

## COMMUNICATING THE SCIENCE

### Greenbaum Highlights HEI Accountability Studies at Air Pollution Control Agency Meeting

**H**EI President Dan Greenbaum helped open the spring meeting of the Association of Air Pollution Control Agencies (AAPCA) held in Tucson, Arizona, by presenting in a topical session on “New Developments in Risk Science and Causality.” AAPCA is an organization representing some 40 state and local air pollution control agencies and working to assist them in implementing the Clean Air Act; staff from these agencies meet twice each year to discuss technical issues and exchange information with each other and with the U.S. Environmental Protection Agency (EPA).

At the opening session, Greenbaum addressed how the HEI [Accountability Research Program](#) — which is designed to test whether air quality regulations and other actions have the benefits for air pollution reduction and health improvement that were intended — can help test the cause-and-effect relationships between air pollution and health. He described the results of HEI studies stemming from traffic controls employed during the 1996 Olympics held in Atlanta, Georgia, and bans on the sale of coal for home heating in Ireland, as well as studies on the effects of mobile and other control measures taken in Los Angeles, and preliminary results of a comprehensive look at air quality programs in the Atlanta region. He joined a panel that also included Louis

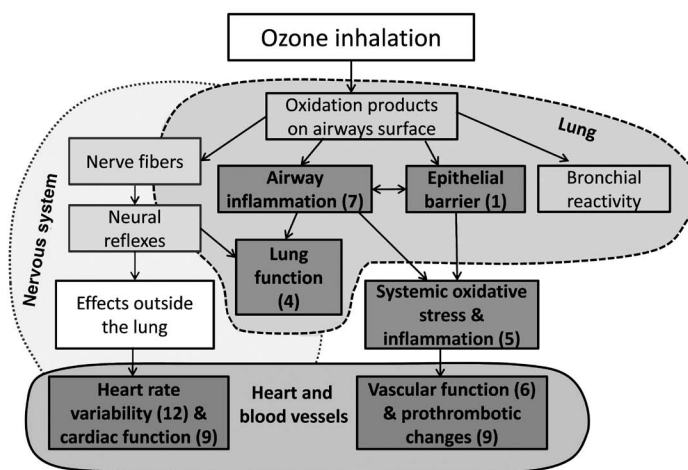
*Continued on page 5*

## NEW HEI RESEARCH REPORT

### HEI to Publish Major Multicenter Ozone Study in Older Subjects

**T**he Multicenter Ozone Study in oldEr Subjects (MOSES) investigated whether short-term exposure to ambient levels of ozone in a controlled exposure setting induces short-term cardiovascular responses in healthy older volunteers. Preliminary results were presented at the 2016 HEI Annual Conference, and the final results are about to be published in HEI Research Report 192, together with a Commentary from the HEI MOSES Review Panel. Briefly, the study of healthy older volunteers exposed to low levels of ozone showed that there were moderate changes in lung function and some markers of lung inflammation and injury after exposure to 70 parts per billion (ppb) ozone (the current National Ambient Air Quality Standard) or to 120 ppb ozone, but there were no changes in a large suite of cardiovascular outcomes.

*Continued on page 2*



Possible pathways by which ozone may cause adverse health effects. Pathways evaluated in MOSES are shown in **boldface**; the number of endpoints evaluated is shown in brackets. (Adapted from Research Report 192, Figure 1.)

## Also in This Issue

Call for Preliminary Applications .....	2
HEI's Annual Strategic Planning Session with Sponsors .....	3
NEW HEI RESEARCH REPORT Air Pollution and Dementia in Older Women .....	3
HEI in the News .....	4
Search for Next Research Committee Chair .....	6

Exposure to ozone has been associated with adverse health outcomes in children and adults. Its effects on the respiratory system are well established and include worsening of asthma (acute effects) and increases in acute deaths and hospital admissions for respiratory illnesses such as chronic obstructive pulmonary disease and asthma (chronic effects). However, the effects of ozone on the cardiovascular system are not as well known, though recent studies have suggested that exposure to ozone may be associated with adverse cardiovascular outcomes, including increased mortality. At the same time, it has been suggested that ozone may lead to adverse health effects at concentrations at or below the current ambient air quality standard. Thus, the HEI Research Committee determined that research was needed to investigate ozone's cardiovascular effects, particularly at low ambient concentrations.

MOSES was funded in 2010 under HEI Request for Applications 10-1, *Cardiovascular Effects of Exposure to Low Levels of Ozone in the Presence or Absence of Other Ambient Pollutants*, which solicited responses from clinical research centers that were equipped to safely conduct human exposure studies, with the goal of creating a multicenter ozone study. After reviewing the applications, HEI selected three centers, led by John Balmes at the University of California–San Francisco, Philip Bromberg at the University of North Carolina–Chapel Hill, and Mark Frampton at the University of Rochester Medical Center. In addition, the New England Research Institute was selected through a 2010 *Request for Qualifications for a Data Analysis Center* to serve as the data coordinating center for the study. HEI formed a special MOSES Oversight Committee to provide guidance during the study design and research phases and also established a Data Monitoring Board.

The MOSES project focused on older participants, who may be more susceptible to the effects of air pollutants. Researchers at the three clinical centers, with input from the HEI Oversight Committee, developed a common protocol for exposing human volunteers to ozone and for analyzing the data. Each center planned to recruit and test approximately 30 participants between the ages of 55 and 70; the final count was 87, and the average age was about 60 years. The subjects participated in a screening visit, a training visit, and three exposure sessions (randomized for 0, 70, and 120 ppb ozone exposures). Exposures lasted 3 hours, during which the participants exercised on a stationary bicycle, alternating 15 minutes of exercise with 15 minutes of rest. Participants stayed at a hotel the night before testing to minimize exposure to ambient air pollutants, and were followed the day before, during, and up to 22 hours after exposure.

The investigator teams measured a large suite of endpoints, including changes in heart rhythm and related parameters, pulmonary function, and markers of endothelial function, thrombosis, lung injury, and both systemic and lung inflammation. Many analyses were done at designated central laboratories that handled recordings or samples from all three clinical centers in order to standardize the analyses of biological markers. Study participants were also genotyped for glutathione S-transferase mu 1 (GSTM1), a gene involved in antioxidant defenses. Individuals who lack the GSTM1 gene are hypothesized to be at increased risk for acute health effects. A statistical analysis plan was developed and power calculation performed with input from the three clinical centers and the Oversight Committee.

Ozone exposure in these older, healthy adults did not affect the primary cardiovascular endpoints identified by the

investigators. The MOSES project did find moderate effects on lung function and on two markers of lung injury and inflammation in these healthy, older adults (a population that had not often been studied in the past), which is consistent with the results of earlier studies in younger adults showing ozone effects on the lung at concentrations similar to the air quality standard. The results were not affected by age, sex, or GSTM1 status. The MOSES Review Panel agreed with the main findings of the study and commended the investigator teams for the high quality of the data and analyses. They noted the absence of cardiovascular effects, although they suggested it is possible that ozone exposure may lead to cardiovascular effects in more susceptible individuals, or may do so when other pollutants are present.

Although the participants stayed overnight in a hotel to reduce exposure to ambient air pollutants during the night before exposure, it remains unclear whether prior exposure to air pollutants during the period leading up to the exposure visits may have had an effect on the baseline values of the health outcomes of interest or on the final results. To investigate this question, the investigators collected personal samples of ozone and nitrogen dioxide during 3 days leading up to the exposures. They also collected data from air pollution monitors located near the clinical centers. A forthcoming report will describe additional analyses of the MOSES data set that include these prior-exposure pollutant data, as well as several sets of sensitivity analyses conducted by the investigators. [H]

HEI Research Report 192 will soon be available for downloading, free of charge, at [www.healtheffects.org/publications](http://www.healtheffects.org/publications). For more information, contact Maria Costantini ([mcostantini@healtheffects.org](mailto:mcostantini@healtheffects.org)) or Annemoon van Erp ([avanerp@healtheffects.org](mailto:avanerp@healtheffects.org)).

## HEI Issues Open Call for Preliminary Applications

HEI has issued Request for Applications (RFA) 17-2, *Health Effects of Air Pollution*, which solicits small research projects on air pollution and health. The RFA provides an application mechanism for investigators whose area of interest falls outside the topics targeted in the current major research requests. RFA 17-2 requests preliminary applications for small, innovative studies on air pollution and health that are relevant to HEI's current priorities as outlined in the *HEI Strategic Plan for Understanding the Health Effects of Air Pollution, 2015–2020*.

HEI encourages interested applicants to submit preliminary applications for projects of up to two-and-a-half years in duration. The HEI Research Committee will generally not consider studies of longer duration. The funding cap for each study will be \$400,000 (total budget), and HEI expects to fund two studies from this RFA. Preliminary applications are due on July 1, 2017. The Research Committee will invite a subset of these applicants to submit a full application, which will be due on December 15, 2017. For more information, please see our [Funding Opportunities](http://www.healtheffects.org/research/funding) page, [www.healtheffects.org/research/funding](http://www.healtheffects.org/research/funding). [H]

## HEI's Annual Strategic Planning Session with Sponsors

HEI's sponsors and Research Committee gathered in Boston on March 6. This yearly meeting provides an opportunity for the sponsors to hear an update on HEI's activities, and for the Committee to hear directly from the sponsors about priority topics HEI should be addressing.

PHOTOS BY MELISSA OSTROW



From left: Tim Wallington, Ford; Kaoru Horie, Honda; and David Foster, HEI Research Committee. In background is Bruce Copley of ExxonMobil.



Susan Collet, Toyota.



Stacey Katz, U.S. Environmental Protection Agency.



HEI Vice President Robert O'Keefe.



HEI President Dan Greenbaum (left) and Howard Feldman, American Petroleum Institute.

### NEW HEI RESEARCH REPORT

## Air Pollution and Dementia in Older Women

Dementia is relatively common in elderly people. Because there is no cure, there has been much interest in identifying risk factors, such as exposure to air pollution (among many other possibilities). To examine whether air pollution might be involved, HEI funded a study that will soon be published as Research Report 193, *Particulate Air Pollutants, Brain Structure, and Neurocognitive Disorders in Older Women*. In this study, Jiu-Chiuan Chen of the University of Southern California, a recipient of HEI's Walter A. Rosenblith New Investigator Award, and colleagues examined possible associations between long-term exposure to ambient particulate air pollution and neurocognitive outcomes (mild cognitive impairment and dementia) and between exposure and changes in brain volumes.


Chen used data from almost 7,500 women, ages 65–80, enrolled in the U.S.-based Women's Health Initiative Memory Study. Exposure to ambient particulate matter (PM) was estimated at their residential addresses using a nationwide spatiotemporal model; diesel PM was assessed at census level. The period covered by the study was 1996–2007.

The investigators observed that exposure to neither ambient PM<sub>2.5</sub> nor diesel PM was associated with mild cognitive impairment or dementia in the women. Some positive and negative associations were reported between particulate air pollution and brain volumes,

but their clinical significance remains unclear and the findings differ from previous research.

In its independent review of the study, the HEI Review Committee commended Chen and colleagues for conducting a novel study, one of the few to evaluate a potential relationship between long-term exposure to ambient particulate air pollution and neurocognitive outcomes and brain volumes. A high-quality neurocognitive outcome assessment, the inclusion of brain imaging data, and the availability of detailed individual-level covariate information were strengths of the study. On the other hand, the Committee had less confidence in the results for diesel PM than for ambient PM<sub>2.5</sub> because the exposure assessment was based on a screening tool that the Committee considered to be less suitable for epidemiological studies and that was prone to substantial measurement error. Also, the Committee questioned the emphasis on statistically unadjusted findings in the report and thought the investigators could have taken additional steps to increase consistency in the analyses and reporting and to further explore the potential for selection bias.

The Committee noted that the number of air pollution studies on dementia-related outcomes remains small and that evidence from the current study, along with previous results, provides impetus for further research — particularly in light of an aging world population.

HEI Research Report 193 will soon be available for downloading, free of charge, at [www.healtheffects.org/publications](http://www.healtheffects.org/publications). For more information, contact Hanna Boogaard ([jboogaard@healtheffects.org](mailto:jboogaard@healtheffects.org)). 

### Health Effects Institute

75 Federal Street, Suite 1400  
Boston, MA 02110-1817, USA  
Phone: +1-617-488-2300  
Fax: +1-617-488-2335  
[www.healtheffects.org](http://www.healtheffects.org)

Richard F. Celeste, *Chair, Board of Directors*  
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 all published HEI reports are available for downloading, free of charge, from the website.

#### Production Staff for *Update*:

Hilary Selby Polk, *Managing Editor*  
Hope Green, *Editor*  
Annemoon M.M. van Erp, *Webmaster*  
Ruth E. Shaw, *Cameographics, Layout and Composition*

### SIGN UP: HEI NEWSLETTER ONLINE

To sign up for e-mail delivery of *Update*, go to "Newsletter Sign-up" at the bottom of our home page, [www.healtheffects.org](http://www.healtheffects.org).



## HEI in the News

### Major Media Cite *State of Global Air* Data on Population Effects

With its data showing that air pollution is the leading environmental cause of health burden worldwide, the *State of Global Air 2017* inaugural annual report and website, released by HEI this past winter, quickly captured headlines in numerous leading news outlets.

State of Global Air is a collaborative project of HEI and the Institute for Health Metrics and Evaluation at the University of Washington–Seattle, with additional expertise from the University of British Columbia, Canada. The project's [interactive website](http://www.stateofglobalair.org) ([www.stateofglobalair.org](http://www.stateofglobalair.org)) was launched February 13 along with its [annual report](http://www.stateofglobalair.org/report) ([www.stateofglobalair.org/report](http://www.stateofglobalair.org/report)). Both provide global and country-level data on air quality and its potential impact on human health, and the health and air pollution data are available for downloading free of charge for all users. Here is a sampling of the media coverage the report received:

“You’re More Likely to Die from Air Pollution in India than China, Study Says” (*Washington Post*, February 14, 2017)

“India Reported 1.1 Million Deaths Due to Air Pollution in 2015, Says a Global Study” (*Times of India*, February 14, 2017)

“Air Pollution Around the World Takes a Staggering Toll” (editorial, *Washington Post*, March 5, 2017)

“India’s Air Pollution Rivals China’s as World’s Deadliest” (*New York Times*, February 14, 2017)

“India Air Pollution Deaths Poised to Exceed China’s” (*Financial Times*, February 14, 2017)

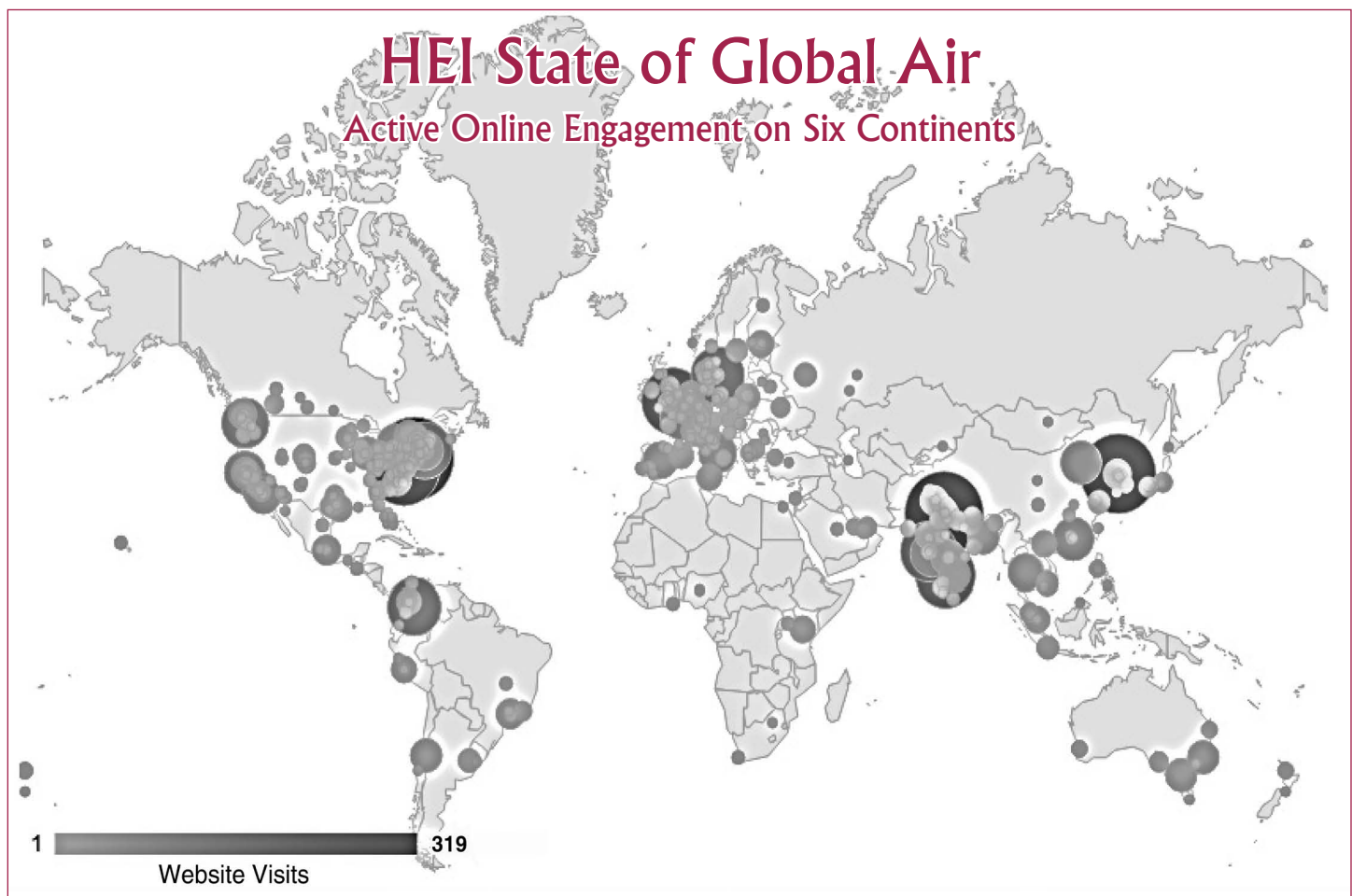
“China, India Account for Half World’s Pollution Deaths in 2015: Study” (Reuters, February 14, 2017)

“The Foul Air We Breathe” (editorial, *The Hindu*, February 16, 2017)

“Our Polluted Planet” (editorial, *The Lancet*, February 25, 2017)

“India’s Air Rivals China’s as Deadliest in the World, Says Study” (*Hindustan Times*, February 15, 2017)

Data from *State of Global Air 2017* also were cited in numerous Chinese news outlets. [\[HEI\]](#)



During the first 2 months after its launch, the State of Global Air website received more than 11,000 visits from users around the world. Larger, darker circles denote cities with higher user activity.

Anthony (Tony) Cox, Jr. of Cox Associates and the University of Colorado, who is editor of the journal *Risk Analysis*; Roger McClellan, advisor, Toxicology and Human Health Risk Analysis, and former chair of EPA's Clean Air Scientific Advisory Committee; and Steven C. Packham, Utah Division of Air Quality.

Presentation slides from the AAPCA meeting are available for viewing at [www.csg.org/aapca\\_site/events/2017SpringMeetingPresentations.aspx](http://www.csg.org/aapca_site/events/2017SpringMeetingPresentations.aspx). For more information, please feel free to contact Dan Greenbaum ([dgreenbaum@healtheffects.org](mailto:dgreenbaum@healtheffects.org)).

## HEI Briefs Key Legislators on Accountability Research Program

In May, accountability was again in focus when HEI President Dan Greenbaum and Vice President Bob O'Keefe, accompanied by Director of Science Rashid Shaikh, were invited to brief Lamar Smith (R-Texas), chairman of the House of Representatives Committee on Science, Space, and Technology — along with other members of the committee and its staff — on HEI's [Accountability Research Program](#). The briefing, entitled "Holding Regulations Accountable: Do Air Quality Actions Accomplish Predicted Benefits?" reviewed the basic principles of the "Chain of Accountability" that HEI first described in 2003 as part of Communication 11, [Assessing Health Impact of Air Quality Regulations: Concepts and Methods for Accountability Research](#). Greenbaum and O'Keefe then highlighted several studies that HEI has funded of short- and longer-term air quality actions in Atlanta, Georgia; Dublin, Ireland; and Southern California.

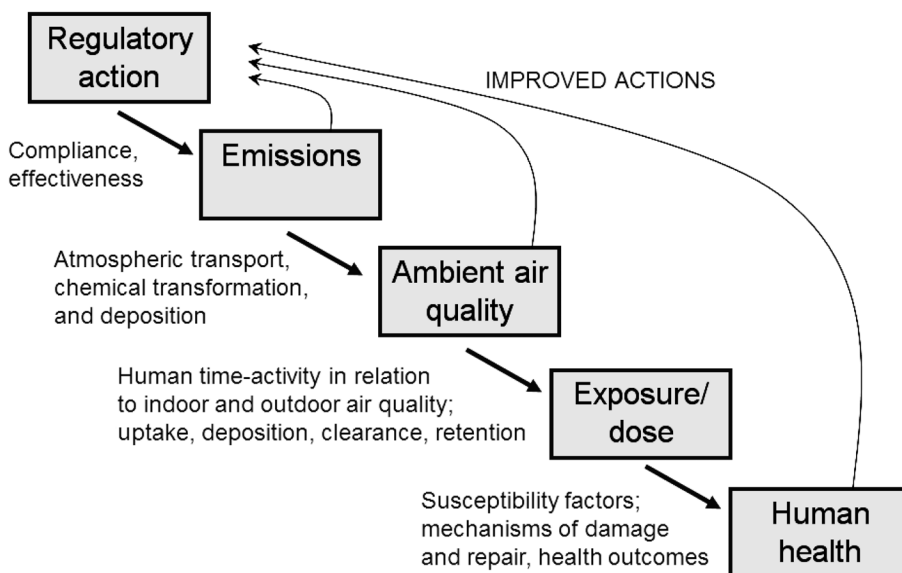
The committee chair and members asked a number of probing questions — regarding the findings of health effects such as exacerbation of asthma, the strength of different models used in air quality analyses, and the potential usefulness for more such studies after each governmental rule is implemented. Following the briefing, Greenbaum, O'Keefe, and Shaikh discussed in detail with committee and member staff the next steps in HEI's accountability research, as well as a range of broader air pollution and health research issues, such as the role of toxicology and human exposure studies, statistical methods, and more.

For more information about the briefing or HEI's Accountability Research Program contact Dan Greenbaum ([dgreenbaum@healtheffects.org](mailto:dgreenbaum@healtheffects.org)), or Bob O'Keefe ([rokeefe@healtheffects.org](mailto:rokeefe@healtheffects.org)), or visit [www.healtheffects.org/accountability](http://www.healtheffects.org/accountability).

## Shaikh Describes Strategies, Methods at Coordinating Research Council Workshop

In February, accountability was the topic of a session co-organized by Rashid Shaikh, HEI Director of Science, and Howard Feldman, of the American Petroleum Institute, at the [8th Coordinating Research Council Mobile Source Air Toxics Workshop](#), held in Sacramento, California. Shaikh gave a talk titled "Accountability Research: Pitfalls and Opportunities," in which he highlighted

## Chain of Accountability



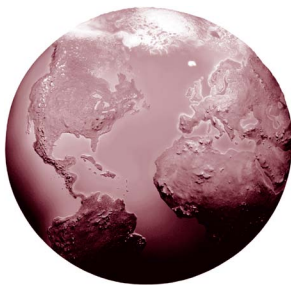
HEI diagram showing relationship of regulatory action and health effects of air pollution.

the variety of strategies, approaches, and methods useful in accountability research and some challenges that such studies encounter. Other speakers during the session were Rob Harley and Jason Su, both from the University of California–Berkeley; Lucas Henneman, Georgia Institute of Technology; and Jim Gauderman, University of Southern California.

## HEI Contributes to Discussions on Unconventional Oil and Gas Development

As HEI initiates its new [Energy Research Program](#), which focuses on the potential for population exposure and health effects from unconventional oil and natural gas development, the program's director, Donna Vorhees, has been contributing to regional and national discussions. Two recent examples:

- "Roundtable on Technical Innovation, Policy, and Shale Gas Development," conducted on March 29 as part of Carnegie Mellon University's Energy Week 2017. The two primary objectives for the Roundtable were to (1) identify technological innovations related to shale gas development and barriers to their implementation and (2) identify policies to counter these barriers.
- "Aspen Institute Dialogue Series on Shale Production and Governance," a three-meeting, nonpartisan policy dialogue that convenes 25 individuals from the regulatory community, industry, academia, and nongovernmental organizations to examine shale governance approaches and make recommendations to better anticipate and address potential environmental risks. The first two meetings were held in the fall of 2016 and winter of this year; a third took place in early June. [HEI](#)




## Health Effects Institute

75 Federal Street, Suite 1400  
Boston, MA 02110-1817

## HEI Seeks Nominations for Next Chair of Research Committee

**T**he HEI Board of Directors is seeking help in identifying candidates for the position of chair of the HEI Research Committee. David Eaton (University of Washington–Seattle) will step down as the chair next summer, when his eight-year term expires.

The Research Committee helps HEI in identifying critical research areas, planning HEI's research program, selecting the best projects, and overseeing ongoing research. The chair leads a group of 8 to 10 scientists with expertise and insights into the various aspects of HEI-sponsored research, interacts with sponsors, and collaborates with staff. HEI is looking for a scientist holding a Ph.D. or M.D. who is a thought-leader in the health research community and has some experience with the use of scientific information in policy making processes. He or she should be a consensus builder who can help lead HEI as it continues its tradition of excellent research of the highest scientific integrity on air pollution, health, and emerging fuels and technologies — both in the national and international contexts.

Please send your nominations to Rashid Shaikh ([rshaikh@health-effects.org](mailto:rshaikh@health-effects.org)) and, if possible, include the curriculum vitae of your nominee(s). 

Mark Your Calendar!  
HEI Annual Conference  
2018  
April 29–May 1  
Chicago, Illinois