Learning about Clinical Trials

A Guide for Individuals and Their Loved Ones

INTRODUCTION

Clinical trials help researchers answer important medical questions, providing information that may help with the development of future treatment options. For many individuals, clinical trial participation may be a consideration.

Clinical trials are conducted to determine if investigational treatments (such as new drugs, procedures, or medical devices) are safe and effective. This brochure explains what a clinical trial is and what it may involve to help you make an informed decision about participation.

If after reading this brochure you have questions or would like to learn more, please speak with your doctor.

Clinical Trials Overview

Clinical trials are conducted to test investigational drugs so that the regulatory authority can decide whether they can be approved for use as a treatment. Researchers must scientifically prove that an investigational drug is safe and effective in order for it to be approved.

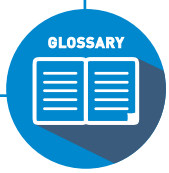
Researchers may test an investigational drug:

- at different doses or for different lengths of time
- against the standard (approved) treatment
- against a placebo (an inactive substance designed to have no effect on health)
- by itself

Participation in a clinical trial is voluntary. You can withdraw at any time and for any reason (or no reason at all) – and doing so will not affect the care you may be receiving now or may receive in the future.

Glossary of Terms

This brochure contains many terms that may not be familiar to you. If you would like to learn more about some of them, please go to the Glossary of Terms at the end of this brochure.



CLINICAL TRIAL DESIGN

The design of a clinical trial is agreed upon by the clinical trial sponsor (typically a medical device, pharmaceutical, or biotech company) and the regulatory authority. The regulatory authority must review and approve the design, making sure it follows the national rules and laws for conducting a clinical trial.

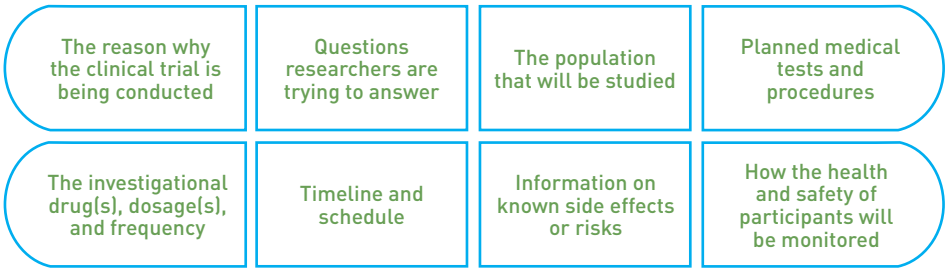
Careful and thoughtful planning goes into the design of a clinical trial. It may include input from physicians, advocacy organizations and patients to help make sure the questions being asked have meaning for people living with the disease. The length and size of a clinical trial is also carefully considered to ensure that it will answer specific research questions.

Types of Clinical Trials

There are two main types of clinical trials. Interventional trials are conducted to determine whether an investigational treatment, or a new way of using an approved treatment, is safe and effective. Observational trials do not involve the use of an investigational treatment. Instead, researchers focus on collecting data about the disease. The data may be used by researchers in the future to help with the development of potential new treatments.

WHAT IS A PROTOCOL?

All clinical trials follow a detailed plan, called a "protocol." It explains the purpose of the trial as well as many details regarding how it will be conducted. It includes information about:



WHAT IS A PLACEBO AND WHY IS IT USED?

Some clinical trials include the use of a placebo to help researchers evaluate the effect, if any, the investigational drug has on symptoms. (A placebo is commonly used in phase II and phase III clinical trials.)

- A placebo is designed to look like the investigational drug but has no active ingredients.

In randomized clinical trials, participants will receive either the investigational drug or a placebo. Researchers compare the results of the group receiving the investigational drug to the group receiving a placebo to determine if the investigational drug is having the desired effect. The use of a placebo helps to speed up a clinical trial as researchers can more quickly observe any differences between the groups.

RANDOMIZATION: A CLOSER LOOK

The process that determines whether a participant will be assigned to the group receiving the investigational drug or the group receiving a placebo is called randomization. This process is done by chance, like flipping a coin.

In some clinical trials, neither the participant nor the principal investigator knows to which group the participant has been assigned. This is called "double-blind," and it is designed to eliminate potential bias on the part of the principal investigator. In other clinical trials, called "blinded," only the participant does not know to which group he or she has been assigned.

How Are Clinical Trial Participants Protected?

Regulatory authorities make sure that the rights of participants are protected by requiring that all clinical trials are approved and monitored by special committees called Institutional Review Boards (IRBs) and Ethics Committees (ECs). These are independent committees responsible for protecting the rights, welfare, safety, and well-being of clinical trial participants.

These committees are responsible for:

- Ensuring that steps are taken to protect the rights, safety, and welfare of participants.
- Reviewing the clinical trial protocol, informed consent forms, recruitment methods, and all written information provided to participants.
- Monitoring aspects of a clinical trial and requiring that any serious changes in health are reported.

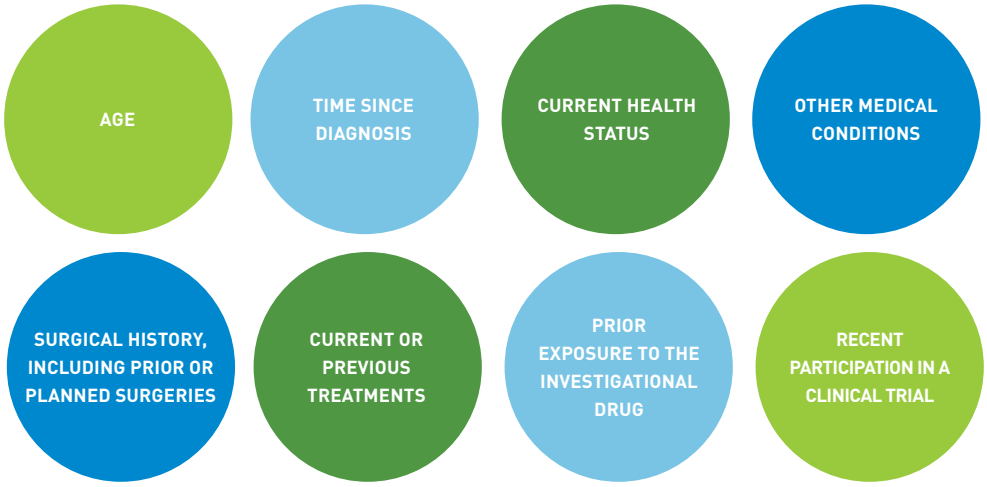
Before a research center or hospital can participate in a clinical trial, the protocol, as well as any documents that will be provided to participants, must be reviewed and approved by an IRB or EC.

How Is the Clinical Trial Population Chosen?

All clinical trials have guidelines about who can and cannot participate. These are called eligibility criteria (or inclusion / exclusion criteria), and they are determined by a discussion between the clinical trial sponsor and the regulatory authority. Eligibility criteria help researchers conduct a trial safely and efficiently while helping produce reliable results.

Eligibility criteria help researchers establish a group of participants that share similar qualities. This allows researchers to evaluate the investigational drug and compare its effect, if any, among participants who have similar characteristics. Eligibility criteria also help researchers identify individuals who can safely participate in a clinical trial.

KEY ELIGIBILITY CRITERIA MAY INCLUDE:



The principal investigators and the clinical trial staff evaluate potential participants through a screening process that may include:

- a review of the patient's medical history
- medical tests and evaluations
- a discussion with the potential participant (or loved ones) to help the principal investigator make a decision about whether the patient's status and medical history meet the eligibility criteria for participation.

The final decision about whether an individual may be able to participate is made by the principal investigator.

Not everyone interested in a clinical trial may have the opportunity to participate. This could be because their current health status and medical history may not match the eligibility requirements.

If you or your loved one is not able to participate in a clinical trial after completing the screening process, the principal investigator may be able to discuss the possibility of participating in another trial now or in the future.

Who Is Involved in Conducting a Clinical Trial?

There are many people involved in planning, organizing, and conducting a clinical trial. They may include:

CLINICAL TRIAL SPONSOR

A clinical trial sponsor can be a company (e.g., medical device, pharmaceutical or biotech), a non-profit institution, or a government organization. The sponsor initiates, manages, and funds a clinical trial.

REGULATORY AUTHORITY

Each country has its own regulatory authority with its own regulations, or laws, for conducting a clinical trial. The regulatory authority reviews and approves the protocol, and ensures that the clinical trial follows national regulations.

INSTITUTIONAL REVIEW BOARD (IRB) / ETHICS COMMITTEE (EC)

An IRB or EC is an independent committee that includes medical, scientific, and non-scientific members, whose responsibility is to protect the rights, welfare, safety, and well-being of clinical trial participants. Each clinical trial location is monitored by a specific IRB / EC. It is responsible for reviewing all clinical trials, as well as conducting ongoing reviews of active clinical trials.

PRINCIPAL INVESTIGATOR

The principal investigator is usually a medical doctor who is responsible for managing a clinical trial at an individual research center or hospital. The principal investigator is sometimes called the "study doctor," and he / she is usually helped by other doctors, nurses, and clinical research coordinators who are part of the study team.

The Four Phases of Clinical Trials

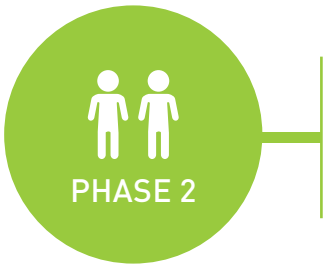
Developing a new medical treatment is a long and complex process, averaging 10 – 15 years from start to finish. This is because there are several steps in place that are designed to evaluate whether an investigational drug is safe and effective before it is approved by a regulatory authority.

Once an investigational drug is identified, testing is performed in the laboratory before it can be tested in humans. This initial testing may take several years. Approximately one in every 1,000 investigational drugs will make it to human testing.

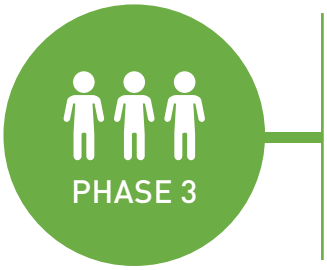
Following the completion of each phase, the sponsor will evaluate the results and decide if the investigational drug will advance to the next phase.

AN OVERVIEW OF THE FOUR PHASES

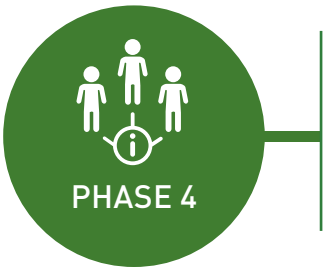
The investigational drug is tested in a small group of people to evaluate its safety, determine a safe dose, and identify side effects. Sometimes phase 1 trials involve a group of healthy volunteers who are generally paid for participating.



The investigational drug is given to an increased number of people with the disease. Researchers look to identify initial signs that it may be effective and further evaluate its safety.



The investigational drug is given to an even larger number of people with the disease to confirm its effectiveness, monitor side effects, and collect information that will allow the investigational drug to be used safely. During this phase, the investigational drug is often compared to a placebo.

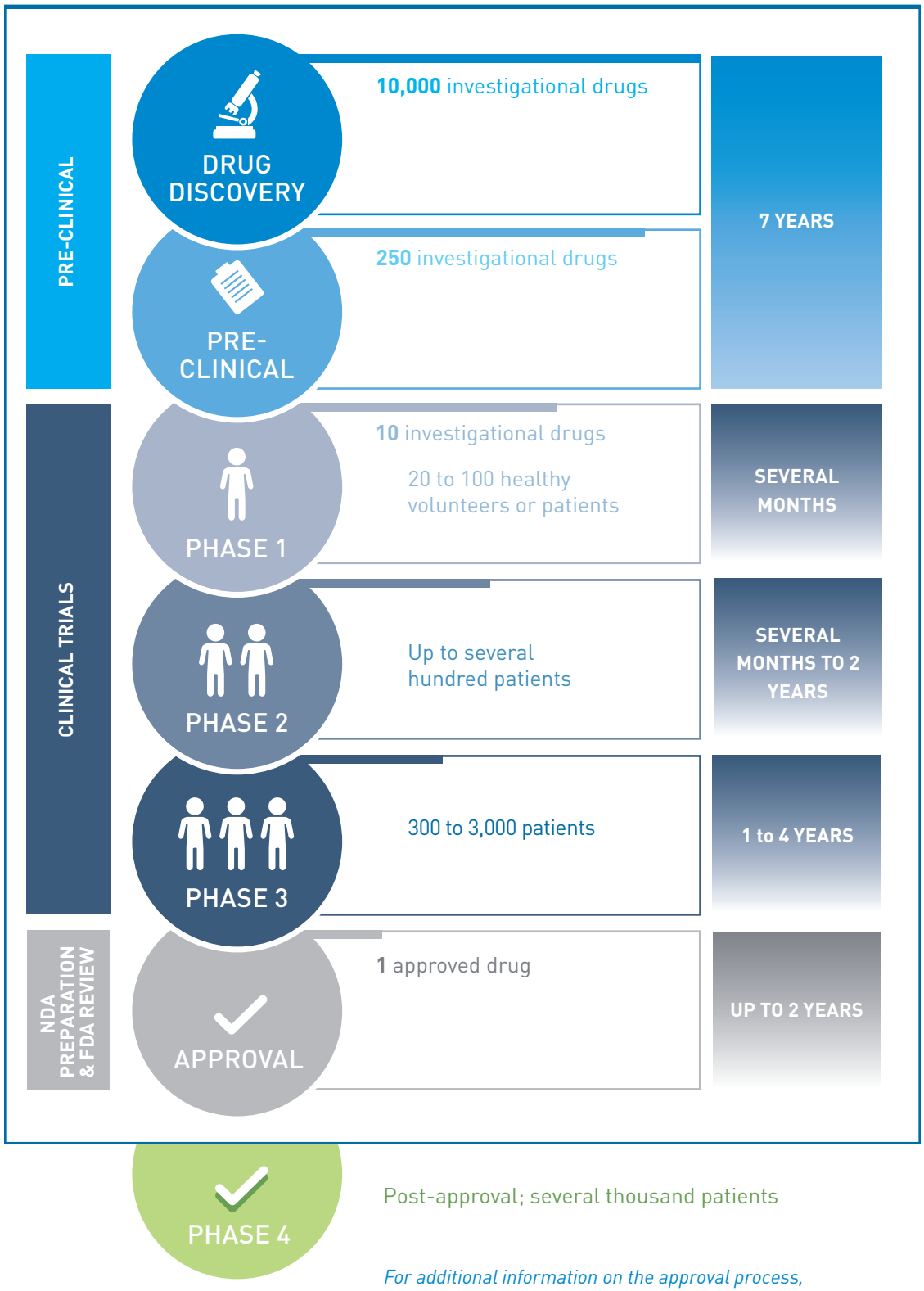


After an investigational drug has been approved and made available to the public, researchers gather information on its effects in various populations and any side effects associated with long-term use.

Extension Trials

Some clinical trials have an extension trial that participants may be eligible to participate in following the completion of the main trial. In most cases, during an extension trial, all participants receive the investigational drug over a longer period so that researchers can study its long-term effects.

THE CLINICAL TRIAL PROCESS EXPLAINED



For additional information on the approval process, please refer to the section at the end of this brochure.

Why Consider Participation?

Individuals may choose to participate in a clinical trial for a variety of reasons, including:

To help advance knowledge about the disease

To contribute to medical research and to the development of a potential treatment

To help others impacted by the disease in the future

Potential access to an investigational drug

Appointments with the study team

Clinical trial-related care, monitoring, medical tests and assessments

HOW DO I LEARN ABOUT THE POTENTIAL RISKS AND BENEFITS OF PARTICIPATION?

Clinical trials are investigational in nature. There is no guarantee that participating in one will provide a medical benefit, and in fact there may be risks involved – some known, some unknown. Although efforts are made to control potential risks, some may not be avoided because they may not be known.

When potential risks are known, they must be fully explained by the clinical trial staff to potential participants (or parent or guardian, depending on the age of the participant). They may include unpleasant or even serious side effects. If new risks are learned during the trial, this information must be shared as well.

Participants may or may not experience a benefit from the investigational drug. However, there may be other potential benefits to participation that include:

- contributing to medical research
- clinical trial-related care and monitoring
- potential access to an investigational drug

As part of the decision-making process, you will be given a chance to discuss the potential risks and benefits of participation with the principal investigator. You should make a decision only after you fully understand them.

WHAT IS THE INFORMED CONSENT PROCESS?

If you are interested in participating in a clinical trial, you will be given an opportunity to ask the principal investigator questions. You will be provided with an Informed Consent Form that explains the details of the trial, including its purpose, length of time, required procedures, key contacts, and any possible risks and benefits. You may take the form with you to review and discuss it with loved ones or friends while you consider participation.

If you decide to participate, you must provide your consent by signing the form. This process is called the informed consent process, and it is a standard process for participation in a clinical trial.

As you consider your decision, please remember:

- Participation in a clinical trial is always voluntary and you can change your mind at any time.
- Deciding not to participate will not affect care that may be provided now or in the future.
- Participants may withdraw at any time and for any reason – doing so will not affect the care they would normally receive outside of a clinical trial.
- The principal investigator is required to inform clinical trial participants of any new developments that may affect or influence their decision to participate. The IRB / EC plays a role in overseeing clinical trials to make sure this occurs.

For some individuals, it is a possibility that their participation may be ended, without their consent, if they become too sick or other medical issues develop.

SPECIAL CONSIDERATIONS FOR CHILDREN

By law, children are not allowed to give informed consent until they are 18 years of age. However, if your child is seven years of age or older, he or she may be asked to provide their assent. By giving their assent, they are agreeing to take part in the clinical trial. Whether your child will be required to give their assent is determined by the regulatory authority.

WHAT ARE THE RESPONSIBILITIES OF PARTICIPANTS?

There are certain responsibilities that clinical trial participants (or their parent or guardian, depending on the age of the participant) are asked to follow. These may include:

- Following all instructions given by the study team.
- Attending all scheduled visits.
- Completing questionnaires about the status of the participant between visits.
- Telling the principal investigator of any new health-related problems. (Even if you don't consider them to be caused by the clinical trial or the investigational drug, any small change is very important to report.)
- Telling the principal investigator about any new medications or changes in doses or the frequency of medication.
- Being mindful about discussing the clinical trial with other participants, including whether or not you think you or your loved one may be receiving a placebo.

TRAVEL SUPPORT

Some clinical trials may include travel support and reimbursement for parking, meals, and other expenses. This may be helpful for individuals that need to travel a long distance to the clinical trial location, or that have a lengthy appointment or overnight stay.

PLANNING AHEAD TO MEET WITH THE PRINCIPAL INVESTIGATOR

When you meet with the principal investigator for the first time, you may have many questions. Here are a few tips to help you plan so that you are prepared.

- Think about questions you may want to ask and write them down in advance so that you don't forget to ask any of them.
- Bring a family member or friend to support you with asking questions.
- Write down the principal investigator's response to your questions so you can review them later with your family members.

Make sure you leave with an understanding of the potential risks and benefits involved with participation and the side effects that could occur. These are important things to consider during the decision-making process.

SUGGESTED QUESTIONS TO ASK THE PRINCIPAL INVESTIGATOR

When meeting with the principal investigator to discuss participation, you may want to consider asking some of the following questions:

- What is being studied?
- If researchers are studying an investigational drug, why do they believe it may be effective?
- How long will participation last?
- How often will I have to visit the hospital or clinic? Will any of these visits require an overnight stay?
- Is there a chance of receiving a placebo?
- What types of medical tests and procedures will be performed?
- What are the possible risks / benefits of participation?
- Will the results of the clinical trial be available to participants?
- Who will pay the costs associated with participation?
- Will I be reimbursed for other expenses?
- Is travel support included?
- Is there a planned extension trial?

EXPANDED ACCESS PROGRAMS

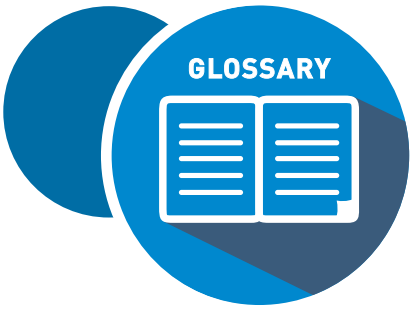
If you or your loved one is not eligible to participate in a clinical trial, expanded access – also called "compassionate use" – may be an option to explore. Laws in some countries allow drug companies to provide investigational drugs to patients outside of a clinical trial – however, expanded access programs are highly regulated and patients must meet several criteria in order to be eligible.

The purpose of expanded access is to provide treatment for a patient's disease, rather than to collect data about the investigational drug.

ACCELERATING THE APPROVAL PROCESS

Several countries have programs to speed the development and approval of investigational drugs designed to treat serious and life-threatening conditions, as well as rare diseases. These programs help ensure that investigational drugs for these conditions are approved and available to patients as soon as it is known that the drugs' benefits justify their risks. These programs call for earlier attention to drugs that have promise in treating such conditions.

Investigational drugs that meet an unmet medical need, and that show an increased benefit over available treatments, may be moved through the clinical trial review and approval process more quickly than others.



GLOSSARY OF TERMS

Listed below are some of the common words and terms associated with clinical trials, along with their definitions

Blinding

The design of a clinical trial in which participants do not know whether they have been assigned to receive the investigational drug or a placebo. Blinding is done to prevent the unintentional bias that can occur when assignments are known.

Double-blind

The design of a clinical trial in which neither the participant nor the principal investigator knows whether the participant has been assigned to receive the investigational drug or a placebo.

Expanded Access

When drug manufacturers provide investigational drugs to patients with serious diseases or conditions who cannot participate in a clinical trial, or when no other treatments are available.

Informed Consent

The process by which a person provides his / her consent, or agreement, to participate in a clinical trial. This occurs after the patient has reviewed the informed consent form and has an opportunity to ask the principal investigator any questions he / she may have about participation.

Institutional Review Board (IRB) / Ethics Committee (EC)

An independent committee that includes medical, scientific, and non-scientific members, whose responsibility is to protect the rights, welfare, safety and well-being of clinical trial participants.

Interventional Trial

Interventional trials are conducted to determine whether an investigational treatment or a new way of using an approved treatment is safe and effective.

Observational Trial

Observational trials collect health information. They do not involve the use of an investigational treatment. Instead, researchers focus on collecting data about the disease. The data may be used by researchers in the future to help with the development of potential new treatments.

Open-label

A clinical trial in which everyone involved (participant, doctor, and study team) is aware of the drug and dosing levels. In open-label trials, no one receives a placebo.

Placebo

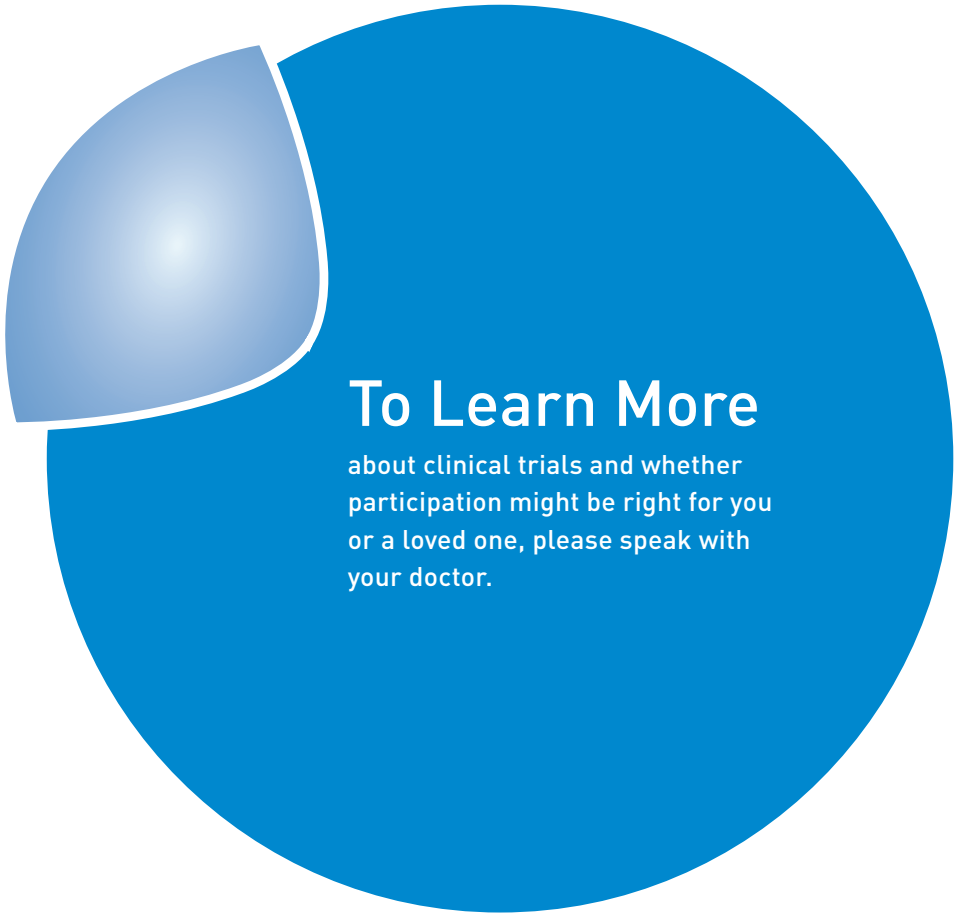
An inactive substance that looks like the drug being tested. It is used as a control to eliminate any psychological effects testing may present.

Randomized Controlled Trial

A type of clinical trial where participants are randomly assigned (like flipping a coin) to a particular group. Depending on the trial, participants may be assigned to receive a placebo, the investigational drug, or a particular dose of the investigational drug.

Standard Treatment (Standard-of-Care)

Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals.



To Learn More

about clinical trials and whether participation might be right for you or a loved one, please speak with your doctor.

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