


Clinical Trials: **Your Questions Answered**



**Alzheimer's Disease Research
Macular Degeneration Research
National Glaucoma Research**

Clinical Trials:

Your Questions Answered

The nonprofit BrightFocus Foundation is an international leader in supporting innovative research to find cures for Alzheimer’s disease, macular degeneration, and glaucoma. Guided by scientific review panels of world-class researchers, we invest in promising and rigorous science to end diseases of mind and sight. Through free publications such as this one, we share research findings and helpful tips with those impacted by these diseases, including families and caregivers.

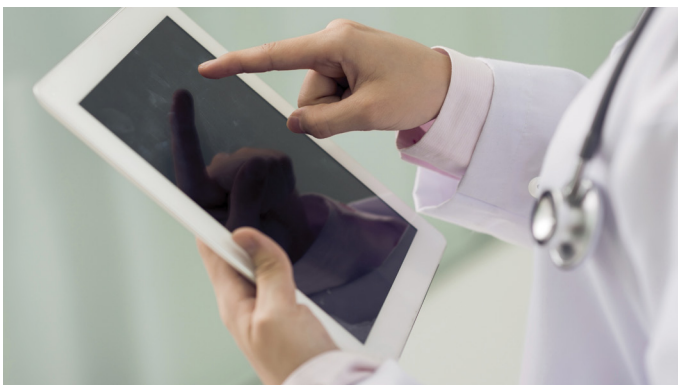
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Clinical trials play a critical role in the development of new treatments and are the culmination of years, often decades, of work done by researchers to find ways to slow, treat, or even cure diseases like Alzheimer’s disease, macular degeneration, and glaucoma. Unlike earlier phases of research, clinical trials are completely dependent on the volunteer participation of patients and others who are personally invested in seeing new treatments become available.

Many people express a wish to learn more, or would like to participate in clinical trials, but lack the information about how to get involved. Researchers rely on volunteers to bring their research closer to their ultimate goal of providing the public with better options to manage their conditions, and older individuals in particular are in demand. The reality is many breakthroughs are delayed due to a lack of volunteers.

BrightFocus Foundation is here to help you understand what clinical trials are, what volunteering for a trial means to you, what you should consider before participating, and how you are helping researchers impact the lives of millions of people. This brochure will also address other ways you can help health research if the clinical trial course is not for you.



What Is Involved in Bringing a New Treatment to Market?

A new treatment or cure cannot come fast enough for someone who suffers from a mind- or sight-stealing disease. However, it is a long and difficult journey to bring new treatments to market, one that involves decades of painstaking research and testing, and billions of dollars in cost.

The word “treatment” most often refers to a new drug that can cure, modify, or reduce the symptoms of a disease. However, it may also refer to a new technology or device, or a new approach to surgery. This brochure focuses on clinical trials leading to treatments and devices that are regulated and approved by the U.S. Food and Drug Administration (FDA). There may be other dietary and lifestyle approaches to preventing or treating a disease that do not fall under FDA jurisdiction, such as supplements, but they are not discussed here.

The journey from a scientific breakthrough by a researcher to a treatment you can access at your local pharmacy is a long one. Even after positive results are reported on a promising idea, there are many twists and turns on its path to FDA approval.

The final stages on this path are clinical trials that depend on the volunteer participation of patients and others who hope to find better approaches to managing diseases. In return for enrolling, many trial-related expenses are often paid. You may have the opportunity to participate in a clinical trial that helps advance new treatments and cures.

What Are Clinical Trials?

Clinical trials are the final phase of the research process, and the step in the process that ultimately determines whether or not a treatment will be approved for use by humans. Extensive research has already taken place in laboratories and in animal models before human trial volunteers ever get involved. During this process, the list of potential treatments is whittled down to a small number of promising candidates selected to go through the rigor of testing in humans.

Why Are Clinical Trials Necessary?

Clinical trials are undertaken to test whether a new drug or device is safe and effective, which requires successive levels of proof that it will effectively treat people who have a certain disease or condition. This series of clinical hurdles is referred to as Phase 1, 2, and 3 clinical trials, and each phase is closely regulated by the FDA to ensure that all steps are done properly and adhere to strict standards governing the drug approval process.

By establishing safety and effectiveness, these trials will ultimately determine whether a drug or device will receive approval by the FDA, and the conditions for which they can be marketed and sold in the United States.

Who Sponsors Clinical Trials?

Clinical trials are sponsored by government agencies, private organizations, and research teams who are seeking ways to improve the health of people living with chronic and life-threatening illnesses. Sponsors include:

- Government agencies such as the National Institutes of Health (NIH), the Department of Defense (DOD), and the Department of Veterans Affairs (VA)
- Pharmaceutical, biotechnology and medical devices companies
- Health care institutions such as academic medical centers and health maintenance organizations (HMOs)

Clinical trials take place in a variety of locations, including hospitals, universities, doctors' offices, or community health clinics.

Source: www.nih.gov/health-information/nih-clinical-research-trials-you/basics

Clinical trials answer the following questions:

- Is a new device or treatment safe to use?
- Does the new treatment have a positive or negative effect on patients' disease?
- Is the new treatment better than the current standard treatment, or other treatments that might be available?
- Which patients benefit the most from the new treatment?

Today's clinical trials will lead to new standards of care in the future.

How Do Clinical Trials Work?

Each of the three phases of clinical testing has a specific purpose in determining the safety of a treatment for use by the public.

Phase 1 clinical trials evaluate the safety of a drug or treatment and to determine how well it works. This testing normally takes place with a small group of healthy volunteers. The trial sponsor monitors potentially serious adverse events—that is, any toxic, undesirable, or unwanted effect that causes death or danger to health, like a disability or permanent damage, birth defect, heart attack, or other serious medical condition.

At the end of Phase 1, the results are collected, analyzed, and submitted to the FDA for permission to proceed to Phase 2 clinical trials. However, if the results show that the treatment was associated with one or more serious adverse events, then the FDA may not give permission to proceed to Phase 2. Sometimes early clinical trials are discontinued for that reason, or the sponsor may voluntarily withdraw the treatment from regulatory consideration.

If the trial meets the primary outcomes, as proposed in the application to the FDA, then the FDA permits the trial to proceed to Phase 2.

Clinical Trials at a Glance

This table compares Phase 1-4 trials by purpose, number of participants, and approximate length of time.

Type of Clinical Trial	Primary Purpose/ Questions Answered	Numbers Enrolled (approx.)	Typical Length (approx.)	Treatments continuing to next stage (%)
Phase 1	SAFETY & DOSAGE Is the treatment safe? What are its side effects? How is it metabolized and excreted (if drug)?	20-100 healthy volunteers or people with the disease or condition	Several months	Approx. 70% (may vary by disease and severity)
Phase 2	EFFICACY & SIDE EFFECTS Is the treatment effective? Does it work in people with a certain disease or condition? How do results compare with different treatment or placebo? [Safety and side effects continue to be studied.]	Hundreds of people with the disease or condition	Several months to 2 years	33%
Phase 3	SAFETY & EFFICACY Is the treatment safe and effective when used in ways resembling “real life?” Is it effective in different populations? At different dosages? When used in combination with other drugs?	Hundreds to thousands of people with the disease or condition	1-4 years	25-30%
Phase 4	POSTMARKET SAFETY MONITORING Have any serious unexpected adverse events occurred? Should the labeling reflect these risks? Does the public need to be informed in other ways? Should its use be limited or the treatment withdrawn from the market?	All people using the treatment after it has been approved	Ongoing after FDA approval	

Source: Center for Drug Evaluation and Research, U.S. Food & Drug Administration

Phase 2 clinical trials test the right dosage and effectiveness in treating a particular disease. This testing normally takes place with a larger number of volunteers who have the disease, and typically involves assigning participants to different treatment groups, where each group can receive different doses or delivery of the treatment.

At the end of Phase 2 trials, the health of the group(s) of patients who received the different types of treatment is compared to the control groups. However, if the results show that the treatment did not work better than the current standard of care or even caused acceleration of the disease or other unexpected serious adverse events, the FDA may not give permission to proceed to Phase 3, and the trial may be discontinued from the regulatory approval process until modifications can be made.

Phase 3 clinical trials are the ultimate test of whether a treatment is safe and effective for a wide variety of people, and typically involve a much larger group of volunteers than Phase 1 and 2 trials (see chart on page 5). Just like Phase 2 trials, the plan normally involves assigning participants to treatment or control groups. There can be more than one treatment group, especially if the treatment involves a combination of drugs or different components. Participants can expect to receive either the treatment being tested or an equivalent single or combined treatment for comparison (treatment groups), or a placebo treatment (control group).

After completion, the health of the patients who received the different types of treatment are compared to the control groups.

If successful, sponsors may now apply for a New Drug Application (NDA). The NDA contains



A Note about Repurposed Drugs

Sometimes researchers discover that a drug or treatment that has been approved for one disease has the potential to be considered for treating a different disease. When that happens, the sponsor may seek FDA approval to test the drug for another disease or symptom. If a Phase 1 safety profile has already been established for the drug in a similar human population, then “repurposing” can sometimes shorten the drug pipeline by allowing a drug to go straight from preclinical investigation into Phase 2 clinical trials.

all of the discoveries made at every stage of the process (starting from the basic investigation/ drug discovery stage through the results of the Phase 3 clinical trials), and is submitted to the FDA for their consideration.

If approved, the trial sponsors will now have the necessary approval to manufacture and sell these new treatments, making them available to patients.

Does the FDA Monitor a New Treatment after Approval?

They do. **Phase 4 clinical trials** (also called Post-Market Surveillance and Adverse Event Reporting) take place after a treatment is approved by the FDA to be manufactured and sold in the United States. For the entire time a treatment is on the market (or longer), the FDA monitors its impact on public safety and whether it has been associated with any potential serious adverse events.

Who Can Participate in Clinical Trials?

People with a medical condition as well as healthy individuals may consider participating in clinical trials. Each trial has its set of guidelines, or protocols, and volunteers must meet the criteria as outlined to qualify for enrollment. Before making a decision and giving informed consent (see page 8), each person should learn as much information as possible about the trial.

Many people choose to become involved because they hope to improve their health or be cured, and also wish that for others with the same condition. Whether that happens depends on the many factors, and yet there are many additional benefits to participation:

- You are helping the cause of research.
- You may find a treatment better than your current one.
- Your participation may result in new treatments for people who are now suffering, or will later.
- You have the satisfaction of knowing you are helping speed the availability of new treatments in health care.
- You help medical science know more about individual diseases.

Enrolling in clinical trials requires a time commitment, even to learn whether you are eligible. And there are possible risks to consider along with the benefits. There may be side effects, or the treatment you receive may be no more effective than the current care you are receiving. However, even if that happens, you will have helped in some important ways listed above. The decision is yours to make with your family and doctor.

Trials Designed with Your Safety in Mind

While trial designs vary, it is quite typical for enrollees to be split up into a group that receives a new drug or therapy and another group of “controls” who receive either the current standard of care or a placebo treatment that has no benefit, i.e., a sugar pill or harmless injection. If the trial is “blinded,” then it’s possible that both you and the study directors will not know which group you are in.



Thus, the possibility exists that after enrolling in a trial, you may not receive the study drug for a period of time if you are placed in a control group. Sometimes the chance of being randomized to the placebo group is addressed by crossover designs where everyone gets the drugs, but at different times. Still other trials are designed so that all enrolled patients wind up receiving the drug at the end of the study if it is found to be effective.

The important thing to remember is this: in order to get the FDA’s approval to run the trial, researchers have to make sure their design protects the safety of all participants, both subjects and controls. Nonetheless, be sure to ask questions about trial design—including how the risks of being assigned to a placebo group will be handled—when you meet with study directors and/or your doctor.

What Is Informed Consent?

Informed consent is a legal protection enforced by the FDA that ensures you have been given detailed information about possible risks and benefits before agreeing to participate in a clinical trial. It requires sponsors to provide complete information to potential volunteers, and to make sure it has been understood, before enrolling them. The information must be written in easy-to-understand language, and you must be given an opportunity to discuss the information in at least one personal interview. If you do not understand all of the information, ask a doctor or other medical professional to help.

The FDA requires sponsors to provide the following information as part of the informed consent process:

- Explain that the potential treatment is unproven and not yet approved.
- Verify the purpose and length of the study.
- Outline possible risks and benefits.
- Disclose that the FDA may look at personal health records, but those records will be kept confidential.
- List other treatments or current standard of care that you may want to consider instead of the treatment being studied in this trial.
- Provide you with detailed information about what medical treatments will be made available to you if you get hurt in the trial, where you can find them, and who will pay for them.

- Inform you about who to contact with questions about the study, your rights, and the development of side effects.

You must sign a form to show that you understand the information. It is not a binding contract, though, and it is important to remember that you can leave the study at any time.

In addition to being an enrollment requirement, informed consent is a continuing process throughout the clinical trial to ensure that updated information is provided to participants.

The ethical and legal codes that govern medical practice also apply to clinical trials. Please note that some of the other protections for clinical trial volunteers are in the form of institutional review boards, data monitoring committees, and regular FDA inspections of data and facilities at the various trial site locations. In addition, confidentiality is protected and individual participants' names will remain private.



Questions to Ask before Enrolling in a Clinical Trial

You will learn the answers to many of your questions during the informed consent process, but here are some additional questions you may consider asking the research team before you join a trial:

- What kinds of tests and exams will be performed during the study? What is involved in each test?
- What are my other treatment choices and how do they compare with the treatment being studied?
- Are there possible advantages over my current treatment(s)?
- Does the study compare standard and experimental treatments or will there be a placebo group? Will I know which treatment I am getting?
- What side effects can I expect from the treatment being tested? How do they compare with side effects of the standard treatment?
- Will the new treatment pose a conflict with any other drugs/treatments that I am currently receiving for the same or a different medical condition?
- How often does the study require me to go to the doctor or clinic?
- Will I be hospitalized? If so, how often and for how long?
- Who will be in charge of my care?
- How will you keep my doctor informed about my participation in the trial?
- What are the costs to me? Will my health insurance pay for it?
- Will I be reimbursed for other expenses (e.g. parking fees, mileage)?
- What type of follow-up care is part of this study?
- How will I know that the treatment is working? Will results of the trials be provided to me? Who will be in charge of my care?

Notes:

How Can I Learn about Clinical Trials?

Your primary care provider or a specialist may tell you about a clinical trial if he/she thinks you might qualify as a candidate. However, some physicians may have little or no contact themselves with clinical research.

Stay informed. You may initially find trials that you are not qualified or eligible to enroll in. Check back periodically to see if new trials have been listed, and share the information with others who may be eligible or interested. This brochure provides a list of resources starting on page 11 to help you become informed about clinical trials. You can also find this information at www.brightfocus.org/clinical-trials

What Should I Consider When Making a Decision about Participation?

Many factors have to be weighed when reaching a decision about whether to enroll in a clinical trial. There should be a full discussion between you and your medical care team. Do not hesitate to ask additional questions of the research team and healthcare professionals associated with the clinical trial. You may want to bring a family member or caregiver with you, or even a recording device like your cell phone to help make sure all of your questions are answered and documented for future reference.

Can I Leave a Clinical Trial?

Participation in a clinical trial is voluntary, which means you can leave a clinical trial at any time. Before you leave a clinical trial, please let the research team know you have decided to withdraw and your reasons for leaving the study. Also ask them for direction on how your participation may impact your care outside the trial. This will help the team to prepare information for their detailed report on the clinical trial to the FDA.

Are There Other Ways to Participate in Health Research?

Maybe you have decided a drug approval trial is not for you. Or you cannot find one convenient to your location. Or you do not qualify based on the entry criteria. If any of these are true, there are still ways you can participate in health research. You may still have the opportunity to participate in research.

Participate in Other Studies. Some prevention research looks at whether things like vitamins, exercise, or similar lifestyle changes that don't require FDA approval might prevent a disease or condition from developing or getting worse. There are long-term studies (sometimes called "longitudinal studies") that track healthy people or people with a particular disease for years to see how they fare over time. You will find studies like these listed at www.clinicaltrials.gov and other resources listed at the end of this brochure, and they may be suitable for people who are not comfortable being randomized into a treatment or non-treatment arm.

Join Registries and Genetic Research

Efforts. If you are being treated for a disease or condition, your doctor may be able to contribute information about your health and treatment to a “registry” or data bank of information kept on large numbers of people with the disease. In some cases, these registries involve sampling and keeping track of genetic information; thanks to millions of people worldwide who were willing to provide this information (usually anonymously), new genes associated with diseases and conditions are being discovered. And if you happen to have a highly inheritable disease or form of a disease, there are researchers who might like to study you and your family to gain more information.

Donate Tissue. There’s an enormous amount of information to be gained from postmortem studies of tissue donated by individuals who had a disease or condition. Most donor

registries are nonprofit organizations that provide these specimens to medical schools and research labs at minimal or no cost. Healthy individuals also have the option of donating their eyes and other organs for use by the living. More information is listed in “Where Can I Find More Information?” below.

Follow and Share Results. While it takes a long time for a new treatment to be discovered and approved, scientific research yields new information and small breakthroughs every single day. At BrightFocus, this information appears in our print newsletters and on our website. Keep hope alive by tuning into these accomplishments and informing others about scientific progress.

Where Can I Find More Information?

Services to Identify Clinical Trials and Sign up as a Volunteer:

Antidote. A free service connecting patients with clinical trials by using an easy-to-understand online questionnaire.

www.antidote.me/
1-888-509-1308

CenterWatch Clinical Trials Listing Service.

This service provides information about clinical research, including listings of active industry and government-sponsored clinical trials, research on new drug therapies, and drugs recently approved by the FDA.

www.centerwatch.com
1-866-219-3440



Clinicaltrials.gov. An online registry and results database hosted by National Institutes of Health (NIH) that lists all publicly and privately supported clinical studies being conducted with human participants around the world. Follow prompts to look for active clinical trials located near you for a specific medical condition.

www.clinicaltrials.gov

eyeGENE®. Aims to advance studies of eye diseases and their genetic causes by giving researchers access to DNA samples, clinical information, and patients looking to participate in research studies and clinical trials.

<https://eyegene.nih.gov/>
(301) 435-3032

National Institutes of Health (NIH). Provides information on government-sponsored human trials and recruitment, with locations, purpose, eligibility requirements, and phone contacts.
www.nih.gov/health/clinicaltrials

They also provide information on health registries:

www.nih.gov/health-information/nih-clinical-research-trials-you/list-registries
(301) 496-4000

ResearchMatch. This free and secure registry brings together people who are trying to find research studies, and researchers who are looking for people to participate in their studies.

www.researchmatch.org

Additional Resources to Answer Your Questions:

Center for Information and Study on Clinical Research Participation (CISCRP). A nonprofit organization that educates the public about clinical research; what it means to be a clinical research volunteer; and questions you should consider before, during, and after your participation in clinical trials.

www.ciscrp.org/education-center
1-877-633-4376

U.S. Food and Drug Administration (FDA). The “For Patients” section of the FDA website links to information about clinical trials and the drug and device approval process.

www.fda.gov/patients/

Drug Safety & Reporting:

MedWatch (FDA Safety Information and Adverse Event Reporting Program). A website maintained by the FDA with safety information about drugs commercially available in the United States, including a searchable database. Consumers and healthcare professionals can voluntarily report a serious adverse event, product quality problem, or another type of failure that is suspected to be associated with the use of an FDA-regulated drug, biologic, medical device, dietary supplement, or cosmetic. Suspected counterfeit medical products can also be reported through the same online reporting form.

www.fda.gov/Safety/MedWatch/default.htm
1-888-463-6332

Information About Online Reporting

www.fda.gov/Safety/MedWatch/HowToReport/default.htm

Organ and Tissue Donation:

Eye Bank Association of America. A network of eye banks around the country recover corneal tissue from donors and prepare it to surgeons' specifications for sight-restoring transplant procedures.
<http://restoresight.org>
(202) 775-4999

NIH NeuroBioBank (NBB). Supported by the National Institute of Mental Health, the National Institute of Neurological Disorders and Stroke, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the NBB brings together multiple stakeholders to facilitate research advancement through the collection and distribution of human post-mortem brain tissue.
<https://neurobiobank.nih.gov>

U.S. Department of Health and Human Services. An online resource offering information about "the basics" of organ, eye, and tissue donation, and about who these gifts may help under the U.S.-run Organ Procurement and Transplantation Network.
www.organdonor.gov/index.html

The above organizations are not affiliated with BrightFocus Foundation. BrightFocus is not responsible for the content of these websites and does not endorse any particular programs offered by these organizations.

BrightFocus is at the forefront of brain and eye health, supporting innovative research around the world and promoting better health through our three programs:

Alzheimer's Disease Research
Macular Degeneration Research
National Glaucoma Research



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