Clinical research is an important process that provides opportunities to develop significant advances in medical practice. As a clinical scientist for almost 20 years, I have enjoyed the privilege of collaborating with many colleagues on projects designed to enhance analgesia in patients with cancer and in those who are recovering from surgery. My prior clinical research sites included Walter Reed Army Medical Center, Medical College of Pennsylvania, and Thomas Jefferson University; I have recently conducted studies at Methodist Hospital (with Anesti Gianitsos, DO) and at the former City Avenue Hospital (with Saul Jack, DO, and Alexander Nicholas, DO).

By designing human studies and submitting them for approval at many different hospitals, I have gained an appreciation for the review process. This experience expanded my knowledge of clinical research and of the regulations that govern this type of professional activity.

To perform investigations in humans, approval must be obtained from an Institutional Review Board (IRB) at each site from which volunteers will be recruited. The Office for Protection from Research Risks (OPRR), Department of Health and Human Services (DHHS), is responsible for ensuring that citizens of the United States do not participate in a clinical study unless they want to—and then only after giving their consent through a formalized process. Such authority can be found in the Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects. This protective approach stems from the Nuremberg Code, written immediately after World War II because of Nazi experimentation, whose first statement is “The voluntary consent of the human subject is absolutely essential.”

Although federal policies regarding experimentation on patients have been in force for decades, some health professionals are unaware of the distinction between standard practice and research. According to the OPRR Belmont Report, practice refers to “interventions designed solely to enhance the well-being of an individual patient or that have a reasonable expectation of success,” and research is “an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby, to develop or contribute to generalizable knowledge.” Other aspects that define research usually include enrollment of subjects, management of data, and preparation of progress and final reports. Activities that meet these criteria are defined as research even if they are conducted under a program that is not considered research for other purposes (for example, some demonstration and service programs).

A major factor in classifying an activity as research is the formal development of a hypothesis, that is, the question that is to be answered from a systematic investigation. The principal investigator (PI) has the major responsibility for developing the project. A protocol is written; this document describes in great detail why the study is necessary and how it will be conducted. A general format includes the following:

- purpose;
- background (discussion of previously published studies on same topic);
- methods;
  - types of patients that will be recruited (list of inclusionary criteria) or excluded (list of exclusionary criteria);
  - how many patients will be enrolled;
  - experimental design;
- risks;
- statistical procedures [not necessary in pilot studies]; and
- expected results.

To enroll subjects who volunteer for a study, an informed consent document must be signed. This consent form, which has to be approved by the IRB, must include the following:

- purpose of the study;
- type of personal medical data that will be collected;
- type of test(s) that will be performed;
- number of times the patient will be tested;
- risk(s) involved; and
- potential benefit(s).

The consent form must be written at an educational level that ensures—as much as possible—that the average patient can clearly understand it; most often, this means using language that a child in sixth grade could understand. To those of us who usually compose articles at a professional level, this task is not an easy one. We have to downgrade the complexity of our statements. For example, stating in the consent form that a “5-mL blood sample” will be taken means nothing to the average patient; it should be translated into something like “about a teaspoonful of blood.”

Writing the consent form properly means that volunteers will have clear knowledge of the process to which they are submitting themselves. They will understand that this treatment may not help their condition, and that it may even be harmful. They will also know that they can pull out at any time and, if so, will continue to receive the best medical care that their physicians can provide.

The PI submits the protocol and consent form to the appropriate IRB for

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approval. All decisions by the IRB (approval; approval with modifications; disapproval) are final and not subject to review by any administrative officer of the facility where the research is to be performed. The PI also ensures that all data are collected, supervises and monitors patients while enrolled in the study, and prepares progress and final reports that are submitted to the IRB.

A well-designed protocol maximizes the chance that if positive effects do occur as a result of the experimental treatment, they will be observed and documented. A properly prepared consent form will give the patient all information necessary to make the best possible decision whether to volunteer—and a fully informed patient is one who is less likely to sue if damages occur during the study.

References

