

EU-US Biomedical Sciences Research Infrastructures and Initiatives

International Cooperation on Clinical Trials

Embassy of France, June 6, 2012

NIH mission: Science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.

The NIH:

- **Conducts** research in its own laboratories on its Bethesda campus and in several other locations
- **Supports** research of non-federal scientists in universities, medical schools, hospitals, and research institutions throughout the United States and overseas
- **Translates** scientific information into clinical guidelines and community programs
- **Trains** research investigators – supports doctoral and post-doctoral training through both training and research grants.
- **Fosters communication** of medical information to professionals and the public
- **Over half the funds support basic science.** Virtually all of the work which leads to the development of new drugs, diagnostics and devices comes from work supported by the NIH. Industry picks up and commercializes findings. Universities own the Intellectual Property.

NIH is not a ministry of health, but a research institution. It has a budget of just over \$30 billion, 83% is distributed across the US and the globe. Approximately 1/3 of this amount goes to support research infrastructure at institutions, and supports non-federal research as well as that supported by NIH.

The NIH supports clinical research infrastructure across the US in four ways.

1. Individual investigator research grants come with overhead which is negotiated by the federal Office of Management and Budget (OMB) which varies by institution, but generally runs between 50 and 95% of the “direct” cost of the grant. These “indirect costs” go not to the investigator but to the institution to pay for costs of running a research enterprise – administrative costs, running the IRB, keeping the lights and water on, etc.
2. Institutions get grants to build new research buildings. This process is run centrally at NIH – all construction grants are handled by the former National Center for Research Resources, now the National Center for Advancing Translational Science. These are supplemented by bonds at very favorable rates and have provided incentives to build capacity.
3. The CTSA program, run from NCATS, has built research institutes and infrastructure at 60 different centers across the US, and is now in the process of enhancing the consortial activities of these separate entities. The CTSA provide protocol development assistance, informatics, community resources for conduct of research, pilot funds, and have begun addressing cross-cutting needs for US institutions. Many of the institutions have international partners and collaborators.
4. Individual institutes and centers fund clinical research, including centers and networks, in specific disease areas. For example, the NCI supports Cancer Centers at institutions, which bring together multiple disciplines, create core facilities and enhance engagement of investigators in cancer research. The NIAID supports AIDS clinical trials networks. The NICHD supports multiple networks in pediatric and maternal medicine. The NHLBI – my institute – supports relatively little long term infrastructure, and creates networks when three conditions are met: a robust portfolio of clinical research questions; an organized investigator community; and effective leadership and governance.

All of these investments are reviewed periodically, undergoing renewal processes. Each of the entities mentioned is able to collaborate in international research – NIH Intramural, extramural institutions, the CTSA consortium.

The NHLBI is the third largest of 27 Institutes and Centers, with an annual budget of \$3.1 billion. It is what is called a *categorical* institute, meaning that it focuses on the function and diseases of specific organ systems – heart, lungs and blood. Sleep disorders and blood safety are also within the mission of the NHLBI. Other institutes, such as Child Health and Human Development and the Fogarty International Center, address research which takes place in certain populations (children) or settings (international). Virtually everything in the NHLBI portfolio has global importance. Half of all deaths around the world are caused by heart disease, chronic lung disease, cancer, and diabetes, 80% in low and middle-income countries.

Extrapolating from the prevalence of known (and in many cases, shared) modifiable risk factors for chronic, non-communicable diseases, at least half of these deaths are preventable. We know more or less what needs to be done, but we do not know how to do it.

Collaboration among International Entities: Partnerships are paramount: NHLBI collaborates with other parts of NIH, other federal agencies, professional organizations, and other governments as well as with industry, non-profits, and patient and professional organizations. When researchers, industry, and policy makers work together, we are all more effective.

Global Health: Challenges and Benefits

Effective evidence-based prevention and treatment of disease contribute to peace and economic stability all over the world. A multitude of factors drive the need for cooperative global health research.

- There are common risk factors for heart and lung diseases which overlap with those for diabetes and cancer, including nutrition, smoking, indoor and outdoor air pollution, and physical inactivity.
- Research conducted in global settings offers creative and effective approaches to control chronic diseases in the United States, decreasing health costs and improving the nation's economic status.

- International studies on rare diseases that afflict Americans will advance understanding and lead to new therapies that studies based in one nation alone could not achieve.
- Approaches which work in some settings may or may not work in others, for many reasons. Because of genetic, environmental and cultural diversity, it is important to get information in multiple settings if we are to truly understand diseases and interventions.

NIH is a funder, not a sponsor of international clinical trials – if commercialization is part of the goal of a study, NIH usually plays a small role unless it is an orphan disease. Industry plays a primary role in commercialization. NIH's role in international clinical trials is driven by public health need, not product development.

- NIH funds investigators on their home territory—they know first-hand the regulations, policies, cultural issues, local guidelines and practices—they can also implement findings quickly because of this.
- International sites participate in many US-based trials, especially in those in which the economics of medical care provide dis-incentives for clinicians to enroll participants on some studies.
- NIH is very aggressive insisting that research data obtained with public support and funds be widely shared.

International participation has been essential to completion of a number of important NHLBI trials, especially those examining medical interventions compared to surgical or radiological interventions.

Despite notable gains, conducting international clinical trials — and doing global health research in general — is very hard — systems are not set up to collaborate, and there are major cultural differences among institutions and countries, as well as between government, non-profits and industry.

Infrastructure is vital for all of us, and we very much appreciate role of the European Clinical Research Infrastructures Network (ECRIN), which supports

multinational clinical research projects in Europe via coordinating centers, support, and services.

Challenges include protecting participants, harmonizing rules and policies to the best extent possible

- Participant engagement and protection
- Regulatory issues
- Health care issues
- Currency exchange rates

Conclusion

All clinical research is a massive team effort. International clinical research is a huge team effort.

Science and health know no borders. Governments and policies do have distinct boundaries, but we are all facing similar problems.

Communicating the Role of research: As scientists and public health leaders, it is our job to find out what works. We reach out to policy makers at all levels of government, to help implement research findings in ways that make sense in local settings and with the regional differences in health care, cultural norms, and a host of issues unique to individual countries and communities.

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