State of California
AIR RESOURCES BOARD

RESEARCH PROPOSAL

Resolution 07-36

September 27, 2007

Agenda Item No.: 07-9-2

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 2633-257, entitled “Cardiopulmonary Health Effects: Toxicity of Semi-volatile and Non-Volatile Components of Ultrafine PM,” has been submitted by the University of California, Irvine;

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 2633-257, entitled “Cardiopulmonary Health Effects: Toxicity of Semi-volatile and Non-Volatile Components of Ultrafine PM,” submitted by the University of California, Irvine, for a total amount not to exceed $501,484.

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 2633-257, entitled “Cardiopulmonary Health Effects: Toxicity of Semi-volatile and Non-Volatile Components of Ultrafine PM,” submitted by the University of California, Irvine, for a total amount not to exceed $501,484.

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 $501,484.

I hereby certify that the above is a true and correct copy of Resolution 07-36, as adopted by the Air Resources Board.

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Lori Andreoni, Clerk of the Board

ATTACHMENT A

"Cardiopulmonary Health Effects: Toxicity of Semi-volatile and Non-Volatile Components of Ultrafine PM"

Background

Studies of mice exposed to fine and ultrafine particulate matter (PM) 50 meters from a freeway showed that these exposures had significant biological activity. The appearance of airway allergy biomarkers was associated with elemental and organic carbon fractions of the aerosol. When exposures were performed 150 meters downwind of the freeway the biological activity was greatly diminished and there were no measurable exposure-related effects (Kleinman et al., 2005). The reason for this change in toxicity is not known. The size and composition of the ultrafine particles undergo rapid changes at the same time that the toxicity is reduced with distance from roadways. However, if these changes are responsible for the changes in toxicity of the particles, the phenomenon cannot be effectively tested using collected samples because of the apparently short-lived duration of causal agents involved. The problem can be addressed with in-vivo inhalation studies.

Many of the organic chemical constituents of PM emitted from vehicles are semi-volatile, existing simultaneously in the gas and particle phases at equilibrium. Changes in ambient temperature and gas phase concentrations of these components can affect the measured particle size distributions due to evaporation or condensation and may also be dependent on the dilution ratios and dilution air conditions used during sampling.

Objective

The objective of this project is to determine how the toxicity of ultrafine particles depends on the semi-volatile and non-volatile fractions of PM emitted from vehicles and other sources.

Methods

Dr. Sioutas of the University of Southern California (USC) and colleagues have developed a thermal denuder coupled to a Versatile Aerosol Concentration Enrichment System (VACES). The thermal denuder heats the aerosol to a specified temperature to evaporate and remove volatile components, and then returns the aerosol to the original temperature. The VACES can increase the concentration of the processed aerosol by factors of 20 to 30 to provide adequate concentrations for performing acute in-vivo toxicology exposure studies. The investigators will use an in-vivo rodent exposure system in combination with the VACES-thermal denuder technology to separately study the cardiopulmonary effects of PM, before and after the removal of the semi-volatile components. The PM will be studied at sites scheduled for detailed chemical and physical characterization examination of PM emitted by specific sources by Dr. Sioutas and colleagues as part of the Southern California Particle Center research program.

Dr. Kleinman of the University of California, Irvine (UCI) will examine acute and chronic cardiopulmonary inflammation, vascular injury and myocardial function using genetically susceptible mice implanted with electrocardiogram telemetry devices to test the

hypothesis that exposure to ultrafine particles composed of semi-volatile compounds causes inflammation and oxidative stress resulting in pulmonary and cardiovascular injuries. Endpoints will include markers of inflammation, histological examinations for evidence of vascular and myocardial pathology, ventricular hypertrophy and biomarkers of lipid, protein and DNA oxidation. The in-vivo biological responses will be correlated with physical and chemical composition of the particles and the in-vitro potential of these particles to produce free radicals and induce cytotoxicity.

The rodent model will be the Apolipoprotein E -/- mouse which has already been established to be sensitive to the atherogenic effects of concentrated ambient particles and which has high levels of both low-density lipoproteins and high-density lipoproteins.

Expected Results
The expected results of this project are to improve the understanding of the mechanism of toxicity of freshly emitted combustion aerosols and to identify fractions of the aerosol causally related to health effects.

Significance to the Board
Understanding of the mechanism of toxicity of freshly emitted combustion aerosols and identifying fractions of the aerosol causally related to health effects will aid ARB in developing air quality regulations to better protect the health of California residents.

Contractor:
University of California, Irvine

Contract Period:
36 Months

Principal Investigators:
Michael T. Kleinman, Ph.D.
Constantinos Sioutas, Ph.D.

Contract Amount:
$501,484

Basis for Indirect Cost Rate:
The State and the UC system have agreed to a ten percent indirect cost rate.

Past Experience with this Principal Investigator:
Michael T. Kleinman is a Professor of Community and Environmental Medicine at UCI. He has been studying the health effects of exposures to environmental contaminants found in ambient air for more than 30 years. He holds a MS in Chemistry from the Polytechnic Institute of Brooklyn and a Ph.D. in Environmental Health Sciences from New York University. He is a Professor and Co-Director of the Air Pollution Health Effects Laboratory in the Department of Community and Environmental Medicine at UCI. He has published more than 90 articles in peer-reviewed journals dealing with the uptake and dosimetry of inhaled pollutants in humans and laboratory animals. Constantinos Sioutas, ScD, is currently the Fred Champion Professor of Civil and

Environmental Engineering at USC. He is also the Co-Director of the Southern California Particle Center and Supersite. Dr. Sioutas received his Doctor of Science degree in Environmental Science and Engineering at Harvard University, School of Public Health, in 1994. Dr. Sioutas' research focuses on developing technologies for measuring the physico-chemical characteristics of air pollutants and determining their toxic properties. Since 1993, Dr. Sioutas has authored over 150 peer-reviewed publications, and holds 14 U.S. patents in development of aerosol instrumentation.

Prior Research Division Funding to UCI:

Year	2007	2006	2004
Funding	$0	$104,027	$450,446

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

University of California, Irvine

Cardiopulmonary Health Effects Toxicity of Semi-Volatile and Non-Volatile Components of Ultrafine PM

DIRECT COSTS AND BENEFITS			
1.	Labor and Employee Fringe Benefits	$ 137,048	
2.	Subcontractors	$ 231,760	
3.	Equipment	$ 15,500	
4.	Travel and Subsistence	$ 8,960	
5.	Electronic Data Processing	$ 0	
6.	Reproduction/Publication	$ 0	
7.	Mail and Phone	$ 0	
8.	Supplies	$ 62,952[1]	
9.	Analyses	$ 0	
10.	Miscellaneous	$ 19,880	
	Total Direct Costs		$476,100
INDIRECT COSTS			
1.	Overhead	$ 25,384	
2.	General and Administrative Expenses	$ 0	
3.	Other Indirect Costs	$ 0	
4.	Fee or Profit	$ 0	
	Total Indirect Costs		$25,384
TOTAL PROJECT COSTS			**$501,484**

[1] Genetically modified and ID-chipped mice will be purchased from Jackson Labs at a cost of $95 (shipping included). A total of 108 mice will be purchased in Years 1 and 2. Jackson Labs will surgically install transponders in 20 mice per year at a cost of $127/mouse. Having the mice implanted by the supplier allows us to have them shipped directly to the USC vivarium and will avoid an unacceptable quarantine period which would be triggered if the mice were implanted at UCI. There will be 5 histological or immunohistochemical evaluations for 36 mice per exposure study at a cost of $25 per evaluation to determine injury patterns in heart, lung and artery samples. Protein array assay materials and supplies will be purchased from Linco for assays of cytokines and acute phase proteins in sera and tissue homogenates.

Attachment B

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

Subcontractor: University of Southern California

Description of subcontractor's responsibility: Dr. Sioutas of USC will act as co-PI on this project and will coordinate field exposure activities between the USC and UCI staff. USC will operate the particle concentrators / thermal denuders and will collect filter and bioassay samples for analyses of PM composition and toxicology studies. USC will analyze filter samples, and under Dr. Sioutas' supervision provide atmospheres of PM with and without vapor phase components for mouse exposures.

	DIRECT COSTS AND BENEFITS		
1.	Labor and Employee Fringe Benefits	$ 159,747	
2.	Subcontractors	$ 0	
3.	Equipment	$ 0	
4.	Travel and Subsistence	$ 0	
5.	Electronic Data Processing	$ 0	
6.	Reproduction/Publication	$ 0	
7.	Mail and Phone	$ 0	
8.	Supplies	$ 0	
9.	Analyses	$ 0	
10.	Miscellaneous	$ 24,089	
	Total Direct Costs		$183,836
	INDIRECT COSTS		
1.	Overhead	$ 47,924	
2.	General and Administrative Expenses	$ 0	
3.	Other Indirect Costs	$ 0	
4.	Fee or Profit	$ 0	
	Total Indirect Costs		$47,924
	TOTAL PROJECT COSTS		**$231,760**