

The NIH Roadmap

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The National Institutes of Health (NIH) is at a critical moment in its prestigious history. As the 21st century unfolds, discovery in the life sciences is accelerating at an unprecedented rate. Although the sequencing of the human genome presents vast opportunities for researchers, it also creates a series of challenges that will redefine the ways that medical research is conducted and, ultimately, how research leads to improvements in health.

The 5-year doubling of the NIH budget, completed in FY 2003, both picked up the pace of discovery and heightened public expectations. As I assumed the directorship of NIH, early discussions with legislators, administration officials, and institute directors, as well as public, patient advocacy, and scientific leaders convinced me that NIH needed to examine its portfolio with an eye to identifying critical scientific gaps.

The NIH earned its reputation for success because of the vitality of its institutes, centers, and offices and because of the diverse ways in which it funds and conducts research—all fostered by decentralization inherent to its organization and funding streams. This characteristic serves the agency well and should be preserved. However, as science grows more complex, it is also converging on a set of unifying principles that link apparently disparate diseases through common biological pathways and therapeutic approaches. Today, NIH research needs to reflect this new reality.

Over the past year, NIH and its leadership have been engaged in a process dubbed the “NIH Roadmap.” This process was designed to ask the kind of probing questions that a complex research organization should periodically pose, especially when in transition. The roadmap was purposefully focused on efforts that no single or small group of institutes or centers could or should conduct on its own, but that NIH as a whole must address to ensure both efficient and effective

discovery. This was not a reexamination of the strategic plans of each institute or the development of a wholly new comprehensive plan for the sake of being responsive to every interest and constituency. This would have led to a reasoned, but impractical, plan. Rather, the goal was to define a compelling, limited set of priorities that can be acted on and are essential to accelerate progress

across the spectrum of the institute missions.

Our consultations began first with the scientific community and public constituencies, representing over 300 of the nation’s biomedical leaders from academia, government, and the private sector. We asked participants to address three key questions: What are today’s most pressing scientific challenges? What are the roadblocks to progress and what must be done to overcome them? Which efforts were beyond the mandate of one or a few institutes, but were the responsibility of NIH as a whole?

Through these consultations, three major themes emerged—New Pathways to Discovery, Research Teams of the Future, and Re-engineering the Clinical Research Enterprise. These ideas were examined by 15 working groups, each led by institute directors, with input from the NIH Council of Public Representatives and the Advisory Committee to the Director.

In June, the NIH leadership met to make final selections of key initiatives to be launched in FY 2004 based on the following criteria: Is the initiative truly transforming—will it dramatically change the content or the process of medical research in the next decade? Would outcomes from the initiative be used by, and synergize the work of, many institutes? Can the NIH afford not to do it? Will the initiative be compelling to NIH stakeholders, especially the public? Does the initiative position the NIH to do something that no other entity can or will do?

At this juncture, working groups with thematically related initiatives were combined and reorganized into nine implementation groups (see the table) responsible for developing the proposals into tangible activities to be launched in FY 2004. The initiatives are complex, so their implementation will be gradual and tailored to specific short- and long-term goals. Some efforts will reach fruition rapidly; others will require longer incubation periods before being fully realized.

NIH ROADMAP—THEMES, IMPLEMENTATION GROUPS, AND INITIATIVES*

New Pathways to Discovery

Building Blocks, Pathways, and Networks Implementation Group

National Technology Centers for Networks and Pathways
Metabolomics Technology Development
Standards for Proteomics and Metabolomics/Assessment of Critical Reagents for Proteomics

Molecular Libraries and Imaging Implementation Group

Creation of NIH Bioactive Small-Molecule Library and Screening Centers
Cheminformatics
Technology Development
Development of High-Specificity/High-Sensitivity Probes to Improve Detection
Comprehensive Trans-NIH Imaging Probe Database
Core Synthesis Facility to Produce Imaging Probes

Structural Biology Implementation Group

Membrane Protein Production Facilities

Bioinformatics and Computational Biology Implementation Group

National Centers for Biomedical Computing

Nanomedicine Implementation Group

Planning for Nanomedicine Centers

Research Teams of the Future

High-Risk Research Implementation Group

NIH Director’s Innovator Awards

Interdisciplinary Research Implementation Group

Interdisciplinary Research (IR) Centers
Interdisciplinary Research Training Initiative
Innovations in Interdisciplinary Technology and Methods (Meetings)
Removing Structural Barriers to Interdisciplinary Research.
NIH Intramural Program as a Model for Interdisciplinary Research
Interagency Conference on the Interface of Life Sciences and Physical Sciences

Public-Private Partnerships Implementation Group

Designation of a Public-Private Sector Liaison
High-Level Science-Driven Partnership Meetings

Reengineering the Clinical Research Enterprise

Clinical Research Implementation Group

Harmonization of Clinical Research Regulatory Requirements
Integration of Clinical Research Networks
Enhance Clinical Research Workforce Training
Clinical Research Informatics: National Electronic Clinical Trials and Research (NECTAR) Network
Translational Research Core Services
Regional Translational Research Centers
Enabling Technologies for Improved Assessment of Clinical Outcomes

* For further description see www.sciencemag.org/cgi/content/full/302/5642/63/DC1

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However, we will begin to implement all 28 initiatives in 2004, with a clear focus on making viable, enduring changes that will lead to improvements in health. Let me outline the themes and initiatives in more detail.

New Pathways to Discovery. This theme addresses the need to understand complex biological systems. Future progress in medicine will require quantitative knowledge about the many interconnected networks of molecules that comprise cells and tissues, along with improved insights into how these networks are regulated and interact with each other.

New Pathways to Discovery also sets out to build a better “toolbox” for today’s biomedical researchers. To fully capitalize on the recent sequencing of the human genome and many new discoveries in molecular and cell biology, the research community needs wide access to technologies, databases, and other scientific resources that are more sensitive, more robust, and more easily adaptable to researchers’ individual needs.

Roadmap initiatives within this theme address technologies and approaches necessary to meet contemporary research challenges, including building blocks and pathways, molecular imaging, the development of small-molecule libraries, bioinformatics and computational biology, nanomedicine, and structural biology. We will issue new Requests for Applications (RFAs) in FY 2004 for National Technology Centers for Networks and Pathways, National Centers for Biomedical Computing, Centers for Innovation in Membrane Protein Production, as well as investigator-initiated grants for related research in structural biology, metabolomics technology development, and proteomics. In addition, we will support development of new screening centers for bioactive small molecules, a publicly accessible cheminformatics reference database to be housed at NIH’s National Center for Biotechnology Information, and a database and core facility dedicated to synthesizing and distributing molecular imaging probes. The agency will also begin planning a series of nanomedicine centers that will be launched in 2005. These centers will focus on quantitative measurement of biological processes at the nanoscale and the engineering of new tools to intervene at the nanoscale or molecular level. This research will help scientists construct synthetic biological devices, such as miniature, implantable pumps for drug delivery or tiny sensors to scan for the presence of infectious agents or metabolic imbalances.

Research Teams of the Future. The scale and complexity of today’s biomedical research problems increasingly demand that scientists move beyond the confines of their own discipline and explore new organizational models for team science. NIH wants to stimulate new ways of combining skills and disci-

plines in the physical and biological sciences. The Director’s Innovator Awards will encourage investigators to take on creative, unexplored avenues of research that carry a relatively high potential for failure, but also possess a greater chance for ground-breaking discoveries. In addition, novel partnerships, such as those between public and private sectors, will be encouraged to accelerate movement of scientific discoveries from bench to bedside.

Solving the puzzle of complex diseases, from obesity to cancer, will require a holistic understanding of the interplay between factors such as genetics, diet, infectious agents, environment, behavior, and social structures. To devise and use the state-of-the-art technologies developed from the roadmap effort, we will need the expertise of nontraditional teams of biological scientists, engineers, mathematicians, physical scientists, computer scientists, and others. The private sector will play an essential role in this new paradigm, and federal agencies will be required to do more collaborating with industry and each other. We recognize that the research teams of the future will look and feel vastly different from their predecessors.

Effecting these changes will require cultural and scientific adjustments and experimentation with new approaches. The implementation group responsible for the Research Teams of the Future devised a plan to meet these challenges with a series of initiatives that provide mechanisms for high-risk strategies, interdisciplinary research, and public-private partnerships. For example, it has been suggested that investigators do not submit their most innovative applications to the NIH because they think the NIH is risk-averse. We have heard that peer review typically values likelihood of success more than potential impact and that some funding decisions are too conservative. To encourage high-risk research, NIH will solicit nominations for the Director’s Innovator Awards, which will provide support to a highly select group of individuals who have the potential to make extraordinary contributions. They will be evaluated in terms of their exceptional creative abilities, potential for ground-breaking discovery, evidence of focused and skillful habits of mind that predict perseverance and thorough exploration of his/her ideas, and, most important, prospects for making seminal biomedical research advances.

To build the research workforce of the future, the agency will issue RFAs to promote collaborative efforts, including Exploratory Centers for Interdisciplinary Research and Training for a New Interdisciplinary Research Workforce. These programs will be augmented by conferences and symposia on timely issues, such as methodological innovations and peer review. To expedite the formation of productive public-private partner-

ships, the NIH will establish a central point of contact to support and encourage NIH activities involving these partnerships.

Reengineering the Clinical Research Enterprise. Although biomedical research has succeeded in converting many lethal diseases into chronic, treatable conditions, continued success requires that the United States recast its entire system of clinical research. Over the years, clinical research has become more difficult to conduct. However, exciting basic science discoveries demand that clinical research continue and even expand, while striving to improve efficiency and better inform basic science. This is undoubtedly the most difficult but most important challenge identified by the NIH Roadmap process.

Clinical research needs to develop new partnerships among organized patient communities, community-based physicians, and academic researchers. In the past, all research for a clinical trial could be conducted in one academic center; that is unlikely to be true in the future. In these initiatives, NIH will promote creation of better integrated networks of academic centers that work jointly on clinical trials and include community-based physicians who care for large groups of well-characterized patients. Implementing this vision will require new ways to organize how clinical research information is recorded, new standards for clinical research protocols, modern information technology, new models of cooperation between NIH and patient advocacy alliances, and new strategies to reenergize the clinical research workforce.

Critics of the nation’s current clinical research system have cited several factors that promote inefficiency, including poor integration of existing clinical research networks, inadequate training mechanisms for clinical investigators, inconsistent data standards and database requirements, and lack of information. In addition, successful clinical research relies on public trust, and any proposal that addresses the nation’s investment in this area must be sensitive to the needs of the most important NIH constituency, the American people.

The NIH annually funds and conducts billions of dollars of clinical research—\$8.4 billion in FY 2003—addressing the full panoply of public health problems that confront the nation. As such, we have a vested interest in catalyzing the transformation of policies throughout the federal government, while maintaining an emphasis on the integrity and effectiveness of federal and institutional systems of oversight. In the upcoming year, the NIH will design pilot programs for a revolutionary National Electronic Clinical Trials and Research (NECTAR) network. These pilot programs will begin to develop an infor-

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POLICY FORUM CONTINUED FROM PAGE 64

matics infrastructure that will link current and emerging clinical research information systems so that data and resources can be shared within and across clinical research networks, across studies and across institutions, reducing duplication and avoiding unnecessary overlap between trials. We expect NECTAR to help streamline clinical research and to accelerate the pace of discovery and application of clinical findings.

We intend to issue RFAs for technologies that improve assessment of clinical outcomes and for regional translational research centers. We will expand efforts to provide advanced training in clinical research, through the Institutional Career Development Award

Program and the NIH Clinical Center Clinical Research Training Program. NIH Clinical Research Associates (trained and certified health-care providers) will enroll and follow patients in clinical trials, ensuring that principles of integration will become routine in the clinical research culture.

Roadmap initiatives will also be unique in the manner in which they are funded. All institutes and centers decided to create a new funding mechanism through a common pool of resources agreed upon and contributed to by all of them on the basis of the multiyear roadmap plan. The plan will be administered centrally, but executed by lead institutes or centers as appropriate on behalf of the whole of NIH. This ensures that a steady multiyear and flexible stream of funding is available

and also institutionalizes a corporate process for decision-making about trans-NIH priorities. It reflects, in our opinion, a maturation of the NIH toward a more adaptive management of the NIH portfolio—an approach that will enable rapid responses to emerging opportunities that do not fit clearly within the mission of a single or small group of institutes.

The extraordinary participation of hundreds of NIH staff, extramural scientists, and the lay public in developing these initiatives is a reflection of the profound commitment of NIH and its stakeholders to do whatever is necessary to rapidly exploit the revolutionary advances of the past few years for the benefit of our people.

For more information, visit <http://nihroadmap.nih.gov>