



NBAC Facts

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PRESIDENTIAL BIOETHICS COMMISSION ISSUES REPORT ON CLINICAL TRIALS RESEARCH IN DEVELOPING COUNTRIES

Study finds difficulties in applying U.S. research regulations to clinical trials conducted in developing countries; Makes recommendations for research design, ethics review, post-trial access to research products

BETHESDA, Md., April 30, 2001 – The National Bioethics Advisory Commission (NBAC), seeking to improve the ethical conduct of international clinical trials, today recommended a series of steps aimed at reducing the potential for exploitation of research participants in developing countries, ensuring that studies are responsive to the health needs of the country, and seeing that post-trial access to successful research products is improved.

These conclusions come as part of the Commission's final report on ethical issues in international research. The report calls for a range of changes in the conduct of research in developing countries to ensure that participants are adequately protected and to add safeguards in the way U.S. researchers and sponsors conduct clinical trials involving competent adults in developing countries. The report, *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries* (www.bioethics.gov) was delivered on April 18 to President Bush following 18 months of study.

The Commission's report comes at a time when there is increasing interest in international research ethics, as both individual countries and international organizations are reviewing their own guidelines and procedures. The Commission assessed whether existing U.S. regulations are appropriate in the international context, in light of the increasing number of U.S. collaborations with scientists from developing host countries and the growing number of clinical trials conducted by private companies in developing countries.

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This trend raises concerns because of the potential for researchers and sponsors from more prosperous countries to exploit participants from developing countries heavily burdened by disease. In delivering the report to the President, Harold T. Shapiro, NBAC chairman and President of Princeton University, said, “The potential for such exploitation is cause for a concerted effort to ensure that protections are in place for all persons participating in international clinical trials.”

Considerable clinical research in developing countries is conducted or sponsored by the U.S. government or by pharmaceutical companies seeking product approval by the U.S. Food and Drug Administration. Some have questioned the motivations of researchers and sponsors when the product being tested is unlikely to be available to those in the host country, or the trial could instead have been conducted in the U.S. Others question whether it is appropriate to “export” U.S. research regulations without taking into account local context.

“Though no simple answers emerge, we have identified principles that ought to govern such research,” said Shapiro. “While we cannot remove all of the risks from research at home or abroad, we can reduce the risk of exploiting vulnerable populations.”

The Commission’s recommendations include the following:

Substantive ethical requirements: NBAC recommends that when conducting clinical trials abroad, U.S. researchers and sponsors and others subject to U.S. regulations should comply with substantive ethical requirements for the protection of human research participants. These requirements include: prior review by ethics review committees; minimization of risk and having a reasonable risk/benefit ratio; voluntary informed consent by each participant; and an equitable distribution of the burdens and benefits of the research.

Responsiveness to health needs: NBAC recommends that clinical trials being conducted in developing countries should be limited to those studies that are responsive to the health needs of the host country. The Commission wrote: “No population, especially a vulnerable one, should be the focus of research unless some of the potential benefits of the research will accrue to that group after the trial.”

Research design: A critical issue in clinical trial design concerns control groups. Although placebos are frequently used, it is increasingly common to compare an experimental intervention to an existing established effective treatment. NBAC recommends that researchers and sponsors design clinical trials that provide members of any control group with an established effective treatment, whether or not such treatment is available in the host country. Any study that would not provide the control group with an established effective treatment should include a justification for using an alternative design to be assessed by ethics review committees.

Community involvement: By consulting with the community, researchers often gain insight about whether the research question is responsive to their health needs. NBAC recommends that researchers and sponsors involve in the design and implementation of research representatives from the community in which potential participants will be drawn.

Voluntary informed consent from participants: The requirement to obtain voluntary informed consent from human participants before they are enrolled in research is a fundamental tenet of research ethics. NBAC recommends that researchers should not propose, sponsors should not support, and ethics review committees should not approve research that deviates from this substantive ethical standard.

“Informed consent should be an ongoing process throughout the research and not merely an initial documentation of willingness to participate in the research,” said Shapiro.

“In addition, U.S. regulations focus primarily on the informed consent document and require written consent,” said Shapiro. “This is impossible for illiterate individuals and such documents may be viewed as dangerous to sign in countries with oppressive regimes. Ethics review committees should be allowed to waive the requirement for written consent when alternative means are available to ensure participants’ comprehension and voluntary participation.”

Making consent culturally appropriate: The report states that belief systems in some cultures do not explain health care interventions with the same concepts that are used in modern medical science. NBAC recommends that researchers, in consultation with community representatives, develop procedures to ensure that potential participants understand the information provided in the consent process. “Researchers should develop culturally appropriate ways to disclose this information,” said Shapiro.

Researchers should obtain permission from community leaders where culture or custom requires. Similarly, it is customary in some societies for members of a potential participant’s family to be involved in the informed consent process. When a potential participant wishes to involve family members, NBAC recommends that researchers should take steps to accommodate this request.

Researchers should use the same informed consent procedures for women and men. An exception would be allowed only if it were impossible to conduct research on a common, serious health problem that affects only women without supplementing a woman’s consent with permission from a man. In none of these cases should permission from another person replace the requirement of the individual participant’s informed consent.

Post-trial benefits: An increasingly relevant question in international research is what should be provided to research participants, and by whom, after a trial has ended, and whether anything should be made available to others in the host community or country. Concern about the lack of access to adequate health care by a large majority of the population is a profound ethical challenge for researchers and sponsors. NBAC recommends that researchers and sponsors make reasonable, good faith efforts before the initiation of a trial to secure continued access for all participants to needed experimental interventions that have been proven effective for the participants.

In addition, research proposals submitted to ethics review committees should include an explanation of how new interventions that are proven to be effective from the research will become available to some or all of the host country population beyond the research

participants themselves. Whenever possible, agreements should be negotiated prior to the start of the research to make interventions available.

Ethics review: Efforts to enhance research collaboration must account for the capacity of ethics review committees in developing countries to review research, and the need for U.S. researchers and sponsors to ensure that their research projects are conducted according to the ethical standards applied in the United States. To accomplish this, NBAC recommends that protocols must be reviewed and approved by a U.S. Institutional Review Board and by an ethics review committee in the host country, unless the host country or host country institution has in place a system of equivalent substantive ethical protections.

Equivalent protections: Current U.S. regulations allow for the Office for Human Research Protections (OHRP) to determine whether another country's guidelines provide protections for research participants that are equivalent to those provided by the U.S. regulations. If so, the other country is free to follow its own guidelines instead of the U.S. regulations. NBAC found that, to date, OHRP has neither provided criteria for determining what constitutes equivalent protections nor made any determinations of equivalence. The Commission recommends that the U.S. government identify criteria and a process for determining whether the human participants protection system of a host country or a host country institution has achieved equivalent substantive ethical protections.

Building capacity: It is important to increase the capacity of developing countries to become more meaningful partners in collaborative research. Where applicable, U.S. sponsors and researchers should develop and implement strategies that assist in building local capacity for designing, reviewing, and conducting clinical trials.

The National Bioethics Advisory Commission (NBAC) was established by Executive Order 12975 in October 1995 to advise the National Science and Technology Council and other appropriate government entities regarding bioethical issues arising from research on human biology and behavior. The Commission is comprised of physicians, theologians, ethicists, scientists, lawyers, psychologists, and members of the public.

The report is available at our web site at www.bioethics.gov.

For a hard copy of the report, please contact the NBAC Office at (301) 402-4242, or by fax at (301) 480-6900.

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