



Continuing Education

Ethics in research and healthcare access

Learning Objectives

Describe ethical issues related to drug discovery and development.

List the requirements of informed consent and describe related ethical dilemmas.

Describe ways in which data integrity and privacy are protected.

Describe ethical issues related to research in children and use of placebos.

Describe ethical issues related to managed care and prescription drug access.

This second article in a three-part series discusses ethics in the areas of research and healthcare access. Ethical issues are examined in relation to: drug discovery and development, informed consent, data integrity and confidentiality of patient records, research in children, use of placebos, managed care, and prescription drug access.

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During drug discovery and development, ethical questions can arise that are related to the prioritization of research, the selection of clinical sites and pressure from special interest groups.

Drug development begins with basic research designed to discover new chemical compounds. In some cases, discovery programs produce a surplus of candidate drugs, and this causes an ethical dilemma in terms of how to prioritize these research leads to bring the greatest good. Many argue that the usual economic business rule – targeting business toward the activity that will bring the greatest return on investment – should not apply to selection of areas for medical research because people's health and lives are at stake. However, this approach is contrary to the principle of maximizing long-term owner value and business success, and there is concern about how research should be funded in areas where monetary return on investment is inadequate.

Another ethical issue stems from the selection of locations for clinical trials. When selecting sites outside the United States for clinical studies, the decision cannot be focused on costs or convenience alone. The most important considerations for man-

ufacturers are the quality of the local infrastructure and the site's relevance to the area of research. There may be concerns about the stringency of the regulatory control within the country and the rules in place to govern clinical trials. However, it remains the responsibility of the trial's sponsor to ensure that ethical standards are established for supervising subjects at the study site.

Drug candidates go through a series of scientific evaluations to gain the approval of the Food and Drug Administration or regulatory agencies in other countries. The purpose of clinical research is to determine if and when the drug under study can be released to the public (that is, when the benefits outweigh the risks). Some special interest groups, such as those representing patients with AIDS or cancer, have pressured pharmaceutical companies and the FDA to bring products to market before all of the clinical studies have been completed, and this presents an ethical dilemma. Although there are circumstances that allow accelerated development or regulatory review (such as those involving exceptional medical need or rare diseases), the steps taken and the reasons for the acceleration must be carefully documented. The legal and ethical burden of accelerated development is the

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responsibility of the sponsor, with the FDA bearing much of the burden as well.

Informed consent

Informed consent is a central issue in medical research and reflects the moral principle of autonomy, which requires that people be allowed to make life choices according to their own goals and values. Although informed consent in clinical studies is required by law, it is primarily an ethical obligation. According to the Office of Human Subjects Research, informed consent requires:

- Disclosure of relevant information about the research to prospective subjects.
- Their comprehension of the information.
- Their voluntary agreement, free of coercion and undue influence, to participate in research.

Many consent documents contain clinical language such as “placebo-controlled study,” “randomized-controlled study” and “double-blind study,” and these terms must be explained to the subjects using clear, understandable language to ensure the validity of consent. The informed consent document must be written at a reading level that is understandable to the potential research subjects. Short sentences, paragraphs with proper headings and nonscientific terms should be used. The document should be clear, complete and able to stand alone; the author should assume that the subject will not have an opportunity to discuss the content with a researcher.

In some cases, ethical dilemmas occur when individuals who are mentally challenged apply to participate in clinical studies, and the question arises as to whether or not these individuals are capable of understanding the informed consent document and deciding for themselves. On the other hand, individuals who are mentally challenged may, depending upon their physical ailment, benefit from receiving the experimental drug. Each case involves difficult decisions and requires careful analysis of the principles involved.

Although a person may be mentally competent to decide whether or not to participate in a clinical study, there may be external constraints on autonomy that interfere with the person’s ability to make decisions. For example, there may be situational factors that affect the decisions of prisoners or members of the military, who might not ordinarily participate if they were not living in a controlled situation.

Protecting data integrity and privacy

Various safeguards are instituted to protect the data integrity and privacy of client medical records. Data integrity refers to the overall quality of the data, which in turn determines the quality and usefulness of the research results. If data are not accurate or up-to-date, decisions made based on the data will be faulty. To guard the integrity of study data, pharmaceutical companies and other sponsors of clinical studies must ensure that a specialist is assigned as a guardian to

Categories of research involving children

Category 1

Research that does not involve greater than minimal risk to children

Category 2

Research that involves greater than minimal risk but presents the prospect of direct benefit to the individual child-subject

Category 3

Research involving greater than minimal risk and no prospect of benefit to the individual child-subject

- In order to approve research in this category, an IRB must determine that:
 - The risk of the research represents no more than a minor increase over the minimal risk.
 - The intervention or procedure presents experiences to the child-subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations.
 - The intervention or procedure is likely to yield general knowledge about the subject’s disorder or

condition that is of vital importance for understanding or amelioration of the disorder or condition.

Category 4

Research not otherwise approvable under one of the above categories, but which the IRB determines presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children

- In these cases, the IRB will forward the research for review by the Deputy Director for Intramural Research.
- If he agrees, the study will be forwarded to the Secretary of HHS, who may approve the research after consultation with a panel of experts.
- The panel must determine that the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children and that the research will be conducted in accordance with sound ethical principles.

oversee data processes from the time of data collection through any transformation and use.

Institutional Review Boards (IRBs) were established in response to misconduct involving abuses of human research subjects. IRBs are set up at each sponsoring institution and must be composed of no fewer than five experts and laypeople with varying backgrounds. They are used to ensure the rights and welfare of subjects before and during participation in clinical studies.

To meet the requirements for the ethical use of medical record information, access to selected research-related information must be blocked while allowing access to information needed for patient care. Another concern relates to questions regarding when disclosure of treatment information is ethically permitted. It is permitted by law in certain cases, such as when requested by a subpoena or court order issued in a civil lawsuit or criminal proceeding.

The Health Insurance Portability and Accountability Act (HIPAA) of 1996 was enacted to protect the privacy of health information that identifies individuals; it is based on the ethical principle of autonomy, or respect for the individual. HIPAA establishes minimum federal standards for protecting the privacy of individually identifiable health information and confers certain rights on individuals, including the right to:

- Access and amend their health information.
- Obtain a record of when and where their protected health information (PHI) has been shared with others.

HIPAA acknowledges that there are legitimate needs to use, access and disclose PHI for the purpose of research. It establishes conditions under which covered entities can provide researchers with access to and use of PHI when necessary to conduct research.

Other research issues

Two areas with special ethical implications are the involvement of children in clinical research and the use of placebos.

Research in children. This area of research requires special ethical and regulatory considerations because children's physical and intellectual capacities are different from adults'. According to National Institutes of Health policies, four categories of research are permitted for any protocol involving children. The IRB and the principal investigator must determine which category the study belongs to (see figure on page 37). The FDA's current Pediatric Rule – Best Pharmaceuticals for Children Act – requires pharmaceutical companies to study new and marketed drugs and biologics in children to determine their safety, efficacy and dosing. The rule encourages pharmaceutical companies to conduct studies of patented drugs that are used in pediatric populations and are not labeled for such use by extending market exclusivity for approved drugs by six months. In addition, the rule authorizes studies of off-patent drugs by the federal government or others with the expertise to conduct pediatric clinical trials.

Placebo-controlled studies. A placebo is an inactive compound that is indistinguishable from material being tested in experimental research and may or may not be known to the physician and/or subject. Placebos are used in clinical studies to compare the effects of the placebo with those of the experimental drug. There are several schools of thought regarding the ethical use of placebos in studies.

One view is that a placebo should be used as a control unless there is an increased risk of death or irreversible morbidity associated with its use. Advocates of this view argue that it is ethical to use placebos even when there are proven interventions to treat a medical condition. They argue that in some cases, therapies known to be effective are no more effective than placebos because of variable responses to drugs in particular populations, unpredictable effects and high rates of spontaneous improvement in patients.

Another view is that if an effective therapy exists, the use of placebos is unethical and should be prohibited. Those who hold this view argue that placebo controls are not appropriate because the clinically relevant question is whether a new drug is better than standard treatments.

Proponents of both of these views agree that a placebo-controlled study should be prohibited under the following circumstances:

- If life-saving or life-prolonging treatment is available.
- If subjects assigned to take a placebo would be substantially more likely to suffer serious harm than those assigned to receive the investigational drug.

Distribution of healthcare

The complex issues of managed care and prescription drug access generate many ethical questions.

Article Summary

- During drug discovery and development, ethical questions can arise related to the prioritization of research, the selection of clinical sites and pressure from special interest groups.
- Informed consent is a legal and ethical obligation that requires certain activities and conditions.
 - Ethical dilemmas can occur when individuals who are mentally challenged apply to participate in clinical studies.
- Various safeguards are instituted to protect data integrity and privacy of client medical records.
 - The Health Insurance Portability and Accountability Act was enacted to protect the privacy of health information that identifies individuals.
- Two areas with special ethical implications are the involvement of children in clinical research and the use of placebos.
- The complex issues of managed care and prescription drug access generate many ethical questions.

Managed care. Managed care integrates healthcare delivery with health insurance in a specific population of covered enrollees, with the objective of controlling costs and boosting efficiency. Serious ethical issues arise, as the system of managed care, by its nature, creates physician incentives to reduce costs. The major ethical issue related to managed care has to do with patients' lack of ability to make autonomous decisions. Those who receive care should have some input regarding the care they receive, and those who set limits on what is available should be accountable to more than their stockholders.

With a focus on efficiency and productivity, physicians in a managed care environment frequently have less time to spend with each patient. In addition, they must often limit prescription medicines to those on the managed care organization's formulary and restrict access to costly diagnostic tests and treatments. Also, patient access to medical specialists and the freedom to choose providers can be more limited under the managed care structure.

Managed care policies can create ethical conflicts for physicians who have to choose between controlling costs and providing all the care they believe a patient needs. On the other hand, under traditional fee-for-service arrangements, physicians may have an incentive to overtreat patients.

Prescription drug access. Escalating costs have made it necessary for insurers, benefit providers and pharmaceutical companies to make difficult decisions related to the fair distribution of pharmaceuticals and the setting of limits. These decisions are not always readily understood or accepted by the public. Ethical questions related to prescription drug access include whether pricing is reasonable and whether existing efforts to help the indigent are adequate. In 2003, members of the Washington-based Pharmaceutical Research and Manufacturers of America provided free prescription medicines to more than 6.2 million patients in the United States. PhRMA, with participating pharmaceutical companies, maintains and financially supports several interactive Web sites, including RxHope.com and HelpingPatients.org, where physicians and patients can find assistance.

Pharmaceutical company district managers must make certain that their healthcare representatives are aware of the resources available to assist patients with the cost of prescribed medications so that representatives can share this information with the physicians they call on.

The final article in the series will discuss ethics in the workplace.