Chapter 5
Should You Participate in a Clinical Trial?

Almost every month there is news about a laboratory breakthrough that may eventually lead to a new treatment for multiple sclerosis, yet the Food and Drug Administration (FDA) has approved only a few new drugs for MS. How can this be so?

In the United States, clinical research on new medications and treatments is conducted under extremely rigorous and exacting methods which are mandated by the FDA. Developing a therapy for humans is a highly complex process. There are unique ethical and financial issues to consider and many regulations to follow. These experimental trials require carefully designed study protocols that are developed and executed by highly trained clinician-scientists. They also require the willing participation of individuals with MS. Many people with MS are interested in participating in experimental drug trials but are concerned about the risks and commitment involved. Participation may require substantial amounts of donated time. Sometimes the drugs are expensive. In some studies, patients may take a pill regularly for years without knowing if it is a new drug or a placebo/"sugar pill". What are the risks, benefits, and “rules” regarding being involved in experimental research? This chapter is designed to clarify the phases involved in experimental drug trials and identify the key issues that potential participants should consider before becoming involved.

Why Conduct a Clinical Trial?

Before a new treatment can be approved for public use, the Food and Drug Administration requires that the treatment be tested. Clinical trials provide a controlled, scientific way of testing new treatments for safety and effectiveness.

Investigational New Drug (IND) Status: By law, a drug company can make a new drug available to a person who may benefit from it before a full FDA review is completed, but only if
the FDA agrees. A drug made available before FDA approval is called an Investigational New Drug. Usually an IND is made available to individuals in a formal clinical trial.

**What is a Placebo-Controlled Study?**

Typically, someone who is not directly involved in the study randomly assigns either the active drug or a placebo to each patient. Neither the individuals participating in the study nor the study physicians monitoring the participants know whether the subject is on an active drug or the placebo. Placebo controlled studies appear in drug development phases II and III.

This "placebo control" method, while frustrating for people who end up on a placebo instead of the actual drug, is very important to ensure the value of the treatment being studied. It is essential to sort out what the real benefits of a treatment are compared to the "wishful thinking" that goes on when people try a new therapy. Both patients and their doctors are subject to that "wishful thinking", so "blinding" both parties is very important.

**What is an Open Label Study?**

An "open label" study means that both the investigator and research subject know that they are taking the active drug. Open label studies are often conducted at completion of a phase II or III study.

**Phases of New Drug Development**

FDA regulations mandate a standard series of new drug development phases. If you are invited to participate in a study, the investigators will tell you the pre-clinical results and which testing phase is involved.

**Pre-Clinical:** This phase consists primarily of animal and/or laboratory studies to determine if a new drug has biological relevance to the disease in question. During this phase, researchers also test for animal toxicity. No human testing occurs at this time.
**Phase I:** After evaluating the pre-clinical studies, the FDA may allow a drug to be tested in humans. Studies during this phase usually involve small numbers of healthy humans. The term "healthy humans" means healthy people without any disease including MS. This phase is designed to determine if the drug has some unexpected or major toxic effect.

**Phase II:** If Phase I results suggest that the drug is safe, the FDA may give permission to proceed to Phase II. This phase will begin small scale testing in fewer than 100 people with the disease for which the medication is indicated. This phase of testing will continue to monitor the drug's safety but also try to determine if it is effective in the disease in which it is being tested.

**Phase III:** If Phase II testing suggests the drug is safe and effective, the experiment is repeated in a larger number of research subjects (usually between 200 and 500) at several different centers throughout the USA and sometimes other countries. Random assignments of active drug and placebo are used in these Phase III studies. Upon the completion of the Phase III testing, the FDA reviews all the clinical studies to date and will determine if the drug should be approved and marketed for general use.

**Phase IV:** Even after the FDA approves a drug for general release, the drug company remains obligated to conduct further studies. During these Phase IV studies, researchers continue to monitor the drug's safety among the larger number of people now taking it. Some drugs have serious side effects that only occur in one of many hundreds of cases. Therefore, Phase IV studies are critical to identifying side effects that may not have appeared in the smaller Phase III test groups.

**What Is Informed Consent?**

Informed consent is a process designed to ensure that participants are fully informed about all aspects of the study before they agree to become involved. The FDA requires informed consent from all clinical trial participants. As part of the informed consent process, the investigator and potential
participant discuss the study's pros and cons. During this discussion the participant is free to ask any questions about the study. The participant should have all questions answered satisfactorily before participating in any clinical trial.

A "consent form" is a written document, which outline the specifics of the study:

- study visit schedule
- necessary testing
- medication side effects
- risks/benefits

Each study participant must then sign this written consent form indicating they fully understand what the study entails.

What is an Institutional Review Board?

An Institutional Review Board (IRB) is an outside committee that reviews all research protocols and consent forms for ethical and safety issues. IRB committee members are made up of medical and lay persons. This committee has the right to either approve or not approve the research protocol as well as the consent form. The research physician must obtain prior IRB approval before conducting any clinical trial. The major role of an IRB is to protect the welfare and rights of human research subjects.

Your Rights as a Human Research Subject

Before you agree to participate in a study, you have the right to be fully informed about the purpose of the study and about any potential benefits and risks to you, alternative treatments for your condition, and any costs to you or your insurance carrier.

You have the right to drop out of the study at any time and for any reason without penalties of any kind. The investigators may explain the reasons they want you to stay in the study, but they may not coerce or penalize you in any way. If you do decide to drop out, the investigators are not obligated to re-enroll you.
Your decision whether or not to participate in a research project should have no effect on the willingness of physicians in the study to provide you with high quality medical care.

If, during the course of the study, investigators learn anything new that might affect your willingness to be in the study, they are obligated to inform you promptly. This includes any newly discovered risks of the drug being studied or the emergence of alternative treatments for your condition.

If you are denied entry into a study, you have the right to know why.

**The Investigator's Rights**

The investigator has the right to make the final determination about whether or not you are an appropriate candidate for the study. The basis for these decisions is usually explained in the study protocol.

The investigator has the right to expect you to participate in all aspects of the study as appropriate. Once enrolled, you cannot pick and choose which parts of the study you will comply with and which you will not. However, as noted above, you always have the right to drop out of a study.

The investigator has the right to expect you to answer all questions pertinent to the study honestly and fully.

The investigator is not obligated to tell you which treatment you are on in a placebo-controlled study unless it is important to your health and medical treatment.

Participation in any study is not recommended unless you feel comfortable with the investigators and their staff. If you feel uncertain about any aspect of the investigation, you should ask about it directly. Similarly, the investigators want to be sure that you are well informed and joining the study for the "right" reasons.

**In Summary**
Over the years, there have been numerous clinical trials for individuals with MS, both looking at disease modifying, as well as symptom treatment medications. In the future, we will see FDA approval of some exciting new medications for the treatment of MS.