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ASSOCIATION OF
AMERICAN
MEDICAL COLLEGES

2450 N Street, NW, Washington, DC 20037-1127
Phone 202-828-0400 Fax 202-828-1125
www.aamc.org

Jordan J. Cohen, M.D., President

On

NIH: Re-engineering Clinical Research

Presented by

Eugene Braunwald, M.D.
Hersey Distinguished Professor of Medicine
Harvard Medical School
Chairman, TIMI Study Group
Brigham and Women's Hospital

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Good morning. Thank you Mr. Chairman and members of the subcommittee for inviting me to testify today on this important subject.

I am a Professor of Medicine at Harvard Medical School. I have conducted clinical research on heart disease for almost 50 years, from 1955 to 1968 at NIH, then at the University of California, and since 1972 at Harvard. I have also served as Chief Academic Officer and Faculty Dean at Partners HealthCare, an integrated academic health care system that includes two Harvard affiliated hospitals – Massachusetts General and Brigham and Women’s.

Clinical research is the neck of the scientific bottle through which all scientific developments in biomedicine must flow before they can be of real-world benefit to the public. I believe that the academic community has an essential role to play in loosening this bottleneck and I am pleased to be representing the Association of American Medical Colleges (AAMC). The AAMC represents the nation’s 126 accredited allopathic medical schools, some 400 major teaching hospitals and health systems, and more than 105,000 faculty through 96 academic and scientific societies. The Association is the most appropriate representative of the academic community in this policy arena because the performance of clinical research is a defining characteristic of medical schools and teaching hospitals. The AAMC membership conducts a very large share of the biomedical and behavioral research performed in this country, and has been the source of many of the dramatic breakthroughs that have revolutionized biology and are transforming medicine. My testimony today will focus on the role of academia in clinical research and where there is room for improvement.

The AAMC has been concerned about the clinical research enterprise for several years and convened a consensus development conference in 1998, out of which came a broadly inclusive definition of clinical research that led to the conception of a national “clinical research enterprise,” and recommendation of actions to strengthen that enterprise. That conference led to the establishment of the Clinical Research Roundtable in the Institute of Medicine (IOM) and an AAMC Task Force on Clinical Research. The Task Force was charged with assessing the opportunities and challenges facing clinical research in medical schools and teaching hospitals, and developing a set of findings and recommendations to strengthen clinical research in those institutions. The Task Force report, *“For the Health of the Public: Ensuring the Future of Clinical Research”* was issued in January 2000. It concluded that the future of clinical research in medical schools and teaching hospitals is synonymous with the viability of their defining academic missions and their commitment to advancing the health of the public. The conclusions of the Task Force still hold true today and my testimony will focus on the ideas generated by the Task Force and the current thinking in this important policy arena.

Too often, clinical research has been considered synonymous with clinical trials. Clinical research is a component of medical and health research intended to produce knowledge essential for understanding human disease, preventing and treating illness, and promoting health. Clinical research embraces a continuum of studies involving interaction with patients, diagnostic clinical materials or data, or populations, in any of these categories: disease mechanisms; translational research; clinical knowledge, detection, diagnosis, and natural history of disease; therapeutic interventions including clinical trials; prevention and health promotion; behavioral research; health services research; epidemiology; and

community-based and managed care-based research. This broad and inclusive definition is responsive to the dynamic changes that are taking place within the biomedical and health sciences and in the organization and financing of health care. The support and conduct of this research enable advancements across diverse fields of science to be applied to human health and may well transform the practice of medicine and the delivery of health care in this century.

Both the opportunities and challenges that we face in clinical research today are greater than at any time during my professional lifetime. The basic research resulting from the doubling of the NIH budget and the sequencing of the human genome have provided vast possibilities for improving human health, by improving diagnosis, treatment and prevention. Opportunities now exist to prolong useful life by combating the major chronic illnesses such as cancer, hypertension, stroke, heart attack, arthritis, emphysema, Alzheimer's disease, and mental illness.

Actually, at no time in human history has the potential been greater for translating biological knowledge and technological capability into powerful tools for preventing and treating disease and caring for our communities' health.

However, the landmark developments in genetics, bioengineering, neuroscience, and molecular and structural biology that have occurred during the past twenty years will mean little in practical terms if clinical researchers are unable to translate this science into new and effective medical and health practices. Without a robust and coherent national program of clinical research that enjoys the participation and harnesses the full strength of all components of the health sector, the impact of revolutionary advances in the biomedical and health sciences on the health of the public will be greatly slowed. And the national program of clinical research that now exists is anything but robust or coherent.

The major blocks in biomedical science are now at the interface of basic research and clinical care. The lack of coordination of the clinical research enterprise has led to a fragmented cottage industry of investigators each going in their own separate directions. There are great inefficiencies as teams are assembled for specific projects, then quickly disbanded when the project is completed and funding ceases. Regulatory burdens are enormous and growing; they impose delays, costs, and daunting disincentives on clinical researchers and dissuade many bright young medical graduates from choosing careers in clinical research. Information systems available to clinical investigators and designed to support clinical research are relatively primitive. Most of these systems are based on the financial and administrative needs of provider organizations, and virtually all are inadequate for clinical research.

Advances in information technology will be critical to the future of clinical research and to improvements in health care in the 21st century. The creation of federated, inter-operable databases is essential to help exploit the power provided by the Human Genome Project to enrich our understanding of human diseases, guide the development of therapeutics and preventives, identify potential subjects for clinical trials, and track long-term outcomes through post-trial and post-marketing surveillance. There is presently a profound lack of public or private investment in technology development in the clinical research arena, perhaps due to the lack of financial incentive; I believe that this is an area of urgent need that should be an attractive target for novel public-private partnerships. Since progress in this area is

almost certain to increase efficiency in all aspects of clinical research, it is imperative that academia and the federal government work together to develop principles for the standardization, collection and sharing of research data, as well as a nationally inter-operable clinical research information system that is designed to meet the needs, and exploit the opportunities, now presented in clinical research.

Protecting the integrity of research and sustaining the public's trust is as important a building block for clinical research as other more tangible items such as informatics, molecular libraries, and physical facilities. The AAMC and its members recognize that academic medicine and the American public have forged a special relationship rooted in trust that is nowhere more evident, or more fragile, than in clinical research involving human participants. The safety of human participants in research is of the utmost importance and must continue to be our highest priority. In this regard, the AAMC is pleased to have played a leadership role in recently creating the Association for the Accreditation of Human Research Protection Programs (AAHRPP). AAHRPP is a non-profit entity that the AAMC believes can help to lead the nation's clinical research community beyond compliance to a culture of conscience and responsibility in every investigator, every individual who participates in clinical research, and every supervisor of the research.

To accomplish this will require that clinical researchers operate under a standard policy on conflicts of interest that is clear and absolute. For example, it is my understanding from discussing this issue with colleagues at the NIH that some of the rules have been ambiguous. This ambiguity must be removed, but at the same time industry should not be deprived of valuable advice and consultation, nor academic research of the enrichment provided to both governmental and academic scientists, through appropriate consultative interactions. The recent reports by an AAMC task force on individual and institutional financial interests in clinical research provide a helpful framework for structuring and monitoring such interactions.

In a paper published in the February 18, 2004, issue of the *Journal of the American Medical Association* (JAMA), Kotchen, et al., state "[I]t appears that the greatest threat to clinical research, however, is the relatively small and shrinking pool of clinical investigators." AAMC President Jordan Cohen, M.D., made similar arguments in a November 2003 commentary, stating "the NIH's grand vision will become reality only if we can produce a steady supply of well-trained physician-scientists who are both clinically and scientifically competent, and offer them attractive, stable career pathways."

It has been my privilege to train a number of successful clinical researchers. The route is not an easy one. After obtaining the MD degree, an internship and residency, and rigorous research training in a specialty are required, and a first faculty position is not usually obtained until the persons are in their mid or late thirties. Success depends in large part on being able to obtain funding, which in turn depends on the fortunes and sometimes the whims of the sponsoring agency. Instability of funding coupled with the need to support a family is the greatest deterrent to talented young physicians considering a career in clinical research.

The answer to this problem lies with both the research sponsors and the academic partners. The NIH has been responsive to the recommendations of the 1997 Nathan Report, and has established a number

of clinical research training mechanisms such as the K awards and the loan repayment programs authorized by the Congress. We need to continue to increase training opportunities in all areas of clinical research by providing additional mentoring programs, expanding the existing federal loan repayment programs, and most importantly by providing longer commitments of support to the most creative, energetic and humane clinical researchers. Just as important, once they finish their training, clinical investigators must be supported not only with adequate opportunities for funding for their research but also with “nurturing environments” that offer reasonable, long-term career paths.

There are many important tasks ahead in developing a workable clinical research enterprise. One of the first challenges is in the organization of the system. I believe that we need a balanced tripartite system. One partner must be the federal government, which supports clinical research through several agencies, including the NIH, the Department of Veterans Affairs (VA), the Centers for Disease Control and Prevention (CDC), and the Agency for Healthcare Research and Quality (AHRQ). The NIH, as the lead agency, has developed a visionary plan for clinical research in its Roadmap initiative, a plan that we support with enthusiasm. The second partner is academic medicine – the medical schools and teaching hospitals where most innovative, hypothesis-driven clinical research is conducted. A large majority of clinical researchers in this country are faculty members and the trainees at these institutions are the future clinical investigators. These institutions are represented by the AAMC.

The third partner is industry – largely the pharmaceutical, biotechnology and information technology industries. Industry provides ideas, resources, and expertise that are essential to bringing a product to market and actually making it available to the public. Each of the three partners has a stake in the success of the other. Stable clinical research networks involving multiple medical schools and hospitals and their patients should be created and tied together with modern information systems, and these networks should conduct research sponsored by both the government and industry. Many projects should have dual sponsorship. The stability and resources of these networks, in turn, will attract the most creative young physicians who are eager to engage in a career of research. After training at our medical schools they can then conduct clinical research in a variety of sites, including academic, industrial and federal laboratories, as well as teaching hospitals and health systems.

The ultimate winner, of course, will be the public, which has the greatest stake in the outcome of this noble effort.

Once again, thank you for the opportunity to testify before you today. I would be pleased to respond to any questions you might have.