

A GUIDE
TO
PARTICIPATION
IN

CLINICAL
RESEARCH
STUDIES

UNIVERSITY OF
CINCINNATI

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This guide, authorized by the Institutional Review Board of the University of Cincinnati, was written to help people decide whether or not to enter a clinical or drug research study. This guide will also explain the basic information about clinical or drug research studies.

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The UC IRB gratefully acknowledges the help of the members of the UC Division of Infectious Diseases / Infectious Diseases Center and The Network for permission to use the material from their booklet *Should I Join an AIDS Drug Trial?* We have modified the language so that it is universally applicable to any clinical or drug trial. Although the statements often refer to drug trials because these are most common, the same questions and answers pertain to all clinical trials whether or not drugs are involved.

Understanding Clinical Research Studies or Drug Trials

What is a drug trial?

A drug trial is a carefully controlled experiment in which people take a drug that has either 1) never been approved by the U.S. Food and Drug Administration (FDA) or 2) been approved by the FDA for one medical condition but is being studied for the treatment of a second. A drug trial determines if a drug works and if it is safe. Drug trials are also called clinical research studies.

The effects of the drugs being tested in trials are not known. It's important to be aware of the risks, as well as any possible benefits of participating in a clinical trial. Every drug trial is different, so it's important to find out exactly what might be expected to happen before you join.

Why are drug trials done? Why can't I just take the drug I want?

Drug trials are done to find out which ones work, and which ones don't. Every drug sold in the U.S. must first be approved by the Food and Drug Administration (FDA). The FDA carefully reviews the information from drug trials to determine that the drug is safe and that it works. If the drug is safe and effective, the FDA gives permission for the drug company to sell it. It is usually against the law to sell a drug if it has not been approved by the FDA. An insurance company, Medicaid or Medicare usually will not pay for a drug or treatment that has not been reviewed and approved by the FDA.

What drugs are being tested?

People are taking many different things to try to fight diseases. Most trials test drugs, although some are now testing other possible treatments, such as vitamins. In some trials, more than one type of treatment, or a combination of drugs is being tested. In others, a new medical device may be tested.

Types of Trials

After a drug has been tested in the lab and in animals, it is tested in people. There are three types, or phases, of trials that are done with people.

Phase 1: Is the drug safe?

A Phase 1 trial is usually the first time a new drug is given to people after tests are done in animals. This type of trial is done to find out if the drug is safe for people to take. Everyone in a Phase 1 trial gets the drug being studied, but because most Phase 1 trials also try to find out what the best dose (amount) of the drug is, people are often given different doses. A drug in a Phase 1 trial has not been tested in many people, so very little is known about it. This makes Phase 1 trials riskier than Phase 2 or Phase 3 trials. Phase 1 trials are short, usually less than 2 or 3 months long, and usually involve less than one hundred people. Phase 1 trials usually study how safe a drug is, but they may also look at how the drug affects the body.

Phase 2: Does it work?

If a Phase 1 trial finds that the drug is safe for use in people, a Phase 2 trial will be done. In a Phase 2 trial more people are given the drug to see if it works and to study the side-effects more carefully. In this type of trial, researchers try to find out if the drug has a good effect and continue testing its safety. Phase 2 trials can last from a few months to a few years. There may be hundreds of people in a Phase 2 trial. In Phase 2 trials there are still risks that go along with possible benefits.

Phase 3: What if many people take it?

If the Phase 2 trial shows that the drug seems to work, a Phase 3 trial is started. In this type of trial, many people, sometimes thousands, are given the drug to see how well it works and if it causes problems when people take it for a long period of time. Researchers look for rare side effects, which are only seen in a few people, or only after someone has been taking the drug for many months or years. Most drugs will go through all three phase before they are approved, although drugs for life-threatening illnesses, such as AIDS, may be approved after Phase 2 trials and go through Phase 3 trials after FDA approval.

Sometimes phases are combined and you will see a trial described as Phase 1/2 or Phase 2/3. For some drugs, this speeds up the drug testing process.

An additional type of drug research is called a Phase 4 trial. At the same time that a drug has gone through all three preceding types of trials, and is approved for marketing, the FDA may require the drug manufacturer to obtain further information about the drug's risks, benefits or better ways of administration.

Such studies could include differing dosages and the best time for taking the drug, studies of the side effects over much longer periods of time, or in a different patient population, or other factors affecting safety and effectiveness such as gender, race or age.

Some trials may be linked to the presence of some abnormality in a gene or genes in a patient's genetic background and will try to determine whether this plays a role in the action of a drug.

Will I know what drug I'm taking?

Not always. In a Phase 1 trial, you'll know what drug you're taking and how much. In a Phase 2 or 3 trial you probably won't know what drug you're taking. Phase 2 and 3 trials are usually controlled trials, and people in these trials are divided, by chance, into different groups. Each group takes either the new drug or an approved drug or a placebo.

The group that takes an approved drug or a placebo is called the "control" group. Usually no one, not even the people running the trial, knows who is taking what until the trial is over. This is called a Double-Blind study. If everyone knows who is taking which drug, the trial is called an Open-Label study.

Sometimes the control group takes a placebo. A placebo is a fake pill or shot. Trials use placebos so the researchers can be certain benefits or side effects seen are due to the drug and not some other cause. A placebo used in a trial looks exactly like the drug being tested.

If the drug is a pill, the placebo will be a pill. But if the drug is injected into a vein for two hours, the placebo will probably be injected into a vein for two hours.

Controlled trials are done to make sure the drug really works. If everyone in a trial gets the new drug, there's no way to tell if the drug is making them better or if something else is doing it. They may get better because they're seeing a doctor for the first time, or because they're eating better and taking better care of themselves. So, a new drug is compared to something else or nothing, to see which is better.

If the people in the trial believe they're taking a drug that works, they may feel better even if the drug doesn't work. For example, in one trial that tested a drug to fight diarrhea, half of the people taking the new drug got better, but almost half of the people taking the placebo got better too. This means the drug didn't work any better than a sugar pill.

Being in a Drug or Other Clinical Trial

How do I find a Trial?

Community-based, not-for-profit organizations related to various diseases may maintain up-to-date information about drug trials and treatment programs. Your doctor may also know about drug trials. If you or your doctor is dissatisfied with treatment that is available, he may suggest a specific trial. Some clinics run clinical trials. They have information about the trials that they are doing. Many groups conducting clinical trials advertise in the newspaper, radio and on the Internet.

How do I join a trial?

Every trial has strict rules about who can join. The requirements of a trial are called Inclusion and Exclusion Criteria. Inclusion criteria are things you must have to join a trial; e.g. some special blood component or a particular condition, or a certain age level. Exclusion criteria are things that will keep you out of a trial, such as medications that you may be taking but are not allowed to continue taking during the trial.

When you find a trial that interests you, the first step is to call the trial site. The coordinator will ask you questions. If you meet the basic requirements of the trial, they will arrange for you to visit the site for an interview. During the interview, you'll be asked detailed questions about your health. A medical exam and some blood tests are also usually done.

During the interviews, you should ask questions like:

How long is the trial?

A trial could last from a few days to a few years.

Will I know what drug I'm getting?

In a Phase 1 trial you might. It depends on the type of trial. Ask your study doctor. In a Phase 2 and 3, you might not.

What if I get sick?

Find out who you can call for help 24 hours a day.

Should I stop visiting my own doctor if I participate in the trial?

It's important to go to your doctor for regular checkups.

Joining a drug trial means that you agree to follow the rules of the trial. The rules of the trial are called a protocol, which explains exactly how the trial will be run.

If you don't feel comfortable with the rules – like not being able to make all the appointments, or going to a clinic where the waiting room is full of sick people, discuss your concerns with the people running the trial. Following the rules is the only way the researchers can be sure of getting the information needed about the new drug.

Each trial has a protocol chair. The protocol chair is usually a doctor who helps plan the trial, and who is in charge of all the sites. If you don't qualify for a trial or if you're asked to leave because of one bad blood test, you can ask the protocol chair for an exception.

What's it like to be in a trial?

Every trial is different, so it's important to learn exactly what a trial requires before you participate. Everything you have to do while you're in the trial should be carefully explained to you, including:

How will I take the drug?

In most trials you will take the drug or drugs at home. You will be told exactly when and how to take it. In other trials, you may have to take it in the hospital. A drug may be given in one or more ways:

- Intramuscular (injected into a muscle)
- Intravenous (injected in a vein)
- Subcutaneous (injected under the skin)
- Pill or liquid you swallow
- Spray you breathe in
- Cream you rub on

How often do I have to come to the site?

You may have to visit the site as little as once a month or as often as five times a week. At first, there may be many medical checkups to see what the drug is doing to you. Later in the trial there will usually be fewer checkups. Ask for a schedule so you remember your appointments.

What else will I have to do?

Every trial is different rules,. For example, you may be asked to write down information at home about your daily activities, or you may be told not to eat certain foods. If you think you might need help doing any of these things, ask for it. You should also know the reasons why you might be asked to leave the trial.

Will it cost me anything?

In some clinical trials, the study drug or device is provided to the patient at no charge. Other studies, particularly those investigating new uses of existing drugs,

may require you (or your insurance carrier) to pay for the medication or device used.

Similarly, some clinical trials cover all study related costs, including physician visits, laboratory tests, and other relevant procedures, while other studies do not.

If you do not want your insurance company to know you are in a drug trial, talk about this with the people running the trial. If you do not have Medicaid or insurance, the site may pay for everything or may want you to pay.

Your responsibilities should be detailed in the consent from that you will be asked to review prior to study participation. If you have any questions about your financial obligations be sure to discuss this with the study investigator or their staff.

There may be other costs, like time off from work, subway fares, or baby-sitter and day care costs. Some sites will pay for these and some will not. Get the name and phone number of everyone you talk to and keep all records.

Do I need my own doctor?

Yes, joining a drug trial is not the same as having your own doctor. Drug trials are not designed to provide people with treatment, so it's important that you have a regular doctor or clinic for regular checkups and lab tests while you are in the trial.

Who's in charge of the trial?

The person in charge of the drug trial at each site is called the principal investigator. He or she is usually a doctor, although it could be a nurse or other clinical researcher. There is also a team of doctors and nurses who do the medical exams and the blood tests, etc.

Who protects me when I'm in a trial?

Every institution that conducts medical research involving people is required by the federal government to have an Institutional Review Board (IRB). The IRB is a group of people from various professions who are responsible for protecting the rights of people in a trial. The IRB must approve any trial being done at the institution, and periodically approve continuation of the trial.

Based on the data gathered, the IRB, protocol chair or the principal investigator can change or stop a trial that doesn't do what it promised, exposes people to harm or if unacceptable side effects are observed. You can contact the IRB if you have a problem while in the trial.

The people running the trial will tell you how to contact the IRB. You can also contact the people in charge of the trial.

What if I get sick while I'm in the trial?

If your health gets worse while you're in the trial, the people running the trial will try to find out if the drug is making you sick or if you're sick for some other reason. Keep your doctor informed about everything you are experiencing.

All drugs have side effects. Many are not noticeable, but some are moderate and some may be severe. Some drugs can lead to serious illness or death. If you get sick because of the drug, tell the people running the trial. You may be either taken off of the drug or given a different amount. If the trial is comparing two drugs, you may be offered the other drug. It's important to get the phone number of a doctor or nurse involved with the trial who you can call 24 hours a day, in case you get sick in the middle of the night. Because the drugs in trials might be experimental, a doctor in an emergency room may not know what to do if the drug makes you sick. Ask how you can be prepared if this happens. If you get sick, but not because of the drugs, you may be offered the other drug.

Leaving the Trial

What happens when the trial ends?

When a trial ends, you will have an "exit interview". If you didn't know which drug you were taking, you may be told during this interview. If the trial ends early because the drug didn't work or was too dangerous, you should be told this. You may be able to continue to get the drug after the trial ends, but there is no guarantee of this. Sometimes, only enough drug is made for the trial, and the drug company decides not to make more.

What medical care will I get once the trial is over?

Make sure you know how to get medical care at all times, including after you leave the trial. The trial site may agree to provide you with medical care once the trial is over, but you should discuss this with the study coordinator beforehand. Continuing medical care may not be possible.

Can I get the drug once the trial is over?

Trials sometimes promise people drugs when the trial ends. Please check with your study doctor.

How do I leave the trial?

You can choose to leave the trial at any time, and this should not change the care you get at the hospital or clinic in the future. If you get sick because of the drug and are asked to leave the trial, the people running the trial should make sure your medical needs are taken care of, but they might not pay for it.

What Other Questions Should I Ask?

Answers to the questions listed below will help you make an informed decision about whether or not you want to be part of a particular trial. You have the right to have all your questions answered. Some should be answered in the informed consent form, which the study coordinator will go over with you. Go over your questions with your doctor before meeting with the study doctor.

Feel free to ask any other questions about anything that concerns you.

Don't feel you are asking too many questions or taking up too much time. Clinical trials need human participants like you to find out if the treatment works. You are a volunteer who deserves thanks for your effort.

It is a good idea to write down the answers to the questions so that you can go over them and think about them later. You may want to have a friend with you who can remind you of questions or write down the answers for you.

Some questions can't always be answered, such as the long-term side effects of a new drug. Trials are conducted to find out the answers to questions such as these. Trials are conducted to find out the answers to questions such as these. The trial coordinator will tell you what might happen, but may also have to say that just don't know yet. You will have to decide if you are willing to take the risks that a trial involves.

As long as an experimental treatment is still in any phase of trial, no one can be sure how well it will work, or even if it will work at all. Taking part in a trial may or may not be beneficial to you. The more you are informed about available treatments, the better able you will be to make a decision. Talk to other people who are in a clinical trial, or call a community organization that works with people with this particular condition.

Some Questions to Ask About the Trial and About the Drug

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| <ol style="list-style-type: none"> 1. Will I have to stop taking drugs previously prescribed for me and for how long? 2. Has this drug been used before? For what conditions? What were the results? 3. What other drugs are being used for this condition? How does the trial drug compare in safety and success? What is the evidence that this substance can treat my condition? What are the immediate side effects of this drug? What are the long-term effects of my using this drug? 4. If I have any side effects, how will I be helped to deal with them? 5. What type of drug is being tested? 6. How often must the drug be taken? How will the drug be given in this trial? Pills? Intravenously? By shot? 7. Must the drug be taken in the hospital? Do I have to take the drug at the trial site, or can I take the drug at home? 8. How will taking the drug affect my day-to-day activities? 9. Is this drug available outside of this trial? If so, how can I get it? | <ol style="list-style-type: none"> anything? Will I get the results of these tests/ 2. What tests will be given during the trial? How often? Will I get the results of these tests? When? 3. How often will the researchers tell me how I am doing while I am in the trial? 4. Is this trial confidential? Will anyone outside of the trial know about my health condition without my permission? 5. How will this trial about me be coded to protect my privacy? How will genetic information about me be handled, and what control will I have regarding who may or may not have access to it. 6. Do the consent papers that I am signing describe all of the risks and benefits of my participation in the trial? 7. Will I have the same response from the trial drug as the previous one which I discontinued before entering the trial? 8. What written information will I be given about the trial and the drug? 9. How often will the Institutional Review Board (IRB) review the trial for any changes? |
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Informed Consent

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|---|--|
| <ol style="list-style-type: none"> 1. What tests will be given before I start? Will these tests cost | <ol style="list-style-type: none"> 10. How will I be informed of those changes? If this trial changes significantly, or if I'm put into |
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another trial, will I receive an updated informed consent form to sign??

11. Do I need to have my own doctor to get into the trial?
12. Do I need health insurance to be in the trial?
13. Do I have to pay for lab tests or any other costs?
14. If I experience side effects requiring emergency room treatment, which hospital can I go to and who pays for the treatment?
15. Will I be given any money for participating in the trial?
16. Will the money be reportable to the IRS?
17. Will I be reimbursed for traveling expenses to and from my visits?
18. If I am caring for a child is child care available
19. Will the sponsors of the drug supply it to me free until it is marketed and available by prescription?
20. If I develop health problems as a result of being in the trial, will treatment be available to me even if I leave the trial before it is over?

Food and Drugs

1. If the drug is a pill or capsule, should I take it on an empty stomach? With food?
2. Are there any special foods that I need to eat while in this trial? If I am already on a special diet, may I continue?
3. Are there any foods or other substances that I shouldn't have while taking this drug?
4. Can I drink alcohol? Can I take any over-the-counter (nonprescription) drugs? Aspirin? Cold tablets? Cough syrup? Herbal remedies?
5. Can I use prescription drugs while I am in this trial? Can I use other experimental drugs?
6. Can I take drugs to prevent or treat opportunistic infections, cancers, or any other illnesses I may get?
7. What type of contraceptives can I use Do I have to use contraceptives? Are oral contraceptives permitted? Will my use of contraceptives be monitored? Are pregnant women allowed in the trial?

Leaving the Trial

1. If my condition gets worse while I am on the drug, will I be taken out of the trial?
2. If I am in a placebo group, can I get the drug if my condition gets worse during the trial?

3. If the trial was successful, can I take the drug once the trial is over? If the drug worked for me, can I continue to take the drug even if the trial was declared a failure?
4. How is the success of this trial defined by the protocol?
5. How will decisions about stopping the trial be made? How is failure defined in the protocol?
6. Will my health continue to be checked after I stop taking the drug? Will this be done even if I decide to leave the trial?
7. Will there be long-term follow-up on how I am doing Will this be done even if I leave the trial before it is over or if the entire trial is stopped early by the researchers?
8. How can I find out the results of the trial? Will I be able to participate in future trials of this drug? Will I receive the results of future trials using this drug?

Definitions of Words

Antibodies – Proteins in the blood which recognize and blood foreign substances.

Antiviral – A substance that stops or suppresses the activity of a virus.

Asymptomatic – Infection without symptoms. Someone who is asymptomatic has antibodies to a disease but does not have any visible signs or symptoms of infection.

Clinical Trial – A test of a new or experimental drug in people. Also called drug trials or studies.

Comparison Trial – A trial in which experimental drugs are tested against each other or against an approved drug.

Controlled Trials – Trials in which one group gets the experimental drug and another group gets either a placebo or an approved drug therapy. Participants usually do not know which group they are in.

Crossover – A controlled drug trial in which, halfway through the study, the groups in the trial switch. That is, those taking the experimental drug are given the standard drug and vice versa.

Dose Comparison – Trial that uses different amounts of the same drug. Sometimes the drug is tested against a placebo.

Dose Escalation Trial – In this type of trial, one or a few people, usually under a dozen take a small amount of the drug. If it doesn't hurt them, one or a few more take a larger amount. This continues until the researchers find the largest amount of the drug that can be taken without immediate harm.

Double-blind – A type of drug trial in which people are divided into different groups. One group takes the experimental drug and other groups take different doses, the standard therapy, or placebo. Neither the researchers nor the person in the trial know who is taking what until the trial is over.

Immunomodulators – Drug intended to affect the action of the immune system.

Inclusion/exclusion criteria – The medical or other reasons why a person may or may not be allowed to enter a trial. For example, some trials do not allow pregnant women to join, others do not allow people to take certain drugs, and other exclude people with certain illnesses. Other trials may try to include pregnant or nursing women.

IND or Investigational New Drug – The name given to an experimental drug after the FDA agrees that it can be tested in people.

Informed Consent – The name given to the process during which a person weighs the risks and benefits of a trial, then agrees voluntarily to participate. When someone agrees to be in a trial, they sign an agreement called an informed consent form. If new information about a drug

becomes known, a participant who has given their informed consent will be told of this information, and asked to consent to continue the trial.

Institutional Review Board (IRB) – Every institution or hospital that conducts research involving human subjects must have an IRB that approves and periodically reviews the research. The IRB protects the rights of the people in the trial, determines who can participate in the trial and whether the trial is ethical.

Open-Label Trial – A type of drug trial in which researchers and participants know who is taking the experimental drug or the treatment being given.

Pharmacokinetic Trials – Trials which study how the drug is absorbed by the body. These trials often require a short stay in the hospital.

Placebo – A substance that has no effect on the body (often referred to as a sugar pill) that is given to one group in a placebo-controlled trial.

Prophylaxis – Taking a drug to prevent yourself from getting an illness.

Protocol – A detailed plan stating a drug trial's purpose, drug dosages, length of treatment, how the drug is given, and inclusion/exclusion criteria.

Randomized Trial – A trial in which people are assigned to one of two or more treatments by chance. Usually a computer is used to be sure that everyone has the same chance of getting on any given part of the trial.

Short Form Written Consent – A form that states that everything in the informed consent has been verbally explained to an individual entering the trial. A witness must be present when the trial is explained and this form is signed.

Toxicity – Describes some of the possible side effects of a drug. Also indicates how much of a drug can safely be taken.

Treatment IND – An FDA program that makes experimental drugs available to seriously ill people. Drug companies may charge for the drug, although most don't.

Washout Period – A specified length of time during which active medication is withdrawn from the person entering the trial.