

Minimal Risk: An Issue for Research with Vulnerable Subjects

Boston—The ethical principles governing recruiting members of vulnerable populations as research subjects are the same as those for autonomous adults; researchers and others are concerned, however, about the interpretation of beneficence for these persons, concurred panelists at the twelfth national conference of Public Responsibility in Medicine and Research. The conference was cosponsored by the Boston University School of Medicine here October 10-11. More than 100 physicians, attorneys, and members of institutional review boards (IRBs) discussed such topics as the difficulty of determining competency to consent, involving the family or courts in the consent process, and how risk/benefit analysis may differ for these vulnerable groups—children, the aged, mentally impaired, prisoners, and others. How to protect such research subjects is a challenge to these professionals, conference participants concluded.

George Annas, JD, asserted that human experimentation is underregulated, and the public could be lulled into falsely believing that research is safer than it is simply because the regulations exist. Mr. Annas is chief, health law section, and associate professor, Boston University School of Public Health.

Mr. Annas advocated that the majority of IRB members be public representatives, that IRBs be sufficiently large and funded by the research projects, that they employ subject advocates for protocols involving more than minimal risk, and that a system of reasonable sanctions be developed for unethical research.

Gerald Klerman, MD, pointed out the inherent conflict of interest between the investigator seeking subjects and society. Dr. Klerman is director of psychiatric research, Massachusetts General Hospital, Boston, and professor of psychiatry,

Harvard Medical School. Groups of “intense interest,” he predicted, are persons with dementing diseases (e.g., Huntington’s chorea, Alzheimer’s) and children of parents with psychiatric illness.

Special populations, though different, require same protection

Loren H. Roth, MD, noted that risk can be understood in three senses: whether autonomy has been compromised, whether the subject has been exposed to untoward risk, and whether risk exists under the justice principle [equitable distribution of burdens to benefits]. Dr. Roth described risk as comparative and “having to do with the probability and severity of harm,” with subject satisfaction with the research (mentally ill subjects tend to be on a parity with those presumed competent), and with the question of whether risk/benefit can be analyzed in psychiatric patient subjects. Dr. Roth is professor of psychiatry, University of Pittsburgh, and director, law and psychiatry program, Western Psychiatric Institute and Clinic.

Defining, regulating risk hinges on cutoff point

Barbara Mishkin, JD, deputy director, President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, charged that if the commission’s recommendations, due in December, were not accepted [concerning using members of vulnerable populations as research subjects] “the burden is on the Department of Health and Human Services to explain why.” She argued that current regulations do not prevent research with mentally retarded or disabled persons whose express consent is lacking and that, because a guardian’s permission is

insufficient, special regulations are needed.

Robert Levine, MD, advocated that IRBs ask the investigator for a systematic account of risks/benefits, including the psychological ones and those effecting social injury or economic loss. Components of the protocol, Dr. Levine continued, should be evaluated separately (i.e., research and therapy), lest the “fallacy of the package deal” obtain. Dr. Levine maintained that special populations require procedural safeguards to protect their interests, though he abjured precise definition of “minor increment above minimal risk.” Such a definition, he said, would “reduce the decision to a table” and obviate the need for IRBs in favor of computers. Dr. Levine is professor of medicine, Yale University School of Medicine, New Haven, CT; chairperson, Yale University School of Medicine IRB; and editor, *IRB: A Review of Human Subjects Research*.

Thomas G. Gutheil, MD, asserted that competence has not only cognitive but also affective features, that values (e.g., altruism, selfishness) affect decisions, and that competence cannot be created by drugs, although it can be restored. The fact of guardianship may recapitulate, reawaken, reinforce, or reenact a systemic but pathologic conflict and hence be of greater risk to psychiatric patients, he observed. Dr. Gutheil dismissed the substitute judgment doctrine [how would the guardian feel/act in the patient’s place] and cited a judge’s comment to the effect that “one can no more think like a baby than think like a fish.” He raised the question, What is a meaningful yes? He is director, program in psychiatry and the law, Massachusetts Mental Health Center; associate professor of psychiatry, Harvard Medical School; and associate lecturer, Harvard Law School. ★