The Health Effects Institute
As Public-Private Model to Obtain Credible Science

Robert O’Keefe, Vice President
Health Effects Institute

Fourth National Integrity in Science Conference
July, 2008
HEI-The Idea

• 1977 Clean Air Act Requirements (s.202a4) Auto companies to test health effects of emissions
  – EPA-Industry relationship poor, science contentious, defensive, not advancing understanding

• EPA Administrator\ Industry CEOs
  – …There must be a better way to produce science we can trust

• HEI independent non-profit research institute

• Jointly funded by government (USEPA) & world wide vehicle industry
  – Founding Board
    • Archibald Cox, Harvard
    • William Baker, Bell Labs
    • Donald Kennedy, Stanford, FDA, Science

• Mission: provide independent research on the health effects of air pollution from vehicles (1990s “and other sources in the environment”)

HEI-Funding Model

Joint and equal core funding by government and vehicle industry

- Addresses perception, reality of bias

- 5 year commitment to funding

- long term commitment insulates HEI from either side “pulling plug” over single study

- Other partners involved regularly
- State and national regulators, EU, industry, foundations, development banks, WHO

- Regular inclusion of environmental NGOs
HEI – Science Products

• Four key areas:
  
  • **Targeted Research** - Primary role,
    • PM & gasses, air toxics, fuels and additives
    • Across disciplines, toxicology, epidemiology, exposure
  
  • **Special Literature Reviews** - e.g.
    • Health effects of inhaled MTBE; Diesel exhaust,
    • Exposure to traffic
  
  • **Reanalysis** of key studies e.g.
    • Harvard Six Cities, Pope ACS, Time Series Methods (GAM)

  • **Pollution effects in developing countries** (With WHO, others)
    • Impact assessment, Capacity building

• Emphasis on studies relevant to regulatory agenda
HEI Studies Underway
To Inform Increasingly International Decisions

★ = HEI Study
Having an Impact: 

**HEI in the PM NAAQS**

(Number of HEI Reports cited in U.S. EPA PM NAAQS Documents)
HEI-The Organization

- HEI structured to maintain credibility in often controversial national regulatory debates
  - Independent Board of Directors
  - Separate Research and Peer Review Committees
    - Cannot demonstrate by affiliation or conduct a lack of objectivity relating to health effects of ... emissions
  - Do not take policy positions
HEI-Organization: Board

• Characteristics:
  – Respected senior leaders recognized for integrity, public policy and/or science experience
  – *Not affiliated with HEI sponsors*, nor advocates for one or another side

• Appointment
  – Candidates must be ratified by HEI’s core sponsors (EPA Administrator and majority of members of the vehicle industry)

• *Once elected Board oversees operation of all aspects of operation of HEI without further sponsor approvals*
HEI Science Committees

- Impartial, internationally-regarded subject experts
- Appointed by Board
- Regular disclosure of funding, conflicts

**Research Committee**
- Identifies research agenda
- Awards research through competitive process
- Oversees quality and timeliness of research
- Chair: Mark J. Utell, University of Rochester

**Review Committee**
- Independently peer review all major studies
- Publishes detailed critique of studies and commentary on how research contributes to state of knowledge and implications for regulations
- Process more intensive than most journals
- Chair: Homer Boushey, UC San Francisco; Chair of American Thoracic Society
Key Issues - Transparency

- Full public disclosure of results
  - Comprehensive final reports
  - Positive and negative findings reported
  - Sponsors do not review results before publications are complete
  - PIs encouraged to publish in scientific journals

- Sponsor/Investigator Contact
  - Primarily at large annual meetings, poster sessions
  - Both EPA and Industry (and NGOs, science etc) present

- Access to Data
  - HEI itself has full access to all underlying data for review
  - Following publication, access to data, methods can be provided to other investigators (with confidentiality protected) on request
  - In practice limited requests
Models of Data Access

- Reanalysis
- Internet Based Access
EPA 97’ National Ambient Air Quality Standards:
Key Evidence on Long-Term Exposure to PM & Mortality

- Only two studies in U.S.
  - Harvard 6 cities (Dockery et al)
  - American Cancer Society (Pope et al)
- Observed large relative effect of long term exposure
- Basis of most numeric estimates of PM-related deaths and compelling benefit – cost analysis
- Importance of studies in underpinning new national air standards sparked
  - broad interest in data among industry, congress,
  - attacks on Harvard, investigators and study quality for refusal to release

Question: Could these studies stand up to intense scrutiny?
Pollution Study Sparks Debate Over Secret Data

By Laura Joffe
Staff Reporter of The Wall Street Journal

Harvard University researchers published startling findings in December 1993: Thousands of people were dying annually from inhaling microscopic particles in the air.

The U.S. Environmental Protection Agency may soon adopt regulations to curb the industrial and automotive emissions that produce the specks. Predictably, industry groups are challenging the agency's proposed rules, which will cost billions of dollars to implement.

But the study has also had an unforeseen effect: The researchers at Harvard are facing mounting pressure to release the patient records and other raw data that form the foundation of their study.

Even the EPA has joined the chorus demanding disclosure. "When lots of money and lives are at stake, it's not appropriate to say 'This is my data and nobody should be looking at it,'" says Mary Nichols, the EPA's assistant administrator for air and radiation. Several governors have also called for the release of data gathered in the study, which was mainly financed by the federal government.

But many scientists consider the disclosure demands an ominous threat to fundamental research. Douglas Dockery, the lead author of the 1993 research paper, is negotiating with the EPA to find a compromise solution. He argues that "giving up this data in violation of our agreements would completely cripple our ability to go out and do epidemiological studies of any type."

To reach its conclusions on particle pollution, the Harvard research team studied 8,000 people in six cities for nearly a quarter of a century, one of the biggest long-term studies ever on the health effects of pollution. They concluded that tiny particles of soot, chemicals and metal were responsible for a 20% higher death rate in the most polluted city, the steel town of Steubenville, Ohio, than in the least polluted city, Portage, Wis. The researchers have used the same data to prepare dozens of other studies.

The EPA says its proposed rules to curb the small particles -- it is scheduled to decide whether to adopt them on July 19 -- would add $6 billion a year to the costs of the Clean Air Act. Industry groups, meanwhile, estimate the rules will cost at least $23 billion annually. The rules target particles smaller than three thousandths of a millimeter that are produced mainly by burning fuels. Scientists believe the particles burrow into the lungs and cause ill effects as yet not understood. Based on research at Harvard and elsewhere, the EPA estimates its proposed rules would save 15,000 lives a year, including victims of such maladies as chronic bronchitis.

The release of scientific raw data has been a contentious issue for years. In the 1980s, University of Chicago Prof. Arthur Herbst, who found a higher incidence of cancer in the children of women who had taken the drug DES, was ordered to give up his data during litigation against the manufacturers. But, in a more recent case, researchers at the Mayo Clinic in Rochester, Minn., have so far fended off attempts to subpoena the patient database they used in breast-implant research.

Their study, published in the New England Journal of Medicine in 1994, found that breast implants didn't have the ill health effects plaintiffs had claimed. "I can't help but conclude that the purpose of those subpoenas was harassment," says Marcia Angell, the Journal's executive editor.

In the DES case, the data were released with patients' names blocked out. But Dr. Dockery says that won't work with the six-cities study because other specific information in the records -- such as city and date of death --...
Reanalysis: Major Results

- HEI asked by Harvard, EPA, others to reanalyze studies
- **Results:**
  - Data quality assured
  - Replicated original Results
- **Extended Understanding:**
  - Increased mortality effect as education declines
  - Persistent association between SO2 & mortality even with addition of other variables
  - Among others....
The HEI Reanalysis

HEALTH EFFECTS INSTITUTE

SPECIAL REPORT

Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality

A Special Report of the Institute’s Particle Epidemiology Reanalysis Project
What did the Reanalysis accomplish?

Science:
- Corroborated the original results
- Extended and advanced science
- Maintained data integrity

Atmospherics:
- Largely defused the adversarial atmosphere surrounding the critical discussion of the studies
- Reassured regulatory agencies and policy makers

Studies and PI’s
- Foster collegial, compensated relationship with investigators
- Inoculated studies from future spurious attacks
- Verified confidence in study quality fostered extended analysis in ACS data set...e.g. cancer effects, and global use as basis for extrapolating cost benefit of air pollution mortality
Reanalysis: Some limitations

Limited Use
- Should be rarely employed, if not well considered can be delay tactic to avoid needed action
- Must not supplant routine peer review literature as the standard used for regulatory science
- Takes time of original investigators, others
- Relatively Expensive ($1M over 2.5 years)

Science
- Concerns about bludgeoning data (into submission)
- Not complete substitute for collegial access to data
  - Creativity of single team vs. multiple individual investigators
- Complete acceptance elusive: recent critics “most earlier criticisms remain unaddressed”
Providing public access to data:
iHAPSS: internet Health & Air Pollution Surveillance System

- NMMAPS National Morbidity, Mortality & Air Pollution Study of air pollution and daily mortality & morbidity in 100 largest US cities

- High regulatory relevance for acute effects impact and...

- Numerous requests for data, PI assistance to interpret

- Response: iHAPSS developed by JHSPH and HEI to provide public access via the internet to NMMAPS data & methods

Peng R, Dominici F, Zeger S. AJE 2006
Providing public access to results from the National Morbidity, Mortality, and Air pollution Study to foster replication, new analysis

What’s been done:

- **Data** The entire NMMAPS database publicly available via the iHAPSS website

- **Software**: NMMAPS data package for R; the data are available under a “full access” class of license

- **Methods** A full compendium written in LATEX and R is available for download

- **Documentation** Investigators data-processing pipeline on the iHAPSS website, and papers / related technical reports are available for download

- **Distribution** We use the World Wide Web to disseminate our data and software
  http://www.ihapss.jhsph.edu/
Benefits of the iHAPSS approach

• Facilitates the use of complex public-access data sets
• Provides access to all, not only deep pockets
• Access to methods as well as data
• Allows periodic updating
• Drives enhanced use as a public health surveillance tool
• Highly transparent
• Ultimately freeing to investigators, iHAPSS initially proposed by PIs themselves
• To date use to “muddy the waters” minimal
One New Analysis: Nickel and Vanadium associated with PM10 in 60 U.S. Cities
(Lippmann et al EHP 11-06)

Lippmann and NYU team exploring associations of PM$_{10}$ mortality risk with Fine PM components in NMMAPs dataset (for the 60 MSAs for which FPM speciation data were available).
Thank You!

rokeefe@healtheffects.org
www.healtheffects.org
HEI Board of Directors

• Founding Board
  – Archibald Cox, Harvard
  – William Baker, Bell Labs
  – Donald Kennedy, Stanford, FDA, Science

• Current Board
  – Queta Bond, - Burroughs Welcome Foundation
  – Richard F. Celeste, Chair - Ambassador of the USA India (retired)
  – Jared Cohon - Carnegie Mellon
  – Purnell W. Choppin - Howard Hughes Medical Institute
  – Gowher Rizvi - Ash Institute, Harvard; Ford Foundation
  – Linda Rosenstock – UCLA, NIOSH
  – Prof. Richard B. Stewart - New York University School of Law
HEI Research Committee

- Mark J. Utell Chair University of Rochester
- Melvyn C. Branch, University of Colorado, Boulder
- Ken Demerjian, University at Albany - SUNY
- Peter B. Farmer, University of Leicester
- Helmut Greim, Technical University Munich
- Grace LeMasters, University of Cincinnati
- Sylvia Richardson, Imperial College London
- Howard Rockette, University of Pittsburgh
- James Swenberg, University of North Carolina at Chapel Hill
- Ira Tager, University of California, Berkeley
HEI Review Committee

• Homer Boushey Chair
  University of California, San Francisco

• Ross Anderson, St.
  George’s, University of London

• Ben Armstrong, London
  School of Hygiene & Tropical Medicine

• Alan Buckpitt, University of
  California, Davis

• John R. Hoidal, University of
  Utah Health Sciences

• Brian Leaderer, Yale
  Medical School

• Edo D. Pellizzari, Research Triangle Institute

• Nancy Reid, University of
  Toronto

• William N. Rom, New
  York University Medical Center

• Sverre Vedal, University
  of Washington