State of California
AIR RESOURCES BOARD

Women's Cardiovascular Risk from Particulate Matter Exposure

RESEARCH PROPOSAL

Resolution 15-13

May 21, 2015

Agenda Item No.: 15-4-1

WHEREAS, the Air Resources Board (ARB or 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 2784-282, titled "Women's Cardiovascular Risk from Particulate Matter Exposure," has been submitted by the University of California, Irvine, for a total amount not to exceed $599,129;

WHEREAS, the Research Division staff has reviewed Proposal Number 2784-282 and finds that in accordance with Health and Safety Code section 39701, research is needed to identify additional risk factors which may influence susceptibility to the adverse health effects associated with exposure to particulate matter (PM). The results are expected to help the Board understand why epidemiological studies have found a greater risk of cardiovascular mortality for women than men, which would suggest that women's cardiovascular health be included as an important risk factor in the next PM air quality standards review; and

WHEREAS, in accordance with Health and Safety Code section 39705, the Research Screening Committee has reviewed and recommends funding the Research Proposal.

NOW, THEREFORE BE IT RESOLVED that the Air Resources Board, pursuant to the authority granted by Health and Safety Code section 39700 through 39705, hereby accepts the recommendations of the Research Screening Committee and staff and approves the Research Proposal.

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 Proposal as further described in Attachment A, in an amount not to exceed $599,129.

I hereby certify that the above is a true and correct copy of Resolution 15-13 as adopted by the Air Resources Board.

Tracy Jensen

Tracy Jensen, Clerk of the Board

ATTACHMENT A

"Women's Cardiovascular Risk from Particulate Matter Exposure"

Background
Several epidemiological studies have found a greater risk for premature death from exposure to particulate matter (PM) for older women when compared to men. These studies include the California Teachers Cohort Study, the Women's Health Initiative, the Nurses' Health Study, and the Adventist Health Air Pollution Study. Statistically, heart attacks are more deadly and disabling for women than for men; 38 percent of women die within one year of their first heart attack, compared with 25 percent of men. These and other published studies suggest that women have a greater relative risk of PM-mediated cardiovascular death than men. However, animal studies designed to shed light on the mechanism of toxicity for PM are mostly conducted on male animals, which may have inherently different sensitivities to PM compared to female animals. Results from this study will be among the first to help researchers answer this question and, more importantly, may provide insight into the higher relative risks of PM-mediated cardiovascular death in women. In addition, this study may elucidate which possible physiological factors may make females more sensitive to PM-mediated cardiovascular toxicity.

Objective
This study will investigate the mechanisms of PM2.5 cardiovascular toxicity occurring in females using a rodent model. This project will test the hypothesis that the cardiovascular effects of PM exposure observed in women are due to changes in the estrogen production secreted by the ovaries.

Methods
The experiments will be conducted in a rodent model that has been established in previous studies as suitable for investigating PM-mediated cardiovascular diseases. A subset of the female rodents will be chosen to investigate possible changes in physiology due to aging, such as loss of ovarian function which may affect PM2.5-mediated effects. The experiments will consist of groups of male, female and ovariectomized female mice who are deficient for the Apolipoprotein E (ApoE) protein, which increases their susceptibility for atherosclerosis. The group of ovariectomized female mice will be further subdivided between those who receive replacement hormone therapy and those who do not. All test groups and appropriate control groups will be exposed to concentrated PM2.5 or filtered air for four months and later evaluated for evidence of cardiovascular disease by measuring heart rate variability, atherosclerotic plaque development, and changes in ovarian function.

Expected Results
The results are expected to confirm the hypothesis that female mice have higher levels of biomarkers for cardiovascular disease than male mice when exposed to concentrated PM. In addition, this study will attempt to validate the hypothesis that these results are due to an estrogen-producing ovarian system compromised after PM exposure.

Significance to the Board
The work proposed for this project is in line with ARB's mission to "Base Decisions on Best Possible Scientific and Economic Information." It would identify additional risk factors which would need to be taken into account when evaluating the impacts of exposure to PM. The results are expected to help the Board understand why epidemiological studies have found a greater risk of cardiovascular mortality for women than men, which would suggest that women's cardiovascular health be included as an important risk factor in the next air quality standards review.

Contractor:
University of California, Irvine

Contract Period:
36 months

Principal Investigator (PI):
Michael T. Kleinman, Ph.D.

Contract Amount:
$599,129

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:
Dr. Kleinman is a Professor of Occupational and Environmental Health and the Co-Director of the Air Pollution Health Effects Laboratory in the Department of Medicine at University of California with more than 30 years of experience in laboratory and field studies of environmental contaminants and their effects on health. He has published more than 100 peer-reviewed articles dealing with environmental contaminants and their effects on cardiopulmonary and immunological systems. In addition, over the past 30 years he has been the primary investigator on 12 research projects funded by ARB.

Prior Research Division Funding to the University of California, Irvine:

Year	2014	2013	2012
Funding	$ 0	$ 740,429	$ 519,997

BUDGET SUMMARY

Contractor: University of California, Irvine

Women's Cardiovascular Risk from Particulate Matter Exposure

DIRECT COSTS AND BENEFITS			
1.	Labor and Employee Fringe Benefits	$ 387,384	
2.	Subcontractors	$ 0	
3.	Equipment	$ 0	
4.	Travel and Subsistence	$ 2,794	
5.	Electronic Data Processing	$ 0	
6.	Reproduction/Publication	$ 1,000	
7.	Mail and Phone	$ 1,000	
8.	Supplies	$ 123,320[1]	
9.	Analyses	$ 15,500[2]	
10.	Miscellaneous	$ 13,665[3]	
	Total Direct Costs		$ 544,663
INDIRECT COSTS			
1.	Overhead	$ 54,466	
2.	General and Administrative Expenses	$ 0	
3.	Other Indirect Costs	$ 0	
4.	Fee or Profit	$ 0	
	Total Indirect Costs		$ 54,466
TOTAL PROJECT COSTS			**$ 599,129**

[1] Supply costs include purchasing mice ($25,920), their ECG implants ($37,200) for about 50 percent of the total amount. The supplies relating to preparation of the histology slides also has a high cost of $19,200. Remaining consumable supplies are $41,000.

[2] Integrated air filter samples for detailed chemical characterization; 65 @ $200 per sample ($13,000). Shared instrumentation costs for Aerosol Mass Spectrometer ($2,500)

[3] Animal housing, husbandry and cage washing ($9,915); equipment maintenance and services ($3,750)