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Preserving Public Trust:

Accreditation and Human Research Participant Protection Programs

Committee on Assessing the System for Protecting Human
Research Subjects

Board on Health Sciences Policy

INSTITUTE OF MEDICINE

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Preface

Although it is said that each stage of evolution can be explained (but not predicted) from the earlier ones, it is not easy to apply this insight to the specifically human phenomenon known as clinical investigation. With the possible exception of genes for altruism, it is hard to discern the evolutionary antecedents of the behaviors that characterize what we know as human research. The complex system that sustains research is ultimately premised on trust—trust in the people and organizations that conduct research. In the wake of revelations about lapses in research ethics, such trust must be earned, and trust hinges on concrete affirmation of trustworthiness. But trustworthiness to whom? To those who become the object of study in human research.

Consider first those who join the human research system as participants. Those who are volunteers have little to gain by accepting drugs or answering a survey, each of which has a small but unquantified risk. Although a financial inducement is sometimes part of the lure, these individuals often accept considerable risk in the knowledge that the research in which they join cannot help them but does have the potential to help “unknown others”—surely a remarkably selfless behavior. The other key participants are patients who become the subject of research. At some point, all new drugs and devices are given experimentally to sick individuals who might benefit from the intervention. Even when they are explicitly informed of the relative risks and benefits, many patients choose to enroll in a clinical investigation when their own likelihood of benefiting is small. The outcome of this moment of decision affects in considerable measure how the clinician/researcher discharges his or her responsibility to inform.

Protecting research participants looms especially large in clinical research, where the risks are often the highest, professional roles are conflicted, and ethical lapses have been most salient. The physician doing research is wittingly cast in two different and often conflicting roles. Above all else, he or she is a doctor, sworn first to do no harm and always to act in the best interest of the patient. As investigator, however, the same person is trained to randomize his or her patient's participation to an at least 50 percent likelihood of no benefit and, indeed, to treat all research participants with a neutral regard that puts the sought-after truth ahead of the research participant's immediate interest. As if this dual identity of dedicated physician and disinterested inquirer were not enough of a weight to sustain, the physician researcher has two burdens of (self) interest. One of these, familiar now for more than half a century, is the linkage of research and publication to academic promotion and professional advancement. The other, newer pressure is that of obtaining additional income from sources that have a huge interest in a positive outcome of the research. Many and perhaps most clinical trials are now supported by pharmaceutical and biotechnology companies. Honoraria, speaker fees, paid travel, and further research support may all be available to the bearer of positive tidings. These emoluments, though, are dwarfed by the potential of equity participation in the sponsoring company by the investigator.

The social and economic setting of research also is undergoing dramatic change. At first investigation was almost an avocation of scientists and clinicians whose curiosity and clinically derived puzzlement drove them to undertake a study. Later it was a virtual monopoly of academic health centers, where a dominant professional ethos and the constant gaze of skeptical trainees emphasized probity and ethics. In the 1970s, institutional review boards (IRBs) became increasingly common, applying independent review and intellectual rigor to the evaluation of the science and the protection of the individual subject participants. Now, however, clinical research is a multibillion dollar business with enormous potential profits riding on efficiency, aggressiveness, and positive outcomes. Research pervades marketing, census counting, national surveys of opinion, and myriad other aspects of our daily lives. Outputs of research define congressional districts, legal thresholds for poverty, and marketing campaigns that affect us all. Research is carried out in a ragged congeries of universities, for-profit and nonprofit research organizations, and drug companies. Reassurance about the conduct of some of research comes from professional independent review boards that have no anchor in universities or their academic health centers and that are often organized for profit.

As a result of these changes plus the headlong advance in biomedical science, questions are surfacing around the enterprise and about its dedication to the human being at its center—the research participant. Given the complexity of the current science, can consent ever be truly informed? Given the inevitable asymmetry of the investigator-subject dyad, can real autonomy—the power to say no and the choice to change one's mind—be preserved? Can IRBs of such

different geneses handle the complex responsibilities being laid on them? Can professionalism be sustained without requiring saintliness? Can the occasional sinner be recognized before doing tragic harm? In short, how can a diffuse, chaotic, fast-moving, ever-changing nonsystem of evolutionarily unprecedented human behavior be organized and monitored to maximize its glorious potential and control its dark risks?

Our committee was asked to take up these questions and others with the focus on the safety and rights of the participants who share the clinical research enterprise and who are indispensable to its success. In this first report, done in 6 months, we suggest ways in which accreditation might contribute to a new level of excellence. There are many other points of leverage, however, including decompressing the burdens on IRBs, educating and perhaps certifying investigators, improving research monitoring, and building greater institutional support and infrastructure. In another report to be rendered after more time, more study, and more reflection, we hope to contribute to these larger questions and thus to the research enterprise as a social good.

Daniel D. Federman, M.D., Chair

REVIEWERS

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by Francois Abboud, appointed by the Institute of Medicine, and Mary Jane Osborn, University of Connecticut Health Center, appointed by the NRC's Report Review Committee, who was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Acronyms

AAALAC	Association for Assessment and Accreditation of Laboratory Animal Care
AAHRPP	Association for the Accreditation of Human Research Protection Programs
AAMC	Association of American Medical Colleges
ACHRE	Advisory Committee on Human Radiation Experiments
AMA	American Medical Association
CIOMS	Council for International Organizations of Medical Sciences
DHHS	U.S. Department of Health and Human Services
DSMBs	data safety and monitoring boards
FDA	Food and Drug Administration
GAO	General Accounting Office
HCFA	Health Care Financing Administration
HRPP	human research protection program
HRPPP	human research participant protection program
ICH-GCP	International Conference on Harmonisation Guideline for Good Clinical Practice
IND	investigational new drug application (FDA)
IOM	Institute of Medicine
IRB	institutional review board
JCAHO	Joint Commission on Accreditation of Healthcare Organizations
MCMC	Medical Care Management Corporation
MCOs	managed care organizations

NBAC	National Bioethics Advisory Commission
NCI	National Cancer Institute
NCQA	National Committee for Quality Assurance
NHRPAC	National Human Research Protections Advisory Committee
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
OIG	Office of the Inspector General (U.S. Department of Health and Human Services)
OPRR	(former) Office for Protection from Research Risks
ORCA	Office of Research Compliance and Assurance (VA)
PHS	U.S. Public Health Service
PRIM&R	Public Responsibility in Medicine and Research
VA	U.S. Department of Veterans Affairs

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