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Ethics in Clinical Research

Executives must ensure trial participants' protection and the public's best interest.

Clinical research is no longer the exclusive domain of the academic health sciences center but has extended into the everyday world of the healthcare executive in a wide range of organizational and clinical settings. This trend is a beneficial one in many respects, for clinical research is the R&D of the healthcare world in applying and validating discoveries from the realm of basic science (the bench) to the care of the patient (the bedside). Healthcare organizations have engaged in clinical research at a variety of levels as direct sponsors of research investigators or as part of a broader research network engaged in the conduct of clinical trials.

Total spending on health-related research and development from public and private sources in the United States reached $49.3 billion annually by 2010, according to ACHE's *Key Industry Facts: 2012*. This source of opportunity to advance the research dimension of one's organizational mission while opening new sources of revenue in a world of diminishing resources has proven attractive to clinicians in private practice settings and to community institutions, attracting new entrants to clinical research.

Ethical issues have always had a prominent place in discussion of clinical research. The ethical imperative of "first do no harm" has been violated by some studies in the past such as the infamous Tuskegee syphilis experiment begun in 1932 in which participants were not informed of the nature of the study and in which therapy for treatment of the disease was withheld. In response to public outrage, the study was terminated in 1972, and a formal presidential apology by President Clinton on behalf of the nation followed in 1997. Within the conduct of the study, informed consent by the participants was impossible because the study's objectives and a detailed explanation of relative risks and benefits (if any) of participation had not been disclosed to them.

The Belmont Report of 1979, which was prompted in part by the Tuskegee incident, led to the adoption of recommendations to avert future ethical lapses in clinical research as official U.S. Department of Health, Education and Welfare policy. These policy directives were based on specific ethical principles and were directed primarily toward protection of participants. The directives were specifically applied through policies of informed consent, assessment of risks and benefits, and responsible selection of study participants.

The ethical principle that most prominently figured in the Belmont Report was that of *respect for persons*. This premise has been a driving force in contemporary bioethics and is defined as the obligation of the organization and the executive to protect and preserve individual autonomy (self-determination) of participants in clinical research studies. In this regard, it parallels the drive toward protection of patient self-determination in the clinical setting that is embodied in ACHE's *Code of Ethics*. According to the code, the healthcare executive commits to, "Work to provide a process that ensures the autonomy and self-determination of patients or others served."

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Protection of Subjects

Federal regulation for protection of clinical trial volunteers in federally sponsored research projects has been highly developed through the Institutional Review Board mechanism of the U.S. Department of Health and Human Services. Many healthcare executives are part of organizations sponsoring their own IRBs or are members of research networks that assume IRB responsibilities. In the work of IRBs, the attainment of participants' informed consent is a central value, much as

informed consent is essential to patient safety and self-determination in the clinical setting.

In their 2002 "Clinical Trial Volunteer's Bill of Rights," Kenneth Getz and Deborah Borfitz summarize the gist of these regulations for protection of subjects. Key elements involve informing the participant of the purpose of the clinical trial; all risks, side effects or discomforts that might be reasonably expected; and any expected benefits. The participant must be told what will happen in the study and whether interventions such as drugs and devices differ from those used in standard medical treatment. Available options should be discussed and assessed as better or worse than being a participant.

Throughout the clinical trial process, prevention of coercion, which diminishes patient freedom and detracts from the *respect for persons* tenet, is essential. The participant is to be allowed to ask questions about the trial prior to giving consent and at any time during the trial. She or he must have ample time to decide to consent free of pressure. The participant may refuse to participate for any reason before and after the trial has commenced and must be told of any medical treatments available if complications occur. All of the above provisions must be addressed in an informed consent form that is signed, dated and given to the participant.

Protection of study participants has proven crucial in gaining the public's confidence regarding the integrity of research studies and the absence of exploitation of their essential participants. This protection is especially necessary in the successful involvement of minority and underserved populations in studies. The literature demonstrates that variation in success of treatments exists across these lines and that generalizable results cannot be attained without the voluntary involvement of these individuals. In this regard, the ethical obligation of the executive in the conduct of clinical research is again no different than in the therapeutic setting.

Conflicts of Interest

With the increasing fiscal attractiveness of clinical research has come an intensified focus on the obligation to minimize conflicts of interest—on the part of researchers and their organizations—resulting from financial interests that could affect the design, conduct or reporting of research results. In his 2011 book *Ethics in Health Services Management*, Kurt Darr defines conflict of interest as "a duality of competing interest when duties are owed to two or more persons or organizations and meeting the duty to one makes it impossible to fulfill the duty to the other."

Further, without full disclosure of conflicts to participants, the *respect for persons* principle is undermined, as the participant is giving consent based on incomplete information. Just as the American Medical Association's *Code of Medical Ethics* mandates that if a conflict develops between a physician's financial interest and the interest of the patient that the conflict must be resolved to the benefit of the patient (Standard 8.03), so must a conflict in the research world be resolved in favor of the public.

The National Institutes of Health promulgated regulations in 2011 to provide added barriers to conflicts of interest through investigator disclosure and formal institutional review. This intensified interest on the part of NIH requires certification of all investigators to meet stringent financial conflict of interest requirements. This was in part prompted by public revelations highlighted in the media of investigators profiting from the distortion of clinical trial results for the benefit of commercial interests from which they stand to profit.

Also of interest is the improper provision of information regarding the probable outcome of trials to investors who will profit if a drug or device can be successfully marketed. Significant interest is considered to be compensation or equity interest exceeding $5,000, intellectual property rights and reimbursed travel to a researcher by a sponsoring entity.

For healthcare executives, clinical research is a new but vital mission essential to the financial and social vitality of the organization and society in general. The ethical imperative for executives is to ensure research is conducted within policies that protect participants in research and that are for the good of the public. ▲

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