State of California
AIR RESOURCES BOARD

Resolution 04-9

March 25, 2004

Agenda Item No.: 04-3-2

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 2541-232, entitled "Effect of GSTM1 Genotype on Ozone-Induced Allergic Airway Inflammation," has been submitted by the University of California, San Francisco;

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 2541-232 entitled "Effect of GSTM1 Genotype on Ozone-Induced Allergic Airway Inflammation," submitted by the University of California, San Francisco, for a total amount not to exceed $497,990.

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 2541-232 entitled "Effect of GSTM1 Genotype on Ozone-Induced Allergic Airway Inflammation," submitted by the University of California, San Francisco, for a total amount not to exceed $497,990.

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 $497,990.

I hereby certify that the above is a true
And correct copy of Resolution 04-9, as
Adopted by the Air Resources Board.

Lori Andreoni, Clerk of the Board

ATTACHMENT A

"Effect of GSTM1 Genotype on Ozone-Induced Allergic Airway Inflammation"

Background

Epidemiological data suggest that asthmatics may be more sensitive to ozone than nonasthmatics. Animal studies provide evidence that ozone can enhance allergic inflammatory responses in the lungs. Controlled studies of the airway inflammatory responses of allergic asthmatics to ozone suggest that ozone enhances responses to inhaled allergen in some, but not all, allergic asthmatics. Data also indicate that genetic variability between individuals may explain the wide range of responsiveness to ozone exposure, in both healthy and asthmatic people. One particular gene, GSTM1, which codes for the antioxidant enzyme glutathione S-transferase, has been implicated as a candidate gene possibly influencing responsiveness to ozone.

Objective

The objective of this project is to determine whether ozone exposure enhances the specific lower airway inflammatory responses of allergic asthmatic subjects during late-phase reactions to inhaled allergen; and whether the GSTM1 null genotype is an important predictor of the susceptibility of asthmatic subjects to develop enhanced late-phase reactions to allergen challenge after ozone exposure.

Methods

This controlled human exposure study will investigate the effect of variants in a gene (GSTM1) in allergic asthmatics. This gene has been identified as involved in responses to ozone, and in mediating airway inflammation. Thirty well-characterized allergic asthmatic subjects will participate in exposures to filtered air (FA) and twice to 0.16 ppm ozone. The subjects will undergo allergen challenge after the FA and one ozone exposure, while the allergen challenge will occur before the second ozone exposure. Bronchoscopy with bronchoalveolar lavage will follow each of the exposures to assess airway inflammation. The subjects will be genotyped to ensure that 50% of the subjects have the GSTM1 null genotype. Exploratory genetic screening will also be done for several other genes that have been identified as candidates for involvement in mediating injury and repair processes in the airway tissues. The fluid recovered after bronchoalveolar lavage will be analyzed for inflammatory cells, and inflammatory proteins. Lung function will be monitored throughout the experimental periods.

Expected Results

This study will address gaps in the knowledge base on air pollution and human health, namely, what are the biological bases for the inconsistent responses reported among individual allergic asthmatics exposed to ozone. The study will also contribute to resolution of questions regarding the influence of genetic variants on responses to ozone.

Significance to the Board
The results of the study are critical to development of ambient air quality standards that are protective of allergic asthmatics. The results will fill in critical data gaps on the responses of asthmatics to ozone.

Contractor:
University of California, San Francisco

Contract Period:
42 months

Principal Investigator (PI):
Dr. Colin Solomon, Ph.D.

Contract Amount:
$497,990

Cofunding:
None

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:
Dr. Solomon has been the principal investigator on several previous contracts with ARB. The quality of his work is excellent. The results of his research have contributed to development of ambient air quality standards by addressing critical gaps in the scientific knowledge base on the health effects of ambient air pollutants.

Prior Research Division Funding to the University of California, San Francisco:

Year	2003	2002	2001
Funding	$0	$0	$0

B U D G E T S U M M A R Y

University of California, San Francisco

"Effect of GSTM1 Genotype on Ozone-Induced Allergic Airway Inflammation"

DIRECT COSTS AND BENEFITS				
1.	Labor and Employee Fringe Benefits	$	232,968	
2.	Subcontractors	$	66,183	
3.	Equipment	$	0	
4.	Travel and Subsistence	$	1,000	
5.	Electronic Data Processing	$	0	
6.	Reproduction/Publication	$	309	
7.	Mail and Phone	$	618	
8.	Supplies	$	46,054	
9.	Analyses	$	0	
10.	Miscellaneous	$	115,817[1]	
	Total Direct Costs			$462,949
INDIRECT COSTS				
1.	Overhead	$	35,041	
2.	General and Administrative Expenses	$	0	
3.	Other Indirect Costs	$	0	
4.	Fee or Profit	$	0	
	Total Indirect Costs			$35,041
TOTAL PROJECT COSTS				**$497,990**

[1] Publication Costs $3,091
Human Subjects Payment:
-Characterization 2,782
-Exposure 6,955
-Bronchoscopy 37,091
-Recovery Time 8,345
-Transport and Parking 2,782
Bronchoscopy Room Fees: 46,364
Sample Shipping 618
Shared Equipment Maintenance 7,789
TOTAL $115,817

Attachment 1

S U B C O N T R A C T O R S' B U D G E T S U M M A R Y

University of California, Berkeley

To explore effect of GSTM1 genotype on ozone-induced allergic airway inflammation we will employ a novel approach of preselecting of the volunteers based on their genotyping, to be exposed to ozone under controlled conditions of the chamber at the Lung Biology Center, UCSF.

DIRECT COSTS AND BENEFITS			
1.	Labor and Employee Fringe Benefits	$ 48,067	
2.	Subcontractors	$ 0	
3.	Equipment	$ 0	
4.	Travel and Subsistence	$ 3,600	
5.	Electronic Data Processing	$ 0	
6.	Reproduction/Publication	$ 0	
7.	Mail and Phone	$ 2,400	
8.	Supplies	$ 500	
9.	Analyses	$ 5,100	
10.	Miscellaneous	$ 500	
	Total Direct Costs		$ 60,167
INDIRECT COSTS			
1.	Overhead	$ 6,016	
2.	General and Administrative Expenses	$ 0	
3.	Other Indirect Costs	$ 0	
4.	Fee or Profit	$ 0	
	Total Indirect Costs		$6,016
TOTAL PROJECT COSTS			**$66,183**