Re-Engineering the Clinical Research Enterprise

The 21st century is witnessing an increasing need to move research results more quickly to clinical settings. Clinical research is a vital component of progress toward improving America's health. But while clinical research helps assure that new treatments are safe and effective, it is a lengthy and sometimes inefficient process. The current system of clinical research must be re-engineered if it is to respond to these changing scientific and health care needs. Meeting these demands will require new and more efficient approaches to discovery and clinical validation of research results. The initiatives within this theme of the NIH Roadmap for Medical Research aim to contribute to accelerating and strengthening clinical research by adopting a systematic infrastructure that will better serve the evolving field of scientific discovery. The NIH recognizes the complexity of the issues affecting clinical research and is collaborating with other key agencies to address this theme.

Specifically, the initiatives of this theme area include: Clinical Research Networks and NECTAR, Clinical Outcomes Assessment, Clinical Research Training, Clinical Research Policy and Analysis Coordination, and Translational Research.

Clinical Research Networks and NECTAR

Because of the vast number of diagnostic measures, preventive therapies, and treatments that must be evaluated through clinical trials, intervention- and disease-specific clinical research networks have evolved and operate simultaneously, but independently, of each other. As a result, researchers must sometimes duplicate data that already exist because they are either unaware of, or do not have access to, the data. As a result valuable opportunities to evaluate coexisting health conditions in large groups of patients are lost in the process.

Initiatives have been to capture best practices of existing clinical research networks and to test the feasibility of integrating and expanding clinical research networks. Through the NIH Roadmap, NIH is exploring how to enhance and expand existing networks and their interoperability through funding a series of pilot studies. In addition, standardizing data reporting would enable seamless data- and sample-sharing across studies. Ultimately, the goal is to have a common informatics platform that can offer economies of scale and allow complex research programs to benefit from a common infrastructure. These efforts include determining the feasibility of a National Electronic Clinical Trials/Research Network (NECTAR). The following studies have been funded in fiscal year (FY) 2004:

Clinical Research Network Inventory
The overall goal of this effort is to determine best practices in clinical research networks by conducting an inventory of existing networks. This project is examining organizational and

management structures of existing networks and will evaluate the types and volume of studies being conducted. Other parameters to be analyzed include network performance, informatics infrastructure, and training procedures.

Integrating Clinical Research Networks
This initiative will test the feasibility of integrating and expanding existing clinical research networks. A particular focus is on assessing the capacity for interoperability among networks. This will broaden the kinds of research questions that can be addressed and will enhance the efficiency of conducting clinical research. The long range goals are to develop networks that are based on common infrastructure elements, such as informatics, governance, common language, and training activities, that conduct research in both academic and clinical care settings. Successful models can be used by other networks and for dissemination to the clinical research community.

Clinical Outcomes Assessment

Currently, assessment of chronic disease outcomes relies heavily on subjective reports of symptoms and health-related quality of life items. Important targets for disease treatment include patients' subjective experiences, which cannot be measured with laboratory tests and x-rays. Despite a proliferation of tools to measure such factors, these instruments do not allow comparisons among clinical studies.

This initiative, entitled Dynamic Assessment of Patient-Reported Chronic Disease Outcomes, supports researchers who will develop and implement a publicly available system of a large item bank and Computerized Adaptive Tests. As members of a network, the Patient-Reported Outcomes Measurement Information System (PROMIS), scientists funded through this FY 2004 initiative are developing a computerized system to measure patient-reported outcomes more efficiently in study participants with a wide range of chronic diseases and demographic characteristics. This effort will lead to more sensitive and efficient testing of major chronic disease symptoms and functioning, such as pain, fatigue, and quality of life. Ultimately, such a system will also be useful in clinical practice to assess patients' treatment responses and to inform them of therapy modifications.

Clinical Research Training

One of the most important factors determining the health and vitality of the clinical research enterprise is the scientific workforce. Through the NIH Roadmap, NIH is finding ways to expand and diversify the clinical research workforce by optimizing training and career development programs for the many necessary players required to conduct successful clinical investigations. These players include physicians, dentists, nurses, dieticians, epidemiologists, biostatisticians, and informatics specialists. Tomorrow's clinician must be trained to work in the interdisciplinary, team-oriented environments that characterize today's emerging research efforts.

The clinical research workforce must be sufficiently large to catalyze the translation of research discoveries to patient care at the community level. Within this set of NIH Roadmap initiatives are the following programs: Multidisciplinary Clinical Research Career Development, National Clinical Research Associates, and the NIH Clinical Research Training Program.

<u>Multidisciplinary Clinical Research Career Development Program</u>
This initiative, funded in FY 2004 and scheduled for re-announcement in FY 2005, will train health professionals from a variety of disciplines or specialties in the knowledge and skills required for the discipline of clinical research. The programs will foster the career development of doctoral-level health professionals to become the next generation of clinical researchers who will conduct clinical research in multidisciplinary, collaborative settings. These individuals, who will be trained in team research settings and will be known as NIH Clinical Research Scholars, will be expected to become leaders in various fields of clinical research that are critical to the NIH mission.

<u>National Clinical Research Associates</u>
The lack of a diverse clinical research workforce comprising both community-based practitioners and academic researchers is a major barrier to clinical research. By assessing the feasibility of developing and training a cadre of community-based practitioners, NIH seeks to enhance the efficiency of clinical research networks and extend the generalizability of the results obtained in these studies. Ultimately, these National Clinical Research Associates (NCRAs) are envisioned to function as clinical investigators by participating in clinical research in a practice setting, in the context of delivering health care. The NCRAs will participate in clinical studies, assist in patient recruitment, administer experimental treatments, report data, and be among the first to integrate new research findings into routine healthcare delivery.

<u>NIH Clinical Research Training Program</u>
This program, on the NIH campus, was established in 1997 to provide medical and dental students an intensive one-to-two year experience in clinical or translational research after completion of their clinical rotations. The size of the program doubled in FY2004 from 15 to 30 students. Through this program, selected medical and dental students obtain stipends and academic and administrative support. The program also hosts an annual Clinical Investigator Student Trainee Forum for medical and dental students in clinical research training programs across the country. Additional information on this program is available at http://www.training.nih.gov/crtp/index.asp.

Clinical Research Policy and Analysis Coordination

Currently, clinical research is impeded by multiple and variable requirements for addressing what are fundamentally the same oversight concerns. Considerable variability among and within agencies creates uncertainty about how to comply with regulations and policies, hampering the research enterprise's overall efficiency and effectiveness. The CRpac program thus aims to harmonize federal requirements that pertain to the conduct of clinical research, facilitating compliance with pertinent regulations and policies and ultimately creating a more effective oversight framework.

NIH has established working groups with its sister agencies to make progress in high priority policy areas. Some of the goals of this initiative include the development of clear, effective, and coordinated rules for clinical research; maximally effective human subjects protections; more comprehensive analysis and sharing of research data; and overall enhanced quality and productivity of the research enterprise.

Translational Research

To improve human health, scientific discoveries need to be translated into practical applications. Such discoveries typically begin at "the bench" with basic research--where scientists study how diseases develop and spread--then progress to the clinical level, or the patient's "bedside." Researchers have become increasingly aware that this bench-to-bedside approach to translational research is really a two-way street. Not only do basic scientists deliver to clinicians new tools to examine in patients, clinical researchers also make novel observations about the nature and progression of disease that can stimulate basic investigations.

While translational research has proven to be a powerful process that primes the entire clinical research engine, there are many ways the process could be improved, among them building a stronger infrastructure. Key to building this infrastructure will be enhancing interactions between basic and clinical scientists, and easing the movement of powerful new tools from the laboratory into the clinic.

Regional Translational Research Centers
Through the NIH Roadmap, NIH will support planning grants in FY2005 and FY2006 for the development of regional translational research centers that would provide sophisticated advice and resources to better enable scientists to master the many steps involved in bringing a new product from the laboratory to clinical use. Such resources include support in regulatory affairs, clinical informatics, biostatistics, and patient recruitment. An RFA for planning grants for these centers will be issued in the fall of 2004, while RFAs for the centers themselves will be issued later in FY2005.

Translational Research Core Services
The Re-engineering theme also acknowledges the need for translational research core facilities that can provide clinical researchers access to sophisticated manufacturing capacity, along with expert advice to ensure that drug-development regulations are observed. For an initial pilot phase, core facilities will be provided through resources already assembled in support of the National Cancer Institute's Rapid Access to Innovation Development (RAID) program, which currently provides these facilities only to members of the cancer research community. Their availability to the broader research community should expedite discoveries for other major public health challenges. By early FY2005, this program will be in position to receive applications for drug-development planning, small molecule preparation and pre-clinical testing.

The NIH Roadmap for Medical Research is a series of far-reaching initiatives designed to transform the Nation's medical research capabilities and speed the movement of scientific discoveries from the bench to the bedside. It provides a framework of the priorities the NIH must address in order to optimize its entire research portfolio and lays out a vision for a more

efficient and productive system of medical research. Additional information about the NIH Roadmap can be found at http://nihroadmap.nih.gov. For more information on the Re-engineering the Clinical Research Enterprise initiatives, please go to http://nihroadmap.nih.gov/clinicalresearch/index.asp

The National Institutes of Health (NIH), an agency of the U.S. Department of Health and Human Services, is the primary Federal agency for conducting and supporting basic, clinical, and translational medical research. NIH is comprised of 27 institutes and centers and investigates the causes, treatments, and cures for both common and rare diseases. For more information on the NIH, please visit the NIH Web site at http://www.nih.gov.

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