HEI HEALTH EFFECTS INSTITUTE

update

WINTER 2012–2013

Review of Ultrafine Particles Examines Wide Range of Health Studies

A new HEI report, *Understanding the Health Effects of Ambient Ultrafine Particles,* concludes that while there have been a growing number of laboratory and field studies of the effects of ultrafine particles (UFPs), the evidence to date has "not provided consistent findings on the effects of exposures to ambient levels of UFPs, particularly in human populations."

After reviewing more than 300 toxicologic studies in animals, controlled human exposure studies, and epidemiologic studies, an HEI expert panel concluded in the report: "The current evidence does not support a conclusion that exposures to UFPs alone can account in substantial ways for the adverse effects that have been associated with other ambient pollutants such as $PM_{2.5}$ [particulate matter ≤ 2.5 µm in aerodynamic diameter]."

"There is extensive evidence today that the complex mix of fine airborne particulate matter known as $PM_{2.5}$ can contribute to a variety of cardiovascular, respiratory, and other health effects," said HEI President Dan Greenbaum. "But despite a large number of studies of the smallest particles (or particles less than 0.1 microns in size), our expert panel found that the evidence to date has not confirmed the hypothesis of some in the scientific community that these ultrafine particles are the principal reason for these broader $PM_{2.5}$ health effects."

Particulate matter emissions are a complex mixture, containing particles of a variety of sizes and composition, and there have been continuing questions from the scientific and policy communities about whether some components or characteristics of that mixture, or particles from some sources, are more toxic and deserving of priority efforts for control. Ultrafine

Continued on page 3

Victorian "Painted Ladies" border San Francisco's Alamo Square Park.
SAN FRANCISCO TRAVEL ASSOCIATION PHOTO BY CAROL SIMOWITZ

Timely Topics, Great City Highlight HEI Annual Conference

This spring HEI will host its Annual Conference from April 14 through 16 at the Palace Hotel in San Francisco, California's beautiful "City by the Bay." Each day's presentations will highlight the most significant new research findings on air pollution and health. Technical sessions include the following:

Beyond $PM_{2.5}$ Mass: What Have We Learned? Reductions in ambient levels of particulate matter (PM) mass continue to be the major focus of regulatory discussions in the United States, Europe, and Asia. Considerable resources

Continued on page 5

Also in This Issue

NEW HEI RESEARCH REPORT

Air Quality Gains During 2008 Beijing Olympics Improve Cardiovascular Responses

The city of Beijing has some of the worst air pollution in the world. In the run-up to the 2008 Olympic and Paralympic Games held there, the Chinese government launched a series of policies to reduce local and regional emissions in the greater Beijing metropolitan area. These aggressive but temporary controls on air pollution from vehicular traffic and industrial sources were intended to result in a short-term but dramatic decline in air pollution levels during the Games.

Volunteers for the study were primarily medical residents who worked at Peking University First Hospital.
PHOTO BY JUNFENG ZHANG

As part of its Health Outcomes Research program, HEI funded a study to evaluate the impact of changes in air pollution levels before, during, and after the Games on cardiopulmonary responses in a group mainly composed of healthy medical residents living close to the hospital in which they worked in Beijing. The results appear in the soon-to-be-published HEI Research Report 174, *Cardiorespiratory Biomarker Responses in Healthy Young Adults to Drastic Air Quality Changes Surrounding the 2008 Beijing Olympics*. The team was led by Junfeng (Jim) Zhang, then of the University of Medicine and Dentistry of New Jersey–Environmental and Occupational Health Sciences Institute in Piscataway, and currently of the University of Southern California in Los Angeles.

The main hypothesis of Zhang and colleagues was that levels of cardiovascular biomarkers — end points in physiologic pathways considered to be associated with the adverse effects of particulate matter (PM) — would change during the Olympics when air pollution levels would be reduced and that these changes would reflect improvements in health effects. They also proposed that the biomarkers would revert to pre-Olympic levels following relaxation of the air pollution controls after the Games.

Each day the investigators measured the concentrations of multiple pollutant gases and of PM and its components; nearly all measurements were made at one site in the center of Beijing, at the hospital where the 125 young subjects (ages 19–33) worked. The investigators also evaluated several cardiovascular biomarkers in the subjects at each of six clinical visits — two before, two during, and two after the Games.

The key findings were that during the Olympics, concentrations of all measured pollutants decreased as compared with their pre-Olympics levels, except ozone (which increased). The largest decreases (40–60%) were found for the pollutant gases sulfur dioxide, carbon monoxide, and nitrogen dioxide, but particulate pollutants — $PM_{2.5}$ (PM with an aerodynamic diameter of 2.5 μm

Continued on page 3

NEW HEI RESEARCH REPORT

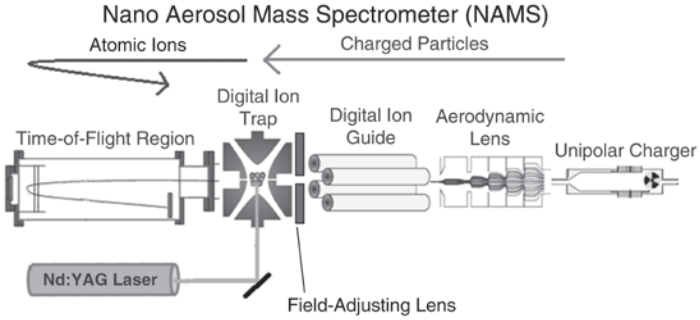
Innovative Tool Helps Identify Nanoparticles from Motor Vehicles

HEI will soon publish Research Report 173, *Selective Detection and Characterization of Nanoparticles from Motor Vehicles,* by Murray V. Johnston of the University of Delaware and colleagues.

The investigators studied the composition of individual nanometer-size particles, approximately 30 nm in diameter, near a major roadway intersection in Wilmington, Delaware, using an experimental monitoring instrument they developed: the nano aerosol mass spectrometer (NAMS). Nanoparticles, also known as ultrafine particles, have been of particular interest to health scientists; some have hypothesized that these tiny airborne particles may be more toxic than larger particles because of their physical characteristics and composition (see related article on the recent publication HEI Perspectives 3: *Understanding the Health Effects of Ambient Ultrafine Particles*).

Previous research has identified motor vehicle traffic as an important source of nanoparticles in urban areas. However, little is known about the formation, growth, and change in composition of particles near roadways. In earlier work, Johnston and colleagues developed the NAMS to study individual nanoparticles and analyze their composition continuously. For the current study, they focused on nanoparticles near a major roadway intersection in order to test and refine the instrument's performance in a real-world setting; additionally, they wanted to assess whether the instrument could aid in identifying the contribution of motor vehicles emissions to ambient nanoparticle concentrations in the vicinity of the intersection.

In its independent evaluation of the study, the HEI Health Review Committee wrote that the investigators had demonstrated that the NAMS is a useful new tool for quantifying the major components of nanoparticles with a high time resolution, an important feature for measuring traffic-related nanoparticles. Although the NAMS is a complex instrument that still requires additional refinement, the committee believes the research team showed that the NAMS could be used in conjunction with other currently available instruments, including particle counters, as well as with traffic cameras and meteorologic data, to assess the contribution of local traffic and various types of vehicles to short-term spikes in nanoparticle concentrations near intersections. The Review Committee commented that the study could both advance the refinement of nanoparticle-speciation monitors and demonstrate their usefulness for apportioning the contributions of different types of vehicles to nanoparticle concentrations in a near-roadway environment.



Schematic drawing of the nano aerosol mass spectrometer, showing the main components and the particle and ion path through the instrument. (From HEI Research Report 173.)

Research Report 173 will soon be available for downloading, free of charge, at *http://pubs.healtheffects.org;* printed copies can be purchased from HEI. For more information, contact Katherine Walker (*kwalker@healtheffects.org*).

ULTRAFINE PARTICLES *(Continued from page 1)*

particles — which are emitted from a variety of sources including traffic, industry, and cooking — have gained special attention because of their potential for traveling deeper into the lungs, bloodstream, and brain. They are important as well because a number of regulatory actions in Europe and the United States have required new filters on diesel engines to reduce UFP emissions, while at the same time fuel economy rules are encouraging the use of more fuel-efficient gasoline engines that may increase UFP emissions.

The report — the latest in a series of HEI Perspectives that attempt to provide broader insights from HEI's research — was prepared by an expert panel formed by HEI, led by Mark Frampton (University of Rochester and member of the HEI Review Committee), and composed of six multidisciplinary scientific experts (see sidebar). At HEI, Senior Scientist Katherine Walker led the project and several other staff members contributed. The team reviewed more than 300 studies and syntheses of data to arrive at its conclusions, and its report was further peer-reviewed by 10 outside experts who had not participated in the review's preparation.

The panel found that despite the substantial number of studies completed to date by HEI and other research institutions, challenges and limitations remain. "The fact that the current database of experimental and epidemiologic studies does not support strong and consistent conclusions about the independent effects of UFPs on human health does not mean that such effects, as one part of the broader effects attributable to $PM_{2.5}$, can be entirely ruled out," said Mark Frampton, chair of the panel. "There are limitations in the evidence base, including deficiencies in exposure data, and numerous challenges in comparing and synthesizing results of existing studies."

Overall, the panel's major findings can be summarized as follows:

- Motor vehicles, especially diesel engines, have been important sources of the UFPs to which humans are exposed, but motor vehicle emissions are likely to change substantially in the years ahead.
- UFPs clearly differ from larger particles in their lung deposition, lung clearance, and potential for translocation to other parts of the body.
- Experimental and epidemiologic studies provide suggestive, but not consistent evidence of adverse effects of short-term exposure to ambient UFPs.
- Currently, there is no strong evidence that effects of short-term exposure to UFPs are dramatically different from effects of exposure to larger PM; information on long-term exposure is not available. HEI

HEI Perspectives 3 can be downloaded free of charge from *http://pubs.healtheffects.org*. For more information, contact Katherine Walker (*kwalker@healtheffects.org*).

HEI Review Panel on Ultrafine Particles

Mark Frampton (panel chair) *University of Rochester, New York, and HEI Review Committee*

Michael Brauer *University of British Columbia, Vancouver, Canada, and HEI Review Committee*

Michael Kleeman *University of California–Davis*

Wolfgang Kreyling *Helmholtz Institute, Neuherberg, Germany*

Leonidas Ntziachristos *Aristotle University, Thessaloniki, Greece*

Stefanie Ebelt Sarnat *Emory University, Atlanta, Georgia*

OLYMPICS *(Continued from page 2)*

or less) and its components elemental carbon and ultrafine particles — also dropped substantially. As for health findings, levels of several cardiovascular markers in the study subjects declined during the Olympics. Large percentage decreases were observed in multiple markers of airway inflammation, oxidative stress, and coagulation. After the Olympics, when the special controls on emissions were lifted, the observed concentrations of most pollutants were higher than the levels observed during the Games.

In its independent review, the HEI Health Review Committee considered the study an important contribution to the literature regarding short-term interventions and their impacts on acute health responses. It is one of the first studies, and to date the most comprehensive, to evaluate changes in biologic end points associated with the control measures taken to reduce air pollution during the 2008 Beijing Olympics. The committee agreed with Zhang and colleagues that the changes observed in several cardiovascular biomarkers during the Olympics were generally consistent with the investigators' hypothesis that they would find changes reflecting a decrease in adverse effects.

The committee pointed out two important limitations of these observations. First, the relationship between the short-term changes observed in this study and their long-term consequences in terms of disease or other adverse outcomes is not known. Second, these observations were made in young, healthy subjects and so may not reflect changes that might be seen in susceptible populations, such as those with preexisting cardiorespiratory conditions (e.g., asthma or cardiovascular disease). The committee also recognized that the study was not designed to identify whether the changes in effects per se were directly attributable to the air pollution controls imposed by the government interventions.

Overall, the committee found that the study by Zhang and colleagues provides important supporting evidence that air quality interventions can improve health-related biomarkers, with the potential for beneficial health effects. HEI

Research Report 174 will soon be available for downloading, free of charge, at *http://pubs.healtheffects.org*; printed copies can be purchased from HEI. For more information, contact Geoffrey Sunshine (*gsunshine@healtheffects.org*).

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Daniel S. Greenbaum, *President*

HEI is a nonprofit organization funded jointly by government and industry to research and evaluate the health effects of air pollution. An overview of HEI, information on its current research program, and a list of published HEI Research Reports are available on request or from the Web site.

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Benchmark Study Finds Ambient Air Pollution Among Top Global Health Risks

A new systematic analysis of all major global health risks — from factors such as smoking, diet, and environment — has found that ambient air pollution in the form of fine particles is a more significant public health risk than previously known. According to the study, factors such as smoking and nutrition pose the highest global risks, but $PM_{2.5}$ (particulate matter ≤ 2.5 µm in aerodynamic diameter) is now considered to be among the top 10 global risk factors, contributing to 3.2 million premature deaths worldwide and 74 million years of healthy life lost in 2010. Approximately two-thirds of those deaths are estimated to have occurred in the developing countries of Asia.

The analysis — the 2010 Global Burden of Disease (GBD 2010) — was published in December in a special issue of the leading British medical journal *The Lancet* (*www.thelancet.com/themed/global-burden-of-disease*). It applies consistent methods to the largest global database ever assembled to estimate premature mortality and years of healthy life lost from a wide variety of risks: smoking, diet, alcohol, HIV-AIDS, household and outdoor air pollution, and many other factors. Its extensive analysis was subjected to detailed peer review to ensure the highest quality of analysis, and a consistent approach was used across all risk factors to ensure that they could be assessed using the comparable techniques.

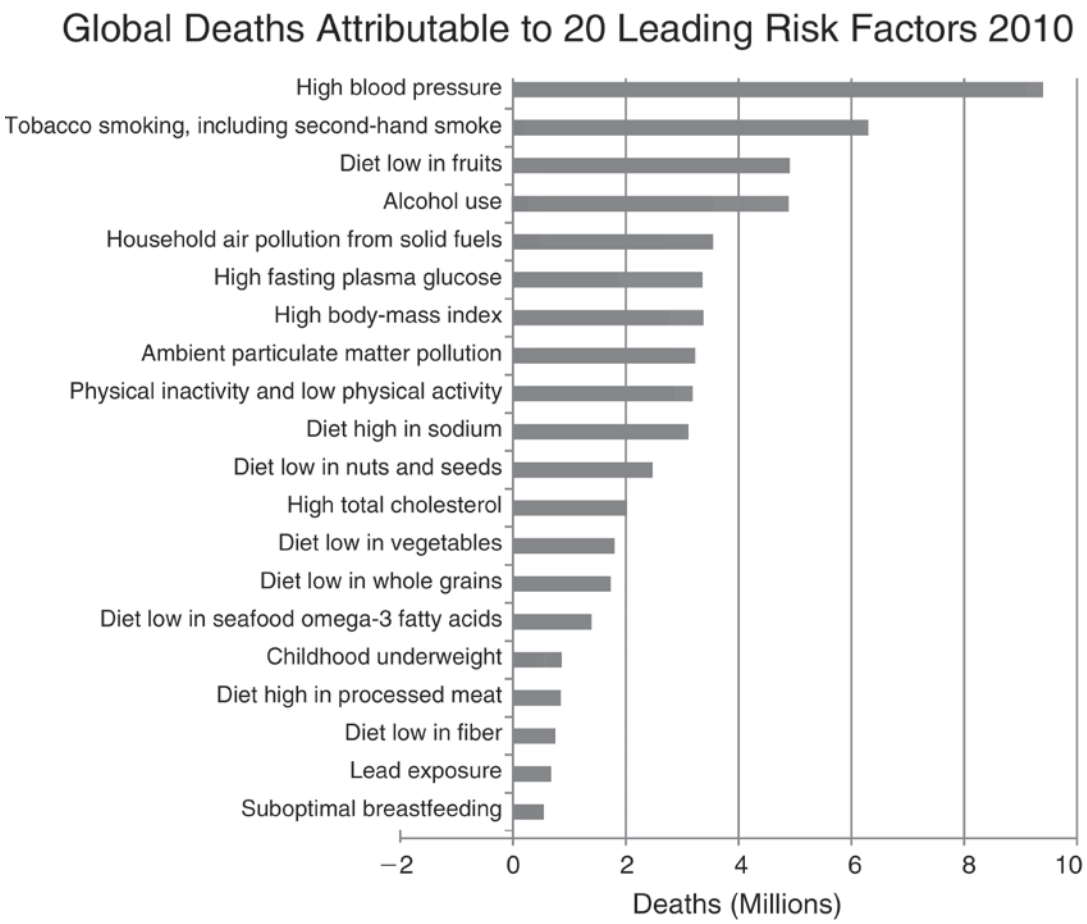
For the first time, ambient air pollution ranks among the top four or six risks in the developing countries of Asia. Together with household air pollution from the burning of solid fuels, as in coal stoves, it is responsible for a substantial burden of disease in low- and middle-income countries. *The Lancet* reports that the study's findings "suggest that a large burden of disease in many parts of the world is attributable to particulate matter pollution, which is substantially higher than estimated in previous analyses."

GBD 2010 was produced by a rigorous, peer-reviewed scientific process involving more than 450 global experts and led by the Institute of Health Metrics and Evaluation at the University of Washington in Seattle, along with four partner institutions: the World Health Organization, the University of Queensland, Australia, Johns Hopkins University, and Harvard University. The ambient air pollution analyses were conducted by an international team led by Aaron Cohen, HEI principal scientist, and H. Ross Anderson of St. Georges, University of London.

Earlier GBD assessments had reported smaller air pollution–related burdens of disease. Air pollution's increased importance in this 2010 update results from two major factors. First, compared with the previous estimates, new global estimates of particulate air pollution exposure in both urban and rural areas, based on ground-level measurements and satellite remote sensing and global chemical-transport models, were better able to capture the full extent of global population exposure. Second, a new detailed analysis of the relationship between outdoor levels of air pollution and effects on mortality and illness — based on the latest health effects research — resulted in increased estimates of effects for each incremental increase in pollution.

Because exposure to air pollution affects cardiovascular disease and other leading causes of disease and death worldwide, the global burden of disease linked to air pollution is substantial. "There is a wide range of risks that affect global health," said Robert O'Keefe, HEI vice president. "However, this analysis places air pollution among the top risk factors in the world today — with the greatest impacts among people in the developing countries of Asia." HEI has organized workshops in February in Delhi and in March in Beijing to bring these new results to the attention of the Indian and Chinese public health and policy communities.

Further information on GBD 2010 is available at *www.healthmetricsandevaluation.org/gbd.* For further information on the ambient air pollution analysis, contact Aaron Cohen (*acohen@healtheffects.org*).



SOURCE: INSTITUTE OF HEALTH METRICS AND EVALUATION

have been invested in research to identify the components, sources, or specific PM size fractions whose control would most effectively protect public health. This session will present major contributions of HEI's National Particle Component Toxicity (NPACT) initiative and similar European research programs. A panel will then lead a discussion of what the findings suggest for future research avenues and air quality regulation.

From Particle Exposure to Cardiovascular Effects: How Well Do We Understand the Mechanisms? This session will review current evidence for the different mechanisms by which cardiovascular effects may occur after humans are exposed to PM. Speakers will discuss the challenges in interpreting results of studies in animals and humans and examine how the gaps in our current knowledge point to possible future research directions.

HEI Update This session will focus on the progress of HEI's research and review programs and publications. Highlights will include the institute's ongoing work on ozone and health outcomes, HEI's review of ultrafine particles (see related story), and plans for new research on near-road exposure assessment and other areas. HEI will also introduce the recipient of the 2012 Walter A. Rosenblith New Investigator Award.

Beijing to Long Beach: Measuring the Effectiveness of Air Quality Actions Many research projects have evaluated the effectiveness of actions undertaken at the local and national level in an attempt to improve air quality and, consequently, public health. A number of actions focused on reducing traffic congestion, but having the potential to simultaneously reduce air pollution, have also been evaluated. This session will look at studies of the Chinese government–mandated curbs on emissions during the Beijing Olympic Games, low-emissions zones in Europe and the United States, and other traffic measures now in place in many European locations, as well as plans to evaluate upcoming regulations to reduce sulfur and mercury emissions from coal-fired power plants in the eastern United States.

The Golden Gate Bridge spans 1.7 miles across the San Francisco Bay.
SAN FRANCISCO TRAVEL ASSOCIATION PHOTO BY JACK HOLLINGSWORTH

The Future of Studies of Long-Term Exposure to Air Pollution Over the past 20 years, prospective cohort studies have identified important associations between long-term exposure to air pollution and mortality from chronic disease. Their findings currently provide the basis for estimating the public health impact in the United States and internationally. Research in this area continues to evolve in response to the limitations of data and methods and the need to address new scientific questions. This session will highlight new approaches to study design, methods for exposure assessment, and ways to evaluate the incidence of chronic disease that offer promise for future research on long-term exposure.

The Evolution of Diesel Engines: Progress and Remaining Questions In the past decade, diesel engine technology has undergone major changes to meet increasingly strict emissions standards. In this session the speakers will discuss regulations and approaches to reducing emissions of diesel engine exhaust, present results of emissions and health testing of new-technology heavy-duty diesel engines (the Advanced Collaborative Emissions Studies, or ACES), and introduce HEI's upcoming reevaluation of the diesel epidemiology literature.

Program updates and hotel registration information are available at *www.healtheffects.org/annual.htm*.

Science Workshop in Brussels to Inform European Union Policies

At the end of January, HEI co-organized a workshop titled "Understanding the Health Effects of Air Pollution: Recent Advances to Inform EU Policies" at the European Commission (EC) headquarters in Brussels, Belgium. In attendance were 200 representatives of European public authorities responsible for air policy development, adoption, or implementation and members of the broader stakeholder and research communities.

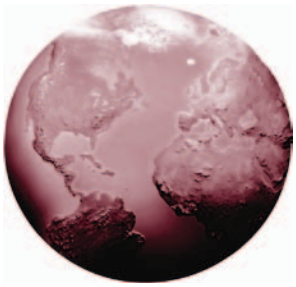
The EC has declared 2013 the "Year of Air" to focus on the importance of clean air for all people and to call for action to improve air quality across the European Union (EU). Last year the EC, in partnership with the World Health Organization (WHO) Regional Office for Europe, began reviewing the latest health-science research on major air pollutants — such as particulate matter, ground-level ozone, and nitrogen dioxide — as an important step in evaluating whether to update Europe's air quality policies.

The overall goal of the workshop — organized by the EC's Directorates-General for Environment and for Research and Innovation, the WHO Regional Office for Europe, and HEI — was to inform regulatory and other policy decisions concerning air quality and its significance for public health. Presentations highlighted current scientific findings from Europe and the United States, including results of recent HEI studies, and literature reviews by the WHO Regional Office for Europe, the Directorate-General for Research and Innovation, and others. Important questions that were addressed included the following:

- What are the latest findings on the health effects of air pollution — in particular, what evidence is there for adverse effects on cardiovascular and respiratory health?
- Is there a concentration below which no adverse health effects of the major pollutants are expected to occur?
- Can we identify specific sizes, sources, or constituents of particulate matter — such as traffic, black carbon, fine and ultrafine particles, and diesel exhaust — that are most strongly associated with adverse health effects?

Participants also summarized how science has advanced our understanding of air pollution's impact on health and what uncertainties remain and identified significant areas for further research.

To view the workshop program and presentations, visit *www.healtheffects.org/Workshops/Brussels2013/brussels2013-agenda.htm*.



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ACES Emissions Testing and Animal Exposures Now Complete

Emissions testing and animal exposures have been completed in the Advanced Collaborative Emission Study (ACES), the most comprehensive study ever undertaken to characterize the emissions and health effects of new-technology diesel engines. Data analysis is now progressing full steam ahead, and some preliminary results will be presented in April at HEI's Annual Conference in San Francisco. This work will set the stage for the first systematic comparison of emissions and health results from the testing of new and older diesel technology.

During Phase 2, which ended in December, investigators characterized emissions from three 2010-compliant heavy-duty engines from participating manufacturers Cummins, Detroit Diesel, and Volvo, under the oversight of the nonprofit Coordinating Research Council (CRC) and its panel of experts. These engines are designed to meet strict federal standards for emission of nitrogen oxides that went into effect in 2010, in addition to meeting the very stringent standards for particulate matter emissions mandated in 2007. The results of the engine characterization will be published in mid-2013 after review by CRC and its panel.

Phase 3B involved lifetime inhalation exposure of rats to exhaust from a 2007-compliant heavy-duty diesel engine at the Lovelace Respiratory Research Institute (LRRI) in Albuquerque, New Mexico. In December, the female rats completed the planned 30 months of exposure. The exposures of male rats were stopped in October, after 28 months, because of their lower survival rate — which was not unexpected. All animals will undergo detailed histopathologic analyses of several organs and tissues, as was done in previous diesel bioassays, with a focus on investigating whether tumors developed. After the results undergo a quality-control review by a Pathology Working Group, appointed by HEI and led by Gary Boorman of Covance, in North Carolina, the final report from LRRI is expected to be submitted to HEI in mid-2013. To ensure the highest quality, the report will then be reviewed by the HEI ACES Special Review Panel and a detailed Commentary will be prepared.

HEI expects to publish the Phase 3B report containing chronic results in the spring of 2014. Included will be two reports from LRRI on health end points and detailed exposure characterization during the inhalation exposures, as well as three reports from the ACES ancillary studies led by Jeffrey Bemis, Daniel Conklin, and Lance Hallberg. (HEI Research Report 166, published in September 2012, contains results of 1- and 3-month subchronic exposures, as well as some 12-month results.) HEI