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The Public Stake in
Biomedical Research:
A Policy Perspective

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Support of biomedical research is one of the rare themes that unify members of Congress and administration officials, the two political parties, and the public. Although the private research sector has grown larger and more powerful than the public sector, the symbol of this support continues to be the National Institutes of Health (NIH), the most visible public research endeavor. During the last two decades, as both domestic and defense spending generated hot debates, the NIH budget got unprecedented backing. Urged by disease lobbies, eminent scientists, movie stars, former first ladies, famous athletes, and even news people, Congress and the Clinton administration moved the NIH budget from less than \$11 billion in 1993, when Harold Varmus, M.D., became the NIH director, to \$15.6 billion in 1999. Over the same period of time, research-based pharmaceutical firms' investment in research and development (R&D) went from approximately \$12 billion to an estimated \$24 billion. Congress and the administration agreed to \$17.9 billion for 2000, with the stipulation that the NIH delay spending \$7.5 billion of the amount until the end of the federal fiscal year.

The impact of biomedical research on Medicare and Medicaid expenditures, as well as other public and private health care outlays, is significant as well. "The United States leads the world both in demand for health care advances and in the research and development (R&D) that produce these advances," Burton A. Weibrod and Craig L. LaMay asserted in a recent *Health Affairs* article. "The primary reason for the increase in the health sector's share of the Gross Domestic Product over the past 30 years is technological change in medicine."

The biomedical research enterprise is traditionally an amalgam of public and private partners and competitors. On the public side, in addition to the NIH, the enterprise includes agencies focused on access, cost, and quality; disease prevention and health promotion; drugs, food, cosmetics, medical and diagnostic devices, and other products; and services provided under the Medicare, Medicaid, and Child Health Insurance Programs (CHIP), as well as under the Department of Veterans Affairs (VA). On the private side, the enterprise encompasses pharmaceutical firms, biotechnology companies, and medical equipment manufacturers that, regardless of their proprietary status, take guidance from regulators. Moreover, public and private academic health centers (AHCs), managed care organizations (MCOs), and other providers serve as loci for funded projects, while practiced-based research networks (PBRNs) and contract research organizations (CROs) act as conduits for funds for a

range of activities. Sometimes more compartmentalized than continuous, these activities include basic, translational, clinical, and outcomes research.

But even as the U.S. biomedical research enterprise is heralded for the drugs and procedures it has developed to fight a bevy of diseases and conditions, it is the subject of dire warnings, particularly in clinical research. Throughout the 1990s, scientists sounded alarms of crisis in the proportion of effort and funding devoted to patient- and population-oriented research and in the number of investigators available to conduct such research. Various groups convened under separate auspices to address the crisis and to develop recommendations to help resolve it. Hosts included the NIH, the Institute of Medicine (IOM), and the Commonwealth Fund; the Association of American Medical Colleges (AAMC), the American Medical Association (AMA), and the Wake Forest University School of Medicine collaborated to convene focus groups and a consensus-seeking conference.

While there is near unanimity on the importance of biomedical research in this country, there is considerable dissension over the priorities that drive various aspects of the field. There is also contention over implementation of research priorities in the public and private sectors and the interface between the two. Moreover, there is considerable disagreement over the leadership of biomedical research. This has come about as the private sector has surpassed the public sector in the extent and financing of projects and as the traditional tripartite mission of AHCs—service delivery, medical education, and research—has come under challenge in the rapidly changing health marketplace. Likely to add fuel to the debate is the recent announcement by Varmus—the *de facto* leader of the biomedical research arena—that he will leave his post as NIH director at the end of this year to head the private Memorial Sloan-Kettering Cancer Center. Rep. John Porter (R-Ill.), chairman of the House Appropriations Committee subcommittee that has jurisdiction over NIH spending, is leaving, too, creating a zone of uncertainty.

Whether biomedical research is undergoing a crisis or is evolving to respond to changes in the health care environment is a key question. Attempts to answer it are likely to consume the field and the policy community for some time to come. To focus the debate, NHPF is launching an examination of the concerns confronting biomedical research, as well as the conflicting priorities and the operational realities that are crucial to its success. Centering on the policy implications—especially in the interaction of the federal and private sectors and

their impact on the public's health—the Forum will conduct a series on the purpose, process, financing, and benefit of different aspects of biomedical research in this country.

THE FEDERAL COMPONENTS

The biomedical research complex is generally considered to be nearly a half-century old, especially if viewed through the lens of the NIH. The NIH actually traces its history to the authorization of a Marine Hospital Service in 1798; the establishment of a Hygiene Laboratory at Marine Hospital, Staten Island, in 1887; and the renaming of the Hygiene Laboratory as the NIH in 1930. However, the NIH was an insignificant player in biomedical research until Congress started directing funds to it in the post-World War II years. During the 1950s, the NIH grew rapidly as it became a key part of a research complex supported by the federal government and the pharmaceutical industry. The postwar advancement of AHCs as medical service, education, and research entities spurred this growth.¹

Today, the NIH includes the Warren Grant Magnuson Clinical Center, an intramural research facility at its campus in Bethesda, Maryland, that has half the designated research beds in the country, and 75 General Clinical Research Centers, extramural research facilities located at AHCs throughout the nation. NIH also has the following institutes:

- National Cancer Institute (NCI),
- National Eye Institute,
- National Heart, Lung, and Blood Institute,
- National Human Genome Research Institute,
- National Institute on Aging,
- National Institute on Alcohol Abuse and Alcoholism,
- National Institute of Allergy and Infectious Diseases,
- National Institute of Arthritis and Musculoskeletal and Skin Diseases,
- National Institute of Child Health and Human Development,
- National Institute on Deafness and Other Communication Disorders,
- National Institute of Dental Research,

- National Institute of Diabetes and Digestive and Kidney Diseases,
- National Institute on Drug Abuse,
- National Institute of Environmental Health Sciences,
- National Institute of General Medical Sciences,
- National Institute of Mental Health,
- National Institute of Neurological Disorders and Stroke, and
- National Institute of Nursing Research.

The NIH also includes the following:

- National Library of Medicine,
- John E. Fogarty International Center for Advanced Study in the Health Sciences,
- National Center for Research Resources,
- Center for Information Technology, and
- Center for Scientific Review.

As already indicated, other federal agencies are also important components of the biomedical research complex:

- The youngest is the Agency for Health Care Policy and Research (AHCPR), which Congress is currently in the process of renaming the Agency for Health Research and Quality (AHRQ). Established in 1989, it conducts health services research on access, cost, and quality issues. Among other units, it has centers to probe practice and technology assessment, primary care, outcomes and effectiveness, and quality management and improvement.
- The Centers for Disease Control and Prevention (CDC) date to 1946, when the CDC was called the Communicable Diseases Center. The CDC received its current name in 1970. The agency works on disease and injury prevention and environmental health. Among other components, it has centers focused on chronic disease; HIV, socially transmitted diseases, and tuberculosis; infectious diseases; immunization; occupational safety and health; genetics; and public health practice.
- The Food and Drug Administration (FDA) dates to 1927, when it was established as the Food, Drug, and Insecticide Administration. It became the FDA in 1930. Responsible for food, cosmetic, drug, medical device, and radiation-emitting product safety (as well as medicines and drugs for pets and farm animals), it

operates through a number of centers, some of which focus on research. Examples are the Center for Biologics Evaluation and Research, Center for Drug Evaluation and Research, and National Center for Toxicological Research.

- The Health Care Financing Administration (HCFA), established in 1977 to bring the administration of the Medicare and Medicaid programs under one agency, has a research and demonstration arm that investigates delivery of services for the two programs and for CHIP, created in 1997. Administrative costs are less than 3 percent for the agency, which has responsibility not only for administering the two public health delivery and financing programs but also for implementing federal quality assurance standards in clinical laboratories, nursing homes, hospitals, home health agencies, ambulatory surgical centers, hospices, and other facilities. For example, as part of its responsibility for informing coverage decisions, HCFA has become involved with the NCI in supporting clinical trials for a study on lung reduction surgery for chronic obstructive pulmonary disease.
- The oldest agency is the VA. It achieved cabinet standing in 1989 but goes back to 1917, when the United States entered World War I. Three different agencies administered veterans' programs in the 1920s, until the Veterans Administration, precursor of the VA, came into being in 1930. The VA has four service areas that are involved in R&D. They include the Medical Research Service, which works on fundamental biological processes; the Cooperative Studies Program, which handles clinical trials; the Health Services Research and Development Service, which looks at accessibility, effectiveness, efficiency, and quality; and the Rehabilitation Research and Development Service, which addresses disability and functional concerns. The VA claims such developments as the cardiac pacemaker, the first kidney transplant, a vaccine for hepatitis, and the magnetic resonance image scan for diagnosis.²

The NIH, AHCPR (or AHRQ), CDC, FDA, and HCFA are part of the Department of Health and Human Services (DHHS). In addition to DHHS and VA, the Departments of Agriculture, Defense, Education, and Energy direct, or are involved to some extent in, biomedical research initiatives, too.

While the NIH, aside from an occasional blip, has enjoyed ongoing support, the other agencies have experienced ups and downs. AHCPR, for example, was

almost eliminated in the mid-1990s. Just re-authorized under legislation that extends its purview, it fared better this year than HCFA, which experienced a cut in administrative funds in its FY 2000 appropriation. Researchers and advocates alike are looking at funding allocation decisions, raising questions about research and funding priorities in the decade to come. While traditional allocation debates have centered on basic versus clinical research, translational and outcomes initiatives are increasingly finding their way into discussions of biomedical research funding priorities.

THE PRIVATE COMPONENTS

One of the most striking aspects of biomedical research over the past two decades or so is the expansion of the private sector. The funding balance has shifted from the public to the private sector, resulting in a shift in who calls the shots on decisions over what to fund and how much to allocate.

Although the NIH budget has more than doubled in the past 10 years, its share of total health R&D expenditures in the United States has decreased from about 35 percent in the mid-1980s to about 29 percent today. Over the same period, industry's share of total health R&D expenditures has increased from 34 percent to 43 percent.³

Rapid Growth in Pharmaceutical, Biotechnical, and Medical Device R&D

The pharmaceutical industry invested an estimated \$20.6 billion in 1998, a 10.7 percent increase over the estimated \$18.6 billion it spent in 1997. While the figures are hard to come by, the Pharmaceutical Research and Manufacturers of America (PhRMA) reports that approximately 25 percent of R&D is devoted to research on products acting on the central nervous system and sense organs (which play a role in Alzheimer's, schizophrenia, depression, epilepsy, and Parkinson's). PhRMA indicates that 21 percent goes to products affecting neoplasms, the endocrine system, and metabolic diseases (cancer, osteoporosis, and diabetes); 15 percent to cardiovascular disease; 19.5 percent to parasitic and infectious disease; and 5.6 percent to products for diseases of the respiratory system (including asthma).⁴

Overall, nearly 33 percent of firm-funded R&D is for evaluation of drugs in human clinical trials, 41 percent for pre-clinical R&D functions, 11.8 percent for synthesizing and extracting compounds for evaluation, 14.9 percent for biological screening and pharmacological testing, 5.4 percent for later toxicology and safety

testing, and 8.5 percent for dosage formulation and stability testing.⁵

The smaller biotechnology companies—numbering approximately 1,500, with only about 20 percent having approved products and incoming revenues and only 30 percent or so having “a stock market value greater than \$1 billion”—are in a different situation than the large firms represented by PhRMA. “But the industry is soon to turn a corner, its leaders say, because almost 300 biotech medicines are in late-stage clinical trials,” Neil Munro reported in the *National Journal*.⁶ The field of gene therapy seems to be experiencing its ups and downs, however. The *Wall Street Journal* reported in October 1999 that gene-therapy drugs are in a “delivery shortfall,” as biotech firms seek to resolve various technical problems.⁷

Medical equipment manufacturers and suppliers also have a large stake in biomedical research. Nearly \$70 billion in medical devices and diagnostic products were produced in 1998, according to the Health Industry Manufacturers Association. Most of the medical and diagnostic equipment was consumed in the U.S. market. Examples of products include electro-medical devices and equipment, surgical and medical instruments, diagnostic reagents, orthopedic devices and surgical supplies, and dental equipment.⁸

Addressing the role that the industry plays in biomedical research, Munro contended in his article that biotechnology firms have an “enormous dependency on governing funding, regulation, and protection.” He said that “even the large, mostly cautious, pharmaceutical firms,” which in part are insulated by their international sales, are “sometimes deterred from investigating a controversial area” because a policy change may crimp a controversial product. He underlines the links between the pharmaceutical industry and “drug-safety laws intended to ensure that it cannot market any product until government regulators give permission, while modest profits make it dependent on Wall Street investment capital, which tends to flee from controversy.”⁹ The medical and diagnostic product industry finds that its success, also, is closely linked to government policies, as well as to its ability to raise venture capital to develop new products.

Varying Responses from Managed Care Plans, PBRNs, and CROs

MCOs’ participation in health research has been mixed, with health plans such as Kaiser Permanente involved and others reluctant to devote dollars to the field. However, large MCOs seem to be naturals for the

conduct of research—especially clinical trials, health outcomes initiatives, and health economics studies—because of their pools of physicians and other practitioners, use of ambulatory settings, links to AHCs, and access to patients as potential research subjects. Referring to a study of managed care plans’ impact upon clinical research (for the most part, viewed through the lens of AHCs’ conduct of research), Robert Mechanic and Allen Dobson pointed out in a 1996 *Health Affairs* article:

Managed care plans’ clinical research priorities differ from traditional AMC [academic medical center] activities. As plans become major players in specific markets, there is a growing need for research partnerships. Many of the managed care plans we interviewed already are involved in a range of research activities, including clinical trials, outcomes research, and health services research, although their basic research and clinical trial activities are smaller than those of AMCs. Managed care plans are most interested in applied research that is focused on measuring the cost-effectiveness of treatments for conditions that are common among their enrollees. In contrast, medical school faculty historically have concentrated on basic research and clinical trials, with substantial focus on rare diseases. Much of the research conducted at AMCs is not perceived as addressing the immediate clinical needs of managed care plans or as devoting adequate attention to economic reality.¹⁰

Speaking to the American Association of Health Plans (AAHP) conference in 1997, NIH Director Varmus cited studies in trade journals that accused “market forces” as hindering scientific investigation. While not directly accusing MCOs, he suggested several ways in which managed care plans could step forward: (a) to work with stakeholders from the research community and health care purchasers to develop core principles, (b) to study cost differences between standard care and research-related care, and (c) to develop pilot projects that would encourage plan participants to take part in clinical studies.¹¹

One point of contention has been managed care plans’ refusal to pay health care costs for their members who are involved in clinical trials. Early in 1999, NIH and the AAHP drew up an agreement under which managed care plans would try to increase the number of their patients in NIH-approved and -financed clinical trials. For example, United Healthcare Corporation, acknowledging that only 2 percent of eligible cancer patients are involved nationwide in clinical trials, indicated that the firm would begin by covering the costs of its cancer patients who took part.¹²

While some MCOs may hang back when it comes to clinical trials, other organizations have been eager to move forward. An estimated 35,000 industry- and government-

sponsored trials currently are going on. The demand for trial participants—and the need for mechanisms to organize the various phases of clinical trials and testing of new drug therapies in humans—has given rise to new modalities. The Internet—providing easy access to patients and physicians who are seeking information about investigational treatments—has spurred a network of pharmaceutical companies, research organizations, and provider groups that sponsor clinical trials and design research protocols. For example, a person seeking information may go to www.CenterWatch.com to find trial listings, new FDA drug approvals, and other leads.

PBRNs, “networks of physicians who have agreed to implement research protocols and data collection in studies ranging from pediatric physiology to outcomes assessment,” have been developing since the early 1980s. “There were more than 27 such networks active in 1994, involving more than 6,000 participating clinicians,” according to a 1999 AAMC paper, “The Changing Landscape for Clinical Research.”¹³ They are involved in the conduct of clinical research, outcomes research, and development of clinical guidelines. Examples include the Ambulatory Sentinel Practice Network (affiliated with the American Academy of Family Practice), the Dartmouth Cooperative Project in New England, and the Pediatric Research in Office Settings network (established by the American Academy of Pediatrics), according to the paper.

New entrants to biomedical research in the 1990s were CROs, organizations devoted to performing clinical trials more quickly and more cheaply than AHCs. Examples of CROs include Covance, Parexel, and Quintiles, all of which offer “integrated product development,” ranging from study design to monitoring and management. Organized to outsource clinical services and to establish multiple sites, CROs exist and operate outside AHCs. They may compete directly with AHCs or they may collaborate with them, but their growth generally seems to have contributed to declining participation in trials by AHCs.

A September 1999 report by the General Accounting Office, *NIH Clinical Trials: Various Factors Affect Patient Participation*, indicated that “patients may enter into trials in a range of settings, including community hospitals and physician offices,” but credited the pharmaceutical industry with supporting “the majority of large clinical trials that determine therapeutic efficacy of new drug products.” It said that an official of PhRMA “estimated that drug trials represent about 75 to 80 percent of all approved trials in the United States and that pharmaceutical companies sponsor about 80

percent” of them. The report also stated that PhRMA “estimated that trials of medical devices represent less than 5 percent of all approved trials and that nondrug therapies, such as new surgical or radiation treatments, represent about 10 percent.” The rise of specialty organizations to organize these trials is a phenomenon that seems to receive much less attention in policy circles than the roles of the NIH, AHCs, and even MCOs.

THE PRESSURES UPON AHCs

Beginning after World War II, AHCs became the linchpins for biomedical research. NIH funded research projects through clinical investigators at AHCs. AHCs—buoyed by Medicare dollars from the mid-1960s on—took on tripartite missions that joined service delivery, medical education, and research. Teaching hospitals at AHCs became the disseminators of new procedures, drugs, devices, and even evaluative techniques. As the biomedical research enterprise grew, AHCs—whether operated by public or by private academic institutions—flourished.

“But for all of its appearance of robustness and prosperity, the enterprise remained dangerously undercapitalized and highly leveraged on public support of research and on patient care funds,” contended the AAMC paper. “In sum, clinical research in academic medical centers became extraordinarily susceptible to modifications of federal policies of sponsored research support and changes in the organization, financing, and delivery of medical care.”¹⁴

As the health care marketplace reconfigured, it placed greater value on delivery of services in ambulatory settings and on financing of care through capitated or otherwise discounted arrangements. AHCs, heavily dependent upon acute, inpatient settings and upon commingled patient service, medical education, and research dollars, tended to be less flexible than other providers in responding to the new marketplace incentives. While AHCs had pioneered various medical and management techniques, they tended to overutilize acute and specialty services and to experience excessive costs, both of which turned out to be the Achilles heels of AHCs, according to Gordon T. Moore, M.D., of Harvard Pilgrim Health Care.¹⁵ Another vulnerability was patient flow, as health plans provided many services—even surgical care—in nonhospital settings and diverted acute care to less expensive providers, such as community hospitals.

The Medicare Payment Advisory Commission (MedPAC) took on the higher cost issue directly in

1999, when it examined Medicare's graduate medical education (GME) payment policies:

The higher patient care costs observed in teaching hospitals reflect a number of factors that are likely to strengthen the clinical care Medicare beneficiaries and other patients receive. Compared with other hospitals, teaching facilities tend to undertake more applied clinical research aimed at developing and testing new diagnostic and therapeutic technologies, such as imaging methods, drugs and devices, and surgical procedures. They also tend to hire a more costly mix of staff, including teaching faculty and technical specialists needed to provide advanced training, research, and patient care. Consequently, teaching facilities generally offer a broader and more technically sophisticated array of services, attract patients who are more acutely ill, and furnish care that is more complex and costly, than do other hospitals.¹⁶

As care has become increasingly managed—by private insurers, in state Medicaid plans, and even through Medicare+Choice—AHCs have had fewer opportunities to cross-subsidize and commingle funds. Moreover, as medical economics has changed, the incentives for practitioners to take part in research have altered as well, particularly resulting in a decline in the number of physicians interested in or involved in clinical investigation. All of these shifts have led AHCs—and those who represent them—to point to a crisis in biomedical research and to the clinical investigator as an endangered species.

These changes have also threatened the traditional partnerships (with NIH, with pharmaceutical and medical device companies, and with various providers) under which AHCs have operated. As indicated by David Blumenthal, M.D., in a 1994 *Health Affairs* article, a series of legislative statutes enacted during the 1980s encouraged links between private firms and academic researchers. For a variety of reasons—including new types of research, investment decisions, and proprietary rights—the nature of the relationships appears to be changing and the shape they will take in the future is not at all clear.

RISING TENSIONS AS THE FIELD RECONFIGURES

As the field of biomedical research has evolved in response to a rapidly changing health marketplace and to shifting economic incentives in the field itself, various tensions have arisen or deepened. These in turn are causing policymakers and others in the health arena to look at the pressures on the research enterprise, the

nature of the U.S. system, the process of setting research priorities, the cost implications, and the impact upon the public health. The following are some of these tensions:

- *Competition among advocates of biomedical research directed toward specific diseases.* Jockeying among disease lobbies has concerned observers of the field since biomedical research became a significant part of the federal budget. However, until recently, the concern was fairly minor because disease groups tended to avoid open warfare and, when it was crucial, work together to get as much funding for biomedical research as they could.

By the mid-1990s, however, a new trend had emerged. Although some interest groups still pursued general increases, . . . certain disease-specific interest groups adopted a narrower approach. Citing the success of HIV/AIDS and breast cancer lobbyists in obtaining high levels of targeted research funds, groups representing persons with Parkinson's disease, prostate cancer, diabetes, and other conditions explicitly requested congressional mandated ("earmarked") funds to support their areas of interest.¹⁷

Certainly, the success of the AIDS and breast cancer lobbies set a standard for other disease groups to strive for. AIDS and breast cancer advocates upped the ante as they organized grass-roots support, gained congressional champions and celebrity backers, and sponsored special fund-raising events.

- *Alignment of biomedical research priorities in a pluralistic system.* While countries such as France, Germany, and Japan have government-directed biomedical research, the United States has a decentralized system. While the NIH serves as an empowering agency (as do, to a certain extent, some of the other agencies of government that are involved in the research enterprise), it does not have the power to set overall priorities. Instead, priorities sort themselves out in the marketplace, largely driven by economic incentives. Some believe that this is the strength of the U.S. biomedical research enterprise, while others—worried about the growing dominance of the for-profit sector—contend it results in misalignment of priorities and outcomes. Because of government's strong role as a regulator, however, protection of "the public good"—such as in establishing incentives or subsidies for the development of "orphan drugs" for obscure conditions—is its responsibility.
- *Allocation of biomedical research dollars and efforts between basic and clinical research, as well as among different areas of DHHS.* The conflict over spending

for basic versus clinical research is a constant concern. “The clinical research communities have been less successful than the basic science disciplines in articulating their needs for a nurturing physical and intellectual environment within the context of scientific opportunities and the health care needs of the public,” the AAMC article contended.¹⁸

At the same time, there are those who criticize the emphasis upon basic and clinical research, at the expense of health services, preventive and environmental, quality assurance, and disability-oriented research. Commenting on the current campaign to double the NIH budget, *CQ Weekly* reporter Sue Kirchhoff wrote: “The campaign has intensified a longtime contest for money between NIH and other programs in the Labor/DHHS spending bill, such as Head Start and jobs programs.” She quoted Rep. Nancy Pelosi (D-Calif.) as calling the fight over the funding items in the appropriations bill a “lamb eat lamb” battle. Rep. David Obey (D-Wis.), ranking minority member of the Labor/DHHS appropriations subcommittee, has been one of the major critics of increasing NIH funding at the expense of other social programs.¹⁹

- *Charges of conflicts of interest among researchers and institutions, suppressed discoveries, and challenged intellectual property rights.* As private industry support of university biomedical research rose from less than 4 percent in the 1950s and 1960s to 14 percent in 1997, concern grew over possible conflicts of interest on the part of industry-backed university researchers. According to David Blumenthal, the “distance” between biomedical researchers and industrial organizations decreased during the 1970s and 1980s as a result of several factors. These include the close ties between academic researchers and the biotechnology firms that sprang up during the period, trade and budget deficits in the U.S. economy during the Carter and Reagan administrations, and federal encouragement of public-private partnerships in the Reagan era.²⁰

Various charges have circulated about suppression of research results that might cause “dislocations” in the biomedical research field. Columnist Daniel S. Greenberg has written a steady flow of columns attacking the biomedical research enterprise—and entrepreneurs. In 1998, he contended:

A case in point is the discovery 20 years ago of an amino acid in the blood, homocysteine, that is now considered to be a major source of heart disease, perhaps on a par with cholesterol. But, as

described in the *New York Times Magazine* last year, the discoverer, Dr. Kilmer McCully, was consigned to scientific oblivion because his findings conflicted with NIH’s reigning dogma of cholesterol as the culprit in heart disease.²¹

Earlier—in 1997—the *New England Journal of Medicine* reported that research on spinal fusion surgery, multiple chemical sensitivity, and calcium channel blockers for the treatment of blood pressure had been suppressed. The implication is that researchers must “go along to get along.” At the same time, as delineated in depth by Blumenthal, there is the implication that researchers have strategic alliances, patenting and licensing arrangements, and even partnerships (say, in the creation of new biotech companies) with industry.²² At times, there have been conflicts over intellectual property rights regarding research, particularly when research findings’ translation and application have resulted in lucrative products.

- *Politicization of biomedical research (especially in the congressional setting), as exemplified by the fetal-tissue and stem-cell research issues.* Related to the polarization of the Congress over the “right to life” versus “choice” abortion issue, some research topics have become embroiled in politics, resulting in congressionally mandated bans against or funding restrictions on certain types of research. The most prominent example is fetal tissue research. In fact, NIH has lacked an actual authorization since 1996 because of that issue (although funds have been appropriated).²³ Stem-cell research is just as controversial. “Opponents decry the research as lethal human experimentation, but supporters say it will create marvelous new medical treatments for myriad diseases and ailments.”²⁴
- *Rising costs of health care said to be direct results of advances in biomedical research.* According to Peter J. Neumann and Eileen A. Sandberg, writing in *Health Affairs*:

Spending on health R&D, which reached \$35.8 billion in FY 1995, increased as a percentage of total health expenditures from 3.2 percent in FY 1986 to 3.5 percent in FY 1995. During the same period, health R&D spending as a fraction of total R&D spending rose from 12.5 percent to 20.3 percent.²⁵

Critics, however, point to cost trade-offs such as the prevention of costly illnesses and disabilities as a result of new modalities and the substitution of less expensive drugs or procedures for more costly ones as a result of new developments. And, of course, they

cite improvements in the quality of patients' lives as well as in the number of lives saved.

- *Questioning of the public interest in biomedical research and the benefits to different segments of the population.* While researchers tout improving the health of the public as the overriding rationale for biomedical research, some observers question whether various segments of the public are benefiting. Three researchers, associated with the Robert Wood Johnson Clinical Scholars Program, looked at NIH funding relative to the burden of disease. They found that AIDS, breast cancer, diabetes, and dementia tended to receive relatively generous funding, whatever the measure (incidence, prevalence, or number of hospital days). They indicated that chronic obstructive pulmonary disease, perinatal conditions, and peptic ulcer research was relatively underfunded.²⁶ NIH has also conducted studies on the burden of disease. Critics are quick to lash out, saying that one disease is bleeding funding from another. For instance, when AIDS entered the scene in the 1980s, its success in drawing research monies caused resentment in some quarters and there is currently much debate over the disproportionately low funding for research on breast cancer relative to prostate cancer.

When it comes to segments of the population, various observers have raised concerns about the incidence and mortality of certain diseases among members of various minority groups, as well as about the participation of minorities and women in various aspects of the biomedical research enterprise. For example, an IOM panel indicated that African-American males “develop cancer 15 percent more frequently than white males” and that African-American women are less likely to have breast cancer than white women but are more likely to die from it once it is detected. They said that, compared to the national average, Asian-Americans have higher rates of stomach and liver cancers, Alaska Natives are at higher risk for colon and rectal cancer, and Hispanic and Vietnamese-American women have a greater likelihood of getting cervical cancer.²⁷ As the costs of drugs continue to rise, advocates for the uninsured and underinsured express concerns that they may be denied access to life-saving and life-enhancing treatments solely on the basis of cost.

Among the panel's conclusions were these:

The committee believes that NCI and NIH should improve the accuracy of their assessment of the amount of resources allocated to addressing the

needs of ethnic minority and medically underserved populations. . . . Research has so far failed to take advantage of the diverse populations of the United States in understanding the causes of cancer and reducing mortality. . . . There is little evidence that NCI or NIH has undertaken a thorough assessment of training programs to determine whether these programs are producing adequate numbers of ethnic minority researchers in all appropriate cancer research fields. . . . Ethnic minority participation in NCI-supported clinical treatment trials appears to be proportional to the incidence of cancer among these groups, but it is lower than expected in cancer prevention trials.²⁸

PROPOSALS FOR SETTING AND IMPLEMENTING PRIORITIES

Various groups that convened during the 1990s have numerous recommendations on the form that biomedical research should take. While these recommendations tend to concentrate on clinical research—where most see the bulk of the problems—they include other aspects of biomedical research as well. Although the Forum will look at other proposals too, it will focus on four major initiatives. These include an NIH director's panel study of priority-setting at the NIH, an IOM study of priority setting at the NIH, an examination of AHCs' research mission by the Commonwealth Fund, and an AAMC-AMA-Wake Forest School of Medicine clinical research summit.

The NIH Director's Panel on Clinical Research

The NIH director's panel, chaired by David G. Nathan, M.D., met from 1995 to 1997. Focusing primarily on policy changes that would encourage physician investigators to undertake careers in clinical research, it urged the following:

- Reinforcement of the NIH's commitment to basic and clinical research (underlining the latter).
- Strengthening of the General Clinical Research Centers' infrastructure in individual AHCs and monitoring of the productivity of the Warren Magnuson Clinical Center.
- Extension of the Howard Hughes Medical Institute medical student program from basic science to clinical research.
- Upgrading of training programs and grants.
- Organization and restructuring of study sections that review patient-oriented research applications.

- Encouragement of collaboration between basic scientists and clinical investigators.
- Both in basic science and clinical research, support of collaboration between pharmaceutical and biotechnical companies and training programs in AHCs.
- Initiation of debt abatement for extramural clinical investigators.
- Greater commitment by certain AHCs, such as increased support to clinical research, extension of data managers and auditors to the best clinical investigators, hiring of additional clinicians, and provision of efficient information systems.
- If it is determined that health insurance should support selected clinical trials, participation by all insurance providers.
- Collaboration by health insurers, foundations, pharmaceutical and biotechnical companies, AHCs, and the NIH in developing a joint policy for the support of clinical research and clinical research training.²⁹

The IOM Committee's Examination of Opportunities and Needs

The IOM, in 1998, released the results of a study by its Committee on the NIH Research Priority-Setting Process. Headed by Leon E. Rosenberg, M.D., the committee subtitled its report *Scientific Opportunities and Public Needs: Improving Priority Setting and Public Input at the National Institutes of Health*. The report included recommendations on the following:

- Setting of criteria for priority setting.
- Recommendation of internal and external processes to guide priority setting.
- Suggestion of new mechanisms to increase public participation in the external process.
- Putting forth of ideas for clarifying the congressional role relative to priority setting.³⁰

The Commonwealth Fund Task Force on Academic Health Centers

Established in 1995 under the direction of Blumenthal and Samuel Thier, M.D., the task force is scheduled to work through 2001 on AHC missions. In April 1999, it issued *From Bench to Bedside: Preserving the Research Mission of Academic Health Centers*. The report contains various findings, such as the following: "The United States spends an estimated \$42 billion annually on health-

related research and development" and AHCs "perform approximately 28 percent of all health-related R&D in the United States." It makes one general recommendation: an overall increase in federal support for health services research.

The report contains the following suggestions relative to AHCs:

- Better management of their research enterprise.
- Greater recognition of academic standing and prestige of clinical and health services researchers.
- More investment in cross-disciplinary research programs.
- Increased participation in applied research and development.
- Enhanced positioning relative to managed care.

The report also recommends the following NIH policies and expenditures regarding:

- More funding for construction and renovation of research facilities.
- Increases in percentage of funds provided for projects and for investigators' salaries.
- Maintenance of current levels of support for indirect cost rates.
- Increase in support for clinical research at AHCs.
- Greater support for training of clinical researchers at AHCs.³¹

The AAMC-AMA-Wake Forest School of Medicine Clinical Research Summit

The AAMC, the AMA, and the Wake Forest University School of Medicine—with funding from the Burroughs Wellcome Fund, the Robert Wood Johnson Foundation, the Pew Charitable Trusts, the John D. and Catherine T. MacArthur Foundation, the Merck Company Foundation, the Commonwealth Fund, and the Wake Forest University Ethics and Leadership Fund—undertook a major initiative in 1998. Drawing on focus groups and leaders from diverse sectors of the health community, they addressed what they viewed as a crisis in clinical research: a declining number of physician scientists, a decreasing pool of younger researchers, a steady reduction in cross-subsidization of research in AMCs, a gradual shift toward targeted proprietary research, and a growing scarcity of patient bases for the conduct of clinical studies. Seeing multiple opportunities for clinical research, they underlined that

clinical research is critical to the flow of scientific discovery and developed recommendations to preserve and enhance it.

Saying that clinical research encompasses a wide range of functions, from disease mechanisms to health services research, they outlined eight problems that it faces:

- Need for an agreed-upon definition of “clinical research.”
- Lack of adequate understanding and value.
- Absence of data to monitor and assess the different components of clinical research.
- Inadequate numbers of appropriately trained clinical investigators.
- Insufficient emphasis on incorporating research findings into clinical practice.
- Inadequate coordination of clinical research within and between research entities and disciplines.
- Restricted ability of AMCs to conduct clinical research.
- Lack of a comprehensive, dynamic clinical research agenda.

Those who participated in the three organizations’ consensus process concluded that there is a need for a clinical research roundtable to continue and focus national attention on the needs, priorities, and progress of clinical research and training. They urged that the roundtable be established at the turn of the century so that it can start undertaking its important work and recommended that the IOM be its headquarters. Afterward, the IOM agreed to establish a clinical research roundtable to build on the work of the summit.

The clinical research roundtable would have the following goals:

- To promote dialogue among the scientific community and the general public to create mutual understanding about clinical research and the public’s participation in it.
- To strengthen the ethical underpinnings of clinical research.
- To establish mechanisms to track and disseminate the aggregate levels of financial and other support for each of the major categories of clinical research.
- To create a process to monitor and promote workforce career development across the health

professions to meet the needs and promote the different categories of clinical research.

- To develop databases for patient- and population-based health research.
- To strengthen the linkages between basic science discoveries and their application to improved patient care.
- To ensure AHCs’ ability to conduct research and training.
- To broaden the participation of the health professions in clinical research across all practice settings.
- To develop and monitor strategies involving the dissemination of new clinical research findings and the evaluation of the outcomes of new procedures and treatments.³²

Backing and Leadership

As reflected in the sponsorship of some of the panels, private foundations play a strong role in the biomedical research arena. “Philanthropic organizations historically were responsible for stimulating and enabling the inculcation of science into medical teaching and practice, and the transformation of the nation’s premier medical centers,” the AAMC paper stated. “These organizations contributed \$1.3 billion to biomedical and health-related research in 1997, an increase of nearly 30 percent from \$942 million in 1995.”³³ Whether in providing grants directly for biomedical research, underwriting new facilities, supporting clinical fellowship programs, giving grants for clinical or policy conferences, or engaging in other initiatives, foundations have provided leadership to the biomedical research field.

Various interest groups, whether associated with specific diseases or banded into coalitions to support all or certain aspects of biomedical research, have contributed significantly as well. Examples include disease groups such as the American Arthritis Foundation, the American Cancer Society, and the American Diabetes Association. Coalitions include the Ad Hoc Group for Medical Research Funding (medical and scientific societies, voluntary health organizations, and academic and research institutions), Campaign for Medical Research (also various groups), the Friends of VA Medical Care and Health Research (various organizations interested in veterans’ health care), the National Health Council (a band of voluntary and corporate organizations), NIH2 (a group of pharmaceutical companies), and Research! America (a large alliance of providers, researchers, professional and trade associations, corporate organizations, and others).

These highlight the search for leadership in biomedical research, which is exacerbated by the departure of Varmus and Porter. Various proposals, such as the NIH director's panel recommendations to strength NIH's role, the IOM's call for greater public participation, the Commonwealth Fund task force's efforts to bolster AHCs, and the AAMC-AMA-Wake Forest call for a clinical research roundtable, reflect a quest for leadership in focusing biomedical research's missions and achievements in the first part of the next century.

Some Key Questions

This Forum series will raise numerous public policy questions about the direction and funding of biomedical research in this country:

- Is biomedical research in crisis? What are its problems?
- How are biomedical research allocations made relative to the continuum of basic, translational, clinical, and outcomes research?
- What pressures come to bear on the funding of various aspects of research for specific diseases?
- Once funding allocation decisions are made, in what ways can they change or be changed?
- Is biomedical research mainly based on a medical model? On a health care model?
- What is the public interest in biomedical research? Who or what is the public?
- Is the NIH budget too small? Should it be doubled? If so, why? If so, how?
- What is the impact of biomedical research spending on health care expenditures?
- Are federal research activities too compartmentalized? Too diverse?
- Are government agencies too paternal in their approach to regulation? Not paternal enough?
- What is AHCPR's (or AHRQ's) role in biomedical research? The CDC's? The FDA's? HCFA's? The VA's? What should their roles be?
- Relative to AHCs, if they are to remain prominent in clinical research, how should the necessary infrastructure (for example, technology, information systems, support for faculty) be funded? How do they remain vital relative to changing health marketplace issues? How do they chart—or what part do they play in—the education of the next generation of clinical researchers?
- Should AHCs retain a strong role in biomedical research? Should only some AHCs play a strong role? Should the AHCs' role be divided up among different health care settings, both public and private?
- Should some AHCs cultivate clinical investigator “stars” to conduct research?
- How have public-private partnerships advanced biomedical research to date?
- Are intermediary organizations (for example, CROs) contributing to advancement of biomedical research?
- Are biomedical research needs being met? What is the outlook for the future?
- What impact do proprietary interests have on the conduct and financing of biomedical research? On the sharing of information? On intellectual property rights?
- Should managed care play a greater role in biomedical research? What should its financial contribution be? How should it contribute (for example, to an all-payer fund, by funding health costs of its members in clinical trials)?
- Is the research agenda clear?
- Should there be acknowledged leadership of biomedical research or pluralistic leadership? Who decides? Should there be a national roundtable? A national clearinghouse?

ENDNOTES

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