CLINICAL TRIALS

CLINICAL TRAILS AND RELIABLE MEDICAL INTERVENTIONS

Imagine choosing among medicines and treatments that made bold claims about managing or curing your serious condition without knowing which could be taken seriously. If drugs and treatments were not investigated and held to consistent standards, it would be up to you to make a guess based on word of mouth, advertising messages, simple observations, and folk wisdom.

The clinical trial process, regulated by the U.S. Food and Drug Administration (FDA), is the controlled way that researchers and physicians study promising medicines, devices, procedures, and treatments on people, with the goal of judging their effectiveness and side effects. Clinical trials result in safer and more effective ways of treating medical conditions.

Note: A clinical trial is a specific type of research in which humans are studied to see how they respond to a certain treatment or intervention.

Participants in clinical trials can gain access to groundbreaking treatments that may not be available at other medical centers and without interrupting the important care they may already be receiving. A wide range of participants is essential for successful clinical trials. Learn more about your potential role in the process and decide if a clinical trial may be right for you.

HOW CLINICAL TRIALS START

Medical researchers, both publicly and privately funded, are always looking for ways to prevent, find, diagnose, treat, and manage medical conditions. This research often begins with pre-clinical testing, meaning tests done in a laboratory without human participants. Researchers find an intervention that should work on a target problem and begin testing it in computer models, bacterial cultures, or on isolated human cells. If the intervention seems to work, the testing usually advances to animals, so that researchers can learn how the intervention affects the entire body of animals (and also may affect humans). Preclinical testing itself may take months or years.

Source: Cancer.gov

The drugs, treatments, and medical devices that make it to clinical trials already have shown promise and a reasonable risk-to-benefit ratio. The standards for entering a clinical trial are so strict that only about 5 in 5,000 new interventions that begin the road toward clinical trials are approved for human testing by the U.S. Food and Drug Administration (FDA). Once an intervention is optimized in the

laboratory, a public or private entity (called a sponsor) may apply for an Investigational New Drug (IND) application with the FDA, which authorizes new interventions to enter the health care market. The FDA decides whether it is reasonably safe for the company to move forward with testing the drug in humans. The clinical trial process then usually takes several more years.

Source: FDA

OVERVIEW OF THE CLINICAL TRIAL PROCESS

Institutional Review Board Approval

A planned clinical trial needs approval from the FDA, but also needs the approval of an independent institutional review board (IRB). An IRB is a panel of scientists and non-scientists in hospitals and research institutions that oversees clinical research. IRBs protect the welfare, rights, and privacy of human participants and can approve, disapprove, monitor, and require modifications to clinical trials. The documents they review are called the clinical trial protocols, and they describe:

- The type of people who may participate
- The schedule of tests and procedures
- The medications (or interventions) and dosages to be studied
- The length of the study
- The study's objectives

The IRB remains involved throughout all stages of the clinical trial process, making sure that appropriate steps are taken to protect patients from harm. (See *Participants and Safety* below in this guide).

Source: FDA

Clinical Trial Characteristics and Phases

Clinical trials are the most powerful way to determine which new interventions (such as drugs and therapies) are effective on the population that needs them, because they are delivered specifically to the population in ways that are controlled by researchers. Researchers control who receives the intervention and in what dosage over three phases of clinical trials. At the end of the three phases, they can be relatively certain that the effects observed are due to the intervention and not other factors. The research team also can learn how the intervention affects different people with various forms of the condition it is designed to treat.

Every clinical trial is led by a principal investigator (PI), often a medical doctor. PIs lead research teams that may include doctors, nurses, social workers, and other health care professionals. Clinical trials, depending on their complexity and who is sponsoring the study, can be conducted at hospitals, universities, physician offices, and community clinics. Many trials take place at multiple sites, each having a principal investigator. **Academic medical centers, such as UAB Medicine, host many groundbreaking clinical trials due to having the needed resources and specialists.**

Source: clinicaltrials.gov

CLINICAL TRIAL PHASES

Clinical trials for drugs and other treatments and devices advance through three phases to test a treatment, find the appropriate dosage, and look for side effects. After the first three phases, if researchers find a drug or other intervention to be safe and effective, the FDA approves it for clinical use and continues to monitor its effects.

- A **phase I trial** tests an experimental treatment on a small group of often healthy people (usually numbering 20-80) to judge its safety and side effects and to find the correct drug dosage.
- A **phase II trial** involves more people (100-300). While the emphasis in phase I is on safety, the emphasis in phase II is on effectiveness. This phase seeks to obtain preliminary data on whether the drug works in people who have a certain disease or condition. These trials also continue to study safety, including short-term side effects. This phase can last several years.
- A **phase III trial** gathers more information about safety and effectiveness, studying different populations and different dosages, using the drug in combination with other drugs. The number of participants usually ranges from several hundred to about 3,000 people. If the FDA agrees that the trial results are positive, it will approve the experimental drug or device.
- A **phase IV trial** for drugs or devices takes place after the FDA approves their use. A device or drug's effectiveness and safety are monitored in large, diverse populations. Sometimes, the side effects of a drug may not become clear until more people have taken it over a longer period of time.

Source: National Institutes of Health (NIH)

PARTICIPATION, RISKS, AND SAFETY

Participating in a clinical trial is a way to help advance health care for everyone, and it also may be a way to receive treatments that have not yet been made available as standard care. Treatment received as part of clinical trials is often at no cost, and sometimes participants are paid for their time, but participants may have to commit to extended periods of time and endure some side effects. Although many steps are taken to control the risk to participants, it is up to you to decide if any given clinical trial is right for you.

Researchers carefully decide the criteria for patients to be included (called inclusion criteria) in each clinical trial phase. Along with inclusion criteria, research guidelines determine *exclusion* criteria, or factors such as age, gender, previous treatment history, and type of disease – any of which could jeopardize the accuracy of study results. While some trials seek healthy participants, others are limited to those with a certain condition.

Source: clinicaltrials.gov

Informed Consent

Informed consent is an FDA-required process by which researchers provide potential and enrolled participants with information about a clinical trial, to help them make an educated choice about participation. An IRB reviews the plan for informed consent and sees that it is properly performed. The informed consent process is intended to protect participants and should provide enough information

for a person to understand the risks, potential benefits, and alternatives to the study. The process may involve recruitment materials, verbal instructions, question-and-answer sessions, and activities to measure participant understanding.

Participants must sign informed consent documents before joining a study to show that they were given information on the risks, potential benefits, and alternatives – and that they understand it. This document is not binding; participants may withdraw from a clinical trial at any time during a study.

Source: clinicaltrials.gov

HOW IT WORKS

Tens of thousands of clinical trials are in progress at all times. You can find a searchable database of all active FDA-sanctioned clinical trials at clinicaltrials.gov. Hundreds of trials are underway here at UAB Medicine for general participants and for very specific conditions; you can search our database here. If you are seeing a specialist at UAB, he or she often can recommend a trial for which you meet specific inclusion criteria. At UAB, many of our physicians also are principal investigators or part of research teams, and they can point you to the kind of clinical trial in which you are interested.

Your primary care physician should always be made aware of your participation in a clinical trial, and often it is the research team's responsibility to work with your primary care physician to coordinate care. *It is important to understand that no clinical trial will deprive you of standard treatment that you are already receiving for a condition*.

For those who express interest in a clinical trial, here's how the process works:

1. Study staff explain the trial in detail and gather more information about you.
2. Once you've had all your questions answered and agree to participate, you sign an informed consent form.
3. You are screened to make sure you qualify for the trial.
4. If accepted into the trial, you schedule a first visit (called the "baseline" visit). The researchers conduct cognitive and/or physical tests during this visit.
5. You are randomly assigned to a treatment or control group.
6. You and your family members follow the trial procedures and report any issues or concerns to researchers.
7. You may visit the research site at regularly scheduled times for new cognitive, physical, or other evaluations and discussions with staff. At these visits, the research team collects information about effects of the intervention and your safety and well-being.
8. You continue to see your regular physician for usual health care throughout the study.

Source: NIH

GLOSSARY OF COMMON CLINICAL TRIAL TERMS