

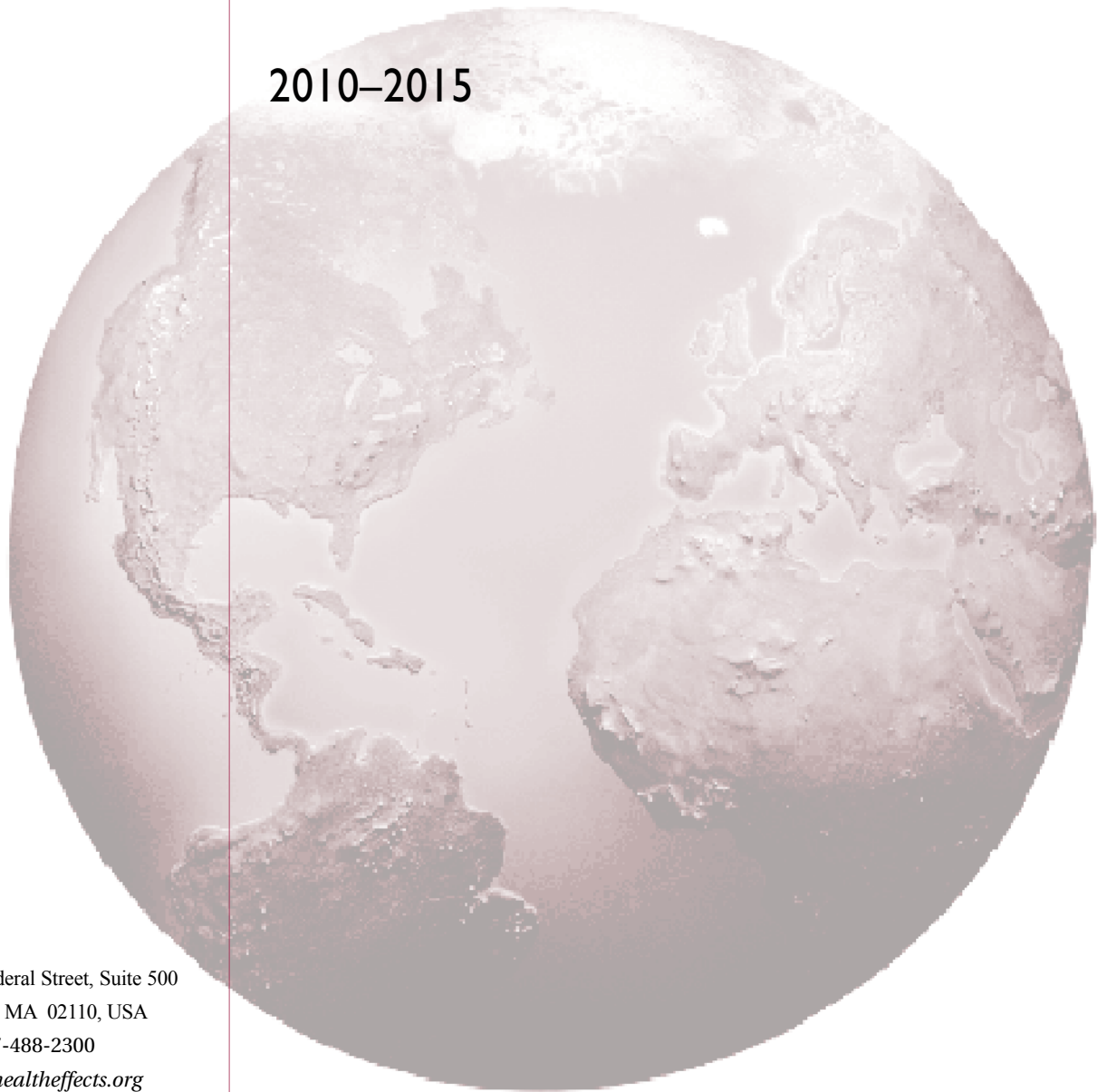


HEALTH
EFFECTS
INSTITUTE

April 2010

HEI STRATEGIC PLAN
FOR UNDERSTANDING THE HEALTH
EFFECTS OF AIR POLLUTION

2010–2015



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HEI Strategic Plan for
Understanding the
Health Effects of Air Pollution
2010–2015

Health Effects Institute
Boston, Massachusetts

Trusted Science • Cleaner Air • Better Health

Publishing history: The Web version of this document was posted at www.healtheffects.org in April 2010.

Citation for whole document:

Health Effects Institute. April 2010. HEI Strategic Plan for Understanding the Health Effects of Air Pollution 2010–2015. Health Effects Institute, Boston, MA.

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ABOUT HEI

The Health Effects Institute is a nonprofit corporation chartered in 1980 as an independent research organization to provide high-quality, impartial, and relevant science on the effects of air pollution on health. To accomplish its mission, the institute

- Identifies the highest-priority areas for health effects research;
- Competitively funds and oversees research projects;
- Provides intensive independent review of HEI-supported studies and related research;
- Integrates HEI's research results with those of other institutions into broader evaluations; and
- Communicates the results of HEI research and analyses to public and private decision makers.

HEI receives half of its core funds from the U.S. Environmental Protection Agency and half from the worldwide motor vehicle industry. Frequently, other public and private organizations in the United States and around the world also support major projects or certain research programs. HEI has funded more than 280 research projects in North America, Europe, Asia, and Latin America, the results of which have informed decisions regarding carbon monoxide, air toxics, nitrogen oxides, diesel exhaust, ozone, particulate matter, and other pollutants. These results have appeared in the peer-reviewed literature and in more than 200 comprehensive reports published by HEI.

HEI's independent Board of Directors consists of leaders in science and policy who are committed to fostering the public-private partnership that is central to the organization. The Health Research Committee solicits input from HEI sponsors and other stakeholders and works with scientific staff to develop a Five-Year Strategic Plan, select research projects for funding, and oversee their conduct. The Health Review Committee, which has no role in selecting or overseeing studies, works with staff to evaluate and interpret the results of funded studies and related research.

All project results and accompanying comments by the Health Review Committee are widely disseminated through HEI's Web site (www.healtheffects.org), printed reports, newsletters and other publications, annual conferences, and presentations to legislative bodies and public agencies.

Dear Colleague:

We are pleased to provide you with this copy of the *HEI Strategic Plan for Understanding the Health Effects of Air Pollution 2010–2015*. We have made great progress in our quest to provide trusted science to inform public and private decisions about cleaning the air we breathe, but there is still much to do.

After extensive consultation with sponsors and many others, we found that two messages came through clearly in the comments HEI received: that we must view our efforts increasingly in a multipollutant context (since exposures are rarely to any one pollutant) and that we must place our efforts increasingly at the nexus of air quality and climate change.

To that end, the *HEI Strategic Plan 2010–2015* is a comprehensive final Plan that charts an innovative, responsive course for the next five years with an important *principal overarching theme*:

HEI will work, through all of its major programs, to **develop and apply next-generation multipollutant approaches** to understanding exposure to and health effects of air pollutants. This is critical to understanding whether there might be joint or synergistic effects of multiple exposures to particulate matter (PM), gases, and air toxics, but equally important to ensuring that, in our efforts to identify the effects of any one pollutant, we don't underestimate other pollutants that may be of equal or greater importance. HEI will pursue these approaches both for traditional air pollutants and at the nexus of air quality and climate.

HEI sees this theme integrated throughout four core program elements:

- *Multipollutant Exposure, Epidemiology, and Toxicology Research* — the completion of the National Particle Component Toxicity (NPACT) initiative studies, and new initiatives on PM/ozone effects, air toxics exposure, traffic, climate-related air pollutants, ultrafine particles, and others;
- *Emerging Fuels and Technologies* — completing the Advanced Collaborative Emissions Study (ACES) and targeted assessments of emerging climate- and air-quality-driven fuels and technologies identified by our Special Committee on Emerging Technologies;
- *The Health Impact of Air Pollution Actions (Accountability)* — targeted new studies of longer- and shorter-term air quality actions; and
- *An International Perspective* — continued attention to global opportunities to conduct science that is relevant to the developed world, and selected further efforts in Asia and the Americas.

We also expect to pursue important cross-cutting issues in all of our efforts, including the effects of air pollution in *sensitive populations* (e.g., the elderly and those of lower socioeconomic status); *innovation* in statistics, new toxicology, and related areas; and a continued focus on HEI's leading role in *validation* of whether existing and new biologic techniques and statistical analyses well represent actual exposures and health effects.

We are grateful to many for their ideas and active involvement in the development of this Strategic Plan: to HEI's sponsors and other stakeholders, to our Health Research and Review Committees, and to our staff. With your help and the continued interest of our sponsors, we look forward to the coming years of accomplishment as we refine and focus our efforts to answer key questions of air pollution and health with timely and relevant science.

Sincerely,



Richard F. Celeste
Chair



Daniel S. Greenbaum
President

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HEI Strategic Plan for Understanding the Health Effects of Air Pollution 2010–2015

THE HEALTH EFFECTS INSTITUTE

The Health Effects Institute is an independent nonprofit corporation chartered to “conduct . . . and to evaluate research and testing related to the health effects of emissions from motor vehicles, and other environmental pollutants, and to provide the results to the public and interested governmental agencies.” Since 1980, HEI has provided high-quality science on the health effects of a broad range of mobile-source and other air pollutants.

This Strategic Plan describes the proposed HEI research program and review activities for the study of the health effects of air pollution for the period of 2010 through 2015. We have attempted to identify and anticipate the major questions on the health effects of pollutants and new technologies likely to be facing policy makers and manufacturers of vehicles and fuels. In its May 2009 Draft Strategic Plan 2010–2015, HEI considered a wide range of choices for its activities in the coming years. Based on a review of these possibilities by sponsors and others, HEI revised the Draft Plan into an integrated set of strategies designed to guide HEI in developing detailed annual research and review plans that will deliver research results on the potential health effects of greatest concern in a timely manner.

MISSION AND GOALS

HEI’s mission is to provide public and private decision makers with independent, impartial, timely, and high-quality science on the health effects of emissions from motor vehicles, fuels, and other sources of environmental pollution. HEI accomplishes its mission by seeking to achieve six principal goals:

- To identify the areas of highest priority for health effects research that target pollutants and issues of greatest concern and respond to the rapidly changing public and technologic environment.
- To fund and oversee the conduct of high-quality research in the priority areas, fostering whenever possible integrated and multi-institute efforts.

- To conduct, as needed, intensive reanalyses of studies, data sets, and methods that are at the center of important policy decisions.
- To provide independent review of HEI-supported research and reanalysis that evaluates, summarizes, and enhances the understanding and credibility of the results.
- To integrate HEI’s research results with those of other institutions into coherent, broader evaluations of the health effects of a pollutant, fuel, or technology.
- To communicate the results of HEI research and analyses to public and private decision makers and the scientific community in an understandable and timely manner.

CONSTITUENTS

HEI’s success depends on cooperation, coordination, and communication among its many constituents. These include the sponsors; the scientific community from which we draw investigators, Research and Review Committee members, expert panel members, and reviewers; and a broad range of external stakeholders across all levels of government, environmental public interest groups, and other nongovernmental organizations.

HEI’s Board of Directors, President, and Senior Staff consult periodically with sponsors, consider and respond to their diverse priorities, and then set the goals of the Institute and oversee its work. The Board, President, and Senior Staff also take into consideration the views of others in the public and private sectors who have an interest in environmental and health issues and who are important audiences for the results of HEI’s work. Without broad stakeholder acceptance of the quality and independence of HEI’s work, the effectiveness and impact of the Institute would be reduced.

HEI’s sponsors provide recommendations to HEI about research priorities on the basis of their projections of research needs associated with regulatory activities, changes in the use of technologies and fuels, and new scientific information that raises concerns. In addition, HEI encourages scientists and others in government, industry, and environmental and health organizations to provide input about priorities for HEI research and to participate in

its activities. HEI believes that the contributions of diverse sponsors and other stakeholders, both in the United States and internationally, will result in a Strategic Plan that is comprehensive and broadly relevant and that stands the best chance of accurately anticipating the emerging questions in science and regulation.

The HEI Research and Review Committees select, oversee, and evaluate the scientific activities of the Institute. The committees are multidisciplinary in nature and are composed of distinguished scientists who are knowledgeable about scientific issues related to the study of the health effects of air pollution. The Research Committee and the Institute's scientific staff develop and oversee HEI's research program. The Review Committee, which has no role in selecting or overseeing the studies, works with other scientific staff members to evaluate and interpret each study. (See Table 1 for a more detailed description of the research and review processes.) The Institute's scientific staff are highly qualified and actively engaged in all scientific activities. Other Institute staff members provide expertise in administration, finance, and scientific publishing. The scientists at universities and research organizations who carry out HEI's selected studies are essential to the quality of HEI's research program and its broad content and diverse approaches. HEI, through the use of highly competitive national and international selection processes, has attracted an expanding community of scientists who develop new collaborations and fresh approaches to the problems of air pollution and public health. Ultimately, the public, whose health is to be protected by standards and decisions based in part on studies funded and reviewed by HEI, is perhaps the most important constituent for HEI, its sponsors, and other stakeholders.

FUNDING

Current Status and Trends

HEI's core budget has been \$7.5 million per year for the last 10 years.* Over the five-year period of the 2005–2010 Plan, HEI spent approximately 82% of its total budget on its research program and 18% on administrative expenses (a level of administrative expense well below most scientific institutions). The core of HEI's annual budget is funded jointly by the U.S. Environmental Protection Agency (EPA[†]) and worldwide manufacturers and marketers of motor vehicles and engines that do business in the United States. The motor vehicle industry's share is contributed by 28 U.S.,

Asian, and European companies in order to maintain compliance with key vehicle-certification provisions of the U.S. Clean Air Act; each company's contribution to HEI is proportional to its vehicle and engine sales in the United States.

HEI has worked extensively to further leverage its core support, attracting supplemental funding for its ongoing research programs, such as the National Particle Component Toxicity (NPACT) initiative, and special scientific projects, such as the Review of the Health Impacts of Mobile-Source Air Toxics, the Advanced Collaborative Emissions Study (ACES), and the Public Health and Air Pollution in Asia (PAPA) program. HEI has found that the economies of scale it can achieve at higher funding levels through such leveraging allow a growing proportion of its funds to be directed to extramural research while still maintaining appropriate levels of research planning, quality assurance, and review, and a more broadly relevant program.

To support these leveraged efforts, the Institute has over the last decade received support from a variety of public and private sponsors. *On the government side*, these include the European Commission; the U.S. Department of Energy (DOE) and Federal Highway Administration (FHWA); and the California Air Resources Board (CARB). *On the industry side*, these include the American Petroleum Institute; the European oil industry (CONCAWE); individual oil companies; steel, pulp, and paper companies; utilities; and emission control companies. HEI's current international activities in Asia have received substantial additional support from the U.S. Agency for International Development, the Asian Development Bank, and the William and Flora Hewlett Foundation.

This additional support has allowed HEI to increase the size of its research program beyond the level that its annual \$7.5 million core budget would allow and is an important variable in the Institute's strategic planning as a means to significantly increase the size and pace of HEI's research programs on certain pollutants in order to meet its core mission.

Future Funding

HEI's funding base rests on core funding provided by longer-term sponsors supplemented by leveraged contributions to HEI's ongoing research program in three- to five-year additional commitments to major programs from new and existing sponsors. The core funding has remained at the same level for the past 10 years.

HEI has used the strategic planning process to identify further opportunities for HEI initiatives. HEI will continue its efforts to leverage its core budget with additional special program sponsors and through joint funding of research programs with other institutions. HEI's ongoing

* Based on the last five audited financial statements of HEI, FY 2003–FY 2008.

[†] A list of abbreviations and other terms appears at the end of the Strategic Plan.

Table 1. HEI Research and Review Processes

Research Process

Research Program Development

- Solicit sponsors' views.
- Develop information on new research areas.
- Assess ongoing research by other institutions.
- Identify critical research needs.
- Develop Requests for Applications for specific research objectives and distribute to scientific community.

Project Selection

- Ad hoc panel of experts reviews applications.
- Research Committee evaluates top-ranked applications for relevance to HEI objectives and contribution to a coherent research program.
- Research Committee recommends studies for funding to the Board of Directors.
- Board approves evaluation process and studies selected.
- Research Committee requests study modifications as needed (for example, eliminating aspects of low interest or changing exposure concentrations).

Project Oversight

- Science staff organizes workshops to encourage interaction and collaboration among investigators conducting related new studies.
- Research Committee reviews progress reports (sometimes augmented by other experts); science staff communicates recommendations to investigators.
- Investigators present results and interact with HEI community at HEI annual conference.
- Research Committee and other experts conduct site visits at investigators' institutions.
- HEI applies quality assurance program for studies with potential regulatory significance.

Final Report

- HEI requires a comprehensive final report at the end of each study.

Special Attributes of the Research Process

- HEI funds extramural research that draws on strengths of scientific community and conducts a broad range of studies.
- Oversight methods encourage formation of coordinated program with communication and collaboration among investigators.

Review Process

Objectives

- Provide critical and impartial evaluation of HEI-funded research.
- Ensure credibility of research findings.
- Place results into scientific and regulatory context.
- Identify future research opportunities.

Process

- External peer reviewers evaluate investigator's final report.
- Review Committee evaluates report and recommends revisions.
- Investigator submits revised final report.
- Review Committee and science staff develop Commentary, which critiques study and interprets findings.

- Editorial staff prepares report for publication.
- Review Committee approves Commentary; Board approves process.
- HEI publishes Research Report on Web site and in print.

Special Attributes of Review Process

- HEI conducts in-depth external and internal review.
- Review Committee's work is independent from Research Committee, which selects and monitors research.
- Results of all HEI-funded work, both positive and negative, are available to the public.
- Review Committee comments on the research and results.

collaborations with the DOE (to support ACES, a large project testing the emissions and health effects of new diesel engines with strong emissions control), and the recently completed collaboration with the European Commission to support Air Pollution and Health: A Combined European and North American Approach (APHENA) are examples of the kind of collaborations that HEI continues to seek and implement, thereby allowing both HEI and a partner institution to gain more research opportunities and benefits than either institution could alone.

This approach has enabled HEI to build a stronger and more influential research program than core funds alone would allow while ensuring, through longer-term commitments of core funds, that HEI's research decisions continue to maintain the high level of independence that is the basis of the credibility of HEI's research. HEI faces the challenge, however, of ensuring that — as the costs of research continue to increase — it can successfully undertake the major initiatives outlined in this Plan.

PROGRESS: HEI STRATEGIC PLAN 2005–2010

PRIORITY RESEARCH AREAS

The *HEI Strategic Plan for Understanding Health Effects of Air Pollution 2005–2010*, issued in April 2005, had four major priority research areas: health effects of the air pollution mixture, emerging technologies and fuels, assessing the public health impact of air quality actions (accountability), and — given the increasingly international nature of industry and the growing understanding of global air pollution levels and their influence on the United States — an enhanced international perspective in HEI's work.

The Plan also had an overarching theme, in view of the accelerating pace of development of techniques and methods used in scientific research, which was to infuse all of HEI's work with innovation and validation.

The Air Pollution Mixture

Polluted air is a complex mixture of vapors, liquids, and solids that varies greatly across the United States and around the world owing to differences in sources and in weather, topography, and other factors. Because air quality regulations usually focus on specific compounds, research has also tended to focus on single pollutants. However, different pollutants can cause similar responses through the same or different mechanisms, and exposure to two or more pollutants together may elicit a response that is additive, more than additive, or less than additive. The Strategic Plan 2005–2010 designated three components of the

ambient pollutant mixture as priority research topics: particulate matter (PM), gases, and air toxics.

Emerging Technologies and Fuels

HEI has been involved since its inception in many activities related to evaluating the health effects of fuels, fuel additives, and new technologies. The research and development of new fuels and technologies have increased substantially in the recent past, driven by new air pollution regulations and by concerns about fossil fuel availability and climate change. As a result, the Strategic Plan 2005–2010 identified a more proactive role for HEI in this area, including the conduct of studies to test certain new technologies.

Assessing the Public Health Impact of Air Quality Actions (*Accountability*)

Air pollution regulations and other actions intended to improve public health can be complicated to implement and costly for industry and ultimately for the public. Regulators are therefore being asked to demonstrate that interventions reduce pollution and that such reductions in turn reduce human exposures and health effects. Many other factors can influence public health outcomes (such as medical care, socioeconomic status [SES], and dietary preferences) and may undergo changes in the same time frame during which air quality interventions are implemented; these factors add to the complexity of conducting accountability studies. In view of the public health importance of these issues, HEI's Strategic Plan 2005–2010 included the conduct of accountability studies as a priority topic for further research.

Enhanced International Perspective

The Strategic Plan 2005–2010 recognized that HEI's efforts to integrate international science into its program to inform U.S. decisions, and to be cognizant of how that same science could help inform decisions in Europe and other developed regions, have borne substantial benefit. Although HEI's core scientific programs in the Strategic Plan 2005–2010 continued to focus on research to inform decisions made in the United States and other developed countries, HEI identified a targeted, modest program in international research to complement its larger domestic program.

Innovation and Validation

An important aspect of high-quality science is to seek out new methods — both experimental (such as “-omics” methods [the emerging molecular biology techniques; for example, genomics and proteomics]) and statistical — in order to design better and more robust studies. In the HEI Strategic Plan 2005–2010, HEI indicated that it would

pursue several overarching activities to keep its work at the cutting edge and would strive to infuse *innovation* and *validation* into everything it does. Additionally, HEI committed to take steps to increase Web-based access to data for studies with broad interest.

ACCOMPLISHMENTS

The Air Pollution Mixture: PM and Gases

In the HEI Strategic Plan 2005–2010, HEI indicated it would conduct several activities related to PM and gases, among them

- Complete, review, and communicate the results of existing studies of the health effects of PM and gases, including key studies of the health effects of long-term exposure, animal and human studies of the effects of exposure to diesel and other particles on allergic response, and individual studies of the mechanisms and health effects of pollutant components.
- Launch a systematic, multidisciplinary program that would use toxicologic, epidemiologic, and exposure research to examine and compare the toxicity of PM components and gases, as well as their sources.
- Conduct an expert review of the current and emerging scientific literature of the health effects of exposure to traffic.

During the five years of implementation of that Plan, HEI made substantial progress, meeting and in some cases exceeding these goals. Specifically, we have initiated over 25 studies and completed more than a dozen studies. We have another dozen studies nearing completion in the HEI Review Process. These include research focused on better characterization of exposure to PM and gases, the potential mechanisms of effects on the heart, the possible role diesel or other particles may play in exacerbation of asthma and allergy, and major analyses of long-term exposure to air pollution in U.S. and European population cohorts.

Several completed studies were communicated to the EPA and other sponsors for consideration in the context of key science decision-making processes, such as preparation of the Integrated Science Assessment for the current review of the National Ambient Air Quality Standards (NAAQS) for PM. These have included studies that

- Better characterize exposure to PM and gases, including studies of outdoor, indoor, and personal exposure to PM and gases in several hundred individuals from a variety of potentially sensitive populations in seven U.S. and European cities;

- Investigate potential mechanisms of effects on the heart and the role of different particle components and sizes;
- Test whether diesel or other particles can cause exacerbation of asthma and allergy, with real-world and controlled human-exposure studies and animal studies recently published or nearing completion;
- Analyze, in two new major studies, the effects of long-term exposure to air pollution in U.S. and European population cohorts;
- Conduct a comprehensive review and synthesis of over 700 studies of *exposure to and health effects from traffic-related air pollution* (Special Report 17 [HEI 2010]); and
- Test whether some components or sources of the complex PM mixture are more toxic than others; the NPACT initiative is under way and will be completed during the 2010–2015 Plan period.

The Air Pollution Mixture: Air Toxics

The overall goal of HEI's air toxics program has been to provide information that will reduce uncertainties in evaluating human health risks associated with exposure to mobile-source air toxics (MSATs). Specifically, in the HEI Strategic Plan 2005–2010, HEI indicated that it would continue to extend efforts to assess and investigate exposure to and health effects of key air toxics, focusing on the EPA's list of MSATs, many of which are also emitted by other sources. These efforts were to include

- Conducting a review and synthesis of current scientific knowledge on exposure to and health effects of major MSATs;
- Completing ongoing studies of population exposure to multiple air toxics in potential *hot spots* (areas likely to have high levels of some air toxics) and other studies of exposure to or health effects of air toxics; and,
- Launching, if feasible, comprehensive studies of health effects at confirmed hot spots.

During the five years of Plan implementation, HEI has

- Published Special Report 16, *Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects* (2007). The report, prepared by a special panel of experts appointed by HEI, focused on the EPA's list of 21 MSATs. The literature on seven compounds high on the EPA's list (acetaldehyde, acrolein, benzene, 1,3-butadiene, formaldehyde, naphthalene, and polycyclic organic matter) was critically reviewed, evaluated, and summarized. The report was widely disseminated through briefings, workshops, the Web, as a CD, and in print.

- Conducted a number of studies on 1,3-butadiene and acrolein, two of the priority chemicals identified by the MSAT panel. Especially important was the latest comprehensive study of mortality among 18,000 men who had worked at least one year in any of eight styrene-butadiene rubber plants between 1944 and 1998.
- Completed, in partnership with the Mickey Leland National Urban Air Toxics Research Center, studies on the *Relationships of Indoor, Outdoor, and Personal Air (RIOPA)* (Weisel et al. 2005; Turpin et al. 2007). The study documented concentrations of volatile organic compounds (VOCs), carbonyl compounds, and PM_{2.5} in indoor, outdoor, and personal air for approximately 100 subjects living in each of three urban areas. The data generated in this study are available at <http://riopa.aer.com>. Under Request for Applications (RFA) 08-1, HEI has now initiated studies to analyze the RIOPA data in greater detail.

Under RFA 03-1, titled “Assessing Exposure to Air Toxics,” HEI funded five studies to assess whether there are hot spots, that, if documented, could be sites for health effects studies. The five HEI studies were chosen to represent a diversity of sites and toxic compounds. One of these studies has been published (Harrison et al. 2009); others have been completed, and HEI is currently working on their evaluation through its Review Committee.

Emerging Technologies and Fuels

In keeping with its long-standing mission to track and assess the health consequences of emerging technologies and fuels, HEI indicated in the HEI Strategic Plan 2005–2010 that it would

- Launch ACES to assess 2007 and 2010 Class 8 heavy-duty diesel engines and fuels; and
- Conduct periodic reviews of current knowledge of key technologies (e.g., alternative fuels and metallic fuel additives).

ACES During the past five years, HEI has met the following goals: ACES is testing and evaluating emissions from new, heavy-duty diesel engines and control systems designed to meet the stringent emission standards for PM and nitrogen oxides (NO_x) in 2007 and for even lower NO_x levels in 2010. ACES has attracted substantial additional funding for selected components from the DOE, engine manufacturers, the oil industry, CARB, and other organizations. It is being implemented by HEI and the Coordinating Research Council.

This study has three phases. *Phase 1* — which has been completed — involved extensive emission characterization for four engines supplied by major manufacturers with control systems that meet the 2007 standards for PM and NO_x and that are being currently marketed. Emissions were analyzed during several cycles at the Southwest Research Institute, and the results — available at www.crcao.org — show that the emissions of PM from the four engines tested were approximately 99% lower than the PM emission levels allowed from 2004 engines and nearly 90% lower than even 2007 national emissions standards for heavy-duty vehicles. *Phase 2*, which will test emissions of 2010-compliant engines, is currently being planned.

Phase 3A of ACES, which has been completed, developed a facility at the Lovelace Respiratory Research Institute (LRRI) to install one of the four 2007 heavy-duty diesel engines tested in Phase 1 and expose animals to engine emissions. LRRI has completed construction of the facility and initial characterization of the exposure conditions and atmosphere. Also, protocols for engine operation, atmosphere characterization, and housing and exposure of animals have been completed. *Phase 3B* — health testing in rodents — will be implemented as the next stage; it is described under “Priority Research Opportunities 2010–2015” later in this document.

Other Major Efforts on Technologies and Fuels During the last four years, HEI has undertaken several other activities directed at gathering information about new fuels and technologies. At its annual conferences, HEI has organized sessions and targeted workshops on biofuels emissions and effects (2008), toxicity testing of emissions from new fuels and technologies (2009), and ultrafine particles (2009). In addition, HEI has held several meetings with sponsors to gather more information about fuels and technologies.

In spring 2009, HEI reconvened its Special Committee on Emerging Technologies (SCET). SCET is a key advisory body established by the HEI Board in 2000 to aid the Institute in identifying emerging fuels and technologies with a high likelihood of coming to market so that HEI can effectively evaluate, plan, and initiate timely research and assessment of their likely health implications and potential unintended consequences. SCET is composed of experts knowledgeable about fuels, technologies, and future trends; they are recruited from industry, government, academia, sponsors, and environmental organizations. SCET is preparing a report for HEI and the HEI Research Committee that surveys and evaluates alternative fuels and emerging technologies and points to needs for future research; this report is expected in May 2010 and will guide

priorities in the next Plan (see “Priority Research Opportunities 2010–2015” below).

Assessing the Public Health Impact of Air Quality Actions (Accountability)

Building on the foundation laid out in HEI Communication 11, *Assessing Health Impact of Air Quality Regulations: Concepts and Methods for Accountability Research* (2003), HEI issued several RFAs for accountability research; funded, oversaw, and completed a number of innovative studies; and undertook key collaborative efforts with others to define and enable this type of research. By defining and supporting work in this emerging field, HEI is also building a larger base of research teams familiar with the concepts and methods needed to conduct these studies. Specifically, in the HEI Strategic Plan 2005–2010, HEI said that it would

- Initiate and complete a substantial first phase of diverse accountability studies;
- Support and help coordinate the development of sustainable tracking networks (as key data sources) by state public health agencies and the U.S. Centers for Disease Control and Prevention (CDC) (who are implementing local and national health tracking systems), as well as the EPA and others;
- Support new research and methods development to assess long- and short-term effects of domestic air quality regulations and other actions on public health; and
- Assess and communicate progress and help define a next generation of accountability studies, in particular approaches to study major regulatory programs.

Accomplishments During the 2005–2010 Strategic Plan Period During the first four years of implementing this Plan, HEI funded nine studies from RFAs issued in 2002 and 2004. These include

- *Short-term actions:* Actions to improve fuels and combustion technologies (a woodstove change-out program in Montana [Noonan et al.]^{*} and reducing sulfur in fuel in Hong Kong [Wong et al.]); actions to reduce vehicular traffic (the London congestion charging study [Kelly et al., Parts I and II, in press] and traffic measures during the Atlanta Olympics [Peel et al., in press]), or multiple actions (air quality improvements during the Beijing Olympics [J Zhang et al.]);
- *Medium- to long-term actions:* Actions to reduce the impact of mobile, area, and stationary sources (a coal ban

in Irish cities [Dockery et al.], the London low-emissions zone baseline study [Kelly et al., in press], and the impact of Title 4 of the Clean Air Act on power plant emissions [Morgenstern et al.]); and

- *Multiple actions:* Broad social change and accompanying air quality changes (air quality improvements after German reunification [Peters 2009]).

The research phase has now been completed on most of HEI’s initial studies, and the first study from the program, investigating air quality changes in the former East Germany, has been published (Peters 2009). The balance of the initial studies will be published in 2010, including the high-profile study of air quality improvements during the 2009 Olympics in Beijing (J Zhang et al.), which completed its research phase and will be published following review.

As part of its commitment to further define methods and approaches to accountability, HEI also published and shared with sponsors and others several documents detailing its experience to date, assessment of lessons learned, and definition of a pathway to future research. These include

- The article “Evaluating the effectiveness of air quality interventions” in the *Journal of Toxicology and Environmental Health* (van Erp et al. 2008); and
- HEI’s Communication 14, *HEI’s Research Program on the Impact of Actions to Improve Air Quality: Interim Evaluation and Future Directions* (van Erp and Cohen 2009).

Building a Stronger Health Surveillance Network In January 2008, HEI organized a workshop, together with the U.S. CDC and EPA, to further the development of indicators of the health effects of air pollution suitable for public health tracking and potentially useful for accountability studies of regulations implemented over a long period of time. Building on the CDC’s efforts to develop an environmental public health tracking program, the workshop recommended approaches for using local data to generate state and sub-state impact estimates for the acute effects of air pollution and for using concentration–response function estimates from the scientific literature to generate local estimates of effects. A final workshop report was provided to the CDC in August 2008 and working papers from the workshop were published in the journal *Air Quality, Atmosphere & Health* in 2009 (Matte et al. 2009).

Expert Workshop on Concepts, Methods, and Future Directions for Accountability Research HEI conducted a broad-based expert workshop in December 2009 to critically review progress to date and future directions of

^{*} Studies cited in this Plan without a date or without stating “in press” have been completed but are in the review process.

research in this area, as described in the “Priority Research Opportunities 2010–2015” section below.

Enhanced International Perspective

HEI has worked successfully to bring the Institute’s high-quality and impartial science to bear on international air quality decisions in Europe and the emerging markets of Asia and the Americas, while maintaining a central focus on its domestically relevant activities. This approach has yielded new HEI sponsors and research partners in Europe, Asia, and Latin America, including foundations, development banks, international agencies, and European industry and governments. This has resulted in HEI and its science now being widely recognized as credible and regularly sought after to inform global science and regulatory decisions taken by governments and international agencies.

In HEI’s 2005–2010 Strategic Plan, HEI said it would

- Apply the best science from throughout the world to inform U.S. and European decisions;
- Continue the PAPA program to inform decisions in the rapidly expanding markets of Asia;
- Conduct limited capacity building to strengthen local scientists; and
- Actively communicate the results of HEI science to sponsors and decision makers.

Accomplishments During the 2005–2010 Strategic Plan Period

Several broadly relevant studies have been completed — funded under the Air Pollution Mixture and Accountability programs — that will inform decisions both in the United States and internationally, including

- The first European study on the long-term health effects of traffic-related and other air pollution in a cohort of over 120,000 participants in the Netherlands (Brunekreef et al. 2009).
- Air Pollution and Health: A Combined European and North American Approach (APHENA), cofunded with the European Union (Katsouyanni et al. 2009).
- Key accountability studies in London, Hong Kong, Ireland, and Germany (Peters et al. 2009).

In addition, HEI brought its rigorous scientific approaches, health studies, and leadership to important international efforts, including the World Health Organization’s (WHO’s) revision of the influential *Global Air Quality Guidelines* (2006). Most recently, HEI has led efforts to organize the outdoor air pollution component of a global consortium of WHO and others to measure current levels and recent trends in all major diseases, injuries, and risk factors to update the estimates of the *Global Burden of Disease*, a

systematic assessment of current levels and recent trends of diseases, injuries, and risk factors, which was initiated by WHO.

HEI also served as an active interpreter of global science and regulatory issues (e.g., PM regulation and science, and manganese and sulfur in fuels) with and for core sponsors in the EPA (specifically, the Office of Air and Radiation and the International Office) and industry (among HEI’s many industrial sponsors doing business worldwide), as well as decision makers in Europe, Japan, and Asia, underscoring the relevance of international activities to domestic needs.

PAPA Program Funded primarily with support from the U.S. Agency for International Development, the William and Flora Hewlett Foundation, development banks, national governments, and others, the PAPA program was undertaken in cooperation with the Clean Air Initiative for Asian Cities (CAI-Asia). Its purpose is to understand the health effects of air pollution in representative Asian cities and to foster science-based, policy-relevant decision making and capacity building in the developing countries of Asia. Accomplishments include the following research.

Research

- Completion of six Asian time-series studies on the short-term effects of air pollution on mortality in China, Thailand, and India, with results generally consistent with effects observed in studies conducted in North America, Europe, and Latin America (publication in 2010).
- Completion of a combined analysis across China, Hong Kong, and Thailand (publication in 2010).
- Publication of HEI Communication 13 (HEI 2008), based on these studies and an accompanying editorial in *Environmental Health Perspectives* (Speizer et al. 2008).
- Submission for HEI peer review of a major study of air pollution, poverty, and health in Ho Chi Minh City (Giang et al.) that assessed the potential associations between admissions for pneumonia in young children of differing socioeconomic status and exposure to air pollution, and determinants of personal exposure for the poor and non-poor. This was the first-ever study of air pollution and health in Vietnam.

Synthesis and Interpretation The PAPA program has also undertaken activities to document, synthesize, and interpret Asia-wide research and create key resources for policy makers, scientists, and stakeholders, including

- **Public Health and Air Pollution in Asia—Science Access on the Net (PAPA-SAN):** This unique Web-accessible compendium of studies of air pollution and health effects

across the Asian continent now includes 421 studies in China, India, and other Asian countries as a useful resource for policy makers and the scientific community.

- **Comprehensive Assessment of Outdoor Air Pollution and Health in the Developing Countries of Asia: A Review and Research Needs Assessment:** HEI staff, International Scientific Oversight Committee members, and other leading experts prepared a major comprehensive review of the Asian literature on the health effects of air pollution. The review updates and expands HEI's 2004 first-ever review of the Asian literature (HEI Special Report 15), and includes a description of trends in sources and exposures, a review of key evidence, and a meta-analysis of studies of acute and chronic health effects of air pollution (publication in 2010).

Capacity Building in Asia HEI has supported targeted capacity building and networking opportunities for Asian scientists through workshops, applied technical assistance, and participation in international scientific meetings, resulting in PAPA-trained scientists successfully competing for and implementing a major 12-city time-series study in China using the PAPA-created common protocol.

Multicity Study of Air Pollution and Health Effects in Latin America (ESCALA) In 2006, with support from the Hewlett Foundation, HEI funded a coordinated regional analysis of the impact of short-term exposures to air pollution in nine cities in Mexico, Brazil, and Chile (Romieu et al.). The study has a special focus on the impact of air pollution on child mortality that is also relevant to regulatory decisions in the United States and Europe. Investigators also explored whether differential effects by socioeconomic position could be observed. This report is currently being reviewed at HEI.

Active Communication of HEI Results HEI's international activities have led to regular invitations to contribute technical expertise to inform sponsor-relevant regional and national regulatory decisions and global evaluations, including the U.S. EPA's trilateral Regional Air Quality Management Meetings to help guide China's environmental five-year plan; CONCAWE-coordinated forums to inform European research priorities; the Society of Indian Auto Manufacturers forum on clean diesel and low-sulfur fuels; and in the United States, congressional briefings with the Woodrow Wilson International Center for Scholars on air pollution and climate co-benefits in China.

Innovation and Validation

HEI's mission is to provide high-quality science that is reviewed, interpreted, and communicated thoughtfully

and completely to the full range of private and public stakeholders in air quality. An important aspect of high-quality science is to seek out new methods, both experimental and statistical, to design better, more robust studies. In the HEI Strategic Plan 2005–2010, HEI indicated that it would pursue several overarching activities to keep its work at the cutting edge. Specifically, HEI would strive to infuse *innovation* and *validation* into everything it does by

- Continuously improving and validating state-of-the-art statistical techniques for epidemiologic analysis;
- Increasing Web-based access to data for studies of broad interest; and
- Identifying the latest genomics, proteomics, and other tools for health investigation, bringing state-of-the-art practitioners into the field of air pollution and health, and working to validate these emerging tools for health and risk assessments.

Innovative Statistical Techniques and Validation

Efforts HEI has had two major research efforts to develop and test statistical techniques for epidemiology studies. It has funded a study by Dr. James Robins that is entering HEI review to develop new, innovative methods to address current approaches used in modeling data to estimate the association between fluctuations in air pollution concentrations and mortality and morbidity rates. Also, HEI funded and published in the fall of 2009 the APHENA study (Katsouyanni et al. 2009), the goal of which was to understand the extent of coherence among findings of time-series studies of air pollution and mortality and hospitalization in cities in North America and Europe. In the wake of earlier challenges posed to the generalized additive models used in many studies, it also conducted rigorous testing of alternative and new approaches. This highly ambitious project shed light on many aspects of time-series analyses but — as is typical of scientific studies — identified remaining important questions.

Methods RFA Humans are almost always exposed to mixtures of pollutants, yet most scientific studies and regulatory regimes are focused on single pollutants. In January 2009, HEI issued a request for applications (RFA 09-1) for studies to develop methods to investigate the effects of multiple air pollution constituents. The RFA was designed to support the development of innovative statistical methods for the characterization of air pollutant mixtures, the study of the health effects of such mixtures, or both, as well as development of methods for investigating the joint effects of air pollution constituents (i.e., exploring how the effects of a mixture as a whole differ from individual or combined effects of its components). In response to this RFA,

HEI received strong responses, many from well-respected investigators, and has now selected several studies.

Increasing Access to High-Quality Research Data HEI is committed to making exposure and health effects data available to the scientific community and the public. To meet this objective, HEI has supported the development of several databases:

- The Internet-Based Health and Air Pollution Surveillance System (iHAPSS) was funded by HEI and developed and maintained by the Department of Biostatistics at the Johns Hopkins Bloomberg School of Public Health. It contains data and analytical software from the National Morbidity, Mortality, and Air Pollution Study (NMMAPS) (www.ihapss.jhsph.edu).
- The HEI Air Quality Database is funded by HEI and prepared and maintained on a continuing basis by Atmospheric and Environmental Research, Inc. It focuses on levels of pollutants at and near the 54 sites in the recently initiated EPA PM_{2.5} Chemical Speciation Trends Network (<http://hei.aer.com>).
- The RIOPA database was posted in November 2008 and contains information collected in the RIOPA study, which was cofunded by HEI and the Mickey Leland National Urban Air Toxics Research Center and conducted in three cities with different air pollution source profiles: Los Angeles, Calif.; Houston, Tex; and Elizabeth, N.J. This database contains information on the concentrations of VOCs, carbonyls, and PM_{2.5} in outdoor, indoor, and personal air for approximately 100 subjects living in each of the three urban areas (<http://riopa.aer.com>).

New Biologic Methods HEI has made every effort to ensure that the studies it funds employ the best experimental techniques and methods. During the last several years, HEI has funded several studies that use cutting-edge techniques in areas as diverse as neuroimaging (Chen et al.), “-omics” techniques (Borchers et al. 2009; Veranth et al., Q Zhang et al.), intravital microscopy (Grigg et al. 2008; Nurkiewicz et al., Sun et al.), and geographic information systems (Levy et al. in press; Paciorek et al.).

Additionally, HEI has a strong interest in identifying new biologic methods that may be applied to toxicologic research. HEI organized a workshop in October 2008 that focused on the availability and utilization of new methods in the areas of genomics, proteomics, systems biology, immunology, neurobiology, and population-based studies. The emphasis in the workshop was on the usefulness of such methods, particularly in exploring exposures at low concentrations.

MEASURING HEI'S EFFECTIVENESS

As described above, HEI has initiated and completed a large number of projects that were undertaken to implement the HEI Strategic Plan 2005–2010. Beyond these activities, however, other measures should be examined to assess how effective HEI's work has been in informing both our scientific and policy audiences. Some questions we have considered are

- How many studies did we start and complete over the last five years in priority areas?
- How well did we disseminate these results in print and through the Internet?
- Did the scientific community make use of these studies in its research?
- Did the policy community make use of these studies when making decisions about air quality standards and other actions?

We have tracked several measures of effectiveness to address these questions.

STUDIES STARTED AND COMPLETED

HEI initiated 54 studies of air pollution, health, and exposure during the 2005–2010 Strategic Plan period and published 29 research reports of HEI-funded studies (Table 2). An additional 17 reports were produced from pilot studies, and 4 other studies were not published; copies of these are available on request from HEI. In addition, five other documents were prepared in several priority areas: among these were special reports on MSATs and the health effects of exposure to traffic-related air pollution, and a review of the literature from Asia on the health effects of air pollution. Finally, HEI also produced three large databases of air pollution information and made them publicly available.

STUDY DISSEMINATION

Since its inception, HEI has distributed scientific reports and summaries of those reports (HEI Statements) to a growing list of HEI sponsors, scientists, and interested parties in government, environmental organizations, and industry. Between 2005 and 2009, HEI distributed more than 5,000 copies of Research Reports and over 25,000 copies of HEI statements. HEI reports are also available online through www.pubs.healtheffects.org. Our Web site has proved to be an increasingly effective means of extending HEI's reach. Web site downloads may be the best measure of the value of HEI publications, because downloading is an active process undertaken by people who

Table 2. Number of HEI Studies and Publications April 2005–March 2010

	Initiated	In Review	Published	Other ^a	Web Databases
Air pollution mix				1	
PM and gases	25	6	12		
Air toxics	4	4	8	1	1
Diesel	5	3	5		1
Emerging technologies and fuels					
ACES	6	1	0		
Accountability	7	5	2	1	
International	3	7	2	2	1
Innovation and validation	4	1			
Total	54^b	27	29^c	5	3

^a HEI Special Reports and Communications.

^b Includes 10 pilot studies.

^c An additional 17 pilot study reports and 4 unpublished reports are available from HEI.

think a report may be of value. HEI has seen substantial distribution of its scientific documents via the Web. Each year, the HEI Web site's publications page is viewed by some 40,000 visitors, leading to over 30,000 downloads of documents.

CITATION OF HEI REPORTS IN THE SCIENTIFIC LITERATURE

Another measure of HEI's impact is the extent to which the scientific community uses its scientific reports. HEI recently analyzed how often HEI Research Reports and other scientific publications published in 2005 through 2009 have been cited in the scientific literature. Results of this analysis suggest that HEI's impact is substantial (see Figure 1).

- The 23 HEI reports published between April 2005 and October 2009 were cited 127 times in more than 50 health and atmospheric science journals (since some of those

reports were published only recently, we would expect citations to rise in the coming years) (Figure 1).

- The work described in the 23 reports also resulted in an additional 92 peer-reviewed scientific articles; these peer-reviewed publications were cited 2371 times in other publications (Figure 1).
- HEI-funded research reports during 2005–2009 generated an average of nearly 109 citations per report (citations of the original report or its related journal articles), an extraordinarily high number of citations for any scientific work.
- HEI reports also continue to be cited long after publication. Some older HEI reports (for example, reports about NMMAPS (Samet et al. 2000a; 2000b), the Reanalysis of the American Cancer Society and Harvard Six Cities Study (HEI 2000), and the Extended Analysis of the American Cancer Society Study (Krewski et al. 2009) continue to be widely cited (see Figure 2).

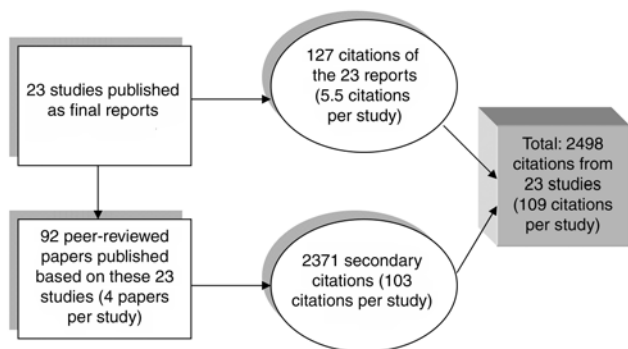


Figure 1. Citations of HEI reports (published from April 2005 to October 2009) and accompanying journal articles in the scientific literature.

ROLE OF HEI IN KEY DECISION-MAKING ARENAS

Beyond HEI's efforts to better inform the science community about the health effects of air pollution, a central part of HEI's mission has been to ensure that its work is effectively communicated, in understandable terms, to the full range of stakeholders in the industry; the environmental community; local, state and federal government; and international agencies. During the current Plan period, HEI scientific results have been presented in many key forums. Examples include

- *Frequent testimony and presentations* — HEI's leaders have continued to present information on the health

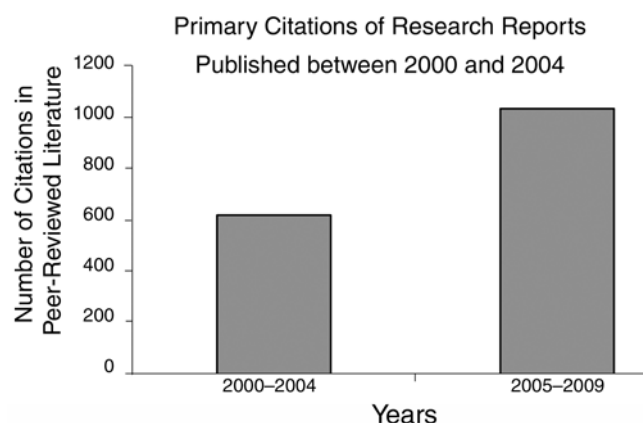


Figure 2. The continuing and increasing rate of citation of reports published by HEI during 2000–2004.

effects of air pollutants before legislative, regulatory, and advisory bodies, including the U.S. Congress, the FHWA, the Clean Air Scientific Advisory Committee, and CARB.

- *Continued contributions to the scientific basis for rule-making by the EPA and others* — HEI's reports have been cited and used during reviews of national ambient air quality standards and motor vehicle emission standards in many countries.
- *Important roles in U.S. and international assessments, analyses, and guidelines* — HEI has continued to play an important role in providing health effects information and design concepts for several important public health tracking and risk assessment efforts. Among these are the CDC's Environmental Public Health Tracking Program and the comprehensive revision of the WHO's *Global Burden of Disease*.

A further sense of HEI's relevance to developing credible science useful to important policy issues can be gleaned from the fact that in several recent policy forums, including a 2007 congressional hearing and a report of the Woodrow Wilson International Center for Scholars (Maynard 2006) on the risks of nanotechnologies, HEI was advanced as a possible model for addressing emerging environmental health issues.

An additional illustration of HEI's impact on decision making is the frequency with which its reports are cited in key regulatory science documents. HEI research played a significant role in the review of the NAAQS for PM. Looking at the most recent science reviews — those prepared for the PM and SO₂ reviews now under way and for the recently completed NO₂ and ozone reviews — there is clear indication of both the broad and continuing relevance of HEI's work, as well as the continuing influence of its older studies (Table 3).

ENVISIONING THE FUTURE: DEVELOPING A RESEARCH STRATEGY TO MEET EMERGING NEEDS

Key to the success of the *HEI Strategic Plan for Understanding the Health Effects of Air Pollution 2010–2015* will be the Institute's ability to anticipate major trends in air pollution policy making and science and then to design research and other scientific programs to meet the needs that emerge from those trends. While decision makers often focus on the decisions they face over the next two to three years, experience has shown that both major policy changes and scientific understanding occur over longer cycles. As initial scientific results are reported, initial decisions are made; then as science matures, decisions are revisited and refined over 5, 10, or more years.

To ensure that HEI's scientific contributions are as timely and relevant as possible, we must identify these major trends and use them to guide strategic planning for both the short and long term. Of course, because no effort to forecast the future can be perfect, any strategic plan must have the ability to adjust to trends as they actually emerge. But at any given point, major trends can be identified that are not only current but are also likely to last for some time into the future and to be major enough to affect the needs of and opportunities for science.

Table 3. Citation of HEI Works in Most Recent NAAQS Science Documents^a

Regulatory Document	No. HEI Works Cited
Integrated Science Assessment for Particulate Matter (Final Report)	66
Integrated Science Assessment for Oxides of Nitrogen — Health Criteria (Final Report)	24
Integrated Science Assessment for Oxides of Sulfur — Health Criteria (Final Report)	12
Air Quality Criteria for Ozone and Related Photochemical Oxidants (Final Report)	30

^a See reference list for full citations of these NAAQS documents.

MAJOR FUTURE TRENDS AND ISSUES

A wide range of larger and more detailed trends and activities is under way — and is likely to continue through the coming five years and beyond. This includes

- Overarching policy and science issues;
- The setting of ambient air quality standards;
- Issues at the nexus of climate change and air quality; and
- New emission standards that will drive new fuels and technologies.

Overarching Policy and Science Issues

A number of overarching *policy issues* concerning the functioning of environmental regulations are likely to influence developments in air quality management programs and air pollution research:

- The need for continued attention to the role and improvement of cost–benefit analysis;
- A need to update and improve risk assessment procedures, including ways to better handle the scientific uncertainties underlying available evidence;
- A need to improve ways of evaluating the impact of policies and of measuring the results achieved by air quality actions (*accountability*); and
- A focus on ensuring the integrity of the scientific processes and the proper integration of science into decision-making frameworks.

Underlying these policy issues are a number of major long-term and cross-cutting *science trends and challenges* as well. Together they are likely to expand the need for new analytical tools and methods, new measurement and assessment strategies, and further multidisciplinary and interdisciplinary forms of research.

- **Multipollutant air quality exposure and effects** — Risk mitigation strategies based on multipollutant approaches are being widely advanced to provide potential gains in both public health effectiveness and cost-efficiency. EPA policy and research offices have recently taken steps toward the goal, such as the creation of pilot air quality management planning projects in several states. The challenges for both policy makers and scientists are significant.
- **Sensitive populations** — Even relatively low exposure levels may not offer an adequate margin of safety to protect the entire population, given the heterogeneity of individual susceptibilities and vulnerabilities. The relative effects of pollutants on populations such as the elderly, children, and the poor could be an important element in regulatory actions and policy decisions.

- **Health tracking and indicators** — Efforts to measure bodily accumulations of substances across a population are seen as vital to a better understanding of the links between sources of pollution and health effects and to crafting targeted measures.
- **Atmospheric transport of pollutants cross-region and cross-boundary** — Research has raised awareness of the extent to which chemical and atmospheric transport processes influence pollutant concentrations in a given locale. Distant or uncertain sources impede management efforts and demand new frameworks for action across political boundaries.

Setting Ambient Air Quality Standards

An array of actions and issues surround the setting of ambient air standards for the major pollutants:

- In the *United States*, over the 2010–2015 timeframe, each of the NAAQS for the criteria pollutants is expected to be reviewed. From a health effects perspective, the most significant remain the reviews for *PM* and for *ozone*, both of which are currently under way. EPA timetables indicate the publication of final rules in 2011 for *PM* and in 2014 for *ozone*.
- In *Europe*, an integrated air pollution strategy, including new limit values, emission ceilings, and control programs, was developed based on the comprehensive assessments and reviews of the health effects science conducted under the European Commission's Clean Air for Europe (CAFE) program. The resulting directive on ambient air quality, with standards set for all major pollutants, including new objectives for $PM_{2.5}$, was finalized in mid-2008. Over the course of the next Strategic Plan period, the European Union will again review the science and the impacts of the measures adopted and identify any needed revisions by 2013.
- The last few years have seen a noticeable increase in the promotion of air quality goals and standards *worldwide*. Shaping some of this activity, in 2005 *WHO* issued revised guidelines on air quality standards that for the first time provided global suggestions, with air quality target levels below the current standards of many countries.
- Two-thirds of the health impacts estimated through *WHO's* evaluations are thought to occur in *Asia*. Among the developing Asian countries, the increasingly stringent measures adopted by *China* and *India* have received great attention, while demands for additional research to meet local and regional needs are likely to remain strong.
- Authorities at the Ministry of Environment in *Japan* have also promulgated, for the first time, ambient standards for fine *PM* ($PM_{2.5}$).

- In the course of these policy deliberations, various questions and areas of research have been repeatedly identified as priorities for future decision making:
 - The possible differences in the health impacts of specific particle components and whether these could translate into source-specific or otherwise targeted management actions;
 - The relative health effects at low levels of ozone and PM on cardiovascular and respiratory systems and the possible interactive effects from combined exposures;
 - The health impact of ultrafine particles, which are a focus of attention because of recent health effects evidence, as well as concerns that emerging technologies could significantly change their relative presence in overall PM concentrations;
 - Questions about the indicators and forms used in standards, including ground-level ozone as an index for photochemical oxidants and the use of mass criteria for fine PM;
 - The identification of threshold concentrations for harmful effects; and
 - The influence of climate change processes on ozone formation, which can appreciably alter approaches to the pollutant.

The Nexus of Climate Change and Air Quality

Another set of major cross-cutting issues is arising from the integration of climate change concerns with traditional air quality programs. A large number of climate-change-related activities have been under way at federal departments and agencies and at the state level:

- There are a number of aspects to the *U.S. EPA's* developing response to the Supreme Court's 2007 ruling that the *Clean Air Act* gives the agency authority to regulate greenhouse gases (GHGs) from the transportation sector. For instance, the EPA recently made an "endangerment finding" that GHGs pose a danger to both public health and welfare, and issued proposed mobile-source GHG emission standards and proposed controls for the largest stationary sources.
- The priority placed by *California* on climate change efforts has led that state to be the first to set GHG emission standards for motor vehicles, as part of a sweeping set of carbon-reduction mandates.
- Although not solely focused on climate change, recent revisions of the *Renewable Fuel Standard* mandate dramatic changes in the nation's transportation fuel supply. These, however, have been the subject of intense criticism and may be revisited, particularly in the context of congressional interest in alternative ways to construct

fuel standards, such as the performance-oriented *Low Carbon Fuel Standard* (LCFS) in California.

- Climate legislation has been accorded high priority in the U.S. Congress, with the likely result that new programs with major implications for the air quality management system will be put in place in the coming years.
- Globally, discussions continue on a framework for international cooperation to replace the Kyoto protocols. Scenarios for post-Kyoto emission reduction strategies hold enormous implications for air quality management. A major issue will be a reworked role for the developing world — particularly the large emerging economies of *India* and *China* — in GHG reduction strategies.

It is increasingly recognized that climate and air quality are closely linked by a number of physical processes. While much further research is needed to better understand the dynamics involved, it appears that some traditional air pollutants can have significant roles in determining the Earth's radiative balance; conversely, global change could significantly affect regional air quality. This raises the possibility that policy decisions about individual pollutants, such as *black carbon* and *tropospheric ozone*, could be driven as much by global change strategies that seek possible *co-benefits* for local health and climate as by traditional local air quality management considerations. It is also the case that choices between GHG reduction actions could be based on the shifts they bring about in their impact on the levels of traditional pollutants.

New Emission Standards That Will Drive New Fuels and Technologies

Over the coming years, *mobile-source control programs* will continue to be important elements for meeting ambient air standards and other air quality goals in the United States and in many countries around the world. Policy attention to mobile sources will additionally be heightened by climate change concerns, with potential new strategies being introduced in the United States and with continued developments in European programs to reduce GHG from transportation.

Over the last decade, *EPA* and air quality authorities in *California* have been especially active in the area of mobile sources:

- Progressively more stringent *U.S. emission standards* have been finalized for both light and heavy-duty vehicles. These have been matched by a new regulatory emphasis on other mobile sources of pollution, some of which had not previously been regulated. Important new rules were finalized for locomotives, large marine engines, off-road equipment, and small engines for boats and garden equipment.

- Alongside these new engine emission standards and various in-use and other vehicle requirements have been a number of *new U.S. fuel standards* for gasoline and diesel and requirements for the use of various *cleaner fuels*, including natural gas. In addition to reflecting broader policy approaches that take into account the total scope of vehicle systems, fuel policies increasingly have been driven by climate change, energy security, and other concerns. Thus, in the last several years, new requirements in the United States have called for increasing the share of *biofuels* in the transportation fuel stock substantially over the coming decade.
- Similar developments occurred in *Europe*, as Euro 5 and 6 standards for cars and Euro V and VI standards for trucks were adopted. Notably, the Euro 6 standards for the first time have set the plan for establishing a particle number standard, although the specific measurement technique and level of the standard have not yet been set formally.
- In many other countries, less-stringent mobile-source pollution controls also have been recently mandated. However, both China and India — where vehicle production has been rapidly growing — have adopted vehicle and fuel standards based on European directives, with the expected result being requirements for Euro 4-level cars in the major cities no later than 2010. As Europe implements its next level of standards, it can be expected that these major economies in Asia will follow suit.

These programs will be implemented during the course of the Strategic Plan's timeframe and beyond. In the near term, their implementation could generate a number of policy issues:

- *There may be continued emphasis on traditional air quality concerns*, because despite the existence of regulatory and nonregulatory emission reductions programs for many years — and despite the development of much cleaner cars and trucks — ambient concentrations of mobile-source pollutants remain above goals. A new level of control following the EPA Tier 2 and California Low Emission Vehicle (CALLEV) 2 standards is likely to follow further evidence of continued health effects occurring at levels below the current NAAQS.
- Possible new mobile-source strategies are likely to also reflect ongoing attention to *air toxics* and accelerated replacements of *older diesel engines*. A focus on assessing remaining risks is likely to be a priority over the course of implementation of the recently adopted MSAT rule, and could lead to its re-evaluation and combination with new fuel strategies. Similar levels of attention are evident in California, where the recent focus of multiple air toxics exposure studies by the South Coast Air Quality Management District on continuing risks from older diesel engines is raising questions about whether

actions are needed under the California Diesel Risk Reduction Plan.

- The focus on the health risks imposed by transportation sources in *near-roadway* and in *other specific environments*, such as ports — where environmental equity concerns may be important — is an emerging concern. Such issues are likely to propel both assessments and policy actions that integrate agencies and tools beyond those typical to the domain of air quality, including novel approaches to traffic demand management; an expanded scope of surface transportation and goods movement planning; and more extensive project development conformity considerations.
- All of these actions taken or concerns raised either explicitly compel or indirectly encourage the *development of new technologies and new fuels*, including renewable fuels. In addition to the need for research on the implications for health of changes in the composition and pattern of emissions, emerging technologies and fuels raise the need for research and assessment on a range of *unintended consequences and sustainability considerations*.

LOOKING AHEAD

Looked at overall, these trends in policy and science lay out a broad and important set of issues for HEI to integrate into its Strategic Plan 2010–2015. Chief among them are an overarching drive toward *enhanced multipollutant approaches to exposure and health* and a need to better integrate HEI's work at the *nexus of air quality and climate*. These larger trends call for HEI to find ways to continue to make an impact through

- Targeted contributions to multipollutant exposure and health science underlying ambient air quality and emission standards;
- Timely assessment of the emissions and health implications of new fuels and technologies being driven by climate and air quality;
- Attention to sensitive populations (e.g., the elderly, children, and those with lower socioeconomic status); and
- Continued efforts — through accountability — to assess the effectiveness of air quality actions in attaining their predicted health benefits.

CHOOSING THE FUTURE

HEI has considered a spectrum of air pollution and climate issues, as well as broader issues, in developing this Plan. The Plan gained insights from extensive consultations with HEI's EPA and motor vehicle industry sponsors; the oil industry and other industries; the broader scientific,

regulatory, and environmental communities; and the HEI Board of Directors, Research Committee, and Review Committee. Figure 3 presents the topics discussed in the Draft Plan, the process for evaluating them, and the priority topics in this final Plan.

HEI received much valuable input in these discussions and also received numerous written comments. In considering this input carefully, HEI staff and committee members addressed several criteria in selecting priority topics for the next five years:

- The current state of knowledge about topics of potential interest;
- Their importance for public health and upcoming regulatory and technology decisions;
- How well they are being addressed by other organizations; and
- The likelihood that scientific work will produce useful findings at this time.

WHAT WILL HEI’S STRATEGIC PLAN 2010–2015 ADDRESS?

Two messages came through clearly in the comments HEI received on its Draft Strategic Plan: that we must view our efforts increasingly in a multipollutant context (since exposures are rarely to any one pollutant) and that we must place our efforts increasingly at the nexus of air quality and climate change. To that end, we have identified a *principal*

overarching theme to guide our Strategic Plan for 2010–2015:

HEI will work, through all of its major programs, to develop and apply *next-generation multipollutant approaches* to understanding exposure to and health effects of air pollutants. This is critical to understanding whether there might be joint or synergistic effects of multiple exposures to PM, gases, and air toxics, but equally important to ensuring that, in our efforts to identify effects of any one pollutant, we don’t underestimate other pollutants that may be of equal or greater importance.

At the same time, HEI will integrate a second overarching theme into its Strategic Plan for the coming five years:

HEI will ensure that its work is increasingly able to *inform key decisions at the nexus of air quality and climate*. There are several areas — especially amid its core multipollutant exposure and health science and in its assessment of emerging technologies and fuels — where HEI can enhance its ability in this important area.

As illustrated in Figure 4, moving forward HEI sees these themes to be integrated into four core program elements:

- Focusing on Multipollutant Exposure, Epidemiology, and Toxicology Research
- Assessing Emerging Fuels and Technologies,
- Measuring the Health Outcomes of Air Pollution Actions (Accountability), and

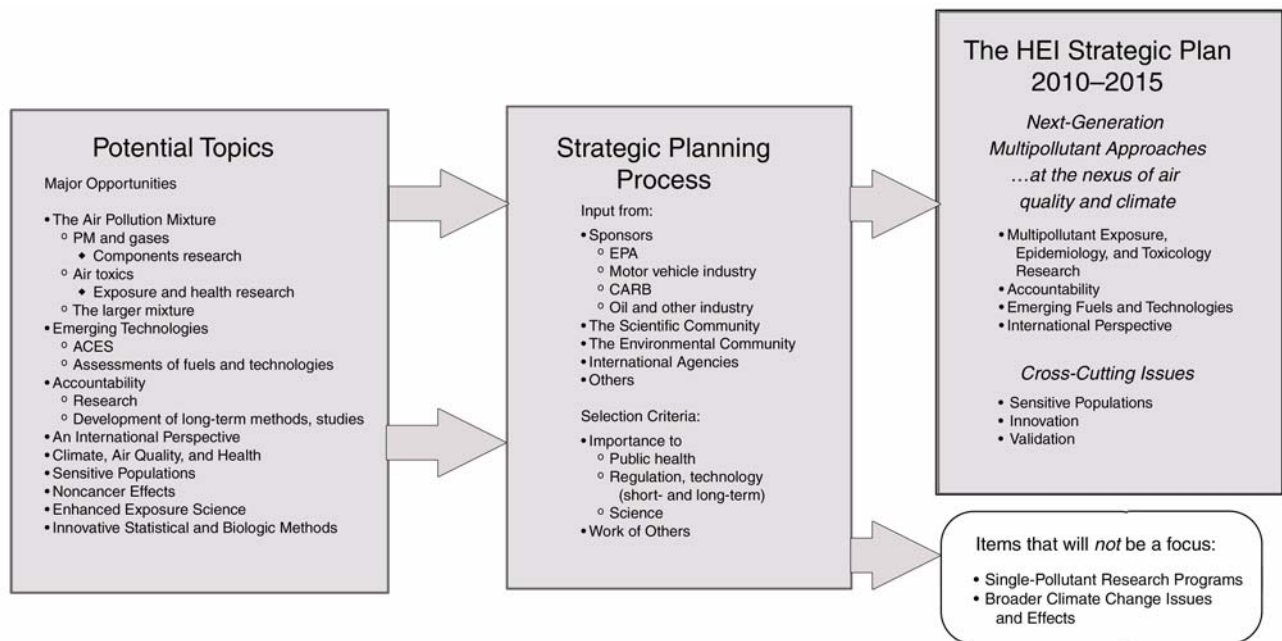


Figure 3. Development of the HEI Strategic Plan 2010–2015.

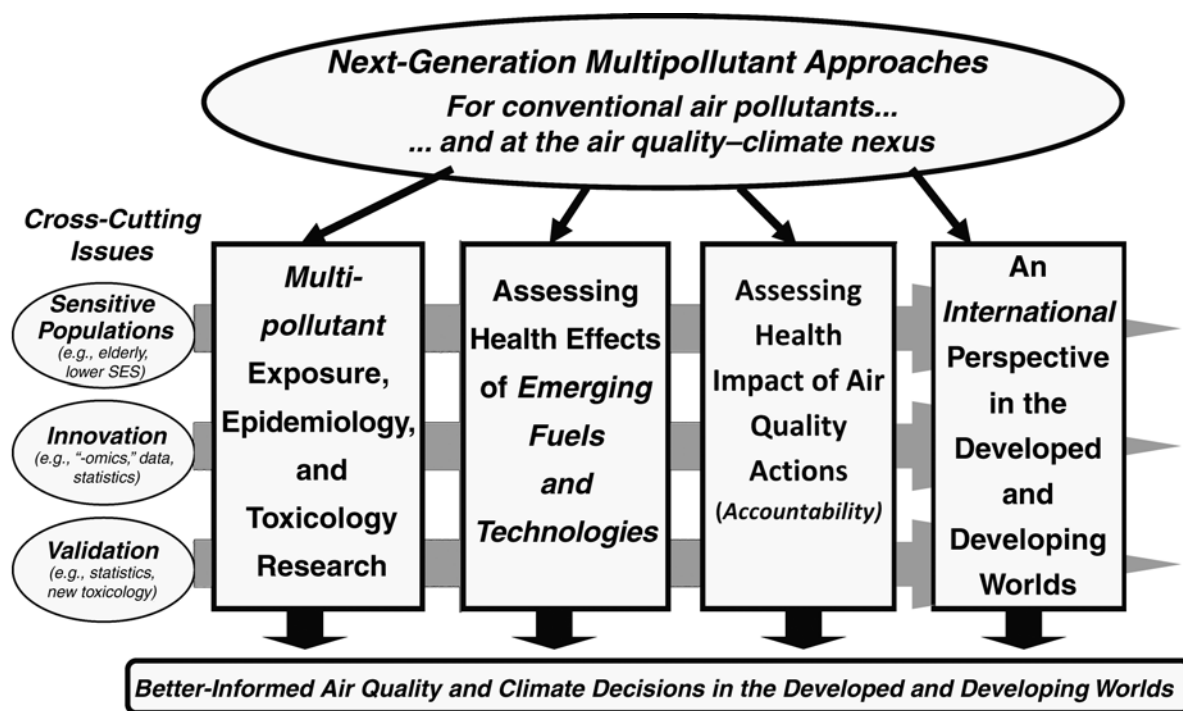


Figure 4. The HEI Strategic Plan 2010–2015.

- Taking an International Perspective.

We also expect to pursue important cross-cutting issues in all of our efforts, including selected *sensitive populations* (e.g., the elderly; the young; those with pre-existing cardiovascular, respiratory or other diseases; and those who may be more highly exposed and/or more vulnerable because of their SES); *innovation* in statistics, new toxicology, and other areas; and continued focus on HEI's leading role in *validation* of whether existing and new techniques and statistical analyses adequately represent actual exposures and health effects.

The next two sections describe in detail the rationale for selecting these topics and the approaches that HEI will take in addressing them ("Priority Research Opportunities 2010–2015"), and the timetable for implementation ("Implementing the HEI Strategic Plan 2010–2015")

WHAT WILL HEI'S STRATEGIC PLAN 2010–2015 NOT ADDRESS?

As is inevitably the case when a science organization has to make choices about where to focus its resources, HEI has, in its new Strategic Plan, chosen not to pursue certain key issues that we have considered and/or that others have proposed:

- HEI will not in the coming years pursue major new programs of research on individual pollutants or categories of pollutants (e.g., individual criteria pollutants, diesel exhaust, individual air toxics) but will focus instead on multipollutant studies of exposure and health, whether in toxicology, or in epidemiology at the local, regional, and national scale.
- Beyond its focus on issues at the nexus of air quality and climate change, HEI would not expect to engage in broader research on the effects of climate change (e.g., changes in sea level or in the spread of mosquito-borne diseases).

PRIORITY RESEARCH OPPORTUNITIES 2010–2015

The HEI Strategic Plan 2005–2010 identified finding ways to improve the understanding of the health effects of the air pollution mixture as a top priority, and focused HEI's efforts on three key components of that mixture: PM, gases, and air toxics. This flowed quite logically from the knowledge that no one is exposed to only one pollutant and from strong recommendations at the time by two committees of the National Research Council on PM Research Needs and Air Quality Management that the nation should

begin the shift from a one-pollutant-at-a-time perspective to a multipollutant perspective.

In the intervening years, the need for this broader approach has become even more compelling, with the U.S. EPA increasingly seeking to *move its programs to a multipollutant perspective*, and Europe attempting to take that perspective in setting its ambient air quality standards through the CAFE process. Yet the science challenges remain: designing studies that systematically investigate a range of pollutants and their potential independent, synergistic, and antagonistic effects is difficult, and made more difficult by a lack of available statistical techniques to allow consideration of the effects of more than a few pollutants at a time.

To those multipollutant challenges has been added the growing awareness of the intersection between *air quality and climate*: the potential effects of different conventional pollutants such as ozone, carbon particles, and sulfate particles on climate; the effects of a changing climate on levels of conventional pollutants such as ozone; and the need, as climate mitigation actions are designed and new technologies developed, to assess those actions for the potential health benefits (in terms of reduced air pollution and health effects) and dis-benefits (e.g., the ability of some pollutants to mitigate against climate change). While many of these issues are the subject of a much wider discussion and debate, HEI is particularly interested in their health effects implications. These issues permeate some areas of HEI research, such as those discussed in the next section and the health issues discussed later under “Emerging Technologies and Fuels.”

MULTIPOLLUTANT EXPOSURE, EPIDEMIOLOGY, AND TOXICOLOGY RESEARCH

With these challenges in mind, HEI has already begun — through its NPACT initiative and its most recent RFA 09-01 (seeking new statistical techniques for analysis of mixtures) — to address these important issues. Following its new Strategic Plan, HEI expects to continue to focus on the key topics of PM, the major gases (ozone, NO₂, CO, and SO₂), and air toxics, with increasing efforts to combine the study of these different pollutants for an integrated approach to the air pollution mixture, and to continue to ensure that statistical issues (such as model selection, sensitivity analysis, and confounding) are addressed in each study. We describe below a number of continuing and new opportunities for the HEI Strategic Plan 2010–2015.

Major Continuing Programs to Be Completed

The NPACT Initiative In 2007, HEI launched this comprehensive initiative to shed light on a key issue regarding the toxicity of PM: *Are all components of PM from various*

sources equally toxic to health, or are some components more toxic than others? The HEI NPACT studies combine coordinated efforts in exposure assessment using sophisticated new techniques, epidemiology focused on PM components and long-term effects, and toxicology focusing on health end points that are relevant to the health effects observed in epidemiologic studies. Two teams of investigators, led by Dr. Mort Lippmann at New York University and Dr. Sverre Vedal at the University of Washington, Seattle, are leading the studies under this initiative. At the end of 2009, the studies were at about the halfway point, with major analyses expected to be completed in 2012 and publication of results after HEI review beginning in 2013.

The Lippmann study has four components:

- **Subchronic animal inhalation toxicology:** Evaluating cardiovascular effects in ApoE knockout mice of 6 months of inhalation exposure to concentrated ambient fine particles at sites in the United States with different source profiles and PM composition: New York City; Sterling Forest, N.Y.; Seattle, Wash.; Irvine Calif.; and Ann Arbor, Mich.
- **Acute biologic effects of resuspended particles of different sizes:** Assessing acute biologic effects of ambient air coarse (PM_{10–2.5}), fine (PM_{2.5}), and ultrafine (PM_{0.1}) particles, — obtained at the sites mentioned above — on epithelial cells, endothelial cells, and cardiomyocytes in vitro, and in vivo when aspirated into the lungs of mice.
- **Time-series analysis of effects of PM components:** Conducting time-series analyses of daily morbidity and mortality effects of individual fine particle components and source-related mixtures in communities throughout the United States that have fine particles of different composition.
- **Analysis of effects of PM components:** Evaluating, with a focus on longevity reduction, the effects of chronic exposure to fine particle components using information from the American Cancer Society cohort and database. The investigators will attempt to link effects to specific components and sources.

The Vedal study focuses on three areas and complements many features of the Lippmann studies:

- **Exposure:** Drawing on participants of the Multi-Ethnic Study of Atherosclerosis (MESA) cohort, the study is estimating exposure using sophisticated modeling, taking into account meteorology, traffic, land-use patterns, nearby sources, air monitoring and speciation data, temporal and spatial variation estimates, home characteristics and infiltration estimates, and time-activity data. Thus, estimates of exposure will ultimately be based on

residential-level estimates of component concentrations and proximity to sources.

- **Epidemiology:** Drawing on participants of the two major cohorts (MESA–Air Pollution [a MESA ancillary study] and Women’s Health Initiative–Observational Study [WHI-OS]), the epidemiologic component of the study will estimate the effects of long-term exposure to PM_{2.5} components and emission sources on cardiovascular endpoints (carotid intima-media thickness and coronary artery calcification).
- **Toxicology:** The study is assessing cardiovascular effects in ApoE knockout mice (in the ApoE^{-/-} mouse model) when exposed for 6 weeks to lab-generated atmospheres. Several endpoints between epidemiologic and toxicologic studies overlap. The oxidative potential of the lab-generated atmospheres and of samples collected at MESA-Air sites is also being assessed.

Statistical Methods for Analyzing the Effects of Mixtures

Under an RFA issued in 2009, HEI is funding three studies focused on the development of novel or enhanced statistical methods for analyzing the effects of mixtures and then testing these methods in existing databases. Dr. John Molitor at the Imperial College, London, plans to cluster joint patterns of air pollution exposures and relate these to health outcomes. He will use recently developed Bayesian dimension-reduction and clustering techniques that will characterize the pollutant patterns contained in two data sets — the HEI RIOPA data and the Environmental Pregnancy Outcome Study from Southern California. Dr. Brent Coull of the Harvard School of Public Health plans to adapt a class of methods, known as *model-based supervised clustering*, as an approach to assessing the joint effects of multiple air pollution constituents. This study would allow both the quantification of differences in a health outcome due to different mixture profiles and the identification of the components that differentiate these mixture classes. He will test his model using epidemiologic data from the Maintenance of Balance, Independent Living, Intellect and Zest in the Elderly (MOBILIZE) study and toxicologic data collected by John Godleski (using concentrated ambient particles). Eun Sug Park, at the Texas Transportation Institute, plans to exploit the high correlations among multiple pollutants to characterize air pollutant mixtures emitted by a few common underlying sources. To achieve this, he will develop enhanced multivariate receptor models and build a coherent statistical model that can estimate health effects specific to sources of multiple air pollutants while accounting for uncertainties in an unknown number of sources and estimating source-specific exposure. He will test his model in two data sets collected, respectively, in Phoenix, Ariz., and

Harris County, Tex. These studies began in early 2010 and are anticipated to be completed during 2012, with the reports being published in 2012–2013.

Better Characterization of the Relationship Between

Indoor, Outdoor, and Personal Exposure HEI published RFA 08-1 in late 2008, titled *Relationships of Indoor, Outdoor and Personal Air (RIOPA): Analysis of Collected Data from the RIOPA Study*. The RIOPA study determined the concentrations of VOCs, carbonyls, and PM_{2.5} in outdoor, indoor, and personal air for subjects living in three urban areas, and HEI has ensured that the data are now well organized and publicly available at <http://riopa.aer.com>. HEI has funded and will complete two studies funded under RFA 08-1. In one study, Stuart Batterman of the University of Chicago plans to use state-of-the-art statistical modeling techniques to conduct further analysis of the RIOPA database. His objective is to identify and characterize exposure distributions, exposures to pollutant mixtures, and dependencies between pollutants and determinants of exposure. In another study, Patrick Ryan of the University of Cincinnati will examine the elemental composition of the RIOPA samples and determine how they vary across individuals and cities. The study is also intended to assess the impact of different factors — including time-activity patterns, housing characteristics, and home proximity to traffic and to pollution point sources — on elemental concentrations. The approaches developed in these two studies are likely to refine exposure assessments and modeling of pollutant concentrations, and may be useful in future large-scale epidemiologic studies.

Completion and Publication of Air Toxics and Other

Studies Initiated under Previous Plans HEI will complete the research phase and publish the studies on PM and air toxics that were initiated under the previous Strategic Plan. During the next 18 months, HEI will publish final reports, along with the Review Committee’s commentaries, on the five studies characterizing atmospheric concentrations and exposures to *air toxics* in areas suspected of higher levels, or so called hot spots. HEI will also publish studies focused on PM and allergic response, mechanisms of toxicity of acrolein and 1,3-butadiene, and improved exposure assessment for acrolein.

Major New Opportunities

Effects of Ozone and PM on the Cardiovascular System

The effects of ozone on the respiratory system have been studied in the past, but very little information is available on the effects of exposure to near ambient levels of ozone on the human cardiovascular system; even less is known about how such effects may be modified due to the presence of

other pollutants. In early 2010, HEI issued an RFA to answer these questions in a systematic fashion. In the first phase of studies under this RFA, investigators will expose human volunteers, age 55 to 70 — a group that is more susceptible to cardiovascular effects than young adults, who have frequently been studied — to ozone at near ambient levels and examine the response of the cardiovascular system (the primary endpoint), along with respiratory and inflammatory effects (the secondary endpoints). The second phase will focus on cardiovascular responses in the same subgroup of the population, but will be measured after exposures in ambient settings to ozone at concentrations similar to those studied in the laboratory but in the presence of other air pollutants — especially PM. Phase II studies will use a protocol as comparable to the controlled-exposure protocol as possible so that the results obtained in the two phases can be compared; these studies may also be performed in two or more regions of the United States to capture the effects of geographic variation. Investigator teams selected under this RFA will work with HEI to develop a common protocol and standard operating procedures. As part of this study, HEI will encourage investigators to supplement established health effects assessment methods with promising, newer methods or analytical techniques, such as those derived from genomic or proteomic research. The studies will fill important gaps in our knowledge regarding the effects of ozone and its interaction with other pollutants.

Research to Further Understand Toxicity among Air Pollutants That May Be Important Climate Agents HEI's NPACT initiative is systematically exploring the relative toxicity of different components of the PM mixture. One important component of ongoing research in this area will be to focus, in a multipollutant context, on air pollutants (such as carbon and sulfate particles, ozone, and NO_x) that can affect human health, that may be affected by changing climate (e.g., ozone), and that also may affect near-term trends in climate change. This could lead to a better understanding of which conventional pollutants should have highest priority for reduction for both air quality and climate reasons, and suggest more effective actions. It could also better inform efforts to estimate the near-term health “co-benefits” of certain actions, as well as the potential “dis-benefits” of actions that might either increase some pollutants (e.g., aldehydes from biofuels) or remove pollutants that mitigate against climate change (e.g., sulfate particles). This will not be a simple area of science; HEI would expect to organize a focused workshop in the early years of the new Plan, as NPACT results begin to become available, to discuss the most effective way to pursue this in an integrated, multipollutant manner.

Multipollutant Air Toxic and Other Pollutant Exposure and Health Studies in High-Exposure Situations Certain special situations and micro-environments may increase the likelihood of elevated exposures to *air toxics, criteria pollutants, and other pollutants such as ultrafine particles*. Although NAAQS-related controls can be expected to reduce many pollutants in such areas, a number of other less-regulated pollutants may continue to pose health concerns. In addition to offering a better understanding of the sources and other factors influencing such exposures, these situations also provide opportunities for methods development for exposure and health assessment. Examples of such situations include exposure near ports, industrial areas or major roads, dense urban areas, and certain occupational environments. HEI has previously supported several studies in locations with suspected elevated concentrations of air toxics. The research phases of these studies are complete, and they are in the midst of the HEI review and publication process. Based on knowledge gained from that experience, HEI will work to identify and implement multipollutant studies of exposure and health in well-documented high-exposure situations. Additionally, short-term peak exposures in certain situations can be high and may be masked by time-averaging; HEI will also seek opportunities for research in situations where the short-term concentrations are elevated.

Filling the Key Gaps Identified in the HEI Traffic Review

The recently published HEI review on traffic, Special Report 17, *Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects* (HEI 2010), has highlighted the importance of filling key gaps in research on exposure and the health of people living in proximity to major roads. The traffic review also highlighted the scientific need to understand the atmospheric transformations and dispersion of tailpipe emissions of air toxics and other pollutants, as well as the spatial and temporal patterns of such pollutants. The review also highlighted the impact of land-use and traffic patterns on pollutant exposure. Given the number of people who live in close proximity to major roads — with potential long-term exposures and health effects — the HEI Research Committee will work with sponsors and others to identify top-priority needs from this review and implement programs of studies to meet those needs. Such studies may include

- One or more areas of atmospheric chemistry and transformation of primary mobile-source pollutants;
- Enhanced investigation of the role of traffic exposure in premature mortality and other end points;

- The relative role of other sources — including stationary sources, brake and tire wear, fugitive dust, and others — in such effects; and
- The possibility of identifying unique “markers” for such exposures.

Based on the extensive HEI-funded work on air toxics hot spots and the traffic review, HEI’s Research Committee and scientific staff will convene, in the early stages of the Plan period, a multidisciplinary workshop to identify the most important needs going forward.

A Review of Emissions, Exposure, and Health Effects from Ultrafine Particles HEI has supported a large number of studies on ultrafine emissions and health (both toxicologic and epidemiologic). The continuing interest in ultrafine emissions, especially from new engine technologies and fuels, and their potential health effects suggest that a comprehensive review of this area has merit. HEI will work with its scientific committees to launch an HEI Perspective or Special Review to help synthesize the state of knowledge regarding ultrafines and automobile emissions — including factors influencing ultrafine emissions, atmospheric transformations, variations in physical and chemical characteristics, the potential for health effects, and the remaining gaps in knowledge.

EMERGING TECHNOLOGIES AND FUELS

HEI has since its inception played a role in assessing new fuels and technologies; topics have included diesel exhaust, particulate traps, cerium, ethanol, methanol, the fuel additive methyl tertiary butyl ether, and manganese. At this point, however, the variety of new fuels and technologies is expanding at an unprecedented rate. Interest in such developments is high, especially given their implications for climate change, as well as conventional pollutant emission reductions. Of special interest would be early identification of any additional emissions from emerging fuels and technologies that, while enhancing fuel efficiency and reducing climate emissions, might at the same time cause increases in other pollutants. In addition, in response to various legislative and regulatory initiatives, there is a growing emphasis on understanding the new fuels and technologies from a full life-cycle perspective (from resource extraction and production through combustion and disposal). Thus, HEI expects that issues surrounding emerging technologies and fuels will occupy a larger portion of its research and review portfolio.

Completion of ACES

Phase 3 of HEI’s ACES program, which includes a chronic bioassay, will be completed in the next five years, and a variety of endpoints will be assessed. These endpoints include neoplastic changes, organ toxicity, pulmonary inflammation, oxidative damage and cell proliferation in respiratory tract tissue, mutagenicity, and cardiovascular endpoints in both rats and mice. Chronic toxicity, including carcinogenicity, will be evaluated only in rats. Rats will also undergo pulmonary function testing. Some of these studies are being done under separate contracts with investigators who have expertise in these areas; the exposure group at the LRRRI will provide the samples for testing. The final reports of ACES will be peer-reviewed intensively by the HEI Review Committee and published. In addition, we expect to plan and move forward with Phase 2, the emissions characterization of and ultimate health effects testing for 2010 engines.

Reinvigoration of the Special Committee on Emerging Technologies

The reconvened SCET will help HEI meet its research-planning goals by surveying and evaluating fuels and technologies, preparing critical summaries of scientific information on them, and identifying particularly important emissions and health effects research issues for HEI and others. This interdisciplinary group of experts is knowledgeable about future trends in automotive engineering and transportation issues, alternative fuels, aftertreatment technologies, health, and other areas.

The newly convened SCET met for the first time at the end of April 2009 and subsequently is producing a report (expected by summer 2010) that will provide a brief overview of selected areas of emerging technologies and fuels, the technologies likely to stay in the marketplace, the state of knowledge about their emissions and potential health effects, and any other topics ripe for further investigation.

Based on the recommendations of SCET, HEI will identify top-priority new, targeted research, as well as timely review and synthesis of information, from among the following potential areas:

- **Emissions from ethanol and other alternative fuels.** There is a strong interest, in the United States and worldwide, in increasing the use of ethanol and other alcohols, ethers, biodiesel, compressed natural gas, and other fuels for transportation. Interest in alternative fuels has also been heightened because of legislative mandates in several countries, including the United States, nationally and at the state level. Frequently, such fuels are blended with gasoline or diesel. However, there is a paucity of information about the emissions

from the use of such fuels. Therefore, there is a need for studies focused on the characterization of the emissions from such fuels, and possibly on human exposure to the emissions and potential health effects. The introduction of such fuels may also provide opportunities for accountability research.

- **Evaluation of NO_x aftertreatment technologies for advanced diesel engines.** The possible emissions and health effects of aftertreatment technologies deployed to reduce oxides of nitrogen (NO_x) from the emissions of advanced diesel engines, such as selective catalytic reduction (SCR) or NO_x adsorbers, need further discussion and review. For example, SCR technology uses urea to remove NO_x; questions have been raised about the emission of by-products such as nitroalkanes, nitropolycyclic aromatic compounds, and aldehydes, many of which are of potential health concern.
- **Gasoline direct injection engines:** To improve the fuel-efficiency of gasoline vehicles, auto manufacturers are increasingly and rapidly adopting gasoline direct injection (GDI). However, GDI is known to increase the emissions of ultrafine PM. Since it appears likely that GDI will be used on a fairly wide scale in the near future, it is important to gain a better understanding of the exposure to and potential health effects from such emissions.
- **Electric and hybrid vehicles.** Electric and hybrid vehicles are entering the market at an accelerating pace and, as in the case of alternative fuels, it seems very likely that they will occupy a greater portion of the automotive fleet in the future. Though the tailpipe emissions from such cars are reduced or eliminated, there are other potential health issues to consider. These include (1) use of highly reactive metals — especially lithium — in the battery and the potential for human exposure to lithium during its entire life cycle (from mining to recycling and disposal); (2) whether there are health effects associated with exposures to electric and magnetic fields during the operation of the vehicles, especially as the proportion of consumers using electric and hybrid vehicles increases; and (3) potential effects of emissions associated with electricity generation. If electricity is generated from renewable sources, this is not an issue. But, in the near term, a large proportion of it will continue to be produced by coal-fired power plants, thus “dislocating” emissions from the tailpipe to the power plants. Fuel-cell vehicles appear likely to arrive in the marketplace five to ten years from now, and this will be an area of continuing monitoring by SCET.
- **Non-tailpipe emissions.** As the emissions of PM from automobile tailpipes continue to decline (at least in the industrialized countries), other non-tailpipe sources of

PM in ambient air will gain more relative importance. Sources of such PM include dust from tire wear and brake linings and fugitive dust. In particular, brake and tire dust often contains metals. The issues arising from such emissions need to be better understood.

- **Studies of metals in fuel additives.** The potential of bio-accumulation of platinum, manganese, and other elements from mobile sources, and their potential toxicity are also areas of concern. Ferrocene, an iron-containing compound that may be added to diesel fuel, is of possible interest depending on the extent of its future use. Manganese is used or is being considered for use in some parts of the world as a gasoline additive as part of methylcyclo-pentadienyl manganese tricarbonyl. Metal additives are frequently emitted as metal-containing ultrafine particles. This area needs further scrutiny and research.
- **Life-cycle issues.** A cross-cutting issue for the use of any technology is its overall impact on humans and the environment throughout its life cycle (from resource extraction and production through combustion and disposal). For example, as discussed above, although electric cars produce no emissions on the street, the power plant — the source of electricity — may well produce emissions. Thus, a close look at the life-cycle issues associated with some of the new technologies — with special focus on their implications for health effects — may be warranted. Life-cycle analyses are of interest from the perspective of many disciplines, such as economics, ecology, and resource management; however, in keeping with its core expertise, HEI will focus primarily on the impact on health effects of any life-cycle factors (for example, health issues associated with the widespread use of metal-ion batteries to power electric and hybrid vehicles).

Based on SCET’s review, HEI and its Research Committee — after consultations with its sponsors — will identify from among these topics the top priorities for the following:

- Timely reviews and/or workshops to get a comprehensive perspective of the state of knowledge — what is known about emissions, their chemistry, atmospheric fate, and exposure and potential health effects (see below under “Synthesis of Information on Important Issues”); and,
- Targeted research to fill key gaps going forward (for example, see some of the ideas discussed below under “Innovation and Validation”).

ACCOUNTABILITY

HEI will maintain a leadership position in accountability, further defining concepts and methods and initiating the next stage of new research in this challenging field. Having completed a first wave of accountability research, HEI is building on the lessons learned from those studies through critical review, publications, and collaborative efforts to identify and exploit new data sources (e.g., health tracking). In December 2009, HEI conducted a workshop to discuss and evaluate more fully the studies supported during the first phase of HEI's Accountability program and to identify the challenges as well as opportunities and strategies for further research. The workshop focused on questions such as

- What are the lessons from the challenges faced in the conduct of previous studies, and how may these lessons be incorporated in the design of new studies?
- To what extent can additional studies of short-term actions deepen our knowledge about the accountability of air pollution controls?
- What opportunities are available for conducting longer-term studies, and what are the best ways for developing novel approaches to detect changes in health outcomes over the longer term?
- How can we stay abreast of policy development at the local, regional, national, and international levels to identify future opportunities?
- What data sources and methods are best suited for these studies?

The detailed recommendations of the workshop are being prepared; among the major findings were the following:

- Further accountability research is needed, especially of long-term, national-scale interventions. This will be facilitated by the development of publicly available platforms for key research data, and will improve the ability to account for other concurrent changes that affect health over the same time frame.
- There is a cross-cutting need for determining if there is "sufficient" exposure contrast before initiating a study.
- Research on shorter-term and small-scale actions remains useful under well-defined circumstances, and may provide supportive evidence for causal relationships if there is sufficient study power.
- We will need an enhanced and targeted method for reviewing upcoming regulatory activities and for screening them to identify the best opportunities for future studies.
- Improvements in monitoring, air quality modeling, and health tracking, together with experience gained from

previous studies, will provide opportunities for high-quality, "second-wave" research.

One important finding is that it would be particularly useful to incorporate accountability research as a fundamental aspect of the design and implementation of policy interventions, particularly of major regulatory programs, which occur over longer periods. Although targeted opportunistic approaches could still be useful, HEI will also pursue more systematic development of a body of evidence in specific areas of regulation and intervention, including some of the following:

- The impacts of the introduction of new fuels and technologies over time (e.g., biofuels);
- The impacts of a series of actions taken over the longer term designed to either reduce emissions from a particular large source (e.g., power plants) or reduce area-wide exposure to a particular pollutant (e.g., implementation of a metropolitan-area implementation plan for ozone);
- The effects of regulatory interventions on populations with exposures to multiple sources in areas with higher levels of pollution (e.g., ports and urban "hot spots");
- Systematic efforts to assess measures aimed at reducing exposure of sensitive populations; and
- Interventions designed to improve air quality significantly for major events (such as the Olympic Games), especially when those actions are likely to be sustainable.

There is also a continuing need, and opportunity, to improve personal bio-monitoring programs that may be able to track reductions in personal exposure over time as a result of interventions (e.g., the ability of the National Health and Nutrition Examination Survey program by the CDC to track reductions in cotinine — a well-validated marker of exposure to secondhand tobacco smoke — as efforts to reduce exposure to passive smoke have been implemented).

To effectively carry out the next generation of accountability research, and consistent with other areas of the Strategic Plan, HEI will work with agencies to strengthen its ability to track and take advantage of upcoming regulatory interventions in the United States, Europe, and other areas where the actions would be relevant to the United States.

Overall, the next generation of accountability studies will build on but also extend beyond opportunistic studies of shorter-term interventions to address larger regulatory programs implemented over longer periods of time. To do this HEI will pursue new or enhanced analytical methods, data from health tracking systems (in partnership with

states and others), and the more systematic linkage of accountability studies to the adoption of major new regulatory initiatives.

AN INTERNATIONAL PERSPECTIVE

Looking ahead, HEI will build on the key themes of multipollutant approaches and research at the air quality–climate nexus as it funds the best research proposals, competitively selected from among the leading scientists in the world. This will enable HEI to take advantage of unique geographic, population, and technical opportunities to fund research that informs decisions in North America, Europe, and Japan. With added support from foundations, international sponsors, and in partnership with the European Union and others, HEI will also selectively enhance its current program of research in the developing vehicle and energy markets of Asia and Latin America in order to inform decisions there and in other parts of the developing world in a manner that encourages globally relevant research results.

In some cases, as noted earlier, HEI will continue to inform decisions taken in the developed world by seeking to

- Target HEI research to projected U.S., E.U., and other international policy trends and timelines, in the process strengthening bridges among HEI and international policy makers to enhance integration of HEI science into key science decision documents;
- Conduct accountability studies of air quality regulations and other interventions in worldwide locations that can produce results relevant in North America, Europe, and Japan;
- Implement studies of long-term exposure to air pollution and health from multiple pollutants (e.g., similar to the Netherlands study completed recently [Brunekreef et al. 2009]).
- Participate in key science oversight and evaluation groups for highly relevant studies (e.g., the European Study of Cohorts for Air Pollution Effects (ESCAPE) study of long-term effects of air pollution, *Global Burden of Disease* updates, and periodic efforts to inform health impact assessment);
- Develop new capabilities to inform decisions at the intersection of air pollution and climate change; and
- Support synthetic research and review in a global context through coordinated assessments of research across multiple continents.

Developing Countries and Emerging Markets

Developing countries in Asia, and to a lesser extent Latin America, are locations where — with additional support from foundations, development banks, industry, governments, and others — HEI can help accelerate the transition to science-based decision making both for traditional air pollutants and at the intersection of air pollution and climate. This approach, accomplished by leveraging existing HEI science capabilities, will also help accelerate the transition to improved public health and more globally consistent regulatory approaches. These developing countries are the world’s most active future markets for new vehicles and fuels and are sources of internationally transported air pollutants and GHGs. With the significant local impacts of air pollution on health, these areas will benefit from high-quality independent science to directly inform health and regulatory decisions by national governments.

HEI, with its internationally distributed research portfolio, PAPA-SAN database, and other research tracking capabilities, as well as its regular interaction with WHO, leading scientists, research institutions, and government experts, is uniquely positioned to selectively review and synthesize regional studies in a global context. This approach, undertaken judiciously (e.g., the APHENA study [Katsouyanni et al. 2009] and the meta-analysis of Asian time-series studies currently being conducted by HEI), will enable progress toward a more synthetic understanding of key differences and similarities among developing- and developed-world populations and inform related policy decisions. New partnerships with potential sponsors in rapidly developing economies such as India and China are expected to help facilitate these efforts.

In these regions HEI will

- Publish all studies and reviews initiated under the previous Plan.
- Maintain selected PAPA activities including
 - The PAPA-SAN database of Asian health studies as a key resource;
 - Periodic review and synthesis of the Asian scientific literature in a global context; and
 - Targeted capacity building and support for Asian scientists to provide the highest-quality research for Asian policy decisions.
- Selectively undertake new studies including
 - Investigating the potential relation between exposure to air pollution and children’s health (e.g. acute lower respiratory infections) as well as reproductive or developmental health effects (including studies to

be funded under RFA 09-2, “Impact of Air Pollution on Infant and Children’s Health in Asia”);

- Pursuing studies at the intersection of air quality, climate, and health; and
 - Conducting studies of the long-term effects in existing cohorts, if technically feasible and if new external funds or funding partnerships are identified.
- Strengthen HEI’s ability to synthesize and independently communicate the results of its research to government, industry, development agencies, and other stakeholders.

Taken together, these activities will maintain HEI as a domestically and globally relevant provider of independent science, regularly called to credibly inform key decisions affecting public health and potential regulation in key forums in the developed and developing worlds (with decisions in the latter arena potentially having both local impact and broader impact on developed countries [e.g., through transport to Japan and the United States from Asia]).

ISSUES THAT CUT ACROSS ALL OF HEI’S WORK

In reviewing the specific issues that HEI might address going forward, a number of specific health effects questions emerged that would not by themselves be programs of research in the new Strategic Plan, but which should be viewed as *cross-cutting issues* that should be integrated into all of HEI’s work:

Sensitive Populations

The Clean Air Act specifically calls for protection of sensitive or susceptible populations. Based on previous health studies, it appears clear that certain groups in the population are, or may be, particularly sensitive to health effects of air pollution. Such groups include the fetus and children who are in active developmental stages; the elderly who may suffer from multiple illnesses; those with asthma, diabetes, obesity, cardiovascular, and other diseases whose underlying pathophysiology makes them more susceptible; and those who are of lower SES and thus may face higher exposures and have underlying health vulnerabilities. Also, in some situations, specific gene-environment interactions may confer susceptibility to individuals who are otherwise resistant to the effects of environmental agents. HEI will integrate such cross-cutting issues into its future research. More specifically, HEI may focus its projects on one or more susceptible groups or explore the role of genetic and epigenetic factors influencing health outcomes by utilizing techniques borrowed from genomics, proteomics, and other new biologic tools.

Innovation and Validation

HEI has done much to advance innovative techniques for improved exposure assessment, statistical analysis, toxicology, and data access under its current Plan. In each of these areas HEI has played two key roles: to *develop innovative methods*, and then to *test and validate those methods* to ensure that they provide high-quality information for better understanding and decision making. Looking forward, there are several key opportunities for incorporating innovation and validation in all aspects of HEI’s work, including

- *Enhanced statistical techniques*: In its new Plan, HEI will continue its decade-long success at identifying, developing, and validating innovative statistical techniques for analyzing the relation between air pollution and health. In addition to implementing the studies resulting from its RFA seeking novel statistical methods to address the mixture (described above), HEI will continue to identify opportunities in all of its studies to develop and test new statistical approaches, especially continuing efforts to test and explain the challenges of model selection for the interpretation of results.
- *New methods for toxicity testing*: HEI will also encourage in its research programs the use of new methods, model systems, and systems biologic approaches for toxicity testing, with the goal of improving exposure- and dose-to-target tissue assessment, genetic or epigenetic factors affecting susceptibility, and species specificity. HEI is also interested in studies focused on mechanisms of action, especially as they pertain to enhancing our understanding of species- or dose-related extrapolations or early markers of pathologic outcomes. Although many other groups at the EPA, National Institutes of Health, and elsewhere are developing such techniques, HEI will use its unique position to apply and test these techniques in challenging areas. In view of the increasing deployment of new fuels and technologies and the paucity of information about the health effects of their emissions, such methods will be particularly useful in the development of more reliable and cost-effective screening tools.
- *New biomarkers*: Although scientists have searched for biomarkers for a long time, advances in proteomics, genomics, systems biology, immunology, neurobiology, understanding of gene-environment interactions, and advances in various measurement methods raise anew the possibility that biomarkers may be found for certain pollutants, and these advances have the promise of providing more reliable methods for dose or exposure assessment and early markers of disease. HEI will encourage the investigators it supports to propose such

approaches in their research, ideally side by side with more traditional and well-validated approaches, to build a broader “tool box,” especially for assessing exposure or health effects.

- *Enhanced public access to data:* HEI has been a pioneer in making the data from its studies available to other investigators and online. In its new Plan, HEI will continue to facilitate and implement new databases to join those it has already implemented.

SYNTHESIS OF INFORMATION ON IMPORTANT ISSUES

Using special expert panels and its scientific committees, HEI has long played an important role in collecting, analyzing, and synthesizing scientific information on important issues facing the EPA and its private sector sponsors. This has taken the form of both Special Reports developed by special expert panels and HEI Perspectives developed by the HEI Review Committee and scientific staff. Examples of such activities include reports on exposure and health effects of oxygenates (HEI 1997) and cerium (HEI 2001) as fuel additives and of MSATs (HEI 2007), and major reanalysis projects such as the Particle Epidemiology Reanalysis Project of the American Cancer Society and the Harvard Six Cities Study (HEI 2000). Very recently, HEI has published a major review of the health effects of exposure to traffic-related air pollution (HEI 2010).

In going forward, HEI expects to continue such activities; two such types of reviews are at the top of HEI’s priority list for the coming five years:

- Potential multiple-targeted assessments of health effects considerations related to the introduction of new fuels and technologies (e.g., the rapidly increasing introduction of biofuels); and
- Exposure to and health effects of ultrafine particles.

IMPLEMENTING THE HEI STRATEGIC PLAN 2010–2015

Based on extensive comments from HEI sponsors, other stakeholders, and the scientific community — and the priority opportunities identified above — HEI has identified the following specific activities and timeline for implementing the HEI Strategic Plan 2010–2015 by *applying next-generation multipollutant approaches to conventional pollutants...and at the air quality–climate nexus*. Assuming adequate resources are available, these specific actions are identified below and in Figure 5.

CROSS-CUTTING ISSUES

In reviewing the specific issues that HEI might address going forward, a number of specific health effects questions emerged that would not by themselves be programs of research in the new Strategic Plan, but which should be viewed as *cross-cutting issues* that should be integrated into all of HEI’s work. These include

- *Sensitive Populations.* These include the elderly; those with asthma, diabetes, cardiovascular, or other noncancer diseases; those of lower SES; and, in coordination with larger national efforts, such as the National Children’s Study.
- *Innovation and Validation.* HEI has done much to advance innovative techniques for improved exposure assessment, statistical analysis, and toxicology, especially to *develop innovative methods*, and then to *test and validate those methods* to ensure that they provide high-quality information for better decisions. Looking forward, there are several key opportunities for incorporating innovation and validation in all aspects of HEI’s work, including
 - Enhanced statistical techniques;
 - New methods for toxicity testing;
 - New health effects biomarkers; and
 - Enhanced public access to data.

MULTIPOLLUTANT EXPOSURE, EPIDEMIOLOGY, AND TOXICOLOGY RESEARCH

In this important area HEI will, first and foremost, bring the major programs it has under way to timely completion. These include

- The NPACT initiative;
- Statistical methods for analyzing the effects of mixtures;
- Better characterization of multipollutant air toxic and criteria pollutant indoor, outdoor, and personal exposure; and
- Completion and publication of air toxic “hot spot” and other studies.

At the same time, and to the extent that resources permit, HEI will initiate targeted planning workshops and new research to

- Test the effects of ozone and PM on the cardiovascular system;
- Further understand the toxicity of air pollutants that can be important climate agents (e.g., black carbon, ozone, and sulfate); and

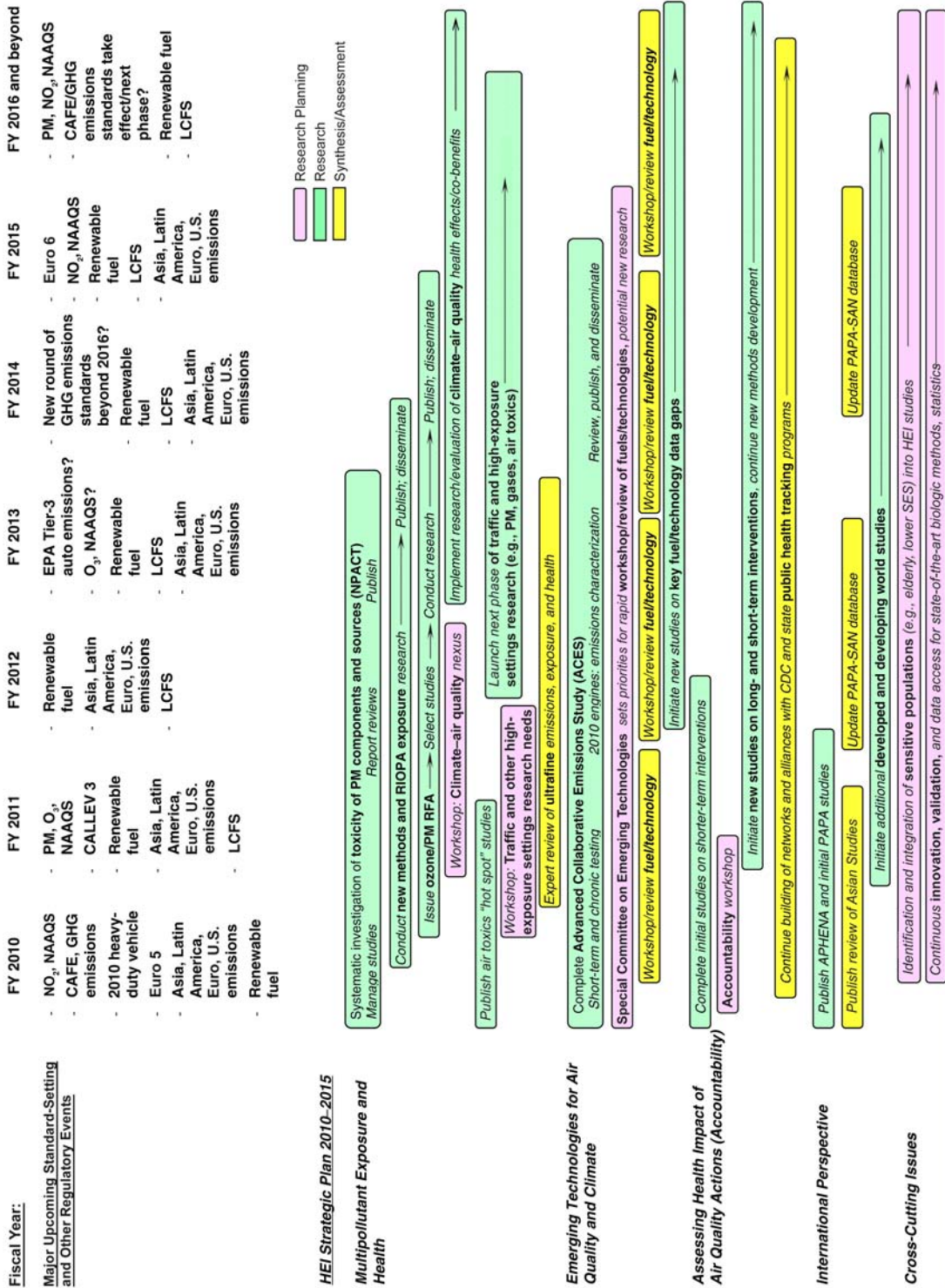


Figure 5. Implementing the HEI Strategic Plan 2010–2015.

- Examine multipollutant exposure to and health effects of PM, gases, and air toxics from traffic (based on the HEI Traffic Literature Review [HEI 2010]) and in other high-exposure situations.

HEI will also work with its scientific committees to conduct a timely review of what we know about *emissions, exposure, and health effects from ultrafine particles*.

EMERGING TECHNOLOGIES AND FUELS

To provide time-sensitive information about the full range of emissions and effects of new technologies and fuels that are being driven by climate, energy efficiency, and air quality, HEI will

- Complete ACES health effects testing and 2010 engine assessment;
- Based on the recommendations of SCET, identify from among the following important topics the top priorities for timely reviews and/or workshops on what is known today about exposure and health as well as targeted research to fill key gaps going forward:
- Emissions from ethanol, other biofuels, and other alternative fuels;
- Evaluation of NO_x aftertreatment technologies for advanced diesel engines;
- Studies of metals in fuel additives and emissions;
- New fuel efficiency technologies and potential effects on ultrafine particle emissions;
- Electric and hybrid vehicles;
- Non-tailpipe emissions; and
- Life-cycle issues: with special focus on their implications for health effects

ACCOUNTABILITY

To effectively carry out the next generation of accountability research, and consistent with other areas of the Strategic Plan, HEI will strengthen its ability to track and take advantage of upcoming regulatory interventions in Europe and other areas relevant to the United States. To set the stage for continued progress, HEI conducted a December 2009 workshop to discuss and evaluate more fully the recent set of studies and to identify the challenges as well as opportunities and strategies for further research. The workshop's detailed findings will be reviewed in spring 2010, but overall, the workshop found that further accountability research is needed, especially of longer-term, national-scale interventions.

One important finding is that it would be particularly useful to incorporate accountability research as a funda-

mental aspect of the design and implementation of policy interventions, particularly of major regulatory programs, which occur over longer periods. Although targeted opportunistic approaches could still be useful, HEI will also pursue more systematic development of a body of evidence in specific areas of regulation and intervention, including some of the following:

- The impacts of the introduction of new fuels and technologies over time (e.g., biofuels);
- The impact of a series of actions taken over the longer term designed to either reduce emissions from a particular large source (e.g., power plants) or reduce area-wide exposure to a particular pollutant (e.g., implementation of a metropolitan-area implementation plan for ozone);
- The effects of regulatory interventions on populations with exposures to multiple sources in areas with higher levels of pollution (e.g., ports and urban “hot spots”);
- Systematic efforts to assess measures aimed at reducing exposure of sensitive populations; and
- Interventions designed to improve air quality significantly for major events (such as the Olympic Games), especially when those actions are likely to be sustainable.

There is, as well, a continuing need, and opportunity, to enhance personal bio-monitoring programs that may be able to track reductions in personal exposure over time as a result of interventions.

To effectively carry out the next generation of accountability research, and consistent with other areas of the Strategic Plan, HEI will work with agencies to strengthen its ability to track and take advantage of upcoming regulatory interventions in the United States, Europe, and other areas where studies would be relevant to the United States.

AN INTERNATIONAL PERSPECTIVE

HEI will continue to inform decisions taken in the developed world by seeking to

- Target HEI research to projected U.S., E.U., and other international policy trends and timelines, in the process strengthening bridges among HEI and international policy makers to enhance integration of HEI science into key science decision documents;
- Conduct accountability studies of air quality regulations and other interventions in worldwide locations that can produce results relevant in North America, Europe, and Japan;
- Implement studies of long-term exposure to air pollution and health from multiple pollutants (e.g., similar to

the Netherlands study completed recently [Brunekreef et al. 2009]);

- Participate in key science oversight and evaluation groups for highly relevant studies (e.g., the European ESCAPE study of long-term effects of air pollution, the *Global Burden of Disease* updates, and periodic efforts to inform health impact assessment);
- Develop new capabilities to inform decisions at the nexus of air quality and climate; and
- Support synthetic research and review in a global context through coordinated assessments of research across multiple continents.

In developing countries and emerging markets HEI will

- Publish all studies and reviews initiated under the previous plan.
- Maintain selected PAPA activities, including
 - The PAPA-SAN database of Asian health studies as a key resource;
 - Periodic review and synthesis of the Asian scientific literature in a global context; and
 - Targeted capacity building and support for Asian scientists to effectively conduct research independently.
- Selectively undertake new studies, including
 - Investigating the potential relation between exposure to air pollution and children's health outcomes (e.g., acute lower respiratory infections and reproductive or developmental health effects);
 - Pursuing studies at the intersection of air quality, climate, and health; and
 - Conducting studies of the long-term effects in existing cohorts if technically feasible and if new external funds or funding partnerships are identified.
- Strengthen HEI's ability to synthesize and independently communicate the results of its research to government, industry, banking, and other stakeholders.

Taken together these activities will maintain HEI as a domestically and globally relevant provider of independent science, regularly called on to communicate on and credibly inform key decisions affecting public health and potential regulation in key international forums.

SYNTHESIS OF INFORMATION ON IMPORTANT ISSUES

Using special expert panels and its scientific committees, HEI will continue to collect, analyze, and synthesize scientific information on important issues facing public

agencies and the private sector. In going forward, two such types of reviews are at the top of HEI's priority list for the coming five years:

- Potential multiple-targeted assessments of health effects considerations related to the introduction of new fuels and technologies (e.g., the rapidly increasing introduction of biofuels); and
- Exposure to and health effects of ultrafine particles.

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ABBREVIATIONS AND OTHER TERMS

ACES	Advanced Collaborative Emissions Study
APHENA	Air Pollution and Health: A Combined European and North American Approach
CARB	California Air Resources Board
CAFE	Clean Air for Europe program
CAI-Asia	Clean Air Initiative for Asian Cities
CALLEV	California Low Emission Vehicle (standards)
CDC	U.S. Centers for Disease Control and Prevention
CONCAWE	Conservation of Clean Air and Water in Europe (research organization of the European oil industry)

DOE	U.S. Department of Energy
EPA	U.S. Environmental Protection Agency
ESCALA	Estudio de salud y Contaminación del Aire en Latinoamérica
ESCAPE	European Study of Cohorts for Air Pollution Effects
FHWA	Federal Highway Administration
GDI	gasoline direct injection
GHG	greenhouse gas
iHAPSS	Internet-Based Health and Air Pollution Surveillance System
LCFS	Low Carbon Fuel Standard
LRRI	Lovelace Respiratory Research Institute
MESA	Multi-Ethnic Study of Atherosclerosis and Air Pollution
MOBILIZE	Maintenance of Balance, Independent Living, Intellect and Zest in the Elderly study
MSATs	mobile-source air toxics
NAAQS	National (U.S.) Ambient Air Quality Standards
	NMMAPS National Morbidity, Mortality, and Air Pollution Study
NPACT	National Particle Component Toxicity initiative
PAPA	Public Health and Air Pollution in Asia
	PAPA-SAN Public Health and Air Pollution Science Access on the Net (Asia)
PM	particulate matter
PM _{0.1}	PM ≤ 0.1 μm in aerodynamic diameter
PM _{2.5}	PM ≤ 2.5 μm in aerodynamic diameter
PM _{10–2.5}	PM between 10 and 2.5 μm in aerodynamic diameter
RFA	Request for Applications
RIOPA	Relationships of Indoor, Outdoor, and Personal Air study
SCET	Special Committee on Emerging Technologies (HEI)
SCR	selective catalytic reduction
SES	socioeconomic status
VOC	volatile organic compound
WHI-OS	Women's Health Initiative—Observational Study
WHO	World Health Organization

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