



NIH BACKGROUND

National Institutes of Health

The NIH Roadmap: Re-Engineering the Clinical Research Enterprise

Clinical research is the linchpin of the nation's biomedical research enterprise. Before a therapy is approved for general use, it must be studied carefully in the laboratory to understand its mechanism of action, effectiveness, and potential risks. The safety and benefits of the therapy for humans are then proven through an orderly series of tests in people. While clinical research helps ensure that new products and techniques that ultimately are made available to doctors and their patients are safe and effective, it is a lengthy and sometimes inefficient process.

To accelerate and strengthen the clinical research process, this set of NIH Roadmap initiatives will re-engineer the clinical research enterprise by adopting a systematic infrastructure that will better serve the evolving field of scientific discovery. This effort, which complements the other initiatives that comprise the NIH Roadmap, will provide the necessary foundation for advancing basic and clinical research. With the NIH Roadmap in action, investigators will be better poised to translate basic discoveries into the reality of better health for our nation.

Although biomedical research has succeeded in converting many diseases once considered uniformly lethal into more chronic, treatable conditions, it has become clear to the scientific community that the United States must recast its entire system of clinical research if such efforts are to remain as successful as they have been in the past. Over the years, clinical research has become more difficult to conduct. However, the exciting basic science discoveries currently being made demand that clinical research continue and even expand, while at the same time striving to improve efficiency and better inform basic science efforts. This is undoubtedly the most difficult but most important challenge identified by the NIH Roadmap process.

At the core of this vision is the concept that 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 the creation of better integrated networks of academic centers that work jointly on clinical trials and that include community-based physicians who care for sufficiently large groups of well-characterized patients. Implementing this vision will require new ways to organize the way 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 re-energize the clinical research workforce.

Translational Research

To improve human health, scientific discoveries must be translated into practical applications. Such discoveries typically begin at “the bench” with basic research – where scientists study the mechanisms and pathogenesis of a disease at a molecular or cellular level – then progress to the clinical level, or the patient’s “bedside.”

Scientists 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.

Translational research has proven to be a powerful process that primes the entire clinical research engine. However, this component of the clinical research enterprise could be optimized and accelerated through a stronger infrastructure.

Key to building a strong infrastructure will be to increase interactions between basic and clinical scientists, and ease the movement of powerful new tools from the laboratory into the clinic. In one approach aimed at accomplishing this, NIH is exploring development of regional translational research centers. These centers would provide sophisticated advice and resources to better enable scientists to master the many steps involved in bringing a new product from the bench to clinical use. Such steps involve laboratory studies to understand a therapy’s mechanisms of action and animal studies to determine how well a therapeutic agent is absorbed into the body, how it is distributed to target tissues, how effective it is, and how likely it may be to cause unanticipated side effects.

Once a potential new drug is developed, sufficient amounts of the drug have to be made according to rigorous standards for testing first in animals and then in people. The clinical research re-engineering initiative also envisions translational research core facilities to provide clinical researchers access to sophisticated manufacturing capacity, along with expert advice to ensure that drug-development regulations are observed. Some of these core facilities will be modeled on, or may evolve through expansion of, the National Cancer Institute’s Rapid Access to Innovation Development (RAID) program, which currently provides these types of resources only to members of the cancer research community. Their availability to the broader research community should expedite discoveries for other major public health challenges.

This initiative will also support translational research by developing new technologies to improve the assessment of clinical outcomes. Many of the most debilitating chronic illnesses gradually erode patients’ quality of life because of the associated fatigue, pain and mood changes. Currently, these critical symptoms cannot be objectively measured in the same way, for example, as blood sugar levels or blood cell counts. More sensitive, well-validated tools need to be developed to improve measurements of these types of symptoms. Technologies, such as a computerized adaptive health assessment, could revolutionize how symptoms and treatment outcomes are assessed. Scientists will be better equipped to understand how patients perceive changes in their health status resulting from new interventions, thereby directing research to therapies that would be most highly valued by patients.

Clinical Workforce Training

Our nation's ability to fully explore the ever-expanding opportunities for medical advances are limited only by our resources, the most important of which is the scientific workforce. To fulfill the promise of 21st century medicine and to make further progress in controlling major human diseases, we must cultivate and train a cadre of clinical researchers with skills commensurate with the increasing complexity and needs of the research enterprise.

The clinical research workforce must be large enough to facilitate bench-to-bedside research, the phased testing of approaches from small to large studies and the translation of proven concepts into medical practice at the community level. Clinicians must be trained to work in the interdisciplinary, team-oriented environments that characterize today's emerging research efforts. Specific training is needed in an array of disciplines important to the conduct of clinical studies, including epidemiology, behavioral medicine and patient-oriented research.

This NIH Roadmap effort envisions two major programs to expand, enhance and empower the clinical research workforce: the establishment of an agency-wide Multidisciplinary Clinical Research Workforce Training Program and a cadre of NIH Clinical Research Associates.

The Multidisciplinary Clinical Research Workforce Training Program will be an NIH-wide effort to train pre- and post-doctoral candidates in clinical research settings that are interdisciplinary and collaborative. The emphasis will be on new strategies and curricula with training opportunities that span a variety of disease areas; a broad range of clinical disciplines, including medicine, nursing, dentistry, pharmacy and other allied health professions; and a wide array of research areas, including biostatistics, behavioral medicine, clinical pharmacology and epidemiology. Generic training programs will be administered by a single institute on behalf of NIH, and programs focused on a specific disease or organ will be administered by the relevant institute. The new program will be coordinated with and complement other NIH training programs that support scholars who wish to become clinical researchers.

In addition, a cadre of NIH Clinical Research Associates will be created. Composed of partnerships between academic and community-based investigators, this initiative will provide a robust and versatile infrastructure of qualified researchers who are well trained to ensure responsible conduct of clinical research and positioned to bring research opportunities to patients and rapidly disseminate the best science-based practices.

Several projects will be required to realize the vision of the Associates. These include a study that will examine the feasibility of involving community practitioners in clinical research and explore possible mechanisms for such involvement. Building on the results of this study, recommendations on ways to reduce barriers to building a model workforce for conducting clinical research are expected to evolve.

Other efforts will focus on the establishment of national core competencies and best practices needed to conduct high-quality clinical research and to translate research into clinical practice. These efforts will apply to researchers working in community or academic settings.

Competencies would include relevant board certification, knowledge of conflict-of-interest regulations and documentation of training in protecting participants in clinical trials. Best practices for research teams might include methods for managing study data, as well as developing cost and staffing estimates.

To train the Associates, the NIH plans to create several nationally recognized regional Centers of Excellence in Clinical Research Training, based on the results of the feasibility and pilot studies. These centers will use an integrated approach to conduct training in “real-world” settings.

Clinical Research Networks

An enriched pipeline of biomedical discoveries, an infrastructure to facilitate their translation from the lab to the clinic and a robust force of clinical investigators will make it possible to test new therapeutic and preventive strategies in larger numbers of patients far sooner than at present. These large studies are often best conducted through networks of investigators who are equipped with tools to facilitate collaboration and information sharing.

Because of the vast number of therapies, diagnostics and treatments that must be evaluated through clinical trials, many clinical research networks operate simultaneously, but independently of each other. As a result, researchers must sometimes duplicate already existing data because they are unaware the data exist or they cannot access them. Standardizing data reporting would enable seamless data and sample sharing across studies. In addition, by enhancing the efficiencies of clinical research networks through informatics and other technologies, researchers will be better able to broaden the scope of their research. Reduced duplication of studies will leave more time and funds to address additional research questions.

This effort will promote and expand clinical research networks that can rapidly conduct high-quality clinical studies that address multiple research questions. An inventory of existing clinical research networks will explore existing informatics and training infrastructures to pinpoint characteristics that promote or inhibit successful network interactivity, productivity and expansion, or broadening of research scope. “Best practices” can then be identified and widely disseminated, further enhancing the efficiency of clinical research networks.

Furthermore, a blueprint for a national informatics network using standardized data, software tools and network infrastructure will evolve from the inventory. The National Electronic Clinical Trials and Research Network (NECTAR) will dovetail with current medical informatics initiatives in the Department of Health and Human Services. It will maximize connectivity among existing and newly created clinical research networks. Researchers will be better equipped and more likely to generate and use data, thereby reducing duplicated efforts and unnecessary overlap between trials. Thus, NECTAR will ultimately assist in accelerating the pace of discovery and development, thereby helping clinical researchers better serve their patients.

Other impediments to efficient clinical research to be addressed through this set of initiatives are the multiple requirements of diverse regulatory and policy agencies. Researchers face a tremendous diversity of requirements in reporting adverse events to NIH, the Food and

Drug Administration, the Office of Human Research Protections and institutional review boards, among others. Clinical researchers must understand and fulfill these varying requirements that often overlap and might even contradict one another.

NIH aims to take a leadership role in working with other agencies to develop better processes and to standardize requirements for reporting adverse events, human subjects protections, privacy and conflict-of-interest policies and standards for electronic data submission. Harmonizing policies and reporting requirements will help minimize unnecessary burdens that slow research, while at the same time enhancing patient protections.

For example, with extensive input, NIH has already designed a more efficient system for reporting adverse events – unexpected or life-threatening problems that occur during a clinical trial. The system is being pilot tested by researchers doing gene therapy studies. Using the pilot system, clinical researchers can submit reports to all relevant oversight groups with a single keystroke, and the data can be analyzed and responded to promptly.

By standardizing the regulatory requirements of clinical research networks and enhancing their interoperability, clinical research will advance more swiftly, and more and better therapies will reach patients nationwide. By creating a partnership with patients and physicians – true “communities of research” – this ambitious set of NIH Roadmap initiatives promises to enhance the scope, resilience, efficiency and impact of the nation’s clinical research workforce, ultimately improving the health of all Americans.

This information is available at the NIH Roadmap Web site (<http://nihroadmap.nih.gov>). For more information on the Re-Engineering the Clinical Research Enterprise initiatives, contact Bill Grigg in the NIH Office of the Director, (301) 496-5787, griggw@od.nih.gov.

###