ASSOCIATION BETWEEN LONG-TERM ULTRAFINE PARTICULATE MATTER EXPOSURE AND PREMATURE DEATH

I. OBJECTIVE

This proposed research is designed to fill the need for a sound epidemiological study on the health effects of long-term exposure to ultrafine particulate matter (UFPM) focused on the risk of premature death. There is a large body of literature showing that fine particulate matter (PM2.5) is associated with premature death, with the most persuasive evidence coming from long-term epidemiological studies. No comprehensive epidemiological study exists for UFPM, though some published research suggests that UFPM may pose a health risk separate from that for PM2.5 mass. While PM2.5 pollution, which includes an ultrafine component, is decreasing in California, we do not know the health risk associated with UFPM exposure. This research project is expected to lead to a clearer understanding of the health effects of exposure to UFPM, including health risk at ambient air concentrations.

II. BACKGROUND

ARB, U.S. EPA, and others have funded toxicological and animal studies on the health effects of UFPM exposure, which have shed light on the potential mechanisms and pathways by which these particles can affect human health. Significant findings in these studies include evidence of cardiovascular effects in animals and humans. Although some UFPM epidemiologic studies have been published, the results are inconsistent, and the studies lacked an adequate exposure assessment at the regional level.

Some studies have examined associations between short-term UFPM exposure and mortality in case-crossover (Forastiere et al., 2005) or time-series studies (e.g. Stölzel et al., 2007; Breitner et al., 2009, 2011); however, these studies relied on central site monitors, which would not have been able to capture regional variation in concentrations. There are no corresponding long-term UFPM mortality studies, even though published results suggest that UFPM may be as toxic as, or possibly more toxic than PM2.5 (for a review of UFPM-related health impacts, see HEI 2013).

The results of the few epidemiologic studies of UFPM are inconsistent, primarily because of the lack of an adequate exposure assessment at the regional level. To date, an adequate exposure assessment has not been conducted largely because UFPM has strong spatial gradients. This is clearly true for California, where ambient concentrations of UFPM have not been adequately characterized by monitoring at the regional level. The proposed study will provide these regional UFPM concentration estimates; moreover, modeled outputs will be validated through comparison with monitored concentrations. These validated concentration data then will be matched with an existing epidemiologic cohort. This integration of approaches will fill the critical need for a sound epidemiologic study on the effects of long-term exposure to UFPM with clinically important health endpoints, such as premature death and hospitalizations.

III. Scope of Work

This project will accomplish the following objectives: 1) estimate daily and annual-average concentrations of UFPM at various representative sites statewide; 2) validate the exposure model through comparison of its output with historical data; 3) conduct additional long-term UFPM monitoring, if necessary, to assess model performance; and 4) perform an epidemiological study with an existing cohort to calculate the relative risk of premature death and other health endpoints from long-term exposure to UFPM.

In carrying out these objectives, the following should be considered:

- A literature review should be conducted to provide adequate background information regarding the methodology selected to obtain daily and annual UFPM concentrations, and its strengths and weaknesses compared to other methods that have been used to estimate regional UFPM concentrations.
- Background literature also should be provided regarding the cohort selected to assess health endpoints, as well as for the endpoints themselves. Justification should be provided for the number of subjects to be included in the study.
- Investigators have a number of different options for determining daily and annual average UFPM concentrations. For example, concentrations may be estimated through the use of UFPM modeling, which could be performed using source-oriented (e.g., chemical transport models) or receptor-oriented (e.g., chemical mass balance) methodology. The use of UFPM surrogates (e.g., CO or NO_X) or combinations of approaches might also be employed.
- Regardless of the method selected for determining daily and annual UFPM concentrations, these data need to be validated. Modeled output should be compared to historical data. Additionally, there should be a comparison between modeled output and current monitoring data.
- Ambient concentrations of UFPM will be paired with an existing epidemiological cohort, such as the American Cancer Society cohort, the California Teachers Study cohort, or the National Medicare cohort. Relevant endpoints include premature mortality and hospitalizations.
- Copies of signed releases from the investigators' institutional human subject review board, confirming approval of the research protocol, will be required after the project has been awarded.
- In order to successfully complete the proposed research, a multidisciplinary team will be needed with expertise in modeling UFPM, UFPM monitoring, and epidemiology.

IV. Deliverables

- Quarterly Progress Reports
- Draft and Final Reports
- Peer-reviewed journal article(s), as appropriate
- All data and analyses generated through the course of this project

V. Timeline

It is anticipated that this project will be completed 36 months from the start date. This allows 30 months for completion of all work through delivery of a draft final report. The last 6 months

are for review of the draft final report by ARB staff and the Research Screening Committee (RSC), modification of the report by the contractor in response to ARB staff and RSC comments, and delivery of a revised final report and data files to the ARB.

VI. BUDGET: $800,000

REFERENCES

Breitner S, Liu L, Cyrys J, Bruske I, Franck U, Schlink U, Leitte AM, Herbarth O, Wiedensohler A, Wehner B, Hu M, Pan X-C, Wichmann HE, Peters A. 2011. Sub-micrometer particulate air pollution and cardiovascular mortality in Beijing, China. Sci Total Environ 409:5196–5204.

Breitner S, Stölzel M, Cyrys J, Pitz M, Wölke G, Kreyling W, Küchenhoff H, Heinrich J, Wichmann H, Peters A. 2009. Short-term mortality rates during a decade of improved air quality in Erfurt, Germany. Environ Health Perspect 117:448–454.

Forastiere F, Stafoggia M, Picciotto S, Bellander T, D'Ippoliti D, Lanki T, Von Klot S, Nyberg F, Paatero P, Peters A, Pekkanen J, Sunyer J, Perucci CA. 2005. A case- crossover analysis of out-of-hospital coronary deaths and air pollution in Rome, Italy. Am J Respir Crit Care Med 172:1549–1555.

HEI Review Panel on Ultrafine Particles. 2013. Understanding the Health Effects of Ambient Ultrafine Particles. HEI Perspectives 3. Health Effects Institute, Boston, MA.

Stölzel M, Breitner S, Cyrys J, Pitz M, Wölke G, Kreyling W, Heinrich J, Wichmann HE, Peters A. 2007. Daily mortality and particulate matter in different size classes in Erfurt, Germany. J Expo Sci Environ Epidemiol 17:458–467.