarized below.

**Study #5: Australian Fires and Perinatal Health Risk**

Dr. Bell will estimate PM<sub>2.5</sub> specifically from Australian fires with fire emissions inventories and Lagrangian modeling. The advanced fire modeling methods and emissions inventory will be made publicly available, which will allow them to estimate daily exposure to PM<sub>2.5</sub> from Australian wildfires. They will then use a retrospective cohort study to estimate associations between adverse birth outcomes and those exposures. Additionally, her study will assess disparities in exposure and in health response for potentially sensitive populations (low socioeconomic status, Aboriginal and Torres Strait Islander populations).

Location: Australia (12 cities)

Duration: 3 years

Start date and anticipated end date: 9/1/2021 to 8/31/2024

Status: in year 1

QA needs: On-site audit during study and off-site of final report

**Study #6: Environmental and Health Benefits of Mobile Sources and Electricity Generating Unit Policies to Reduce Particulate Pollution**

Drs. Ebelt and Rich will assess the impact of selected policies that target emissions from motor vehicles and electricity generating units on PM<sub>2.5</sub>, gaseous pollutants, PM<sub>2.5</sub> components, and source-specific PM<sub>2.5</sub> concentrations in Atlanta GA, New York City NY, and Los Angeles CA from 2005-2019. The investigators will compare changes in estimated PM<sub>2.5</sub> composition resulting from the selected air quality policies and quantify the health benefits of the air quality policies over the study period at each site and within each city in terms of cardiorespiratory emergency department visits and hospitalizations.

Location: Atlanta: GA; Los Angeles, CA; New York City, NY

Duration: 3 years

Start date and anticipated end date: 9/1/2021 to 8/31/2024

Status: in year 1

QA needs: On-site audit during study and off-site of final report

**Study #7: Contributions of Prescribed Fire and Agricultural Burning to Air Quality and Health**

The investigators aim to quantify the impacts of prescribed and agricultural burning on daily fine particulate matter (PM<sub>2.5</sub>) and ozone (O<sub>3</sub>) levels: 1) emissions estimation and 2) model simulations. They will develop a database that contains location and date of prescribed and agricultural fires and estimate emissions using a combination of satellite-enhanced fuel load maps, model-based fuel consumption estimates, and published emissions factors. They will estimate the contributions of fires to daily PM<sub>2.5</sub> and O<sub>3</sub> concentrations using a chemical-

transport model (Community Multiscale Air Quality model). Lastly, they will examine associations between daily estimated PM<sub>2.5</sub> and O<sub>3</sub> concentrations and emergency department visits and cardiovascular outcomes and examine effect modification by sociodemographic factors.

Location: Southeastern, United States

Duration: 3 Years

Start date and anticipated end date: August 1, 2021 and July 31, 2024

Status: In year 1

QA needs: On-site audit during study and off-site of final report

*RFA 20-1B, "Air Pollution, COVID-19, and Human Health"*

RFA 20-1B solicits applications for research on novel and important aspects of the intersection of exposure to air pollution and COVID-19 health outcomes, focusing on two topics: (a) accountability research: What are the effects of the unprecedented interventions taken to control the COVID-19 pandemic on emissions, air pollution, and human health? (b) susceptibility factors: Are individuals or populations who have been chronically or acutely exposed to higher levels of air pollution at greater risk of mortality from COVID-19 compared to those exposed to lower levels of air pollution? Do the effects differ by race or ethnicity or by measures of socioeconomic status? The five new studies funded under this RFA are summarized below.

**Study #8: Long-term exposure to AIR pollution and COVID-19 mortality and morbidity in DENmark: who is most susceptible? (AIRCODEN)**

This study will investigate whether exposure to air pollution increases the risk of severe COVID-19 outcomes and identify the most susceptible groups by socioeconomic status, ethnicity, and comorbidities. The investigators will estimate the association between long-term exposure to air pollution (40-year and 1-year residential mean levels of PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, BC, and O<sub>3</sub>) and COVID-19 mortality and hospitalizations, using Cox regression models, of more than 3 million adults in Denmark. They will adjust for several individual- and area-level factors and assess effect modification by these factors using interaction terms.

Location: Denmark

Duration: 1.25 Years

Start date and anticipated end date: March 1, 2021 and July 31, 2022

Status: In first year

QA needs: Detailed audit of final report

Note: Preference for the same auditor for this study and Study #1 because they use overlapping datasets.

**Study #9: Effect of Air Pollution Reductions on Mortality during the COVID-19 Lockdown: A Natural Experiment Study**

The investigators will estimate ambient NO<sub>2</sub> and PM<sub>2.5</sub> concentrations using a combination of fixed site air quality monitor data and an ensemble model. They will evaluate whether changes in mortality are associated with changes in ambient NO<sub>2</sub> and PM<sub>2.5</sub> levels, before, during, and after

lockdown measures using a difference-in-difference (DiD) analysis. They will also leverage disproportionate reductions in NO<sub>2</sub> and PM<sub>2.5</sub> pollution during the COVID-19 lockdowns to perform stratified analyses to disentangle the short-term effects of NO<sub>2</sub> versus PM<sub>2.5</sub> on mortality. To do so, they will quantify air pollution changes during lockdowns using counterfactual modeling and then apply the DiD approach to estimate the effect of NO<sub>2</sub> exposure, independent of PM<sub>2.5</sub> exposure.

Location: China (Jiangsu), Germany (Northern and Eastern), Italy (Central and Southern), United States (California)

Duration: 2 years

Start date and anticipated end date: April 1, 2021 to March 31, 2023

Status: In year 1

QA needs: Detailed audit of final report

### **Study #10: Ambient Air Pollution and COVID-19 in California**

The investigators will evaluate the chronic and acute effects of air pollution exposure on COVID-19 incidence, mortality, and long-term complications among the approximately 10 million residents of 432 health neighborhoods in Los Angeles, California (CA), with administrative records linked from the Kaiser Permanente Southern California health system. In Aim 1, they will use chemical-transport and land-use regression models to develop chronic (2017-2018) and acute (2020) daily PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> exposure fields across CA at multiple spatial resolutions. Aim 2 will assess the association between air pollution exposures and COVID-19 incidence and mortality. Aim 3 will assess the association between air pollution exposure and new and exacerbated long-term COVID-19 complications up to 18 months following initial SARS-Cov-2 infection. Finally, Aim 4 will assess air pollution exposure and COVID-19 disease progression.

Location: Los Angeles, California

Duration: 2 years

Start date and anticipated end date: February 1, 2021 and January 31, 2023

Status: In year 1

QA needs: Detailed audit of final report

### **Study #11: Race, Ethnicity, and Air pollution in COVID-19 Hospitalization OUTcomes (REACH OUT Study)**

Dr. Stingone and her team propose to evaluate the interactions between chronic air pollution exposure (PM<sub>2.5</sub>, BC, NO<sub>2</sub>, NO, O<sub>3</sub>, and SO<sub>2</sub> via the New York City (NYC) Community Air Pollution Survey) and neighborhood vulnerability in relation to adverse COVID-19 outcomes in NYC. In Aim 1, they will use electronic health record data with more than 37,000 COVID-19 patients from five large hospital systems (INSIGHT clinical research network) to evaluate both single and multipollutant air pollution exposures in relation to COVID-19 hospitalization, inpatient length of stay, ICU admission, ventilator use, and death. They will also complete a validation study, sampling 10% of patients from four hospitals systems to ensure quality of

harmonized data. In Aim 2, they will use vital statistics from the NYC Department of Health and Mental Hygiene to evaluate chronic air pollution exposure and excess all-cause mortality during the pandemic.

Location: New York City

Duration: 2 Years

Start date and anticipated end date: April 1, 2021 and March 31, 2023

Status: In year 1

QA needs: Detailed audit of final report

**Study #12: Air Pollution in relation to COVID-19 morbidity and mortality: a large population-based cohort study in Catalonia, Spain**

The investigators will test whether long- or short-term exposure to air pollution increases the risk of COVID-19 hospital admissions or mortality and to identify vulnerable subgroups in the general population of Catalonia, Spain. They will use electronic health records from primary care, hospital admissions, laboratory testing, and other registries to generate two cohorts: one including nearly the full population of Catalonia (~6 million people) and another, nested, smaller cohort of individuals diagnosed with COVID-19 (sample size not yet reported).

The individual-level health data will be linked to geocoded residential address and modeled and measured air pollutant concentrations of particulate matter, nitrogen oxides and ozone. They plan to use semi-parametric hazard models with time-varying covariates to quantify associations between long- and short-term air pollution and COVID-19 hospital admission and mortality.

Location: Catalonia, Spain

Duration: 2 years

Start date and anticipated end date: February 1, 2021 and January 31, 2023

Status: In year 1

QA needs: Detailed audit of final report

## **APPLICATION PROCESS**

The application process consists of 2 phases:

1. Statement of qualifications (Phase 1)
2. Proposal for auditing HEI-funded research studies (Phase 2)

## **INSTRUCTIONS FOR PREPARING THE APPLICATION**

Interested teams may apply for QA oversight of one or multiple studies.

### **Statement of Qualifications (Phase 1)**

Interested applicants should submit a statement of qualification using Form 1. The Statement should include the following: a) statement of qualifications that includes a list of QA projects completed during the last five years that are relevant to the HEI studies, b) curriculum vitae of the key personnel who would conduct the QA oversight, c) specific studies that the applicant is interested in auditing, and d) list of any actual or potential collaborations between the applicant and the study investigators. The statement of qualifications is non-binding.

Required areas of team expertise include

- Epidemiologic expertise, including experience with use of administrative databases.
- Statistical expertise, including Cox proportional hazard models, regression, and multilevel modeling, preferably with machine learning techniques and causal inference methods.
- Air pollution exposure measurement and modeling, including experience with low-cost sensors, satellite data, dispersion models, and land-use regression modeling.

HEI will invite the most qualified applicants to submit a proposal for auditing HEI-funded research studies.

Deadline: April 4, 2022. Applicants will be informed if they have been selected to submit a proposal and for which studies, within 2 weeks of submitting a complete Statement of Qualifications.

### **Request for Proposals (Phase 2)**

Selected Phase 1 applicants will be asked to submit a written proposal for QA oversight for the specific studies using Form 2. The proposal should include for each study a) proposed scope of work, b) schedule and detailed list of tasks for the audits and hours allocated to each task, c) list of personnel involved and their responsibilities, and d) budget estimate for each study with separate items for personnel costs (indicating the number of hours and the hourly rate of each member of the QA team) and travel costs, if applicable. Please note that HEI does not pay for travel time; however, travel time can be billed if it is used for work related to the visit. HEI will provide additional relevant material (e.g., project plans, progress reports) to the selected applicants.



## RFQP 2022 for QA oversight

Deadline: June 1, 2022. HEI staff will review the proposals based on the quality of the QA plan, expertise of the team, and reasonableness of the proposed costs. A response to all applicants will be provided by June 29, 2022.

Please use the specific Forms 1 and 2 [www.healtheffects.org/sites/default/files/Statement-of-Qualification-Form2018.docx](http://www.healtheffects.org/sites/default/files/Statement-of-Qualification-Form2018.docx) and [www.healtheffects.org/sites/default/files/Request-for-Proposal-Form2018.docx](http://www.healtheffects.org/sites/default/files/Request-for-Proposal-Form2018.docx).

Please direct all questions about the RFQP and application process to Dr. Anna Rosofsky at [arosofsky@healtheffects.org](mailto:arosofsky@healtheffects.org). Submissions should be submitted by email to [funding@healtheffects.org](mailto:funding@healtheffects.org).

### **ATTACHMENTS**

Attachment 1: HEI Quality Assurance / quality control procedures for HEI studies  
<https://www.healtheffects.org/research/quality-assurance>

Attachment 2: HEI Research and Review Processes:  
<https://www.healtheffects.org/research/research-and-review-processes>

Attachment 3: Investigator Commitments (with information on study oversight, progress reports, and audit processes)  
<https://www.healtheffects.org/research/investigators/commitments>