The National Institutes of Health (NIH) is one of the nation’s foremost centers for biomedical research. NIH is divided into an extramural part, which handles biomedical research throughout the country, and an intramural part, based mainly in Bethesda, Maryland. NIH is composed of various Institutes, each of which conducts research on health and disease. Studies involving volunteer subjects (research patients and clinical research volunteers) are carried out in the NIH Clinical Center.

The Clinical Center is the Federal government’s premier biomedical research hospital, where clinical studies of the highest quality are performed. Because the research is funded by the Federal government, there is no cost for care received at the Clinical Center.

Volunteer subjects at the Clinical Center become partners in a special relationship with members of the research teams in the search for better ways to treat disease.

What does it mean to be a volunteer?
The health of millions has been improved because of advances in science and technology, and the willingness of thousands of individuals like you to take part in clinical research. The role of volunteer subjects as partners in clinical research is crucial in the quest for knowledge that will improve the health of future generations. Without your help, the research studies at the Clinical Center cannot be accomplished.

This information is prepared to help you understand what is involved in participating in clinical research. Before you take part in any study, we encourage you to read the booklet and be sure that you have satisfactory answers to the list of questions on the last page. First decide which of the following categories best describes your situation:

- **Clinical research volunteer**: A volunteer subject with no known significant health problems who participates in research to test a new drug, device, or intervention. The clinical research volunteer may be a member of the community, an NIH investigator or other employee, or family members of a patient volunteer. Research procedures with these volunteers are designed to develop new knowledge, not to provide direct benefit to study participants.

Clinical research volunteers have always played a vital role in medical research. We need to study healthy volunteers for several reasons: When developing a new technique such as a blood test or imaging device, we need clinical research volunteers to help us define the limits of “normal.” These volunteers are recruited to serve as controls for patient groups. They are often matched to patients on such characteristics as age, gender, or family relationship. They are then given the same test, procedure, or drug the patient group receives. Investigators learn about the disease process by comparing the
patient group to the clinical research volunteers. Some studies require a major commitment in time and effort on the part of the volunteer, or they may involve some discomfort. The research procedure may also carry some risk. The consent process for clinical research volunteers involves a detailed discussion of all the study’s procedures and tests. After this discussion, he or she will be given a consent document to read. This document details the study being considered. It must be read carefully and signed only when the clinical research volunteer understands what is involved and is prepared to accept the potential risk, discomforts, and inconvenience involved.

► Patient volunteer: A volunteer subject with a known health problem, who participates in research to better understand, diagnose, treat, or cure a particular disease or condition. Research procedures with a patient volunteer help develop new knowledge. Such procedures may or may not benefit individual study participants.

The following should help you better understand how the research is planned and carried out, how to weigh the risks, and how your safety and rights are safeguarded.

What is clinical research?
Patient volunteers have a particular illness or condition that can help research doctors and scientists better understand, diagnose, prevent, treat, or cure it. The research is planned to help others and may not benefit them directly.

As a patient volunteer, you may be involved in studies similar to those described in the section on clinical research volunteers. Benefits of such research may be indirect for you, but may help others.

These studies involve drugs, devices, or interventions designed to prevent, treat, or cure disease. It is important to remember, however, that although such studies may provide direct benefit to patient volunteers, the main aim is to prove, by scientific means, the effects and limitations of the experimental treatment. This may mean that some patients serve as controls by not taking the test drug, or they receive test doses of the drug large enough only to show that it is present, but not at a level that can treat the condition.

What is a clinical trial?
Clinical trials are a means of developing new treatments and medications for diseases and conditions. There are strict rules for clinical trials, which are monitored nationwide by the NIH and the FDA, especially when they involve new drugs. There are three types of study:

► The phase 1 study is used to learn the “maximum tolerated dose” of a drug that does not produce unacceptable
side effects. Patient volunteers are followed primarily for side effects, and not for how the drug affects their disease. The first few volunteer subjects receive low doses of the trial drug to see how the drug is tolerated and to learn how it acts in the body. The next group of volunteer subjects receives larger amounts. Phase 1 studies typically offer little or no benefit to the volunteer subjects.

The phase 2 study involves a drug whose dose and side effects are well known. Many more volunteer subjects are tested, to define side effects, learn how it is used in the body, and learn how it helps the condition under study. Some volunteer subjects may benefit from a phase 2 study.

The phase 3 study compares the new drug against a commonly used drug. Some volunteer subjects will be given the new drug and some the commonly used drug. The trial is designed to find where the new drug fits in managing a particular condition.

Determining the true benefit of a drug in a clinical trial is difficult. Medical research is dogged by the “placebo effect”—the real or apparent improvement in a patient’s condition due to wishful thinking by the investigator or the patient. Medical techniques use three ways to rid clinical trials of this problem.

These methods have helped discredit some previously accepted treatments and validate new ones. Methods used are the following: randomization, single blind or double-blind studies, and the use of a placebo.

Randomization is when two or more alternative treatments are selected by chance, not by choice. The treatment chosen is given with the highest level of professional care and expertise, and the results of each treatment are compared. Analyses are done at intervals during a trial, which may last years. As soon as one treatment is found to be definitely superior, the trial is stopped. In this way, the fewest number of patients receive the less beneficial treatment.

In single-or double-blind studies, the participants don’t know which medicine is being used, and they can describe what happens without bias. Blind studies are designed to prevent anyone (doctors, nurses, or patients) from influencing the results. This allows scientifically accurate conclusions. In single-blind (“single-masked”) studies, only the patient is not told what is being given. In a double-blind study, only the pharmacist knows; the doctors, nurses, patients, and other health care staff are not informed. If medically necessary, however, it is always possible to find out what the patient is taking.

Placebos are harmless, inactive substances made to look like the real medicine used in the clinical trial. Placebos allow the investigators to learn whether the medicine being given works better or no better than ordinary treatment. In many studies, there are successive time periods, with either the placebo or the real medicine. In order not to introduce bias, the patient, and sometimes the staff, are not told when or what the changes are.
If a placebo is part of a study, you will always be informed in the consent form given to you before you agree to take part in the study.

When you read the consent form, be sure that you understand what research approach is being used in the study you are entering. Remember, even with a clinical trial, there is no guarantee that the new approach will be effective for you.

**Are there risks involved in participating in clinical research?**

Risks are involved in clinical research, as in routine medical care and activities of daily living. In thinking about the risks of research, it is helpful to focus on two things: the degree of harm that could result from taking part in the study, and the chance of any harm occurring. Most clinical studies pose risks of minor discomfort, lasting only a short time. Some volunteer subjects, however, experience complications that require medical attention. In rare cases, volunteer subjects have received serious injuries or died of complications resulting from their participation in trials of experimental therapies.

The specific risks associated with any research protocol are described in detail in the consent document, which you are asked to sign before taking part in research. In addition, the major risks of participating in a study will be explained to you by a member of the research team, who will answer your questions about the study. Before deciding to participate, you should carefully weigh these risks. Although you may not receive any direct benefit as a result of participating in research, the knowledge developed may help others. The following section describes safeguards to protect the safety and rights of volunteer subjects.

**Protocol review**

As in any medical research facility, all new protocols produced at NIH must be approved by an institutional review board (IRB) before they can begin. The IRB, which consists of medical specialists, statisticians, nurses, social workers, and medical ethicists, is the advocate of the volunteer subject. The IRB will only approve protocols that address medically important questions in a scientific and responsible manner.

**Informed consent**

Your participation in any Clinical Center research protocol is voluntary. For every study in which you intend to participate, you will receive a document called “Consent to Participate in a Clinical Research Study” that explains the study in straightforward language. A member of the research team will discuss the protocol with you, explain its details, and answer your questions. Reading the consent document and understanding the protocol is your responsibility. You may discuss the protocol with family and friends. You will not be hurried into making a decision, and you will be asked to sign the document only after you understand the nature of the protocol and agree to the commitment.

At any time after signing the consent document, you are free to change your mind and decide not to participate further. This means that you are free to withdraw from the study completely, or to refuse particular
treatments or tests. Sometimes, however, this will make you ineligible to continue the study. If you are no longer eligible or no longer wish to continue the study, you will return to the care of the doctor who referred you to NIH.

Patient Representative
The Patient Representative acts as a link between the patient and the hospital. The Patient Representative makes every effort to assure that patients are informed of their rights and responsibilities, and that they understand what the Clinical Center is, what it can offer, and how it operates. We realize that this setting is unique and may generate questions about the patient’s role in the research process.

As in any large and complex system, communication can be a problem and misunderstandings can occur. If you have an unanswered question or feel there is a problem you'd like to discuss, call the Patient Representative at 301-496-2626. The sooner your concerns are known, the easier they are to address.

Bill of Rights
Finally, whether you are a clinical research or a patient volunteer subject, you are protected by the Clinical Center Patients’ Bill of Rights. This document is adapted from the one made by the American Hospital Association for use in all hospitals in the country. The bill of rights concerns the care you receive, privacy, confidentiality, and access to medical records. Your patient handbook contains this information.

Questions to ask before agreeing to participate in a research protocol
1. What is the purpose of the study?
2. What is required of me?
3. What is my role in the study—am I a clinical research volunteer or a patient volunteer?
4. Will the study directly benefit me?
5. Will the study benefit others?
6. Are there risks? If so, what are they and what are the chances that they will occur?
7. What discomforts are involved?
8. What is the total time involved?
9. Are there other inconveniences?
10. Have I discussed participation in the study with those who are important to me, such as family and friends?
11. Do I wish to participate in this study?
12. When can I decide not to participate in all or part of the study? What will be the consequences?

This information is prepared specifically for persons taking part in clinical research at the National Institutes of Health Clinical Center and may not apply to patients elsewhere. If you have questions about the information presented here, talk to a member of your health care team.

Products/resources named serve as examples and do not imply endorsement by NIH. The fact that a certain product/resource is not named does not imply that such product/resource is unsatisfactory.

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Questions about the Clinical Center?
http://www.cc.nih.gov/comments.shtml
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