

State of California  
AIR RESOURCES BOARD

Resolution 06-4

January 26, 2006

Agenda Item No.: 06-1-1

WHEREAS, the Air Resources Board has been directed to carry out an effective research program in conjunction with its efforts to combat air pollution, pursuant to Health and Safety Code sections 39700 through 39705;

WHEREAS, a research proposal, number 2601-250, entitled "Differences in Inflammatory Responses to Exposures of Concentrated Ambient Particles in Susceptible Volunteers", has been submitted by the University of California, Los Angeles;

WHEREAS, the Research Division staff has reviewed and recommended this proposal for approval; and

WHEREAS, the Research Screening Committee has reviewed and recommends for funding:

Proposal Number 2601-250 entitled "Differences in Inflammatory Responses to Exposures of Concentrated Ambient Particles in Susceptible Volunteers", submitted by the University of California, Los Angeles, for a total amount not to exceed \$629,920.

NOW, THEREFORE BE IT RESOLVED, that the Air Resources Board, pursuant to the authority granted by Health and Safety Code section 39703, hereby accepts the recommendation of the Research Screening Committee and approves the following:

Proposal Number 2601-250 entitled "Differences in Inflammatory Responses to Exposures of Concentrated Ambient Particles in Susceptible Volunteers", submitted by the University of California, Los Angeles, for a total amount not to exceed \$629,920.

BE IT FURTHER RESOLVED, that the Executive Officer is hereby authorized to initiate administrative procedures and execute all necessary documents and contracts for the research effort proposed herein, and as described in Attachment A, in an amount not to exceed \$629,920.

I hereby certify that the above is a true and correct copy of Resolution 06-4, as adopted by the Air Resources Board.

  
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Lori Andreoni, Clerk of the Board

## ATTACHMENT A

### “Differences in Inflammatory Responses to Exposures of Concentrated Ambient Particles in Susceptible Volunteers”

#### **Background**

The idea that particulate air pollution can affect respiratory health effects is now well established. In particular, multiple studies have identified particles generated by incomplete combustion from motor vehicles as being of especial concern. Recent studies illustrate that short-term exposure to some types of PM can lead to adverse health effects. Advances in the immunotoxicology of PM provide strong support for the concept that enhanced inflammation underlies observed respiratory changes following PM exposure. In addition, hourly monitoring studies have shown that PM levels can vary considerably hour-to-hour over the course of a day. There is, therefore, an obvious need to understand if and how ambient PM can impact human health over short exposure time periods.

#### **Objective**

To determine how short-term exposure to ambient particulate matter alters inflammation and airway function in humans.

#### **Methods**

The study will examine the airway and systemic inflammatory changes and related physiology that occur subsequent to exposure to particulate matter. Measurements of lung function by spirometry, non-specific airway sensitivity, and heart rate variability will be determined. Inflammation in the upper and lower airways will also be determined. Key endpoints will be: cellular infiltration, chemokine/pro-inflammatory cytokines, cellular mediators, markers of allergic inflammation, systemic inflammatory changes in blood and exhaled breath, and heart rate variability.

This study will be a single-blind randomized crossover study of controlled exposure to concentrated ambient particles (CAP) and filtered air (FA) in 10 mild to moderate asthmatic GSTM1 null subjects, 10 asthmatic GSTM1 present, and 10 healthy GSTM1 present subjects. Using an established CAP exposure system, responses to exposure to filtered air and 200 ug/m<sup>3</sup> PM for two hours will be determined. GSTM1 is an important genetic marker of PM sensitivity resulting in the inability to make key antioxidant enzymes. The null condition has been found to confer sensitivity to PM as opposed to the normal condition of having the marker present. Another risk factor is the presence of an underlying inflammatory disease (asthma). Decreased heart rate variability has been indicated as a possible indicator or mechanistic link between pollutant exposure and cardiovascular morbidity and mortality. This project proposes to compare individuals with these two risk factors (asthma and GSTM1 null) with healthy individuals without the risk factors.

**Expected Results**

Measures of lung function, inflammatory respiratory responses, and heart rate variability of healthy and asthmatic volunteers as a result of controlled short-term exposures to ambient particulate matter will result. These results will indicate how sensitive individuals respond to short-term exposures to levels of PM encountered outdoors in certain situations, such as on highly polluted days or in areas of very high traffic. The results will also help elucidate the genetic versus disease factors of the sensitivity to air pollutant exposures.

**Significance to the Board**

In order to make effective standards or advisories for short-term PM, studies must be performed to address critical issues such as: what are the health effects observed; and how are PM concentrations and composition related to inflammation? There is at present only limited information to answer these questions. While it is unrealistic to expect any one study to provide all the answers, the proposed study will provide significant data in all these areas.

**Contractor:**

University of California, Los Angeles

**Contract Period:**

36 Months

**Principal Investigator (PI):**

Dr. David Diaz-Sanchez

**Contract Amount:**

\$629,920

**Basis for Indirect Cost Rate:**

The State and UC System have agreed to a ten percent indirect cost rate.

**Past Experience with this Principal Investigator:**

Although we have not worked with Dr. Diaz-Sanchez in the past, he is well respected and a recognized expert in the field with over 60 peer-reviewed publications.

We have worked with the Los Angeles Research Education Institute (LAREI) laboratory, a major subcontractor of this project, in the past on other projects, such as the Southern California Children's Health Study (CHS). The work done by LAREI has been reliable and responsive to our needs.

# BUDGET SUMMARY

University of California, Los Angeles

Differences in Inflammatory Responses to Exposures of Concentrated Ambient  
Particles in Susceptible Volunteers

## DIRECT COSTS AND BENEFITS

1.	Labor and Employee Fringe Benefits	\$ 191,419
2.	Subcontractors	\$ 274,949
3.	Equipment	\$ 15,000
4.	Travel and Subsistence	\$ 3,000
5.	Electronic Data Processing	\$ 0
6.	Reproduction/Publication	\$ 309
7.	Mail and Phone	\$ 0
8.	Supplies	\$ 10,509
9.	Analyses	\$ 69,654 <sup>1</sup>
10.	Miscellaneous	<u>\$ 18,050</u>

Total Direct Costs \$595,718

## INDIRECT COSTS

1.	Overhead	\$ 34,202
2.	General and Administrative Expenses	\$ 0
3.	Other Indirect Costs	\$ 0
4.	Fee or Profit	<u>\$ 0</u>

Total Indirect Costs \$34,202

TOTAL PROJECT COSTS \$629,920

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<sup>1</sup> Analyses

Particle characterization laboratory analyses	\$ 37,200
Heart rate variability measurement analyses	\$ 32,454

## SUBCONTRACTORS' BUDGET SUMMARY

Subcontractor: Los Amigos Research & Education Institute

Description of subcontractor's responsibility: Los Amigos Research Education Institute (LAREI) will recruit subjects and perform particulate exposures and lung function testing. LAREI and Dr. Diaz-Sanchez have collaborated extensively on inhalation exposure studies over the last 6 years. The facility at LAREI is unique in Southern California having access to CAP exposure systems as well as state-of-the-art lung function equipment.

### DIRECT COSTS AND BENEFITS

1.	Labor and Employee Fringe Benefits	\$ 181,672
2.	Subcontractors	\$ 0
3.	Equipment	\$ 0
4.	Travel and Subsistence	\$ 2,100
5.	Electronic Data Processing	\$ 255
6.	Reproduction/Publication	\$ 900
7.	Mail and Phone	\$ 1,200
8.	Supplies	\$ 19,200
9.	Analyses	\$ 0
10.	Miscellaneous	<u>\$ 33,846</u>

Total Direct Costs \$239,173

### INDIRECT COSTS

1.	Overhead	\$ 30,376
2.	General and Administrative Expenses	\$ 0
3.	Other Indirect Costs	\$ 0
4.	Fee or Profit	<u>\$ 0</u>

Total Indirect Costs \$30,376

**TOTAL PROJECT COSTS** **\$269,549**

Additional subcontract to a statistician for \$5,400 labor only