



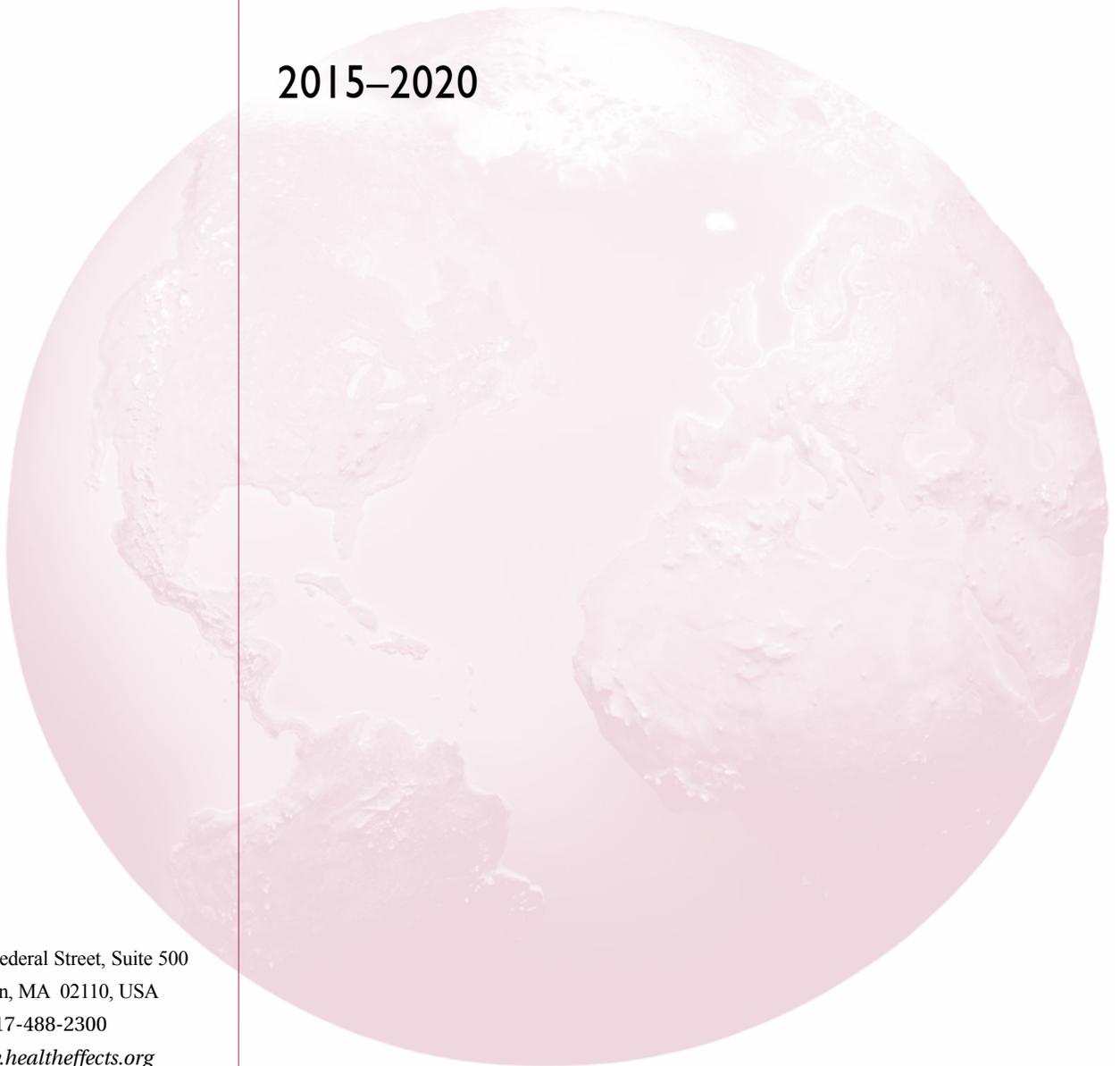
HEALTH
EFFECTS
INSTITUTE

April 2015

HEI STRATEGIC PLAN
FOR UNDERSTANDING THE HEALTH
EFFECTS OF AIR POLLUTION

2015–2020

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HEI Strategic Plan for
Understanding the Health
Effects of Air Pollution
2015–2020

Health Effects Institute
Boston, Massachusetts

Trusted Science • Cleaner Air • Better Health

Publishing history: This document was posted at www.healtheffects.org in April 2015.

Citation:

Health Effects Institute. 2015. HEI Strategic Plan for Understanding the Health Effects of Air Pollution 2015–2020. Boston, MA: Health Effects Institute.

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Compositor: Printed by Recycled Paper Printing, Boston, Mass.

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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's research and analyses to public and private decision makers.

HEI typically 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 research programs. HEI has funded more than 330 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 more than 260 comprehensive reports published by HEI, as well as in more than 1000 articles in the peer-reviewed literature.

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.

HEI Strategic Plan for Understanding the Health Effects of Air Pollution 2015–2020

INTRODUCTION AND SUMMARY

We are pleased to welcome you to the Health Effects Institute's *Strategic Plan for Understanding the Health Effects of Air Pollution 2015–2020*. HEI's success at producing trusted science to inform key decisions relies on our ability to craft this Plan every five years, in order to review what we have done, anticipate the policy and science challenges ahead, and map out the most effective way for HEI to contribute to better decisions on air quality and health. The quality of this Plan depends on our ability to gather input from a wide variety of our audiences—our sponsors in government and industry; the scientific community; environmental and industrial stakeholders; and international, national, state, and local agencies—to ensure that our work, as outlined in the Plan, targets the most important topics.

This Plan follows significant progress under the *HEI Strategic Plan 2010–2015*. In implementing the 2010–2015 Plan, we initiated, conducted, and/or completed over 85 studies, including major investigations of the toxicity of particulate matter (PM*) components (through the National Particle Component Toxicity initiative [NPACT]) and new-technology diesel exhaust (through the Advanced Collaborative Emissions Study [ACES]). We completed and/or launched several major special projects evaluating new fuels and technologies, ultrafine particles (UFPs), and epidemiology studies examining the health effects of exposure to diesel engine exhaust. And we communicated our results throughout the United States, Europe, Asia, and Latin America. Our published research reports, along with their accompanying journal articles, have each been cited in the scientific literature an average of 89 times by other scientists, and our work was cited extensively in key decision documents from the U.S. EPA, the World Health Organization (WHO), the International Agency for Research on Cancer (IARC), and many more organizations.

* A list of abbreviations and other terms appears at the end of this document.

In our consultations for preparing this Plan, we heard one key message: while we should plan for specific actions we will take in the next five years, we should do so *with a clear eye on the much longer time frames for future air quality and climate decisions*. Challenging decisions on air quality standards continue to arise around the globe as the science evolves. Private and public sector decisions on technology to meet greenhouse gas (GHG) goals (e.g., for vehicles and stationary sources) are already aimed at meeting standards set for 2025—and those standards are likely to be extended for many years beyond. Given that, the *HEI Strategic Plan* is built around one overarching theme: *informing decisions on air quality and on climate-driven technology for 2015–2020... and beyond*.

HEI sees this theme integrated into four core program elements: the Continuing Challenges of Multipollutant Science; Accountability and Transparency; Assessing Emerging Fuels and Technologies; and Global Health Science. This document describes detailed plans for HEI's research and scientific activities in each of these areas, including the following:

- *Completion and communication of the results of key studies* on ozone and cardiovascular effects, traffic exposure, diesel engine exhaust, accountability, and other important topics;
- *The launch of major new research initiatives*, including, among others, the examination of potential health effects at lower levels of exposure to air pollutants; new, targeted studies of the health effects of exposure to traffic; the next generation of accountability studies to evaluate the effectiveness of major air quality actions; and, with additional funds, new source-specific assessment of the health impacts of air pollution in developing countries.
- *Targeted scientific review and synthesis*, including an updated review of the health effects of exposure to traffic and the development of systematic toxicity testing

protocols, as well as workshops on key issues pertaining to emerging fuels and technologies.

- *Pursuit of important cross-cutting issues in all of our efforts*, including innovation and testing of statistical analysis and modeling approaches; assessment of at-risk populations; evaluation of the impact of climate change; enhanced exposure assessment; development of new biologic techniques; and evaluation of new health endpoints.

While the *HEI Strategic Plan* is designed to be a clear path forward for us to follow in the coming years, we have found that, in order to be as responsive as possible to the emerging needs of our sponsors and others, we must build in the flexibility to *anticipate and act on the unanticipated*. We fully expect to continue to have that capacity in the coming years.

Given the need to think, not just of the next five years, but beyond, we have also included in the timeline a *Mid-Plan Review* in order to assess progress, to scope out the continuing and likely future policy directions, to make modest adjustments to ensure that HEI is attuning its work to the greatest science and policy needs, and, most important, to consider a longer-term plan—*Vision 2020*—to guide HEI beyond this current five-year plan.

HEI'S MISSION, GOALS, AND STRUCTURE

The Health Effects Institute is an independent non-profit corporation chartered to “conduct... and to evaluate research and testing relating 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 potential HEI research program and review activities for improving our understanding of the health effects of air pollution for the period of 2015 through 2020. We have attempted to identify and anticipate major questions on the health effects of pollutants and new technologies that are likely to be facing policy makers, industry leaders, and others. Based on input from HEI stakeholders, the Plan presents an integrated set of strategies designed to guide HEI in developing detailed annual research and review plans that will deliver research results in a timely manner on potential health effects of greatest concern to decision makers.

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 integrated and multi-institutional efforts whenever possible.
- **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, HEI Research Committee and Review Committee members, expert panel members and reviewers, and a broad range of external stakeholders across all levels of government, environmental public interests, and other nongovernmental organizations (NGOs), as well as industry.

HEI's Board of Directors, president, and senior staff consult periodically with the 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 of 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 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. At each stage, Committee members who might have a conflict in reviewing either an application or a final report recuse themselves from all such deliberations according to well-established procedures. (See Table 1 for a more detailed description of the research and review processes.) The Institute's scientific staff is 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-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

The *HEI Strategic Plan 2015–2020* offers substantial opportunities for building on the base of science undertaken over the past five years in order to apply next-generation

multipollutant approaches to important science and policy questions. In the context of increasingly complex questions about the effects of air pollution at lower and lower concentrations, HEI stands poised to make measurable progress on several fronts: targeted exposure assessment; epidemiology and toxicology studies; health assessment of emerging fuels and technologies driven by climate and air quality concerns; and accountability.

Current Status and Trends

HEI's core budget has averaged \$10 million per year for the last five years. Over the five-year period of the 2010–2015 Plan, HEI spent approximately 82% of its total budget on its research program and 18% on administrative expenses (a level of administrative expenditure well below most scientific institutions). The core of HEI's annual budget is funded jointly by the U.S. 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 25 U.S., Asian, and European companies in order to maintain compliance with 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 also been able to further leverage its core support by attracting additional resources beyond those provided by HEI's core sponsors. Over the last decade, the Institute has received support from a variety of public and private sponsors. On the government side, these include the European Commission (EC); 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 (API); the Truck and Engine Manufacturers Association (EMA); the European oil industry's research organization (Conservation of Clean Air and Water in Europe [CONCAWE]); individual oil companies; steel, and pulp and paper companies; utilities; and emission after-treatment system 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, the William and Flora Hewlett Foundation, and the Oak Foundation.

This additional support has allowed HEI to increase the size of its research program beyond the level that its annual \$10 million core budget would allow and is an important element in the Institute's strategic planning as a means to significantly increase the size and pace of HEI's research programs.

Table 1. HEI Research and Review Processes

Research Process	Review Process
<p>Research Program Development</p> <ul style="list-style-type: none"> • Solicit sponsors’ views. • Develop information on new research areas. • Assess ongoing research by other institutions. • Identify critical research needs. • Develop Requests for Applications to meet specific research objectives and distribute to scientific community. <p>Project Selection</p> <ul style="list-style-type: none"> • Ad hoc panel of experts reviews and scores 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 are selected. • Research Committee requests study modifications as needed (for example, eliminating aspects of low interest or changing exposure concentrations). <p>Project Oversight</p> <ul style="list-style-type: none"> • Science staff organizes workshops to encourage interaction and collaboration among investigators conducting related new studies. • Research Committee reviews progress reports; 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 rigorous quality assurance program for studies with potential regulatory significance. <p>Final Report</p> <ul style="list-style-type: none"> • HEI requires a comprehensive final report at the end of each study. <p>Special Attributes of the Research Process</p> <ul style="list-style-type: none"> • HEI funds extramural research that draws on strengths of the scientific community and conducts a broad range of studies. • Oversight methods encourage formation of coordinated programs, with communication and collaboration among investigators. 	<p>Objectives</p> <ul style="list-style-type: none"> • 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. <p>Process</p> <ul style="list-style-type: none"> • External peer reviewers evaluate investigator’s final report. • Review Committee considers external expert comments, 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. <p>Special Attributes of Review Process</p> <ul style="list-style-type: none"> • HEI conducts an 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 writes a Commentary on the research and results.

Future Funding

In implementing this *Strategic Plan*, HEI expects to continue its efforts to leverage its core budget with additional special-purpose funds and joint funding of research programs with other institutions. HEI's recent collaborations with the DOE (to support ACES, a large project testing the emissions and health effects of new diesel engines with strong emissions controls) and with the European Commission (to support the Air Pollution and Health: A European and North American Approach [APHENA] project) 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 and benefits than either institution could gain 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 quality 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.

MAJOR ACCOMPLISHMENTS 2010–2015

The past five years have seen substantial accomplishments for HEI in all areas outlined in its *Strategic Plan for Understanding the Health Effects of Air Pollution 2010–2015*, issued in April 2010. That Plan identified four major priority research areas: (1) multipollutant exposure, epidemiology, and toxicology research; (2) emerging technologies and fuels; (3) accountability (assessing the health outcomes of air quality improvements); and (4) an international perspective. In addition, HEI identified cross-cutting issues that apply across all research areas: research in sensitive populations, and innovation and validation (including enhanced statistical techniques; new methods for toxicity testing; new health effects biomarkers; and enhanced public access to data).

Major accomplishments include a large number of research projects started and published, such as the NPACT initiative, ACES, and the Multicenter Ozone Study in Elderly Subjects (MOSES); major scientific research planning for studies of traffic-related air pollutants and exposure to air pollutants at low concentrations; and the continued important impact of our work (see later section, “Measuring HEI's Effectiveness”). In addition, HEI initiated an in-depth review of the epidemiology literature on the health effects of diesel engine exhaust exposure that was not part of the

Strategic Plan 2010–2015 but was requested by HEI sponsors and deemed an important addition to the Plan.

The following is a summary of these accomplishments. In addition, a list of currently ongoing studies and forthcoming reports can be found on the HEI Web site at www.healtheffects.org/ongoing.htm. HEI publications can be downloaded at no charge at <http://pubs.healtheffects.org>.

MULTIPOLLUTANT EXPOSURE, EPIDEMIOLOGY, AND TOXICOLOGY RESEARCH

For the past decade, understanding the health effects of the air pollution mixture has been a top priority, following recommendations from a number of scientific organizations, including the National Research Council, that the nation should begin the shift from a one-pollutant-at-a-time perspective to a multipollutant perspective. Yet challenges remain substantial: designing studies that systematically investigate a range of pollutants and their potential independent, synergistic, and antagonistic effects is difficult, and is made even more so by a lack of available statistical techniques to allow consideration of the effects of more than a few pollutants at a time.

HEI initiated, conducted, and/or completed a total of 59 studies in this important research area, including new multipollutant analyses; source mixture studies of traffic and diesel exhaust exposures; evaluations of exposure to air toxics; and a number of statistical, mechanistic, and other types of studies to address cross-cutting issues.

Multipollutant Analyses and Review

HEI completed NPACT—a systematic, multidisciplinary program that used coordinated toxicology, epidemiology, and exposure research to examine and compare the toxicity of PM components, gases, and sources. Under the NPACT program, two major studies were published in October 2013, together with a Synthesis by the NPACT Review Panel, which discussed coherence and consistency in the epidemiologic and toxicologic results and the implications for future research. The NPACT reports were very well received and have made a major contribution to the policy arena by showing that none of the particle components could be definitively excluded as not having an effect on public health, thus supporting the current regulatory approach of targeting the entire PM mixture. The initiative has provided a large number of valuable data sets that can be further explored for specific questions that remained unanswered, as will be outlined under “Priority Research Opportunities” for the period 2015–2020.

HEI completed a thorough literature review of emissions, exposure, and health effects of UFPs, which was published as HEI Perspectives 3 in January 2013, and two reports on the modeling and measurement of UFPs conducted by recipients of the Walter A. Rosenblith New Investigator Award.

HEI is supporting three studies aimed at developing innovative statistical methods for the characterization of air pollutant mixtures and/or the study of the health effects of such mixtures. These studies address a key gap for future multipollutant analyses identified at a jointly sponsored U.S. EPA–HEI Workshop on Multipollutant Analyses held in February 2011.

HEI is supporting MOSES, a large multicenter effort to evaluate the effects of ozone and PM on the cardiovascular system at nearly ambient concentrations. Subject recruitment ended in December 2014, and is being followed by data analysis, report preparation, review, and publication in 2016.

Traffic-Related Air Pollution and Diesel Exhaust

Following the publication of HEI's Special Report 17, *Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects*, HEI has initiated, conducted, and/or completed a number of new studies and special projects to address major gaps identified in that review concerning exposure to and effects of traffic-related air pollution. Among the highlights are the following:

- Following an Annual Conference workshop in April 2012, HEI funded five new studies to improve assessment of exposure to traffic-related air pollutants. Subsequently, HEI funded two additional studies from a request for applications (RFA) for studies of non-tailpipe emissions and of tunnels.
- HEI completed and published studies funded under ACES to evaluate exhaust from new-technology diesel engines with stringent controls for PM and nitrogen oxides (NO_x). The final reports include the emissions characterization of three 2010-compliant diesel engines with PM and NO_x aftertreatment systems (Phase 2 of the ACES program, published in a 2013 report by the Coordinating Research Council), the evaluation of the chamber conditions for the chronic exposure to diesel exhaust in rats (Phase 3A of the ACES program, published in HEI Communication 17), and evaluation of a large number of health outcomes in mice (3 months) and rats (lifetime) exposed to diesel exhaust from a 2007-compliant engine (Phase 3B of the ACES program, published in HEI Research Report 184).

This final Phase 3B report signifies the successful completion of all three phases of the ACES project, a multi-stakeholder project to provide emissions characterization and health effects testing of new-technology diesel engines. It showed that emissions targets were met, and even exceeded, reducing PM and other emissions by more than 90% relative to previous engine technologies without the appearance of unexpected new, toxic compounds. Laboratory rats exposed for their lifetime (up to 30 months) to the 2007-compliant engine emissions showed some lung inflammation and other mild health effects consistent with nitrogen dioxide (NO₂) exposure, but did not show any evidence of tumor formation or pre-carcinogenic effects, in contrast to previous animal studies of chronic exposure to exhaust from “traditional,” pre-2007-technology diesel engines.

- In response to key questions that arose during the course of the 2010–2015 *Strategic Plan* period, and requests from HEI sponsors to act, HEI appointed a multidisciplinary Diesel Epidemiology Panel, chaired by Daniel Krewski of the University of Ottawa, to perform a detailed review of recently published major studies about exposure to diesel exhaust and lung cancer to examine their suitability for quantitative risk assessment. The Panel has conducted additional analyses of the data from the miners study and is preparing a report, which is expected to be published in mid-2015.

Exposure to Air Toxics and PM

During the 2010–2015 *Strategic Plan*, HEI initiated, conducted, and/or completed 14 studies aimed at improving exposure assessment for air toxics and PM, including the following:

- HEI completed its air toxics “hot spot” program and published four reports based on the results. The program was designed to measure exposure in “hot spots” to multiple air toxics with expected high concentrations.
- Capitalizing on the substantial prior investment made in collecting indoor and outdoor air toxics exposure data in its Relationships of Indoor, Outdoor, and Personal Air (RIOPA) study, HEI supported the development of a Web-based database to allow other researchers access to the data for that study, which focused on the relationships between indoor, outdoor, and personal air concentrations of volatile organic compounds, carbonyls, and PM_{2.5} (PM ≤ 2.5 μm in aerodynamic diameter) for subjects living in three urban centers with different pollution sources and meteorology. HEI funded two studies to gain further information and explore the

RIOPA data. At the same time, as a result of making these data widely available, more than 40 independent journal articles have been published that have applied it to indoor and outdoor exposure questions.

Mechanisms of PM and Gaseous Pollutant Effects

HEI continues to fund studies with the goal of improving our understanding of the adverse health effects of PM and gaseous air pollutants and the underlying mechanisms—an understanding that could play an important role in determining causality. During the 2010–2015 *Strategic Plan* period, HEI initiated, conducted, and/or completed some 15 studies on a variety of potential mechanisms. One new, large study will be examining the effects of exposure to air pollution on biomarkers of cardiovascular metabolic risk and blood-borne whole-genome gene expression profiles in a cohort with clinically evident heart disease.

EMERGING TECHNOLOGIES AND FUELS

Since its inception, HEI has played a role in assessing new fuels and technologies. Recently, the variety of new fuels and technologies has been 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 will 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.

HEI's goal during the 2010–2015 *Strategic Plan* period has been to provide time-sensitive information about the full range of emissions from and the effects of new technologies and fuels being developed to address concerns about climate, energy efficiency, and air quality. As a first step, in 2011 HEI published Communication 16, *The Future of Vehicle Fuels and Technologies: Anticipating Health Benefits and Challenges*, prepared by the HEI Special Committee on Emerging Technologies (SCET). HEI addressed two specific recommendations made by SCET:

- The aftertreatment technologies for 2010-compliant heavy-duty diesel engines include both particle filters and selective catalytic reduction (SCR). SCET recommended that HEI study whether the urea–SCR system commonly used to reduce NO₂ emissions may produce toxic compounds. ACES Phase 2 addressed this issue comprehensively.

- SCET recommended conducting a thorough literature review of UFPs. A review examining the emissions, exposure, and health effects of ultrafines was published by HEI as Perspectives 3 in January 2013.

In December 2013, HEI reconvened SCET for a two-day workshop to revisit its earlier report on emerging fuels and technologies and to assess even more recent trends. SCET members, along with many experts from various sectors, spoke about issues of interest to SCET and HEI concerning potential new fuels (e.g., compressed natural gas [CNG]) and the performance of the newest control technologies. These discussions have helped HEI in planning research during the forthcoming *Strategic Plan* period.

In addition to these broader efforts, HEI completed studies on emissions and exposure to modern vehicles, including studies examining secondary nitrogen compounds, the modeling of urban aerosols, the characterization of nanoparticles from motor vehicles, and factors determining UFPs inside (retrofitted) school buses.

ACCOUNTABILITY

HEI has provided a leading role in accountability research (assessing the health outcomes of air quality improvements) by further defining concepts and methods and by initiating the next stage of new research in this challenging field. Having completed a first wave of accountability research, HEI built 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). Overall, the next generation of accountability studies, while continuing to build on opportunistic studies of shorter-term interventions, is aimed at addressing larger regulatory programs implemented over longer periods of time.

Major accomplishments include the publication of eight reports from the first wave of accountability studies, including studies of the effects of traffic-reduction measures during the Atlanta Olympic Games, a congestion charging scheme and a low emission zone in London, a woodstove replacement program, legislation to reduce sulfur in fuel in Hong Kong, implementation of Title IV Phase 2 of the 1990 Clean Air Act Amendments, air quality interventions during the Beijing Olympic Games, and a ban on the sale of coal in Irish cities.

To effectively carry out the next generation of accountability research, HEI issued RFA 11-1, which focused on long-term national air quality regulations and the development of statistical methods to evaluate such complex regulations, and on studies of air quality improvement in

major port areas. This second wave of research includes four new studies examining changes in children's health in response to air quality improvements in southern California, health effects of the Goods Movement Action Plan in California, health effects of air quality regulations in the southeastern United States, and statistical methods to assess national air quality regulations.

HEI also provided continued leadership through workshops on health outcomes research gaps, including a workshop to discuss research needs (the proceedings were published in 2010 as Communication 15, *Proceedings of an HEI Workshop on Further Research to Assess the Health Impacts of Actions Taken to Improve Air Quality*), an October 2012 review article in *EM Magazine*, and a workshop co-organized with the U.S. EPA to identify research needs in advance of upcoming regional and national regulatory decisions to improve air quality.

AN INTERNATIONAL PERSPECTIVE

Over the years, HEI has built on the themes of multipollutant approaches and research at the air quality–climate nexus as it competitively selected from among the leading scientists in the world to fund research that informed decisions in North America, Europe, and Japan. HEI provides domestically and globally relevant independent science and is regularly called on to credibly inform decisions affecting public health and potential regulation in key forums in the developed and developing worlds. With added support from foundations, international sponsors, and in partnership with the European Union (E.U.) and others, HEI selectively enhanced its research program during the past five years in the developing vehicle and energy markets of Asia and Latin America, encouraging globally relevant research results.

In addition to supporting ten studies specifically targeted at providing local, high-quality data in Asian countries, HEI funded in the past five years nine other international studies that provide data relevant to the United States, and participated actively in a number of larger evidence reviews and syntheses. As part of these activities, HEI

- Published a comprehensive review in 2010 of outdoor air pollution and health in Asia (Special Report 18, *Outdoor Air Pollution and Health in the Developing Countries of Asia: A Comprehensive Review*);
- Published five reports from the Public Health and Air Pollution in Asia (PAPA) first-wave research program in China and Thailand, and two reports from the second-wave of research in India;

- Co-organized with the European Commission and WHO (with U.S. EPA, industry, and non-governmental organization involvement) a pan-European workshop and a companion HEI-led briefing for the European Parliament on “Understanding the Health Effects of Air Pollution” designed to inform regulatory decision making in Brussels;
- Led the air pollution analysis in the 2010 and 2013 Global Burden of Disease (GBD) updates, including conducting highly influential and widely reported analyses of estimates for China and India, and organized workshops in China and India to present these country-specific analyses;
- Participated in key science oversight and evaluation groups for highly relevant studies (e.g., the European Study of Cohorts for Air Pollution Effects [ESCAPE] examination of long-term effects of air pollution, reviews of IARC on diesel exhaust and on air pollution, and a review by WHO of the European Air Quality Limit Values); and
- Published reports of studies conducted in Vietnam, Hong Kong, Latin America, London, Beijing, and Ireland, and funded international studies on reproductive outcomes in Taiwan and China, on personal exposure in the United Kingdom, on traffic exposure in Hong Kong, and on cardiac effects in people exposed to air pollution in Germany and the United States.

CROSS-CUTTING ISSUES

Many studies mentioned in the previous sections addressed cross-cutting issues, including evaluating susceptible populations, advancing statistical methods, using new approaches for toxicity testing, and providing access to data. HEI activity in these areas has included

- Funding studies in susceptible populations, such as children, pregnant women, the elderly, and individuals with asthma, diabetes, cardiovascular disease, or other non-cancer diseases;
- Funding studies to advance statistical methods to more accurately understand and interpret data from epidemiologic studies, to develop and validate modeling, and to improve measurement techniques;
- Making data underlying the HEI RIOPA study available on the Web, in the interest of providing broader access to data underlying HEI studies, leading to over 40 peer-reviewed studies of indoor and outdoor exposure (HEI also provided access to PM composition data

through a Web site specifically developed for the NPACT studies); and

- Providing time-sensitive advice to sponsors, the U.S. Congress, and key stakeholders on the best mechanisms for sharing data from important studies while protecting individual privacy.

MEASURING HEI'S EFFECTIVENESS

IMPACT ON SCIENCE

HEI has had a long-term commitment to ensuring that the science it produces is both relevant to decisions and advances understanding across the scientific community. HEI is also strongly committed to tracking the Institute's progress in meeting these goals. HEI initiated and completed a large number of projects undertaken to implement the *HEI Strategic Plan 2010–2015*. Beyond these activities, however, HEI regularly examines other measures to assess how effective HEI's work has been in informing both our scientific and policy audiences. The results of our review of these measures are summarized below.

Studies Started and Completed

HEI initiated 33 studies of air pollution health and exposure over the course of the 2010–2015 *Strategic Plan* period and by March 2015 had published a total of 37 reports (see Table 2). This number includes several reports that were large, complex, and multipart (such as the two NPACT reports and two ACES reports). HEI also published six Communications and Special Reports, including publications

focused on new technologies and fuels, UFPs and their health effects, and outdoor air pollution and health in developing countries. HEI expects to publish a review of diesel epidemiology studies in mid-2015. In addition, HEI made available six unpublished reports (including three pilot studies). By the end of the *Strategic Plan 2010–2015* period, HEI had ten additional reports in the review and publication process. HEI has also continued to maintain two large databases of air pollution information that are available to the scientific community.

Study Dissemination

Since its inception, HEI has distributed scientific reports and summaries of those reports (called "HEI Statements") to a growing list of HEI sponsors, scientists, and interested parties in government, environmental organizations, and industry. Between 2010 and 2014, HEI distributed more than 5,000 printed Research Reports and nearly 32,000 HEI Statements.

HEI reports are also available online through pubs.healtheffects.org. The HEI 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 think a report may be of value. HEI has seen substantial and increasing distribution of its scientific documents via the Web. Each year, the HEI Web site publications page is viewed by approximately 21,000 visitors, who download some 128,000 Research and Special Reports, HEI Statements, and other documents.

Table 2. Number of HEI Studies and Publications, April 2010–March 2015

Topic	Initiated	In Review	Published ^a	Other ^b
Air pollution mixture				
PM, ozone, and other gases	16	4	12	1
Traffic and diesel exhaust exposure	6	0	3	0
Air toxics	3	1	7	0
Innovative statistics	2	3	1	0
Emerging technologies and fuels				1
ACES	0	0	2	2
Accountability (or health outcomes)	4	1	8	1
International	2	1	4	1
TOTAL	33	10	37	6

^aExcluding 3 pilot reports and 3 unpublished reports.

^bHEI Special Reports, Perspectives, and Communications.

Citation of HEI Reports in the Scientific Literature

Another measure of HEI’s impact is the extent to which the scientific community reads and uses its scientific reports. HEI recently analyzed how often HEI Research Reports and scientific papers resulting from HEI-supported work, published in 2010 through March 2015, have been cited in the scientific literature. Results of this analysis suggest that HEI’s impact is substantial (see Figure 1).

- The 37 HEI reports published through March 2015 were cited 356 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.)
- HEI investigators are also actively encouraged to publish in the peer-reviewed literature—during the course of their study or later—and the work described in the 37 reports resulted in 127 peer-reviewed scientific articles. This was an average of 3.4 publications per report, with the highest-impact studies having substantially more associated publications than the smaller, exploratory studies. These peer-reviewed publications, in turn, were cited 2942 times in other publications.
- Thus, the 37 research reports funded by HEI between 2010 and 2014 generated an average of 89.1 citations per report (including citations of the original report and its related journal articles), an extraordinarily high number of citations for any scientific work, for a total of 3298 citations.
- Also, 17 peer-reviewed papers have been published from ongoing studies, which have been cited 86 times.

IMPACT ON POLICY

The full measure of HEI’s effectiveness must include some consideration of how well the science it produces is communicated and put to use in decision making. Similar to the citation counts in the scientific literature, the

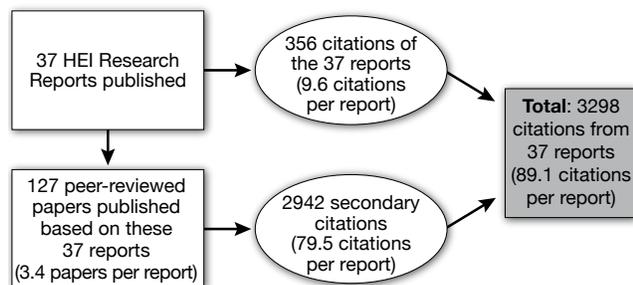


Figure 1. Citations of HEI reports (published between April 2010 and March 2015) and accompanying journal articles in the scientific literature.

number of times HEI reports are cited in regulatory documents helps gauge HEI’s impact. By this measure, HEI has significantly contributed to the scientific basis of norms, standards, and guidelines in the United States and elsewhere. For instance, Figure 2 illustrates a continuing role in the U.S. EPA’s last three reviews of the PM ambient air quality standards. Equally significant, HEI’s reports are also cited in the most recent U.S. EPA assessments for each of the other criteria pollutants as well.

Communication does not end, of course, with the citation of an HEI report in a regulatory document. HEI engages in frequent outreach to leadership and staff from government and core industry sponsors and is often invited to share its science and expertise with a wide set of other public and private actors shaping environmental and public health policy on air pollution. Since 2010, HEI has presented information, provided testimony, and offered technical advice and other assistance in many settings. For example:

- *U.S. governmental agencies and legislative bodies:* The U.S. Congress, FHWA, National Institutes of Health, Occupational Safety and Health Administration, DOE, and California Environmental Protection Agency;
- *Public and private advisory bodies:* The Institute of Medicine, National Research Council, and Clean Air Act Advisory Committee;
- *International organizations and agencies of foreign governments:* The European Commission, European

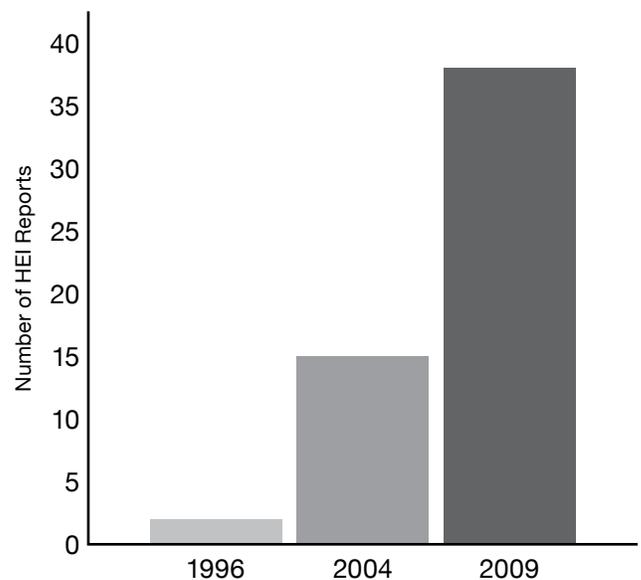


Figure 2. HEI’s impact on documentation for the final PM National Ambient Air Quality Standards. Graph shows the number of HEI reports cited in the PM criteria document or Integrated Science Assessment (ISA) by the U.S. EPA.

Parliament, WHO, IARC, World Bank, China Ministry of the Environment (including the annual Regional Air Quality Management meetings), and India Ministry of Environment and Forests; and

- *Private sector associations and public interest groups:* The American Forest and Paper Association; American Lung Association; API; CONCAWE; EMA; Environmental Defense Fund; European, U.S., and Indian emission control manufacturers; Natural Resources Defense Council; and Union of Concerned Scientists.

THE POLICY CHALLENGES AHEAD

Close attention to the needs and concerns of air pollution policy makers is an indispensable element in HEI's research planning. Air quality goals remain a significant focus of public health regulatory debate in the United States and internationally. This is most apparent in a broad range of policy-setting activities which stress human health impacts at very low pollutant concentrations; assessment of exposures in highly localized environments; protection of children and other sensitive populations; and the integration of climate change and air quality considerations. During 2015 to 2020 and beyond, research agendas will also be driven by changing transportation modes and energy sources and more powerful means of managing and sharing data. Calls for closer scrutiny of the scientific basis of regulatory decisions and the outcomes of adopted measures will increase. The following sections outline key policy drivers likely to be important over the next several years.

AMBIENT AIR QUALITY STANDARDS: INCREASING EVIDENCE, REMAINING UNCERTAINTIES

Reviews Completed or Under Way in the United States, Europe, and China

In the United States, the EPA since 2010 has either started or completed health-based reviews of all National Ambient Air Quality Standards (NAAQS), finding evidence of health effects at low ambient concentrations and tightening standards for several of the pollutants. The ozone standard is currently under review, and the staff assessment has recommended further tightening. Other pollutants are scheduled for review in coming years.

In Europe, similar conclusions about the need for additional health protections were developed by the European Commission last year, after a multiyear review of the European Union air policy. Globally, concerns over air pollution markedly intensified, particularly in Asia,

where extreme pollution levels and new estimates of human health impacts commanded wide public attention. Some of the details are as follows:

- The U.S. and European reviews suggested that recent studies had strengthened the causal determinations made for a number of human health effects and extended the range of effects for which evidence suggesting a causal relationship had accumulated.
- While the recent assessments continue to indicate that PM and ozone pose the greatest potential risks to public health, the health effects associated with NO₂ were also found to be more serious and prevalent than previously thought.
- The European Commission has recently put forward new national emissions ceilings for fine PM and methane. Legislative adoption of these and other control measures is expected over the next few years. In 2013, the Commission deemed current ambient standards insufficient and outlined a program of near-term assessments, with a further consideration of limit values—including areas of high population exposure—to be completed in 2020.
- Dramatic air pollution problems in China, including local health effects and atmospheric transport of pollutants to Japan and the United States, escalated the pace of the country's efforts to improve air quality. Policy responses include the first-ever adoption of an ambient air quality standard for fine particles, stringent emission control measures for coal combustion sources, an expansion of the nation's monitoring network, tightened standards for fuels and vehicles, and an increased commitment to the sharing of air quality information with the public. These are only the first of many actions that will be needed (and reflected in China's five-year plan) to achieve meaningful reductions.

Recent NAAQS and European assessments highlighted a number of uncertainties and limitations that are likely to be key areas for future reviews:

- Whether effects from pollution exposures exist at very low levels of exposure (below current standards) and whether and how current epidemiologic analysis may be applied;
- Continuing emphasis on better protecting susceptible populations, such as children or those with pre-existing health conditions; and
- The nature of exposures in specific microenvironments, and how well monitoring and modeling represent

pollutant concentrations (including exposures identified with the advent of new near-road and urban NO₂ and PM_{2.5} monitoring, and around port facilities).

Source Emissions: Transportation and Energy Choices

Attention to source-specific emissions, particularly from mobile and coal-fired energy sources, has grown around the world, driven by climate, energy, and transportation policy. It is likely to continue to grow during the coming years, despite significant achievements in reducing vehicle emissions.

In the United States, the EPA's Tier 3 program of vehicle emissions and fuel standards is the most recent of an extensive set of measures established over the last decade. In Europe, the adoption of Euro 6/VI marked progressively more stringent emission standards for both light- and heavy-duty vehicles, currently being implemented. China and India, to different extents, are following the European lead. Some specifics are as follows:

- The fast-paced developments in engine technologies and fuels, aimed at improvements in fuel efficiency or to achieve other goals, directly affect emissions. Some emerging technologies (e.g., gasoline direct injection [GDI]) have raised questions about changes in emissions, especially the level of UFP concentrations. Regulatory concern is reflected in the development of a particle number standard for both diesel and gasoline vehicles in Europe and in a continuing interest in California. In the fuels area, increased use of renewable fuels has raised questions about increased levels of aromatics in fuels and secondary PM formation.
- Near-road exposures from existing fleets are likely to be the focus of increased health and regulatory attention because of the deployment of new PM and NO_x roadside monitors (see Figure 3), while offering opportunities to better measure progress as well.
- Air quality concerns around exposure to traffic-related pollutants, including ozone, have focused regulatory attention on real-world and lifetime emissions from vehicles. For example, Tier 3 in the United States extended the required useful life of emission control systems, and the European Union is reexamining and revising its certification testing to better reflect real-world NO_x emissions.
- The emphasis on NO_x controls, even for newer-technology diesel vehicles, is likely to remain especially pronounced in policy discussions in California, where the challenge of meeting the NAAQS-mandated ozone levels is seen as demanding significant actions of

various kinds, and in Europe, where there is concern that diesel engine emissions control technology may not yield the expected NO_x reductions.

POLICIES AT THE INTERSECTION OF AIR QUALITY AND CLIMATE CHANGE

Development of regulatory actions to limit GHG emissions using the Clean Air Act has accelerated the implementation of the U.S. Climate Action Plan. Emission standards are in place or expected for new and existing power plants, and stationary source controls are being developed. Globally, scenarios for post-Kyoto treaty emission-reduction strategies hold enormous implications for air quality management. A major issue will be developing-world GHG reduction targets, especially in India and China, which will drive technology and fuel choices. Some considerations are as follows:

- GHG reduction efforts in the United States have initially focused on motor vehicles, resulting in major changes in vehicle emissions and efficiency. These regulations and harmonization of federal and California programs have accelerated the pace of technologic innovation. The U.S. EPA's new round of GHG standards for heavy-duty vehicles, which would complement the adoption of 2025 targets for light-duty on-road vehicles, will further drive technologic diversity, as will California's planned update of Assembly Bill 32, the "California Global Warming Solutions Act" of 2006. The U.S. EPA is expected to complete a mid-course technology review of the light-duty GHG rules in 2017.
- In recent years, fuel economy and/or GHG emission standards have been established or tightened in Europe, Japan, and China. Gasoline internal combustion engines will remain the near-term technology, but over time a complex mix of future technologic and fuel innovations are envisioned. Assessing the climate and other environmental and health implications of new technologies and emissions will be a key technical and regulatory challenge.
- Looking beyond 2025, the continued desire to significantly reduce GHGs from vehicles is likely to result in further fuel-efficiency targets and even more dramatic fuel and technology changes.

The complex intersection of climate change, air quality, and health will continue to command global policy attention, with increased focus not only on vehicles, but also on other major sources of emissions such as power generation, for which the United States has recently proposed new rules for carbon dioxide (CO₂) reductions. The Fifth



EPA Plans to Monitor NO₂ Concentrations Near Roads in 102 Urban Areas

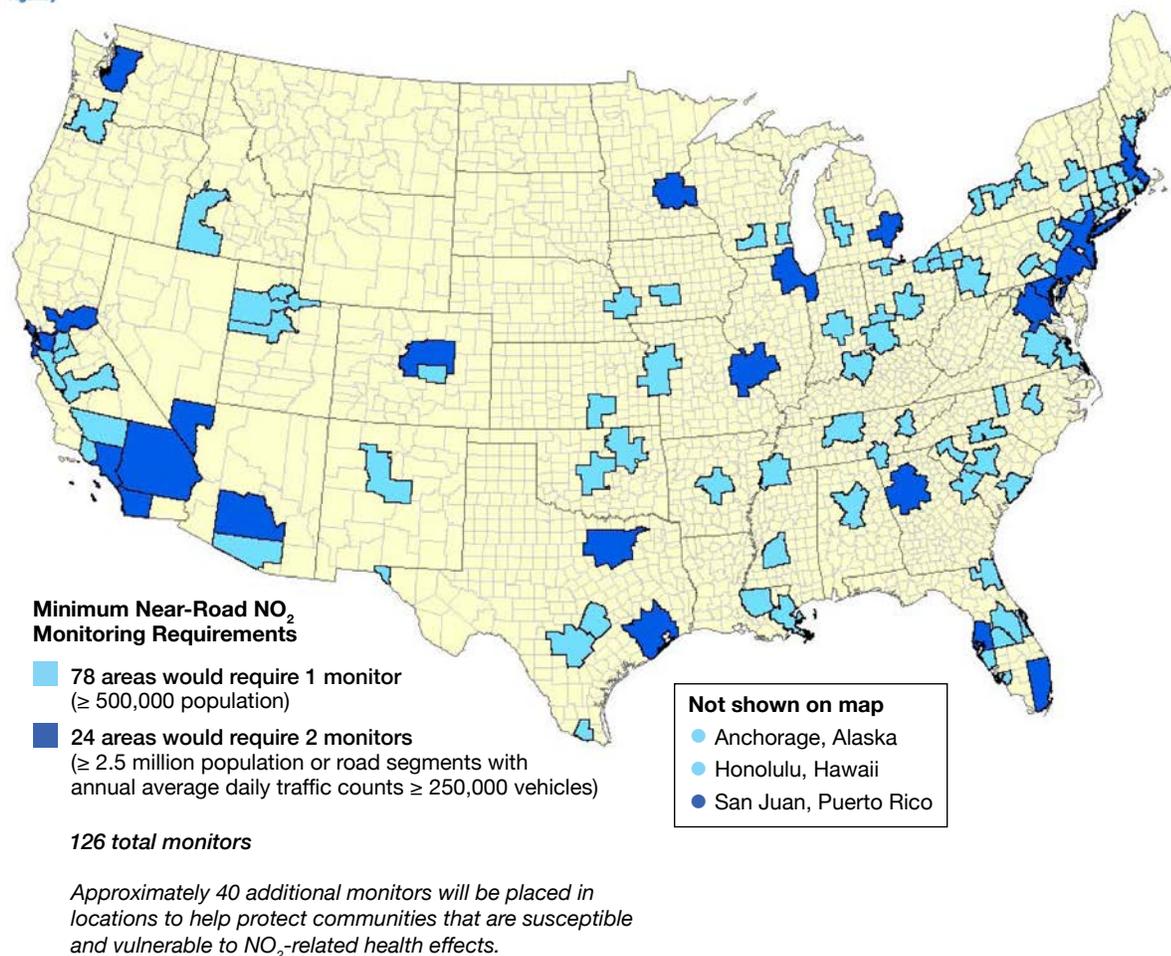


Figure 3. U.S. EPA's proposed near-road monitoring network.
(From: www.epa.gov/oaqps001/nitrogenoxides/pdfs/NO2MonitoringSiteMaps.pdf [accessed 20 March 2015].)

Assessment Report by the Intergovernmental Panel on Climate Change projects air quality impacts from climate change and notes “substantial” health impacts of non-CO₂ climate-altering pollutants and “opportunities to achieve co-benefits from actions that reduce emissions of climate-altering pollutants and at the same time improve health.” Attention to emissions that have both air quality and climate implications, such as ozone and black carbon, has also increased.

REGULATORY EFFECTIVENESS AND TRANSPARENCY

Increasingly stringent and potentially costly regulations have focused attention on the transparency of rule

making, effectiveness of the regulations, and access to data underpinning scientific research. Some of the specifics are as follows:

- The need to better track and understand the health outcomes of major air quality regulations remains a major concern among policy makers and the regulatory community alike. This includes pressure to periodically evaluate the efficacy of U.S. Clean Air Act initiatives mandated nationally and implemented at the state and local levels, as well as ways of evaluating the impact of alternative approaches.
- Access to underlying data is seen as a key tool to evaluate the soundness of regulations and policies and is the subject of proposed legislation in the U.S. Congress, in

administrative policy, and in new procedures urged by the scientific community. This pressure can be expected to continue and expand during the course of this *Strategic Plan*, as federal agencies are engaged in a coordinated effort to develop and implement data access plans.

There is broad interest in regulatory effectiveness and transparency as it touches on fundamental aspects of the scientific process. Questions such as how to best enable innovative approaches to previously unexploited sources of information from often dispersed and enormous data sets are directly relevant to how future air pollution health research will be designed and practiced.

CHOOSING THE FUTURE

HEI has considered a spectrum of air pollution and climate issues, as well as many other broader concerns, in developing its 2015–2020 *Strategic Plan*. A draft Plan for discussion was distributed to participants at HEI's Annual Conference in May 2014. Figure 4 presents the potential topics discussed in that draft Plan, the process for evaluating them, and the selected priority topics in this final *Strategic Plan*. As shown, the draft Plan laid out broad opportunities, as well as many narrower topics, related to concerns about specific pollutants. The Plan was discussed with representatives from HEI's U.S. EPA and motor vehicle industry sponsors, from the oil and other industries, and from the scientific, regulatory, and environmental communities at our Annual Conference and at several smaller meetings over the summer of 2014. The Plan was also discussed at several meetings of the HEI Board of Directors, Research Committee, and Review Committee. Drafts of the initial Plan and a revised version were circulated for comments and suggestions among various sponsor groups and scientific committees.

HEI received much valuable input during these discussions, including 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 by HEI will produce useful findings within the foreseeable future.

WHAT WILL HEI'S STRATEGIC PLAN 2015–2020 ADDRESS?

One key theme among the comments we heard was that, while we must of necessity plan for specific actions that HEI will take in the next five years, we should do that *with a clear eye on the much longer time frames for future air quality and climate decisions*. Challenging decisions on air quality standards continue to arise around the globe as the science evolves. Private and public sector decisions on technology to meet GHG goals (e.g., for vehicles and stationary sources) are already aimed at meeting standards set for 2025—and those standards are likely to be extended for many years beyond. Given that, the *HEI Strategic Plan* is built around one overarching theme: *informing decisions on air quality and on climate-driven technology for 2015–2020...and beyond*.

As illustrated in Figure 5, moving forward HEI sees this theme to be integrated into four core program elements:

- *Addressing the Continuing Challenges of Multipollutant Science*—extending HEI's rigor and innovation in developing next-generation multipollutant approaches to new key questions, including examining evidence of health effects at low ambient concentrations, targeted analysis of potential source effects from traffic, and identification of potential opportunities for development and testing of new statistical techniques in major population databases in the United States and Europe.
- *Accountability and Transparency*—completing the current, and planning the next, generation of HEI-funded accountability studies on key regulatory actions and enhancing our ability to build data access into all HEI work from the inception of the study.
- *Assessing Emerging Fuels and Technologies*—developing a systematic set of toxicity tests and testing for proof-of-concept, as well as facilitating targeted workshops on the state of knowledge of key components of new emissions from vehicle/fuel combinations likely to be considered in meeting upcoming and future vehicle emissions and GHG requirements.
- *Addressing Global Health Issues*—with separate financial support, enhancing U.S.–EC scientific interaction and informing developing world decisions on air quality and climate in Asia and Latin America.

While the *HEI Strategic Plan* is designed to be a clear path forward for HEI to follow in the coming years, we have found that, in order to be as responsive as possible to the emerging needs of our sponsors and others, we must build in the flexibility to anticipate and act on the

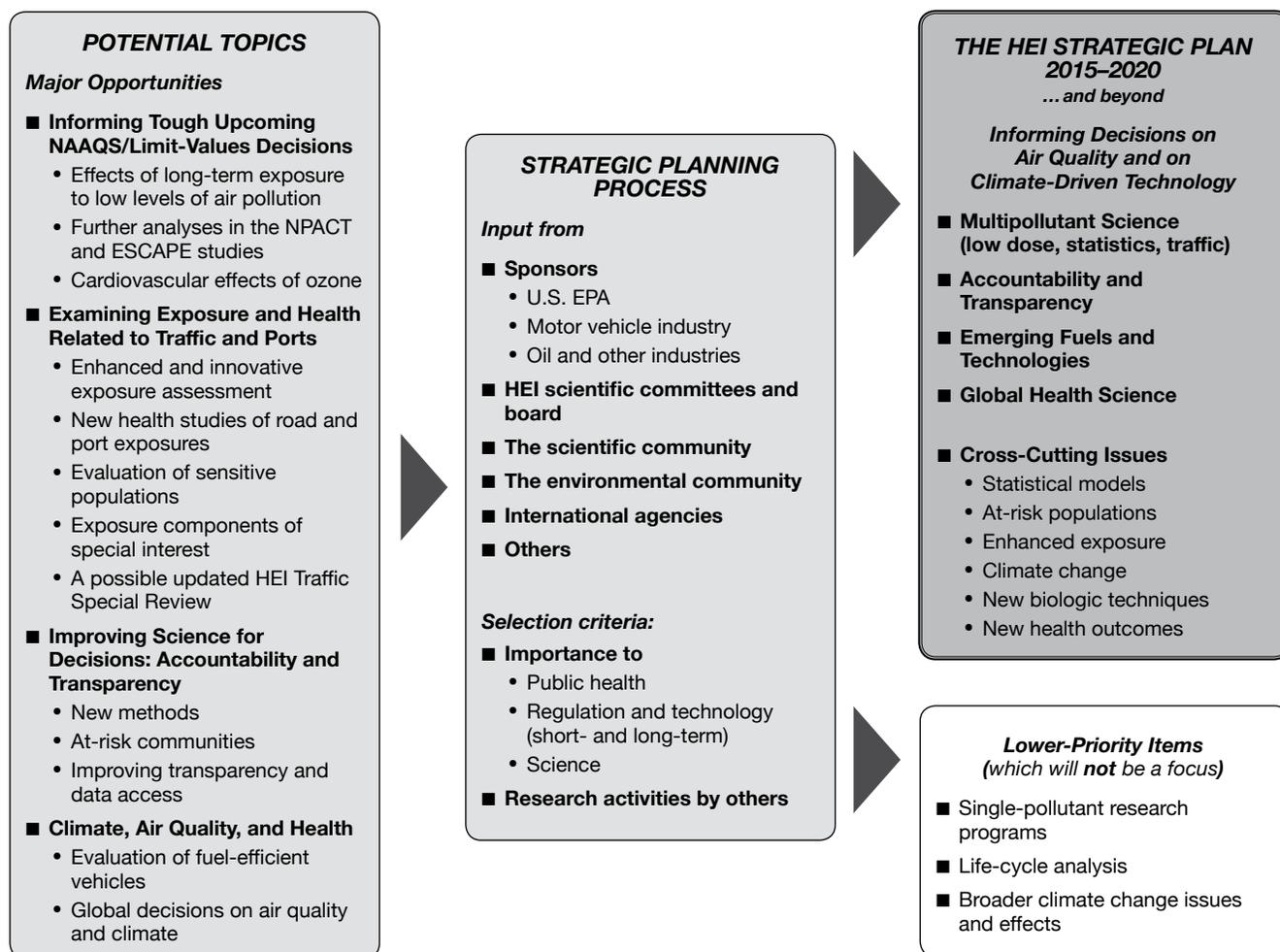


Figure 4. Choosing the future: HEI's planning process.

unanticipated, and we fully expect to continue to have that capacity in the coming years.

We also expect to pursue important cross-cutting issues in all of our efforts, including innovation and testing of statistical analysis and modeling approaches; assessment of selected at-risk populations (e.g., the elderly, the young, those with pre-existing diseases, and those who may be more highly exposed and/or more vulnerable due to their socioeconomic status); evaluation of climate change as a potential modifier of the relation between air pollution and health; enhanced exposure assessment; exploration of new biologic techniques; and consideration of new health endpoints.

In the following sections, we describe in detail the rationale for selecting the four core program areas and the approaches HEI will take in addressing them (see “Priority Research Opportunities”), and the timetable for

implementation (see “Implementing the *HEI Strategic Plan 2015–2020*”).

WHAT WILL HEI'S STRATEGIC PLAN 2015–2020 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 to *not* pursue certain 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 or individual air toxics), but focus instead on multipollutant studies of exposure and health, whether in toxicology or in epidemiology, on a local, regional, and national scale.

The HEI Strategic Plan 2015–2020... and beyond

Informing Decisions on Air Quality and on Climate-Driven Technology

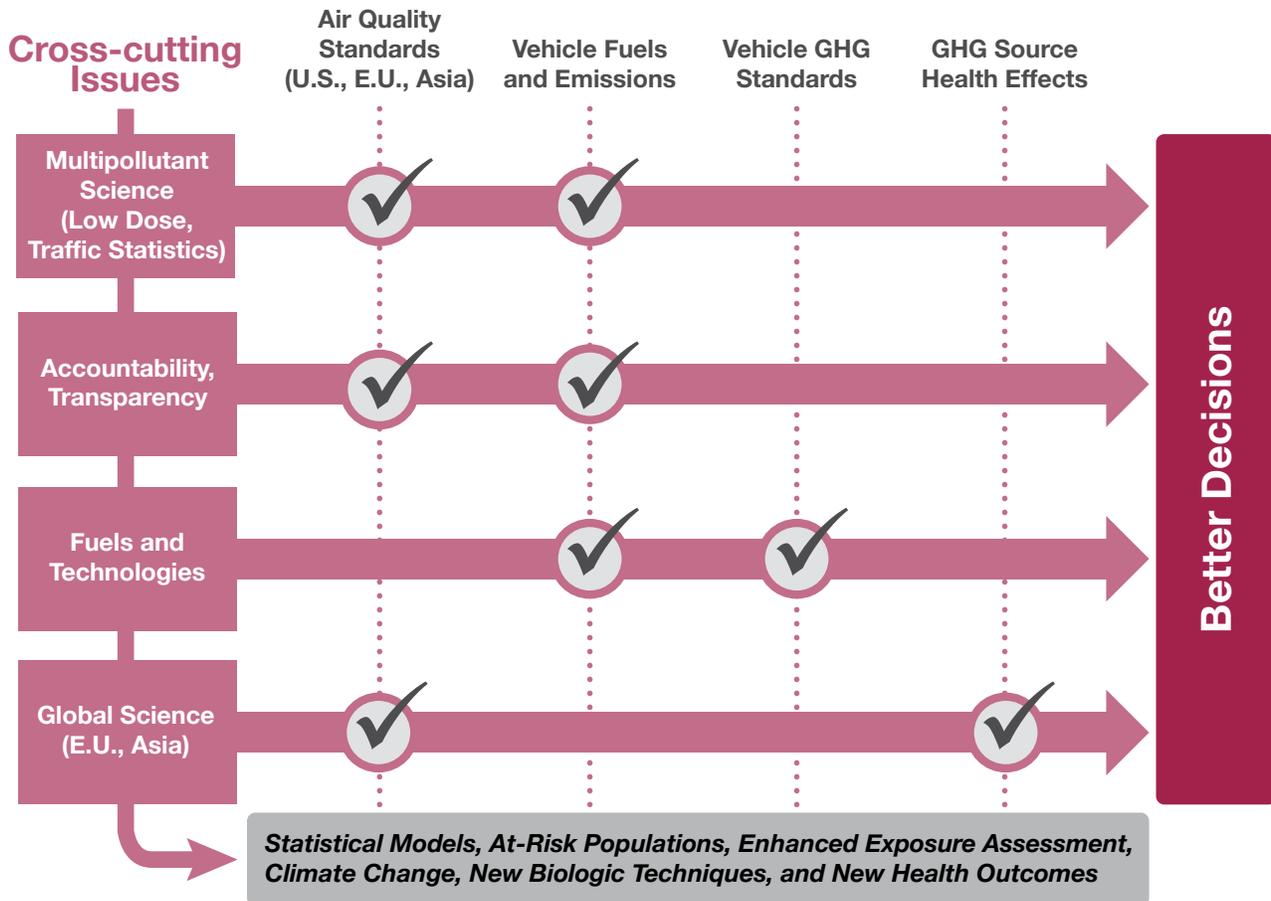


Figure 5. The four core program elements in HEI's Strategic Plan 2015–2020.

- Although there had been some early interest expressed in life-cycle analysis, HEI will not pursue that further in this Plan.
- Beyond its focus on assessing changes in fuels and technologies in response to GHG actions, HEI does not expect to engage in broader research on the health effects of climate change (e.g., concerning sea level rise or changes in the spread of mosquito-borne diseases).

PRIORITY RESEARCH OPPORTUNITIES

Based on the progress HEI has made to date, the challenges for policy and science ahead, and the comments HEI has received on future directions from its sponsors in

government, industry, and the scientific community, we have identified four major areas of significant research opportunities for consideration in the *HEI Strategic Plan 2015–2020*:

- Addressing the Challenges of Multipollutant Science
- Improving Science for Decisions: Accountability and Transparency
- Assessing Emerging Fuels and Technologies
- Addressing Global Health Science

For each of these important areas, we describe below major initiatives that HEI has under way (and will complete in the coming years) or plans to initiate to address key challenges we have identified.

THE CHALLENGES OF MULTIPOLLUTANT SCIENCE

During the *Strategic Plan 2010–2015*, HEI put emphasis on new approaches to understanding multipollutant exposures and health effects. Under this broad area, HEI has now completed several major studies, including those focused on a better understanding of PM toxicity (NPACT), improved statistical methods, air pollution from traffic, and other areas.

Many challenges to a robust understanding of these problems continue, while other research needs (some of which were briefly discussed above) have also become apparent. The consideration of these challenges calls for a new level of rigorous research to answer major uncertainties. During the next five years, HEI proposes to focus its multipollutant research in two broad areas:

- Estimating the effects of exposures to low levels of air pollution
- Understanding emissions, exposures, and health effects of the air pollution mixture

In planning and conducting new research on these topics, HEI will also enhance its resources and ability to catalogue the underlying data and ultimately make them available to other investigators once the studies have been published.

Estimating the Effects of Exposures to Low Levels of Air Pollution

Multipollutant Studies in Large Populations to Estimate the Effects of Exposure at Low Concentrations Levels of ambient air pollution have declined significantly over the last decades in North America, Europe, and other high-income regions. Nonetheless, recent epidemiologic studies report adverse health effects even at these lower levels of exposure. In order to inform future risk assessment and regulation, it is important to know whether adverse effects continue to be observed as levels of air pollution decline still further, and what the shape of the exposure–response function is at those low levels. These issues currently represent the major remaining uncertainties in air quality standards decisions. During the *Strategic Plan 2015–2020* period, HEI proposes to (1) evaluate the most important issues regarding the low-exposure question that need to be addressed before research can be undertaken, and (2) identify opportunities where such research can be implemented.

Large populations will need to be studied in order to accurately estimate air pollution effects at low ambient concentrations. HEI will ask for research groups to

propose study designs based on large populations, either by forming consortia of existing studies or by accessing data for large populations using, for example, administrative databases such as the census. Both approaches entail significant challenges: (1) the requirement of a reliable estimation of exposure and consideration of the level of spatial resolution that will be required—for example, between or within metropolitan areas; (2) resolution of whether a multipollutant approach would be feasible; and (3) the question of how to validate exposure estimates. Measurement error in exposure will need to be quantified and risk estimates adjusted for exposure measurement error, if appropriate. If existing studies are to be combined, a common protocol will need to be developed, including a common approach for characterizing exposure and health outcomes. Studies using large publicly or privately supported administrative databases will need to address issues of data access and confidentiality and will need to develop and apply methods to control for potential confounding from risk factors, such as tobacco smoking, in the absence of detailed personal information.

HEI has formed a scientific committee—consisting of members of the Research Committee and outside experts—to explore the challenges raised above and to advise on the best steps forward. Based on discussions with this group, including the results of an expert workshop held in June 2014, HEI issued an RFA on this topic in December 2014. In addition to a detailed description of design features (e.g., study population, locations, exposure assessment, and health data), applicants were asked to provide an estimate of precision and power to support their proposed population and design. The HEI Research Committee and consultants reviewed preliminary applications in March 2015. Full applications will be reviewed during the summer of 2015, and funding decisions will be made in October 2015.

Effects of Low Levels of Ozone on the Cardiovascular System: Completion and Publication of MOSES

It is well established that exposure to air pollution—particularly PM—contributes to cardiovascular morbidity and mortality. However, studies on the acute effects of ozone have largely focused on pulmonary effects—indeed, such effects are the basis for the current ozone NAAQS—and effects on the cardiovascular system have been largely ignored. Several recent epidemiologic studies that included assessment of associations with specific causes of death have reported stronger associations of ambient exposures to ozone with cardiovascular mortality than with respiratory mortality.

In 2011, HEI initiated MOSES to investigate whether short-term exposure of elderly, healthy volunteers to

ambient levels of ozone in a controlled exposure setting induces acute cardiovascular responses. In the study, which is being conducted in compliance with the latest regulations and guidelines issued by the U.S. Department of Health and Human Services and the EPA for the protection of human subjects, more than 80 volunteers, aged 55 to 70 years, have been recruited to ensure that the study will provide reliable and robust results. The primary outcome of interest is indicators of changes in the cardiovascular system. In addition, pulmonary function, as well as numerous markers of inflammation and oxidative stress, is being recorded. Information about data on the exposure of volunteers prior to testing is also being collected.

In the early part of implementation of this *Strategic Plan*, the MOSES team will analyze data and prepare and submit their final report. The HEI Review Committee will review and publish this report during 2016, along with a detailed Commentary. The investigators will also test a number of secondary hypotheses, including those concerning the effect of prior exposures and genetic polymorphisms.

Understanding Emissions, Exposures, and the Health Effects of the Air Pollution Mixture

HEI envisions three areas of research to improve our understanding of the effects of the air pollution mixture:

- Examining exposures and health effects from traffic and port sources;
- Understanding the changing nature of diesel source emissions and effects; and
- Probing the broader particulate matter mixture and its effects.

Examining Exposures and Health Effects from Traffic and Port Source Mixtures The introduction of cleaner fuels and technologies promises progress for the future as transportation fleets are replaced and the use of new fuels becomes more widespread. However, the advent of increased monitoring and potential regulatory attention to roadside exposures has increased the need for targeted, advanced, and innovative exposure and health research to inform likely future questions on reducing such exposures and effects from traffic. At the same time, the rapid growth in global ocean-going freight movement and the expansion of the Panama Canal have drawn increasing attention to the growth of seaport activity and of goods movement in transportation corridors (roads and rail) leading to and from seaports, and to the potential for increased exposures in communities residing in the

vicinity of such ports and transportation corridors. Questions have also been raised about exposures in communities surrounding airports. More broadly, there is growing attention to the fuller range of potential effects of transportation and mobility decisions on public health. These trends pose several major scientific challenges and opportunities for HEI as it launches its *Strategic Plan 2015–2020*, including the following.

Enhanced, Place-Based Traffic Health Studies HEI Special Report 17, *Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects* and subsequent expert workshops identified a critical need for enhanced traffic exposure assessment that applies the newest sensor and analytic techniques. HEI has already launched five targeted studies—in Atlanta, Georgia; Detroit, Michigan; Hong Kong; North Carolina; and Oakland, California—to enhance exposure assessment, especially for at-risk populations.

As the current exposure studies are completed during the early years of the *Strategic Plan 2015–2020*, HEI will identify opportunities to apply these and other emerging exposure tools to new targeted health studies, especially in sensitive populations. These next-generation studies will pay particular attention to exposures in specific microenvironments and the relation between outdoor and indoor air exposure and will use measurement methods that are currently in development, testing, and validation to allow scaled-up monitoring at modest costs. The new studies may focus on populations in particular transportation corridors and/or neighborhoods surrounding major seaport and/or airport facilities. The presence of industrial sources, significant contributors to both criteria and toxic air pollutants, and exposure to noise, which generally accompanies traffic, may also be included in such studies. The new studies may also take the form of accountability studies of regulatory actions taken to improve air quality near ports or major roads connecting to the ports, similar to the California Goods Movement Action Plan, which is already the subject of an ongoing HEI-funded study in the Los Angeles–Long Beach area (see below).

During the *Strategic Plan 2015–2020*, HEI will also incorporate in its ongoing and new traffic and health studies—in the context of the full traffic mixture—certain special aspects of the traffic pollution mix that are of great interest, including UFPs, the effect of changing fleet composition on emissions and exposure, air toxics, non-tailpipe emissions, and possibly coarse particles. Integrating these aspects into new health studies will not be simple and will likely require the application of some of the innovative multipollutant statistical techniques

developed by HEI and other investigators in recent years. Some topics for inclusion in possible studies are

- *Ultrafine particles*: UFPs were the subject of HEI's 2013 Perspectives 3, *Understanding the Health Effects of Ambient Ultrafine Particles*, which found from the current literature that "the evidence... does not support a conclusion that exposures to UFPs alone can account in substantial ways for the adverse effects that have been associated with other ambient pollutants such as PM_{2.5}." Questions, however, continue to be raised; of particular interest is that UFPs are emitted from light-duty engines that use GDI. In its new traffic and health studies, HEI will explore scientific investigations that might shed light on the role that UFPs may play in health effects in the context of the broader mix of particles, gases (e.g., NO₂), and air toxics emitted from traffic.

- *The changing nature of diesel and gasoline emissions*: During the *Strategic Plan 2010–2015* period, the HEI-sponsored ACES program demonstrated that new-technology diesel engines emit very low levels of PM and other pollutants. It is estimated that approximately a third of the heavy-duty fleet on U.S. roads has new-technology engines. Thus, important and gradually increasing improvement in the levels of roadside pollution, particularly PM, is expected as the fleet continues to turn over. At the same time, there is an increase in the number of light-duty GDI engines, which may be increasing the emissions of some pollutants.

HEI already has plans to characterize changes in real-world PM (and other pollutant) levels: HEI has recently funded a tunnel study, which will compare its results with previous studies at the same location. In the intervening years, however, and in countries outside Europe and the United States, older diesel vehicles will continue to be a significant source of exposure, even as the GDI-equipped fleet increases and the technology evolves. HEI will make special efforts in its new traffic and health studies to integrate source-specific assessment of the contribution of these changing technologies into the assessment of effects.

- *Air toxics*: HEI has a long history of engagement with the effects of exposure to air toxics, including funding of a program of studies on "hot-spots" and publication of a comprehensive report (Special Report 16), *Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects*. As the contribution of diesel engine emissions to air toxics is expected to continue to decline during the next decade, attention continues to be paid to toxics emissions associated with gasoline vehicles. The addition of aromatic compounds

to gasoline, used to boost octane, poses questions in terms of the health effects of direct exposure, the emissions of incomplete combustion products, and their role in the formation of PM. As with the other components of the traffic exposure mixture, HEI will attempt to integrate exposures to the major air toxics (e.g., aldehydes, benzene, and 1,3-butadiene) into its new traffic and health studies. HEI also plans to hold a workshop to better understand the influence of fuel aromatics on PM levels.

- *Non-tailpipe emissions*: With recent and ongoing significant reductions of tailpipe PM emissions from new-technology diesel vehicles, interest in non-tailpipe emissions of motor vehicles is increasing—in particular, how they could affect exposures of individuals living near major roads. Since relatively little work has been done on such emissions, HEI has recently funded a study to characterize such particulate emissions (size distributions, chemical composition, spatial and temporal variation, and exposure assessment) and will explore opportunities for incorporating evaluation of these emissions in the exposure assessment of future traffic and health studies.
- *Coarse (thoracic) particles*: While PM_{2.5} has been the focus of a large number of recent studies, the effects of larger, coarse particles (PM_{10-2.5} [course fraction of PM between 2.5 μm and 10 μm or less in aerodynamic diameter], including brake and tire wear and road dust) cannot be discounted. Both the U.S. EPA and the Clean Air Scientific Advisory Committee (CASAC) have emphasized during the last PM NAAQS review that there is a need for better understanding of possible associations between coarse particle exposure and health effects. In developing its new traffic and health studies, HEI will examine the feasibility of integrating the evaluation of these coarse particle exposures into the exposure assessments.
- *At-risk populations*: A not-insignificant part of the interest in enhanced monitoring of roadside exposures to criteria pollutants such as NO₂ and PM_{2.5} is the disproportionate representation in roadside populations of certain groups, such as those with lower socioeconomic status and peoples of color, who may receive inadequate medical care and/or have other underlying health conditions that may raise their sensitivity to the adverse effects of air pollution. Also potentially of concern are other populations in these settings with certain underlying diseases that can increase sensitivity to the exposures (e.g., children and those with asthma or diabetes). Proximity itself does not establish effects, but rigorous HEI studies with enhanced exposure assessment could

help to determine whether those populations are more susceptible and to better characterize the extent of any health effects.

The State of Knowledge Regarding Health Effects of Traffic-Related Air Pollution After reviewing studies available in the literature through October 2008, HEI published in 2010 a comprehensive assessment of the literature on the sources, exposures, and health effects of traffic-related air pollution (see HEI Special Report 17). During the intervening period, a substantial number of additional studies have been published, and more continue to appear in the literature. Currently, two federal agencies—the Centers for Disease Control and Prevention and the National Toxicology Program—are also reviewing certain aspects of the literature on exposure to traffic pollutants.

In light of these developments, HEI plans to form a panel to systematically review the recent literature and update its 2010 report. One of the goals of the HEI review will be to complement the reports of federal reviews, so that taken together these efforts will provide a comprehensive picture of the state of knowledge regarding the health effects of exposure to traffic pollution. HEI expects to engage in this review during the second half of the *Strategic Plan 2015–2020* period, thus allowing a review of almost 10 additional years of science (approximately 2008–2018).

The Changing Nature of Diesel Source Emissions and Effects In addition to its work on emissions from new-technology diesel engines (specifically, 2007 and 2010 model-year engines), HEI has long played a key role in improving the understanding of exposure to traditional-technology diesel emissions and their effects. As described below and in the section on “Emerging Fuels and Technologies,” HEI plans to continue several such activities, as well as to undertake additional initiatives.

The Diesel Epidemiology Review: Suitability of Current Epidemiologic Studies for Risk Assessment For many years, epidemiologic data have been used to identify the hazards associated with exposure to diesel exhaust. However, the available studies had limitations, which were documented in a 1999 HEI Special Report, *Diesel Emissions and Lung Cancer: Epidemiology and Quantitative Risk Assessment*. Recently, results have been published of several new studies examining the association between diesel emissions exposure and lung cancer (including one from a cohort of U.S. miners); these new studies have attempted to address these limitations and to estimate exposures more precisely than has been possible in the past. These studies contributed to the recent

decision by IARC to designate diesel exhaust as a known human carcinogen (IARC Group 1). In light of these new developments, and in response to strong interest expressed by both our government and industry sponsors, HEI launched its Diesel Epidemiology Review by convening an expert panel, chaired by Daniel Krewski of the University of Ottawa. A final report from the panel is expected in mid-2015.

During the early years of the *Strategic Plan 2015–2020*, HEI will undertake a number of steps to communicate the findings and conclusions of the Diesel Epidemiology Panel. The Institute will hold briefings for its sponsors, publish the report, and make it available widely through print and online. Because old-technology diesel engines are still widely used in developing countries, HEI’s communication efforts will also extend to international as well as country-level meetings and conferences.

Emissions from New-Technology Diesel Engines HEI has recently completed ACES, a comprehensive study to characterize the emissions from 2007- and 2010-compliant heavy-duty diesel engines, along with a detailed study of the health effects in rats exposed for a lifetime to diesel exhaust from a 2007 engine. The results show that pollutant emissions from such modern engines are very, very low and that the emissions produce few, if any, effects of concern—especially for carcinogenicity—in animals. This is the most comprehensive and systematic study of new-technology diesel engine exhaust to date.

During the early part of the *Strategic Plan 2015–2020*, HEI will communicate the results of the ACES animal bioassay study widely. The report from the animal study, accompanied by several detailed appendices and ancillary studies examining other health points, as well as a Commentary by the HEI Review Committee, will be disseminated through print and Web. As in the case of results of the Diesel Epidemiology Panel’s report, the results of the ACES studies are particularly pertinent for developing countries, and HEI will also focus its communication efforts in this area.

Finally, the ACES program has generated a very large amount of information about the characterization of emissions from new-technology 2007 and 2010 diesel engines and an animal bioassay with 2007 emissions. During the first part of the new *Strategic Plan 2015–2020*, HEI will prepare a document that will succinctly summarize the findings of the ACES program and put its findings in the context of prior knowledge of old-technology diesel engine exhaust.

Enhanced Analyses Within the NPACT and ESCAPE Cohorts Recently, the results of two major air pollution

epidemiology efforts have been published: the HEI-funded NPACT initiative and the European Study of Cohorts for Air Pollution Effects (ESCAPE). For NPACT, Drs. Lippmann and Vedal and their respective colleagues performed coordinated U.S.-wide epidemiologic and toxicologic studies of the health effects of PM and its components. Overall, these studies found associations of health effects with exposure to secondary sulfate and, to a somewhat lesser extent, traffic sources, although it was not possible to isolate any source as the primary contributor to effects. Using more than 30 existing cohorts, the ESCAPE study investigated long-term effects on human health of exposure to air pollution in Europe. The investigators have reported associations of PM or NO₂ exposure to health outcomes such as respiratory and cardiovascular morbidity, cancer and natural-cause mortality, and birth and pregnancy outcomes. Importantly, the ESCAPE study suggests the persistence of health effects at exposure levels *below* the European ambient air pollution standards. The strength of both the NPACT and ESCAPE efforts lies in their systematic and careful planning, their wide geographic coverage, and their use of state-of-the-science statistical analyses. Both also relied on a combination of monitored pollutant levels and performed careful modeling to estimate exposures. While they did use different approaches to estimating exposure—across cities versus within cities—this may offer opportunities for comparing these alternative approaches across the different populations.

Many continuing uncertainties about the health effects of air pollution call for further investigation. To gain a better understanding, HEI proposes to explore with the original investigators of these studies (and possibly others) the possibility of performing additional, well-coordinated analyses, including using or developing new analytical methods. To begin this, HEI plans to conduct, in concert with the EC and other relevant agencies, an in-depth workshop with the investigators of these studies, as well as investigators of other recent cohort studies, and other experts in exposure, health, and statistics. The following are some of the most salient questions that could be considered at such a workshop:

- How might the extensive databases for health and exposure from both the NPACT and ESCAPE studies provide a good opportunity for further analyses? Would there be opportunities to apply the innovative statistical methods for characterization of air pollutant mixtures and/or the study of the health effects of such mixtures developed recently by HEI-funded investigators (e.g., Coull, Molitor, Park, Robins, Batterman, and Ryan and their teams) and by other biostatisticians?
- In contrast to reports from North America, some large European studies, including ESCAPE, have not found an association between air pollution and cardiovascular mortality, although they do report associations with cardiovascular morbidity and all forms of natural-cause mortality (including cancer and other causes). The workshop would provide an opportunity to explore factors that may have contributed to these differences and determine whether additional analyses in pooled data sets or alternative statistical approaches might help us better understand the results.
- Will it be possible to apply advanced source apportionment methods to the PM composition data that have been amassed in both programs and use these for epidemiology analyses? This might include, for example, measures of secondary organic aerosol such as organic carbon, and the corresponding findings for elemental carbon, which have been collected as a part of these studies.
- Is there a possibility of collecting further follow-up data in the participating cohorts to enable truly prospective analyses based on the exposure assignments from the 2008–2010 monitoring campaigns? Most, if not all, of the ESCAPE cohorts have ongoing data collections, and having five or more years of additional follow-up could make a big difference for many health endpoints.
- Are there other cohorts (e.g., in Canada, elsewhere in Europe, or in China) that might be usefully included in such discussions?

Based on the results of this workshop, HEI would then consider, in consultation with the EC Directorate-General for Research and Innovation (DG-RTD) and the Directorate-General for Environment (DG-ENV), opportunities for additional research in these important cohorts. Such research would likely take shape in the second half of the new Plan period.

ACCOUNTABILITY AND TRANSPARENCY

HEI's interest and commitment to accountability studies stem in large measure from the importance of assessing whether potentially costly and complex regulations and other interventions are yielding the demonstrable improvements in air quality pollution and public health that were initially projected. In addition, lessons learned about regulatory efficacy from these studies are a means of informing the design and implementation of future efforts to improve air quality. HEI defined initial concepts and methods in this arena with the publication of a major monograph in 2003 (HEI Communication 11). Subsequently, HEI published other documents in the literature and has

funded a successful first wave of studies, which largely evaluated local interventions occurring over relatively short periods of time. HEI built on lessons learned from those first-wave studies to inform a next wave of research to address larger state, regional, and national regulatory programs occurring over longer periods of time and to develop additional tools to conduct such complex studies.

As reported earlier, in 2011 HEI issued RFA 11-1 seeking proposals to study the effects of specific regulatory programs to improve air quality with a focus on large-scale multiyear regulatory programs, complex regulations in large urban areas and around major ports, and improved methods to support outcomes research. Together, these studies signaled a move into the research and development of tools to assess outcomes of core environmental regulations at the state and national level that impact the health of the broader public.

Early during the *Strategic Plan 2015–2020* period, HEI will complete the four studies from that RFA currently under way (on evaluating children’s health and regulations in southern California, goods movement regulations in California, air quality regulations in the southeastern United States, and statistical methods to better assess large national databases). These studies provide some of the first attempts to evaluate large-scale regulations. However, there are many continuing challenges (e.g., concerning concurrent changes in a range of environmental, health, individual, and socioeconomic variables, and involving the implementation of multiple regulations within the same time frame as the regulation of interest). More work remains to be done because evaluation of regulatory effectiveness is critical to ensuring public health and minimizing cost.

Next-Generation Accountability Study

As the second-wave studies reach completion and review during the early part of the *Strategic Plan 2015–2020* period, HEI is planning to gather a small group of experts (similar to what was done after completion of the first wave of studies in a 2009 workshop, and again including members of HEI Committees as well as other interested parties) to review progress and chart next steps. Based on discussions during this second workshop, the HEI Research Committee will plan the next phase of HEI’s Accountability program. Though it may be premature to be specific, some of the areas that are likely to receive attention include the following:

- Studies that are more closely linked to implementation of new regulations, such as

- implementation of NAAQS (e.g., PM_{2.5} and ozone standards);
 - implementation of major stationary-source rules addressing air quality and climate issues, including those addressing emissions from coal-fired utility and industrial sources;
 - implementation of actions to accelerate diesel technology replacement (e.g., expenditures under the Diesel Emissions Reduction Act); and
 - the effects of systematic introduction of alternative fuels over time.
- Measures specifically aimed at reducing the exposure of at-risk populations.
 - Smaller-scale interventions aimed at improving air quality and reducing GHG emissions at the local level (e.g., interventions for improved residential efficiency [and resulting changes to indoor ventilation] or switching fuel from diesel to natural gas).
 - The development of new methods, including enhanced statistics, application of causal models, and potential use of new biomarkers of exposure or early disease in national-scale databases.

Improving Data Access

Throughout its history, HEI has had a commitment to transparency and data access. In addition to maintaining a strong policy on facilitating access to underlying data and methods for the studies it funds, HEI has responded to requests from government, industry, and others to reanalyze studies central to the regulatory process and evaluate their overall strengths and weaknesses and, in other cases, their suitability for use in quantitative risk assessment. Recently, interest in ownership, access, and control of data underpinning scientific research has risen in Congress and in the scientific and stakeholder communities, and requests for HEI involvement have increased. HEI sees activities in this area as an important feature of this Plan.

During the *Strategic Plan 2015–2020* period, HEI plans to conduct one or more workshops at the science–policy interface to identify and promote approaches to data sharing, including identifying opportunities to make data more widely available, as well as challenges to data sharing in the context of confidentiality and other privacy protections. The workshop(s) will also focus on exploring solutions to how scientific data may be shared, an area in which HEI has had some experience.

HEI’s commitment also extends to making data from HEI-funded studies available for reanalysis, replication, and extended analyses by others. Given widespread

interest in both the science and policy communities in this issue, HEI will enhance its ongoing efforts to make all data underlying its studies available following publication and to build on its expertise in this area.

EMERGING FUELS AND TECHNOLOGIES

HEI has long provided critical information on key questions relevant to emerging vehicles and fuels, including emerging diesel technologies, alcohol fuels, and fuel additives such as manganese and methyl tertiary-butyl ether. More recently, HEI undertook a major initiative—ACES—to characterize emissions from new-technology 2007 and 2010 heavy-duty diesel engines and to assess the health effects of emissions from a 2007 engine in laboratory animals. Additionally, through SCET (see next section), HEI has established a mechanism to obtain and provide an ongoing understanding of emerging new technologies and fuels.

In view of concerns about air pollution, climate change, and energy security, there is a desire to find new solutions to enable mobility for the public. Recent regulatory activities in Europe, the United States, the state of California, and many other parts of the world have been specifically focused on combating various aspects of this set of challenges. This situation also provides the impetus for the development and introduction of a broad range of new fuels, technologies, and sources of energy to meet the needs of the transportation sector. Over the next five years, health concerns that may arise from the use of these new fuels and technologies will remain a priority for HEI research.

Special Committee on Emerging Technologies (SCET)

SCET is a key advisory body established by the HEI Board of Directors in 2000 to aid HEI 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 from industry, government, academia, sponsors, and environmental organizations knowledgeable about fuels, technologies, health, and future trends.

In the recent past, HEI has convened SCET for meetings every two to three years. In 2011, HEI published a comprehensive report on new fuels and technologies (Communication 16). In 2013, SCET met to discuss changes that have occurred since the report was published. The deliberations and advice from this meeting proved useful in the preparation of the current plans described in this document. Looking forward, SCET will meet twice during implementation of this Plan for broad overviews and to identify emerging

areas to which HEI should pay particular attention. The membership of SCET will be updated to replace members who have become unavailable and to add additional expertise. Members of SCET with appropriate expertise will also be involved in planning and implementation of plans presented in this section.

Toxicity of Emissions from Emerging Vehicle Technologies and Fuels

In view of current and anticipated policies, emerging technologies (e.g., GDI, hybrids, electric drivetrains, and new-technology diesel engines) and new fuels (e.g., blends of ethanol, biodiesel, CNG, and electricity) are being deployed. The use of some of these—such as 10% ethanol—is already widespread, whereas others—such as GDI and new-technology diesel—are on an accelerating trajectory. With a few exceptions (such as the U.S. EPA–DOE Energy Policy and Conservation Act and HEI’s ACES programs), evaluation of the potential impact from the use of such fuels and technologies has been quite limited. Challenges include selecting “representative” engines, vehicles, fuels, and driving conditions, among others, and the lack of an agreed-upon suite of biologic or health effects testing protocols. The “gold standard” of toxicology—lifetime exposure studies in animals—is time-consuming, expensive, and subject to interpretation. With the exception of ACES, no such studies have been attempted. Several investigators have performed short-term *in vivo* and *in vitro* assays, but in the absence of common and standardized protocols, the results of such studies are difficult to compare. Yet, the need for such evaluations is now more pressing than ever.

To meet this challenge, HEI will undertake the following two-phase initiative:

- The goal of Phase 1 of this work will be to identify a set of toxicity tests that experts agree reflect health effects endpoints of concern, to agree on protocols for these tests, and to assess—and, as needed, modify—the protocols in several laboratories. For this phase, HEI will do the following:
 - HEI will convene a committee of leading experts in biologic testing, both *in vitro* and short-term *in vivo* assays (including proteomics and genomics platforms and high-throughput methods) for several endpoints (such as genotoxicity, oxidative stress, and inflammation). This committee will include experts involved or very familiar with ongoing and larger efforts at toxicity testing, such as those at the U.S. EPA and the National Toxicology Program (including its Interagency Coordinating Committee on the

Validation of Alternative Methods). However, the HEI committee will focus specifically on testing of mobile-source air pollutants, which pose particular challenges.

- Working with this committee, HEI will identify critical pathways and develop an agreed-upon set of appropriate tests and protocols. Smaller working groups with specific expertise in these methods will develop standard operating procedures and other guidelines for performing these tests. The committee will pay particular attention to the testing of emissions in ways that allow both particulate and volatile components to be evaluated. Also, the committee will seek links in HEI's work with the other ongoing toxicity testing efforts mentioned above.
- HEI will also work with a group of laboratories, with the requisite background and facilities, to assess the procedures identified and developed above. The testing phase will establish base parameters of the methods, including reproducibility and specificity, along with other variables for each assay.
- Phase 2 of this effort will test the methods mentioned above on emissions through pilot studies. Recognizing that a robust testing program to characterize “representative” engine and fuel combinations would be a significant undertaking far beyond the resources available to HEI, the goal of this phase will be to leverage ongoing emissions testing efforts at other organizations, such as the University of California at Irvine, CARB, and/or private laboratories (such as the Southwest Research Laboratories), allowing HEI to learn of any challenges to the feasibility of conducting the biologic tests for their intended purposes. If possible, HEI will also include testing of emissions aged in atmospheric chambers along with testing of fresh emissions. These efforts will *not* provide reliable and “representative” information on exhaust from a range of fuel/technology combinations, but will serve as a proof of concept on which future testing programs may be built and, equally important, will provide useful data for future testing programs.

In early conversations, several organizations in the public and private sectors have shown great interest in the efforts just described. Since the biologic testing methods would have been agreed upon and tested with other organizations, we trust that they would begin to use them as well, and a database on the effects of emissions would begin to develop—filling a much needed gap in our knowledge. HEI anticipates that the toxicity testing activities will produce a series of reports and other documents.

Aromatics in Gasoline and PM Formation

There is evidence that the degree of hydrocarbon unsaturation in gasoline, including the contribution from aromatic compounds, is proportional to PM emissions. The use of ethanol blends would be expected to dilute unsaturated hydrocarbons in fuels in proportion to blending levels, and thereby reduce PM formation. However, recent data from the U.S. EPA's Office of Transportation and Air Quality suggest that ethanol's effects on PM emissions are complex and that, at least for certain vehicles, ethanol augments the effect of unsaturation in terms of production of PM. Given that the Energy Policy Act of 2005 mandates the use of increasing amounts of renewable fuels in the coming years, the most recent data on unsaturation and PM raise a potentially significant issue. PM emitted under these conditions has not been characterized, nor have any health effects studies been performed. Additionally, very little is known about the potential impact of such emissions—including primary PM—on secondary organic aerosol formation, which is an important, though not well-characterized, issue regarding population-wide PM exposure.

In view of the importance of the above-mentioned issues, and given the many uncertainties, HEI plans to hold a workshop during the early phase of the 2015–2020 Plan. The goals of this workshop will be to (1) present and summarize the current state of knowledge on all aspects of aromatics in gasoline—including ethanol blends—and PM formation (both primary and secondary) and (2) identify questions and approaches that will provide answers to unresolved questions.

To organize this workshop, HEI will form a small committee composed of experts in the various aspects of this area. HEI will also liaise with government and other sponsors to ensure that the workshop will be responsive to their needs.

Gasoline Direct Injection and UFP Emissions

Starting with the 2007 model-year engines, new developments and regulations have led to a dramatic reduction in the emissions of PM from diesel vehicles. Today, about a third of diesel-powered vehicles on U.S. roads have new-technology engines, and this proportion will increase as the fleet turns over. However, although gasoline engines have traditionally been a relatively minor source of PM, the introduction of engines that employ GDI is raising new questions because such engines emit increased levels of PM in the ultrafine range. The use of GDI is growing because such engines offer improved fuel economy. Though UFP emissions are not specifically regulated in the United States, they are regulated in Europe

under a particle number mandate; debate about a similar policy approach in the United States continues.

Even with the use of GDI, overall emissions of PM from all mobile sources are expected to be below the total PM emissions measured when old-technology diesel was prevalent. Additionally, it appears that UFP emissions from GDI engines can be reduced by refinements in fuel injection that minimize contact with the combustion-chamber walls and valves. Nevertheless, neither the nature of GDI-generated UFPs nor the potential contribution of GDI vehicles to human exposure to UFP has been characterized, and factors that affect UFP emissions from such engines—fuel and blend levels, other engine characteristics, driving cycle, to name just a few—have also not been discussed broadly.

To understand and delineate these issues better, HEI will hold a workshop on GDI engines and UFP emissions during the middle of this Plan period. The workshop will bring together experts in engine/fuel injection design and UFP emissions, the fate of UFP emissions in the near-road environment, and the potential for human exposure, among other areas, and will invite speakers to present state-of-the-science research on GDI and UFP emissions. Workshop participants will also discuss key unresolved issues and how these may be addressed. The workshop will be organized by a small committee, consisting of experts in the various areas relevant to this topic.

Other Important Issues

In addition to the topics discussed above, there are several other issues that HEI will continue to monitor, with assistance from SCET, especially in the context of any health effects concerns they may represent. Such issues include the following:

- *Advanced-technology diesel engines:* Though enormous progress has been made in reducing emissions from diesel engines during the past decade, the technology continues to advance in this area. HEI will seek SCET's advice on whether emissions from these newer engines need attention from a human exposure and health perspective. Two trends are particularly noteworthy:
 - Lower NO_x heavy-duty diesel engines: Given the continuing high ozone levels in California, CARB has indicated that it will seek to further lower the standard for NO_x emissions from heavy-duty diesel engines. Approaches under consideration include better thermal management and new or improved aftertreatment systems (e.g., new SCR formulations, NO_x storage, and alternatives to urea). HEI will have

an initial discussion of NO_x-related issues during its Annual Conference in May 2015.

- Diesel engines without diesel particulate filters: For emissions of PM_{2.5} from some non-road diesel engines, the EPA has set a somewhat less stringent standard than that for on-road engines. Some engine manufacturers are able to meet the lower non-road standard without the use of a diesel particulate filter. It does not appear that emissions from such engines have been well characterized. It is also not known at this point whether further developments would allow the use of such engines for on-road uses, but HEI will work with SCET to track these developments.
- *Potential health effects issues of low-carbon fuels:* As discussed above, the Energy Policy Act of 2005 mandates the use of increasing amounts of renewable fuels in the coming years. At the same time, increasing attention is being paid to the identification and increased use of low-carbon fuels. Though the implementation of the amounts of renewable fuels required under the law is lagging behind for a variety of complex reasons, most gasoline sold in the United States today is a 10% ethanol blend, and biodiesel is often blended with diesel in many parts of the country. All indications are that the use of ethanol and biodiesel—as well as higher blend levels and other fuels—will have an upward trajectory in the years to come. These issues were comprehensively discussed in HEI Communication 16 on new fuels and technologies (2011).

HEI is interested in understanding whether the emissions from the use of such fuels may be important in terms of their public health impact, given that their use is very widespread. There have been some fairly broad research programs on biofuels emissions undertaken by government agencies, private companies, and academic institutions that have characterized emissions. However, because of variation in engine operating conditions, fuel mixes, and emission characterization protocols, the results of the various studies are not easy to compare. HEI considers emissions from new fuels to be an important issue and, working with SCET, will stay abreast of new results and developments in this area.

GLOBAL HEALTH SCIENCE

With supplemental financial support from foundations and international organizations, HEI has worked carefully for many years to extend its work in the United States—both in Europe, where science is often directly relevant to the United States, and in the developed world, in order to provide credible, policy-relevant science and

capacity building to inform decisions in the developing nations of Asia and Latin America. HEI's ability to attract support for such studies greatly leverages the initial investment of the U.S. EPA and industry, taking advantage of unique research opportunities found in the developing world to provide science relevant to decisions in the United States and Europe as well.

Science to understand the health effects of air pollution is much needed in China, India, and developing Asia, where air pollution from a broad range of sources not only directly affects the health of local populations, but also is transported to Japan and the western United States (affecting the health of populations there). Air pollution originating in Asia also contributes a large percentage of global GHG emissions. In addition, the 2010 GBD estimates found that ambient air pollution was associated with over 3.2 million premature deaths worldwide, of which fully two-thirds are in developing Asia.

It is in the interest of regulators and the regulated community alike to support high-quality science, capacity building, and active communication with policy makers in order to engage and equip developing nations to understand and respond to the health, economic, and environmental benefits associated with pollution reduction for local and global benefit. HEI has attracted significant additional support for its international work in the past, including from the European Union and industry to work in partnership with WHO on air quality guidelines and from domestic and international foundations for science at the global level. During the 2015–2020 Plan period, HEI will benefit from similar support and will implement a strong global program through a range of initiatives, including the following:

- *Supporting broadly relevant science in Europe—exploring enhanced analyses within the NPACT and ESCAPE cohorts:* HEI has a strong history of leveraging its core program investments through targeted partnerships to support research, scientific workshops, and periodic reviews of the science in Europe. Examples include joint HEI–EC research support of U.S. and European investigators to facilitate combined analyses of respective populations in HEI's APHENA study and joint scientific workshops in partnership with the European Commission, WHO, European stakeholders, and the European Parliament to inform European consideration of new air quality guidelines in 2013. These initiatives brought together leading scientists and regulators from North America and Europe, including the U.S. EPA, DG–ENV, and member states to gather and review evidence relevant to decisions on both continents.

As described earlier, during the next five-year cycle, HEI expects to conduct, jointly with the EC and other relevant agencies, a workshop to review the data collected for two major air pollution epidemiology efforts—the HEI-funded NPACT initiative and the ESCAPE program in Europe—as well as other population studies, and to determine the best ways forward for potential joint analyses and further detailed testing of the effects of pollutant mixtures.

- *Global Burden of Disease:* GBD is arguably the most comprehensive and credible worldwide assessment of mortality and disease, and the risk factors associated with them, ever undertaken. Overseen by the Institute for Health Metrics and Evaluation (IHME), GBD is a partnership of more than 1000 scientists from 106 countries worldwide working together and with WHO and others to conduct this analysis. HEI led the air pollution working group and worked with IHME and others to calculate and widely communicate the country-specific mortality and morbidity impacts for China, India, and other nations to policy makers, stakeholders, and the media.

Looking ahead, beginning with 2013 data, GBD will now be updated on an annual basis, allowing air pollution and other impacts to be assessed regularly as a tool for measuring progress. HEI will participate through the following:

- Continue to lead the air pollution working group and, in partnership with IHME, update methods and data in order to calculate and communicate highly credible annual analyses in China, India, and other key nations.
- Launch a major new initiative to calculate the source-specific health impacts from the combustion of coal and other sources in China, India, and—resources permitting—Eastern Europe. This initiative is grounded in the belief that focusing more narrowly on health impacts from the combustion of coal and other sources will bring a sharpened focus to the important task of achieving reductions in emissions from a health-impact perspective and that health-based reduction measures will also inform significant GHG reductions.

HEI's work on GBD will be in partnership with leading international institutions (e.g., Tsinghua University and Peking University in China, Public Health Foundation of India, U.S. EPA, and IHME). HEI's collaborative approach will provide local knowledge and understanding and will enhance access to and credibility with Asian governmental decision makers.

Targeted New Research in Asia

One of HEI's major contributions to date has been the building of partnerships with leading local scientists in Asia to conduct high-quality and relevant new studies of air pollution and health. Looking ahead, and pending the availability of foundation and other funding, HEI has identified two potential areas for the focus of new investigations:

- *Long-term cohort study in developing Asia:* The estimates of air pollution and mortality and morbidity in developing Asia calculated by the GBD effort are the highest of any region in the world. However, these estimates are based largely on long-term studies conducted in the developed world (e.g., American Cancer Society cohort). To better inform and calibrate future studies and models using a range of analytic tools including the GBD, the Environmental Benefits Mapping and Analysis Program (BenMAP), and other approaches, and to increase the credibility of results in Asia, there is a strong need for studies of long-term effects in developing Asian populations, especially China. The advent of enhanced ambient air pollution monitoring in China and the increased reliability of satellite-based monitoring have increased the likelihood that existing cohorts may now be suitable for this purpose. During the coming years, HEI intends to work with policy makers and others to identify support (e.g., from the U.S. State Department) to make such a cohort study possible.
- *Studies of air pollution in and around port facilities:* The health effects of air pollution around ports and other centers of goods movement, as described earlier, are of high interest and have prompted ongoing research at HEI. Significant regulations, including national Emission Control Areas and California's port regulations, are already in place in parts of North America. In developing Asia—and Hong Kong in particular—there is strong interest among regulators, environmental NGOs, and segments of industry in building on current regulations requiring low-sulfur fuels in ports to establish emission-reduction programs in Guangdong, Hong Kong, and Macao, and potentially to extend this to other China ports. There is currently a dearth of studies on the impact of shipping emissions on communities in and around ports such as Hong Kong, though emissions are significant and populations are in close proximity. During the coming years HEI will seek to build on its current work in order to understand emissions and health impacts around ports in California and to seek external funding to evaluate the health effects of emissions from shipping in and around major ports in Asia.

Capacity Building

In conducting its work on air pollution and health in the developing world, HEI has always made enhancing the capacity of local scientists to conduct and communicate policy-relevant science a key priority. This was most clearly accomplished in HEI's PAPA program, which paired leading investigators from the developed world with emerging scientific teams from developing countries. This approach has been highly successful, allowing HEI to leverage its cutting-edge research experience by transferring analytic capabilities to emerging investigators, often resulting in their ability to independently obtain funding for new work without Western involvement and to successfully publish in quality scientific journals, increasing the base of quality Asian and other science.

HEI will take a similar approach in the source-specific GBD initiative, where we will establish a high-level International Steering Committee of global experts to help oversee and guide the project and establish a working group of scientists from China, India, Eastern Europe, and other areas. This has the dual benefit of increasing skills among local scientists and also providing enhanced credibility for HEI-funded results because they are produced, not by Westerners alone, but by working in partnership with respected local scientists.

Active Communication with Policy Makers

As noted in the sections on HEI impact above, facilitating high-quality independent science is only one part of having that science seen as relevant and of ensuring that it ultimately be used in decisions by industry and government sponsors. Effective communication of the results is also needed. Since its inception, HEI's global program has sought to systematically and effectively communicate results to decision makers, as well as the public, so that the results are well understood, credible, and can serve as part of the foundation for policy and regulatory interventions.

In Europe, HEI regularly communicates with DG-ENV, DG-RTD, and the European Parliament, and serves on key committees of WHO as they evaluate the current evidence on air pollution and health effects to inform the E.U.'s 2013 Year of Air (e.g., WHO's Review of Evidence on Health Aspects of Air Pollution).

In China, key HEI-funded studies have been translated into Chinese and presented at Tsinghua, Fudan, Peking, and other university seminars and to senior environmental and public health regulators. HEI is regularly invited by both China and the U.S. EPA to join the U.S. delegation to China as part of the annual Regional Air Quality Management forums. When a high-level China delegation came to

the U.S. EPA to meet with the assistant administrator for air, HEI was selected as the entity that could credibly communicate to both the U.S. EPA and the China Ministry for Environmental Protection about the current status of health effects from air pollution in China. HEI actively takes advantage of similar opportunities to present HEI (e.g., on new-technology diesel), local Asian, and GBD results in India and elsewhere in Asia and to a variety of government, diplomatic, environmental, and industrial audiences.

HEI will continue this approach of actively communicating science in understandable terms to these key constituencies in order to enhance understanding and build credibility in developing Asia and beyond for HEI science as reflective of the state of the art.

CROSS-CUTTING ISSUES

In reviewing the major opportunities for new research for the *Strategic Plan 2015–2020*, HEI identified a number of other specific questions on the health effects of air pollution that would not by themselves be programs of research, but which HEI viewed as cross-cutting issues that should be integrated into all of HEI's work. These are described below.

Development, Application, and Testing of Multipollutant Statistical Models and Methods

HEI has had a long-term commitment to—and a record of success in—the examination of key statistical challenges such as model selection and in the development, application, and testing of cutting-edge statistical models and methods to analyze the relation between air pollution and health. Several HEI projects have included strong methodologic components. In addition, HEI has funded studies aimed at methods development through specific RFAs and other mechanisms. In as much as air pollution science is concerned with testing whether it is possible to parse relatively small associations of health and air pollution in the context of myriad other variables, the need for development and improvement in methods continues to occupy a very important place in HEI's future research plans.

Several initiatives described above have highlighted the need for robust methods; this applies most importantly to effects of low-level exposures on health and to many other aspects of exposure research. Thus, HEI will support—as a part of broader projects or through stand-alone projects—research on and testing of multipollutant statistics, spatio-temporal modeling, model selection, measurement error and confounding, effect modification, and causal inference.

A closely related set of issues concerns the applications of statistical methods to large data sets, such as administrative databases, an approach which has been increasing in use. The interest in such large collections of data, as discussed earlier, is in an increase in precision. However, challenges related to selection bias, multiple testing, and regression to the mean—along with the other methodologic research issues mentioned above—need to be addressed so that over- or misinterpretation of data can be avoided. Such research questions will also be a part of HEI's efforts.

At-Risk Populations

HEI is cognizant that there is very good evidence, based on studies in the literature, that certain groups in the general population are, or may be, particularly sensitive to the adverse health effects of air pollution. Such groups may include the fetus and children who are in active developmental stages; the elderly, who may suffer from multiple illnesses; those with chronic disease; and those in lower socioeconomic groups, who may not only face higher exposures but also have underlying health conditions and poor access to health care. In some situations, specific gene–environment interactions may confer susceptibility to individuals or groups. Finally, the differences between indoor and outdoor pollutant concentrations may also play an important role, depending on the time–activity patterns of individuals. In discussing plans for research on exposure to pollution from traffic and ports earlier in this Plan, we raised the issue of at-risk groups who reside in areas more polluted than others and who may share other factors that put them at greater risk.

In this context, individuals with chronic diseases—those with asthma, diabetes, obesity, cardiovascular disease, and other diseases—are of special interest because their underlying pathophysiology makes them more vulnerable to the effects of air pollution. Air pollution may affect both the development of the chronic conditions and acute exacerbations, leading to increased mortality as well as years of healthy life lost.

HEI will integrate such cross-cutting issues into its future research. More specifically, HEI will seek opportunities to focus its projects on one or more at-risk groups or to explore the role of genetic and epigenetic factors influencing health outcomes by utilizing techniques borrowed from genomics, proteomics, and other new biologic tools.

Enhanced Exposure Assessment

One of the cornerstones of HEI's efforts to better assess the health effects of exposure is the care and attention given to the assessment of pollution exposure in each

study. This can be, as HEI noted in its Special Report 17 on traffic-related air pollution (2010), a key determinant of the validity of studies. Looking forward, the importance of assessing both outdoor and indoor exposure continues, but the approaches to doing so have been expanding rapidly, with the advent of remote sensing tools, innovative personal samplers, and emerging mobile apps and technology. HEI is already, in its current studies on traffic exposure, investigating the use of a number of these tools in a search for better estimates of exposure. Continued efforts to enhance exposure assessment will be central to every major research program HEI undertakes under its new Plan.

Climate Change and Health

In addition to the likely changes in fuels and technologies resulting from increased attention to climate change and GHG emissions, which HEI will address through its SCET and vehicle-testing programs, a changing climate also has the potential to be a modifier of risk and increasingly will need to be considered in air pollution and health studies. This may take the form of changing temperatures (which can in and of themselves have effects), changing patterns of exposure to other factors that may affect respiratory health (such as aeroallergens), and potential changes in the levels of key air pollutants such as ozone. HEI will not engage in the next five years in direct research on these climate-related changes and their effects on health, but will need to ensure that any studies it does undertake identify how such changes could modify the relation between air pollution and health (e.g., considering in any relevant study the effects of temperature as a potential modifier or even confounder of effects).

Application of New Biologic Techniques in Air Pollution Health Research

In the recent past, there has been an explosion in knowledge in biology and medical sciences, with a concomitant increase in the availability of new methods to explore biologic and pathologic phenomena. Some of the new approaches are being applied to study problems related to health research. Two examples include the role of genetic polymorphism in asthma and new high-throughput methods for toxicity testing. But much remains to be done. Given the very large number of approaches and techniques from modern biology that may be applied to environmental health problems and the “high-risk” nature of such investigations, HEI does not plan to initiate a specific program in this area. However, we will seek specific opportunities to incorporate new biologic techniques into

HEI-sponsored research. Along similar lines, HEI will encourage investigators to include biomarkers in their research studies. In all these cases, HEI will pay particular attention to questions regarding the specificity, sensitivity, and validity of the proposed methodology.

Other Health Outcomes and Modifying Factors

The effects of air pollution on the respiratory and cardiovascular systems have been extensively studied, and the effects of many other factors (e.g., smoking) on health outcomes have been characterized. During the last decade, researchers have also begun to focus on the influence of exposure to air pollution on other health outcomes, such as reproductive, neurologic, and immunologic effects. However, such efforts have not been very extensive, and there is a need for more research in these areas. HEI will look for opportunities where research in these areas can be incorporated into its ongoing research program.

A particularly intriguing modifying factor that has been recently proposed and studied is the role of the microbiome. The importance of microbial communities in the gastrointestinal system is now quite well recognized. Evidence is also increasing that the gut microbiome can have a dramatic effect on the immune system, at least in laboratory animals. A recently published study concluded that the composition of the gut microbiome influences airway immune defense against allergens and virus infection. HEI will explore this area as a potential opportunity for further research, beginning with a review of the current literature and followed by a few pilot studies.

Capacity Building: Support of Early-Career Investigators

Across its research program, HEI has successfully supported capacity building and career development for promising investigators at the early stages of their career through the Walter A. Rosenblith New Investigator Award program. Since 1999, HEI has supported 19 new investigators at a crucial stage—when they need to establish their own laboratories and research programs and are competing for tenure-track positions. The New Investigator program remains important in the current climate of reduced research spending in which it is becoming increasingly difficult for investigators just starting out to obtain research grants. Given the successful track record of the New Investigator program, HEI is firmly committed to continuing it over the next five years and beyond. Through this program, HEI supports investigator-initiated research in a wide variety of fields, including epidemiology, statistics, toxicology, and exposure science, provided

that the proposed research is in line with the broad research goals described in the current *Strategic Plan*.

IMPLEMENTING THE *HEI STRATEGIC PLAN* 2015–2020

Based on extensive comments from HEI’s Board of Directors, sponsors, other stakeholders, the HEI Committees, and others in the scientific community—and the priority opportunities identified above—it was clear that, while we must of necessity plan for specific actions we will take in the next five years, HEI should do that *with a clear eye on the much longer time frames for future air quality and climate decisions*. Challenging decisions on air quality standards continue to arise around the globe as the science evolves, and private and public sector decisions on technology to meet GHG goals (e.g., for vehicles and stationary sources) are already aimed at meeting standards set for 2025—and those standards are likely to be extended for many years beyond. Looking ahead, there are also trends in urbanization and mobility that will need to be taken into account. Given that, the *HEI Strategic Plan* is built around one overarching theme: *informing decisions on air quality and on climate-driven technology for 2015–2020 . . . and beyond*.

The specific actions we plan to take have been described in this document and are also represented in the attached timeline (Figure 6). Driven to inform the many upcoming policy decisions summarized across the top of Figure 6, HEI has identified specific activities to be undertaken in five key areas:

- The Continuing Challenges of Multipollutant Science
- Accountability and Transparency
- Assessment of Emerging Fuels and Technologies
- Global Health Science
- Cross-Cutting Issues

To be as responsive as possible to the emerging needs of our sponsors and others, HEI, in addition to providing a specific plan of scientific activities, must also build in the flexibility to *anticipate and act on the unanticipated*, and we fully expect to have that capacity in the coming years.

We have also included in the time line a *Mid-Plan Review* to assess progress, to scope out the continuing and likely future policy directions, to make adjustments to ensure that HEI is attuning its work to the greatest science and policy needs, and, most important, to consider a longer-term plan—*Vision 2020*—for HEI. While the Mid-Plan Review

may result in some refinement of HEI’s activities in the later years of this Plan (as has often been the case), its primary focus will be on anticipating what is likely to emerge beyond 2020 (i.e., in the next strategic planning cycle) so that HEI can begin developing appropriate strategies.

THE CHALLENGES OF MULTIPOLLUTANT SCIENCE

In this important area, HEI will, first and foremost, bring to a timely completion the last phases of the major programs it has under way, including

- The Multicenter Ozone Study in Elderly Subjects (MOSES);
- Exploration of innovative statistical methods for analyzing the effects of mixtures;
- Studies of enhanced assessment of traffic exposure; and
- The Diesel Epidemiology Review, including communication of the conclusions.

At the same time, HEI will move to initiate new science and review activities to do the following:

- Test the effects of low levels of air pollution exposure on health;
- Initiate new studies of traffic exposure and health, and investigate special aspects of traffic exposures such as UFPs, air toxics, and non-tailpipe emissions;
- Form a panel to update and revise the HEI literature review of traffic-related air pollution (Special Report 17); and
- Conduct a U.S.–EC workshop exploring NPACT, ESCAPE, and other studies, and considering the feasibility and value of developing new joint analyses in the NPACT and ESCAPE databases; this venture would include the possibility of applying innovative multipollutant statistics and of working to further understand the toxicity of air pollutants such as secondary organic aerosols (e.g., organic carbon).

ACCOUNTABILITY AND TRANSPARENCY

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 the United States:

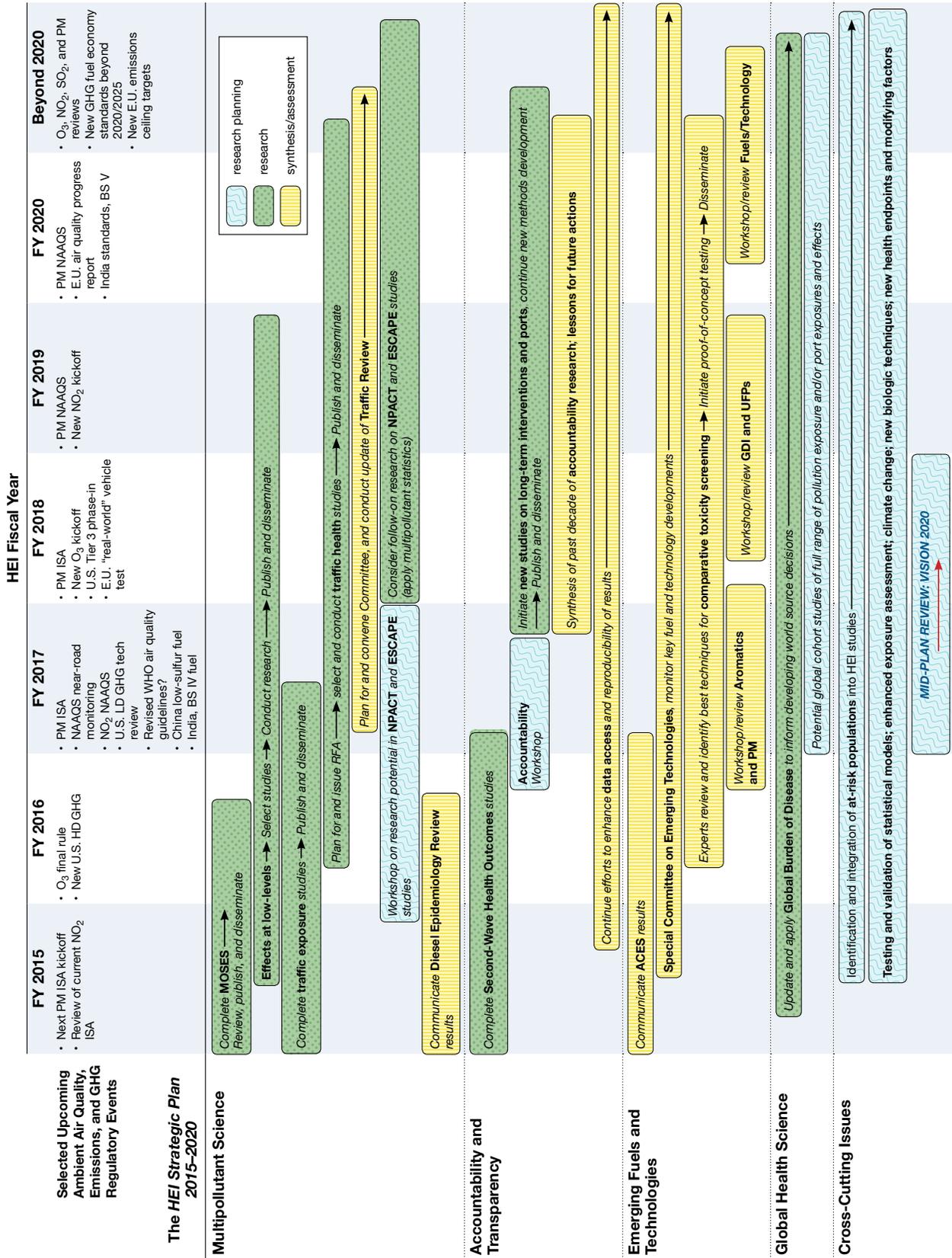


Figure 6. Implementing the HEI Strategic Plan 2015-2020. Time line shows HEI's key research areas selected for the 2015-2020 Strategic Plan period and related upcoming regulatory events.

- First, HEI will complete and communicate the results of the four major accountability studies (assessing health outcomes of air quality improvements) it has under way, examining the potential impacts of major interventions to improve air quality such as the following:
 - Power plants and mobile source actions in Atlanta;
 - Ozone abatement in southern California; and
 - Implementation of the California Goods Movement Action Plan.

Special attention will be paid to communicating the lessons learned in order to inform future decisions.

- Second, HEI will conduct a multi-stakeholder workshop to examine what the lessons from the challenges faced in the conduct of previous studies are and how these lessons may be incorporated in the design of new studies.
- Third, HEI will launch new, targeted studies aimed at key interventions and opportunities (e.g., major rules to reduce coal-fired power plant emissions, new port emissions reductions initiatives, and efforts to reduce exposure for at-risk communities).

Above and beyond its efforts to examine the effectiveness of air quality interventions in improving air quality and health, HEI will continue and enhance its ability to make all of the data from underlying studies that it funds available for broader analysis following completion of the studies.

EMERGING TECHNOLOGIES AND FUELS

To provide time-sensitive information about the full range of emissions from and the effects of new technologies and fuels—the development of which is being driven by GHG rules, energy efficiency issues, and air quality concerns—HEI will

- Communicate the final results from ACES to a wide range of parties, emphasizing both the ACES findings and comparisons with studies on older technologies.
- Plan and test a group of short-term bioassays for emissions from emerging technologies and fuels in order to identify the best techniques for comparative toxicity screening:
 - HEI will implement this activity working with a specially formed committee, other partners, and scientists while remaining cognizant of other efforts in this area, with the goal of facilitating broad use of these assays, allowing for comparison of results.

- HEI will leverage ongoing (non-HEI) work on emissions and fund pilot tests of the methods developed above, as a proof-of-concept exercise.
- Reconvene HEI's Special Committee on Emerging Technologies, to identify evolving issues. In addition, work with SCET—and other experts—to organize key discussions and to stay abreast of other important areas, such as by the following actions:
 - Holding a workshop on aromatics in gasoline and PM formation,
 - Holding a workshop on UFP emissions and GDI engines,
 - Monitoring the advancement of diesel engine technology, including low NO_x and non-diesel-particulate-filter engines, and
 - Monitoring the potential health effects of emissions from the use of low-carbon fuels.

GLOBAL HEALTH SCIENCE

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, and
- Participate in key science oversight and evaluation groups for highly relevant studies (e.g., Worldwide Air Quality Guidelines and the GBD updates).

In the developing countries of Asia and elsewhere, HEI will, with added resources,

- Apply the GBD approach to estimating burdens from specific sources (e.g., coal);
- Selectively undertake new studies, as funding becomes available, on topics including the potential long-term effects of exposure to higher levels of pollution and examination of the exposure and health effects from port activity and emissions; and
- Strengthen HEI's ability to build science capacity and communicate the results of its research to government, industry, development banks, and other stakeholders.

Taken together these activities will maintain HEI's role as a domestically and globally relevant provider of independent science, regularly called on to communicate with

and credibly inform policy makers on key decisions affecting public health and potential regulation in international forums.

CROSS-CUTTING ISSUES

In HEI's planning, a number of specific health effects concerns emerged that would not by themselves be programs of research in the new *Strategic Plan*, but which should be viewed as cross-cutting issues to be integrated into all of HEI's work. These include

- Development, application, and testing of multipollutant statistical models and methods,
- Identification and integration of at-risk populations into HEI studies,
- Enhanced exposure assessment,
- Consideration of climate change and health,
- Application of new biologic techniques in air pollution health research,
- Evaluation of other health outcomes and modifying factors, and
- Capacity building, particularly support of early-career investigators.

CONCLUSION

In summary, during the past five years HEI has continued to make substantial progress in providing timely, relevant, and credible science to inform air quality decisions. Building on that base, HEI stands poised to make even more targeted contributions in the years to come. We look forward to working with our sponsors, the science community, and the broader stakeholder groups to implement this Plan in 2015 to 2020... and beyond.

ABBREVIATIONS AND OTHER TERMS

ACES	Advanced Collaborative Emissions Study
APHENA	Air Pollution and Health: A European and North American Approach
API	American Petroleum Institute
BenMAP	(Environmental) Benefits Mapping and Analysis Program (U.S. EPA)
BS IV or V	Bharat Stage IV or V emissions standards (India)
CARB	California Air Resources Board
CASAC	Clean Air Scientific Advisory Committee

CNG	compressed natural gas
CO ₂	carbon dioxide
CONCAWE	Conservation of Clean Air and Water in Europe (research organization of the European oil industry)
DG-ENV	Directorate-General for Environment
DG-RTD	Directorate-General for Research and Innovation
DOE	U.S. Department of Energy
EC	European Commission
EMA	Truck and Engine Manufacturers Association
ESCAPE	European Study of Cohorts for Air Pollution Effects
E.U.	European Union
FHWA	U.S. Federal Highway Administration
GBD	Global Burden of Disease
GDI	gasoline direct injection
GHG	greenhouse gas
HD	heavy-duty (engines)
IARC	International Agency for Research on Cancer
IHME	Institute for Health Metrics and Evaluation
ISA	Integrated Science Assessment
LD	light-duty (engines)
MOSES	Multicenter Ozone Study in Elderly Subjects
NAAQS	National Ambient Air Quality Standards
NGO	nongovernmental organization
NO ₂	nitrogen dioxide
NO _x	nitrogen oxides
NPACT	National Particle Component Toxicity initiative
O ₃	ozone
PAPA	Public Health and Air Pollution in Asia program
PM	particulate matter
PM _{2.5}	PM ≤ 2.5 μm in aerodynamic diameter
PM _{10-2.5}	coarse fraction of PM between 2.5 μm and 10 μm or less in aerodynamic diameter
RFA	request for applications
RIOPA	Relationships of Indoor, Outdoor, and Personal Air study
SCET	Special Committee on Emerging Technologies
SO ₂	sulfur dioxide
SCR	selective catalytic reduction
UFPs	ultrafine particles
U.S. EPA	U.S. Environmental Protection Agency
WHO	World Health Organization

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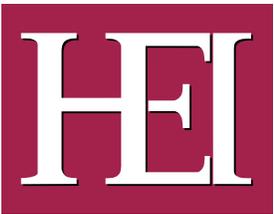
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