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THE CODE SAYS

The AMA *Code of Medical Ethics'* Opinions on Clinical Research

Opinion 2.07 – Clinical Investigation

The following guidelines are intended to aid physicians in fulfilling their ethical responsibilities when they engage in the clinical investigation of new drugs and procedures.

(1) A physician may participate in clinical investigation only to the extent that those activities are a part of a systematic program competently designed, under accepted standards of scientific research, to produce data which are scientifically valid and significant.

(2) In conducting clinical investigation, the investigator should demonstrate the same concern and caution for the welfare, safety, and comfort of the person involved as is required of a physician who is furnishing medical care to a patient independent of any clinical investigation.

(3) Minors or mentally incompetent persons may be used as subjects in clinical investigation only if:

(a) The nature of the investigation is such that mentally competent adults would not be suitable subjects.

(b) Consent, in writing, is given by a legally authorized representative of the subject under circumstances in which informed and prudent adults would reasonably be expected to volunteer themselves or their children as subjects.

(4) In clinical investigation primarily for treatment:

(a) The physician must recognize that the patient-physician relationship exists and that professional judgment and skill must be exercised in the best interest of the patient.

(b) Voluntary [written](#) consent must be obtained from the patient, or from the patient's legally authorized representative if the patient lacks the capacity to consent, following: disclosure that the physician intends to use an investigational drug or experimental procedure; a reasonable explanation of the nature of the drug

or procedure to be used, risks to be expected, and possible therapeutic benefits; an offer to answer any inquiries concerning the drug or procedure; and a disclosure of alternative drugs or procedures that may be available. Physicians should be completely objective in discussing the details of the drug or procedure to be employed, the pain and discomfort that may be anticipated, known risks and possible hazards, the quality of life to be expected, and particularly the alternatives. Especially, physicians should not use persuasion to obtain consent which otherwise might not be forthcoming, nor should expectations be encouraged beyond those which the circumstances reasonably and realistically justify.

(i) In exceptional circumstances, where the experimental treatment is the only potential treatment for the patient and full disclosure of information concerning the nature of the drug or experimental procedure or risks would pose such a serious psychological threat of detriment to the patient as to be medically contraindicated, such information may be withheld from the patient. In these circumstances, such information should be disclosed to a responsible relative or friend of the patient where possible.

(ii) Ordinarily, consent should be in writing, except where the physician deems it necessary to rely upon consent in other than written form because of the physical or emotional state of the patient.

(5) In clinical investigation primarily for the accumulation of scientific knowledge:

(a) Adequate safeguards must be provided for the welfare, safety, and comfort of the subject. It is fundamental social policy that the advancement of scientific knowledge must always be secondary to primary concern for the individual.

(b) Consent, in writing, should be obtained from the subject or from a legally authorized representative if the subject lacks the capacity to consent, following: disclosure of the fact that an investigational drug or procedure is to be used; a reasonable explanation of the nature of the procedure to be used and risks to be expected; and an offer to answer any inquiries concerning the drug or procedure.

(6) No person may be used as a subject in clinical investigation against his or her will.

(7) The overuse of institutionalized persons in research is an unfair distribution of research risks. Participation is coercive and not voluntary if the participant is subjected to powerful incentives and persuasion.

(8) The ultimate responsibility for the ethical conduct of science resides within the institution (academic, industrial, public, or private) which conducts scientific research and

with the individual scientist. Research institutions should assure that rigorous scientific standards are upheld by each of their faculty, staff, and students and should extend these standards to all reports, publications, and databases produced by the institution. All medical schools and biomedical research institutions should implement guidelines for a review process for dealing with allegations of fraud. These guidelines should ensure that:

(a) the process used to resolve allegations of fraud does not damage science.

(b) all parties are treated fairly and justly with sensitivity to reputations and vulnerabilities.

(c) the highest degree of confidentiality is maintained.

(d) the integrity of the process is maintained by an avoidance of real or apparent conflicts of interest.

(e) resolution of charges is expeditious.

(f) accurate and detailed documentation is kept throughout the process.

(g) responsibilities to all involved individuals, the public, research sponsors, the scientific literature, and the scientific community is met after resolution of charges. Academic institutions must be capable of, and committed to, implementing effective procedures for examining allegations of scientific fraud. No system of external monitoring should replace the efforts of an institution to set its own standards which fulfill its responsibility for the proper conduct of science and the training of scientists.

(9) With the approval of the patient or the patient's lawful representative, physicians should [cooperate with the press and media](#) to ensure that medical news concerning the progress of clinical investigation or the patient's condition is available more promptly and more accurately than would be possible without their assistance. On the other hand, the Council does not approve of [practices](#) designed to create fanfare, sensationalism to attract media attention, and unwarranted expressions of optimism because of short-term progress, even though longer range prognosis is known from the beginning to be precarious. With the approval of the patient or the patient's family, the Council, however, encourages the objective disclosure to the press and media of pertinent information. If at all possible, the identity of the patient should remain confidential if the patient or the patient's family so desires. The situation should not be used for the commercial ends of participating physicians or the institutions involved.

Issued prior to April 1977; updated June 1994 and June 1998.

Opinion 2.071 - Subject Selection for Clinical Trials

Ethical considerations in clinical research have traditionally focused on protecting research subjects. These protections may be especially important for those from socioeconomically disadvantaged populations who may be more [vulnerable](#) to coercive pressures. The benefits from altruism that result from participation in research, particularly for severely chronically ill persons, may justify equitable consideration of historically disadvantaged populations such as the poor. With these considerations in mind, the following guidelines are offered:

(1) Although the burdens of research should not fall disproportionately on socioeconomically disadvantaged populations, neither should such populations be categorically [excluded](#), or [discouraged](#), from research protocols.

(2) Inclusion and exclusion criteria for a clinical study should be based on sound scientific principles. Conversely, participants in a clinical trial should be drawn from the qualifying population in the general geographic area of the trial without regard to race, ethnicity, economic status, or gender.

If a subject's primary care physician determines that the subject received a clear medical benefit from the experimental intervention which is now moving towards marketing approval and chooses to seek authorization from the Food and Drug Administration (FDA) for continued use of the investigational therapy during the time period between the end of the protocol and the availability of the drug on the market, the investigator should work with the primary care physician, the product sponsor, and the FDA to allow continued availability of the product.

Issued June 1998 based on the report "Subject Selection for Clinical Trials," adopted December 1997.

Opinion 8.0315 - Managing Conflicts of Interest in the Conduct of Clinical Trials

As the biotechnology and pharmaceutical industries continue to expand research activities and funding of clinical trials, and as increasing numbers of physicians both within and outside academic health centers become involved in partnerships with industry to perform these activities, greater safeguards against conflicts of interest are needed to ensure the integrity of the research and to protect the welfare of human subjects. Physicians should be mindful of the conflicting roles of investigator and clinician and of the financial conflicts of interest that arise from [incentives](#) to conduct trials and to recruit subjects. In particular, physicians involved in clinical research should heed the following guidelines:

(1) Physicians should agree to participate as investigators in clinical trials only when it relates to their scope of practice and area of medical expertise. They should have adequate training in the conduct of research and should participate only in protocols which they are satisfied are scientifically sound.

(2) Physicians should be familiar with the ethics of research and should agree to participate in trials only if they are satisfied that an Institutional Review Board has reviewed the protocol, that the research does not impose undue risks upon research subjects, and that the research conforms to government regulations.

(3) When a physician has treated or continues to treat a patient who is eligible to enroll as a subject in a clinical trial that the physician is conducting, the informed consent process must differentiate between the physician's roles as clinician and investigator. This is best achieved when someone other than the treating physician obtains the participant's informed consent to participate in the trial. This individual should be protected from [the pressures of financial incentives](#), as described in the following section.

(4) Any financial compensation received from trial sponsors must be commensurate with the efforts of the physician performing the research. Financial compensation should be at fair market value and the rate of compensation per patient should not vary according to the volume of subjects enrolled by the physician, and should meet other existing legal requirements. Furthermore, according to Opinion 6.03, "Fee Splitting: Referral to Health Care Facilities," it is unethical for physicians to accept payment solely for referring patients to research studies.

(5) Physicians should ensure that protocols include provisions for the funding of subjects' medical care in the event of complications associated with the research. Also, a physician should not bill a third party payer when he or she has received funds from a sponsor to cover the additional expenses related to conducting the trial.

(6) The nature and source of funding and financial incentives offered to the investigators [must be disclosed](#) to a potential participant as part of the informed consent process. Disclosure to participants also should include information on uncertainties that may exist regarding funding of treatment for possible complications that may arise during the course of the trial. Physicians should ensure that such disclosure is included in any written informed consent.

(7) When entering into a contract to perform research, physicians should ensure themselves that the presentation or publication of results will not be unduly delayed or otherwise obstructed by the sponsoring company.

Issued June 2001 based on the report “Managing Conflicts of Interest in the Conduct of Clinical Trials,” adopted December 2000.

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