Clinical Research and the New Public Partnership – A View from the South

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ABSTRACT. The clinical research enterprise in the United States is in a state of considerable transition. Many, including the US National Institutes of Health through its Roadmap Initiative, have called for a reengineering of the enterprise in ways that will build transparency, public disclosure of trial results, and enhanced public trust. This presentation will set forth a premise for a new public partnership model that will define the clinical research enterprise, in terms of both the relationship between the participant and the investigator in each clinical trial, and the relationship between the public and the clinical research enterprise as a whole. Ten guiding principles to direct this new partnership relationship are suggested.
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The clinical research enterprise in the United States is in a state of considerable transition. The US National Instititutes of Health (NIH) Roadmap Initiative, led by NIH Director Elias Zerhouni, contemplates a "reengineered clinical research enterprise." This reengineered enterprise anticipates new models for clinical research that will be reliant upon dynamic relationships with participants who are viewed as "partners,"[1] and will be founded upon principles of transparency and trust. This presentation will set forth a premise for a new public partnership model that will define the clinical research enterprise, in terms of both the relationship between the participant and the investigator in each clinical trial, and the relationship between the public and the clinical research enterprise as a whole.

The public and its relationship with science and medicine has evolved over the course of the past few decades from a public that was comfortable with paternalism, to a public that came to demand autonomy, to a public that today expects a partnership in the delivery of care, in the determination of treatment choices, and in the operation of the scientific enterprise that it generously funds. This partnership is based upon notions of transparency, equality, and shared decision-making. This informed and transformed public expects to play a direct role in setting scientific priorities and ensuring that the products of science are applied toward improved human health.

It may be an understatement to suggest that recent events in the United States across all sectors have undermined the public's faith in institutions in which it has placed its trust. In large part due to such events, the public is demanding new expressions of cultural integrity from institutions reliant upon its investment and support. Specifically, the public is asking for demonstrations of institutional cultures and operations that value and insist upon each of the following: evidence-based findings as opposed to conclusions supported by opinion; data-driven accountability as opposed to institutional authority; collaboration as opposed to command and control functions; interdisciplinary teams as opposed to "turfs and silos"; earned and informed trust as opposed to blind, assumed trust; and responses that sustain the enterprise and its new relationship with its stakeholders as opposed to "band aid fixes" designed to maintain the status quo. These are global themes that define the public's relationship with institutions in all sectors, but today especially they characterize the public's expectations for science.

The public is setting new standards for its relationship with the clinical research enterprise, which it funds with its dollars and supports with its irreplaceable human contributions. Ten principles for this new public partnership are suggested to sustain and build the clinical research enterprise of the 21st century.

1. Each clinical trial should be viewed as a new clinical trial partnership. Applying a "partnership model" to each clinical trial requires substantial transformations in beliefs, attitudes, and roles on behalf of all involved. The patient who elects to become a subject, becomes something more C a participant who is an empowered partner in the exciting venture of promoting scientific knowledge. Similarly, the physician who becomes an investigator is no longer able to maintain a single focus on providing the best care for an individual patient. Rather, as an investigator, the physician assumes a new fiduciary responsibility to ensure that she and the participant are engaged in a meaningful venture, founded on good science, producing generalizable knowledge, and providing a meaningful return for both partners.
2. The clinical research partnership is reliant upon and defined by joint investment, mutual returns, ethical clarity, and full disclosure. Each partner is propelled into the clinical research venture by dramatically different life experiences, world views, necessities, and expectations.

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Nevertheless, these unlikely collaborators can find, within this partnership, a space where their respective values, goals, and needs overlap.

With this new sense of parity and mutual empowerment comes the potential for enhanced ethical clarity. A partnership model is premised upon the requirements of full disclosure before investment in the venture is made. The participant deserves and must understand that she is involved in the business of research, as opposed to the prospect of therapy. Informed consent as a vehicle for continuously informed participation becomes the essential foundation of the partnership.

This microcosm of a partnership within each clinical trial forms the foundation for the larger model of partnership, which must begin to define the public's relationship with the clinical research enterprise if public trust is to be regained and fortified. The principles and expectations for this larger societal partnership follow.

3. In the new higher level partnership between the public and the clinical research enterprise, the public expects to see manifest coordination and cooperation across the enterprise. The new public partnership in the larger clinical research enterprise holds clear expectations for agencies that fund clinical research. Government agencies that oversee basic research, healthcare applications, healthcare delivery, healthcare entitlement programs, and public health promotion and disease prevention must operate in a collaborative, coordinated fashion. The "baton passing" between agencies must be seamless and swift and never fumbled because of needless inefficiencies or the failure of agencies to align their overlapping authorities.

4. The new public partnership demands new kinds of clinical trials that inform policy and that involve communities. New demands are being made by the US Congress for clinical trials that inform policy decisions. These will be practical clinical trials, conducted in real-life healthcare delivery systems, involving patients with comorbid conditions[2]. Such trials will include comparative drug trials that help payors and the public make informed treatment choices. Communities will be engaged in trial design in new ways that drive participation and compliance and measure outcomes in terms meaningful to individuals and to the community.

5. The new public partnership calls for the use of technologies to speed clinical trial analyses, enhance information transfer, and harmonize reporting of trial events and results. We must develop new systems for postmarket surveillance of exciting, innovative therapies, such as tumor necrosis factor-α inhibitors, brought to market rapidly, with little longterm, population-based history of use. The informed public understands that there is a need for electronic medical records to track outcomes from treatment and to inform future trials. In the US, harmonization of adverse event reporting between agencies is occurring in the area of gene transfer research; this must become a model for the reporting of serious adverse events, in real time, across all large trials.

6. As an essential term of the new public partnership agreement, the public expects – and is entitled – to have meaningful access to information generated by clinical trials. We are seeing the emergence of new societal demands for access to the products of the science funded with public dollars and made possible due to the contribution and assumption of risk of human participants in clinical research. Participants in clinical trials deserve to know the results of the trial in which they have participated. All trials should be registered and all results, including negative results, must be published as part of our social covenant with each participant to deliver generalizable results from the clinical research endeavor. And publications of clinical research that has been funded with public dollars should be made a public resource through placement in an open archive, such as the NIH PubMed Central. Open access is the story to watch.

7. The public asks that its clinical research partners retain adequate control over the information generated from trials and that their independence in analyzing and reporting data is ensured. Investigators, institutions, and internal review boards have duties within the new public partnership to ensure that a study design will render solid data; to retain control over the use of databases, disease registries, and tissue specimens; to have access to all data generated in a multicenter trial – not just the data generated at a single trial site; to have a say in deciding when a trial is to be halted; to refuse to take credit for a ghost-written paper. These are essential elements of the partnership that should not be bargained away in any arrangement between the institution and the trial sponsor.

8. Public trust is the keystone of the new public partnership. Clinical research must remain objective and worthy of trust in the public eye. Highly interwoven relationships between government, academia, and industry have undermined the public's faith in the independence of the scientific enterprise and have outpaced our collective capacity for ethical and convincing responses. This now looms as the largest challenge in rebuilding the public's trust in science and in creating a new partnership that delivers information the public is able to look to, with faith and trust, to inform individuals' health decisions and to foster participation in clinical trials.

Clinical research institutions must build and display cultures that continually and openly value and work to earn public trust. Public trust is not a given, it can never be assumed, and once lost, it is very difficult to regain. Public trust is the bottom-line asset of the nation's clinical research enterprise.

9. The public expects clinical research to be relevant and responsive to public need. For this to occur, the public must be substantially and meaningfully engaged in the process of setting research priorities. "The guarantee of public input and participation in the research priority-setting process for publicly funded research, and the transparency of the process, are essential to promoting public trust in the research enterprise."[3] New mechanisms for dynamic, bidirectional public engagement will require that the public have

access to, understand, and be able to influence the process of research priority-setting. For this to happen, this process itself must become transparent to the public.

10. The public expects scientific inquiry will serve as an ultimate public good. As such, while the conduct of science must occur within the context of ethical and moral codes, scientific inquiry must remain free of improper intrusion by government designed to promote a particular political ideology. This may be a final warning from "the South." As stated forcefully in April 2004 by the former Director of the NIH, Harold Varmus[4], "An increasingly dogmatic faith-based element has invaded government and politics, undermining the evidence-based approaches to problems that most scientists would like their governments to use. In crucial situations, this can produce important mistakes with disastrous consequences, even well beyond the usual confines of science." How government, science, and public interests converge to ensure ethical and value-driven research that nevertheless remains free of improper ideological intrusion is one of the most daunting and pressing issues facing the research enterprise in the 21st century.

The new public partnership with the clinical research enterprise is not for those who resist rapid evolutionary change, rather it is for those determined to fortify an enterprise founded upon shared purposes and recognized by government, industry, academia, and the public as vital to discovery, translation, and improvement of human health.

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