

Step 3: Clinical Research

While preclinical research answers basic questions about a drug's safety, it is not a substitute for studies of ways the drug will interact with the human body. "Clinical research" refers to studies, or trials, that are done in people. As the developers design the clinical study, they will consider what they want to accomplish for each of the different Clinical Research Phases and begin the Investigational New Drug Process (IND), a process they must go through before clinical research begins.

On this page you will find information on:

- Designing Clinical Trials
- [Clinical Research Phase Studies](#)
- [The Investigational New Drug Process](#)
- [Asking for FDA Assistance](#)
- [FDA IND Review Team](#)
- [Approval](#)

Designing Clinical Trials

Researchers design clinical trials to answer specific research questions related to a medical product. These trials follow a specific study plan, called a protocol, that is developed by the researcher or manufacturer. Before a clinical trial begins, researchers review prior information about the drug to develop research questions and objectives. Then, they decide:

- Who qualifies to participate (selection criteria)
- How many people will be part of the study
- How long the study will last
- Whether there will be a control group and other ways to limit research bias
- How the drug will be given to patients and at what dosage
- What assessments will be conducted, when, and what data will be collected
- How the data will be reviewed and analyzed

Clinical trials follow a typical series from early, small-scale, Phase 1 studies to late-stage, large scale, Phase 3 studies.

What are the Clinical Trial Phases?



Watch this video to learn about the three phases of clinical trials.

Clinical Research Phase Studies

Phase 1

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Study Participants: 20 to 100 healthy volunteers or people with the disease/condition.

Length of Study: Several months

Purpose: Safety and dosage

During Phase 1 studies, researchers test a new drug in normal volunteers (healthy people). In most cases, 20 to 80 healthy volunteers or people with the disease/condition participate in Phase 1. However, if a new drug is intended for use in cancer patients, researchers conduct Phase 1 studies in patients with that type of cancer.

Phase 1 studies are closely monitored and gather information about how a drug interacts with the human body. Researchers adjust dosing schemes based on animal data to find out how much of a drug the body can tolerate and what its acute side effects are.

As a Phase 1 trial continues, researchers answer research questions related to how it works in the body, the side effects associated with increased dosage, and early information about how effective it is to determine how best to administer the drug to limit risks and maximize possible benefits. This is important to the design of Phase 2 studies.

Approximately 70% of drugs move to the next phase

Phase 2



Study Participants: Up to several hundred people with the disease/condition.

Length of Study: Several months to 2 years

Purpose: Efficacy and side effects

In Phase 2 studies, researchers administer the drug to a group of patients with the disease or condition for which the drug is being developed. Typically involving a few hundred patients, these studies aren't large enough to show whether the drug will be beneficial.

Instead, Phase 2 studies provide researchers with additional safety data. Researchers use these data to refine research questions, develop research methods, and design new Phase 3 research protocols.

Approximately 33% of drugs move to the next phase

Phase 3



Study Participants: 300 to 3,000 volunteers who have the disease or condition

Length of Study: 1 to 4 years

Purpose: Efficacy and monitoring of adverse reactions

Researchers design Phase 3 studies to demonstrate whether or not a product offers a treatment benefit to a specific population. Sometimes known as pivotal studies, these studies involve 300 to 3,000 participants.

Phase 3 studies provide most of the safety data. In previous studies, it is possible that less common side effects might have gone undetected. Because these studies are larger and longer in duration, the results are more likely to show long-term or rare side effects

Approximately 25-30% of drugs move to the next phase

Phase 4



Study Participants: Several thousand volunteers who have the disease/condition

Purpose: Safety and efficacy

Phase 4 trials are carried out once the drug or device has been approved by FDA during the Post-Market Safety Monitoring

Learn more about [Clinical Trials \(/clinical-trials-what-patients-need-know\)](https://www.fda.gov/patients/drug-development-process/step-3-clinical-research).

The Investigational New Drug Process

Drug developers, or sponsors, must submit an Investigational New Drug (IND) application to FDA before beginning clinical research.

In the IND application, developers must include:

- Animal study data and toxicity (side effects that cause great harm) data
- Manufacturing information
- Clinical protocols (study plans) for studies to be conducted
- Data from any prior human research
- Information about the investigator

Asking for FDA Assistance

Drug developers are free to ask for help from FDA at any point in the drug development process, including:

- Pre-IND application, to review FDA guidance documents and get answers to questions that may help enhance their research
- After Phase 2, to obtain guidance on the design of large Phase 3 studies
- Any time during the process, to obtain an assessment of the IND application

Even though FDA offers extensive technical assistance, drug developers are not required to take FDA's suggestions. As long as clinical trials are thoughtfully designed, reflect what developers know about a product, safeguard participants, and otherwise meet Federal standards, FDA allows wide latitude in clinical trial design.

FDA IND Review Team

The review team consists of a group of specialists in different scientific fields. Each member has different responsibilities.

- **Project Manager:** Coordinates the team's activities throughout the review process, and is the primary contact for the sponsor.
- **Medical Officer:** Reviews all clinical study information and data before, during, and after the trial is complete.
- **Statistician:** Interprets clinical trial designs and data, and works closely with the medical officer to evaluate protocols and safety and efficacy data.
- **Pharmacologist:** Reviews preclinical studies.
- **Pharmakinetacist:** Focuses on the drug's absorption, distribution, metabolism, and excretion processes. Interprets blood-level data at different time intervals from clinical trials, as a way to assess drug dosages and administration schedules.
- **Chemist:** Evaluates a drug's chemical compounds. Analyzes how a drug was made and its stability, quality control, continuity, the presence of impurities, etc.
- **Microbiologist:** Reviews the data submitted, if the product is an antimicrobial product, to assess response across different classes of microbes.

Approval

The FDA review team has 30 days to review the original IND submission. The process protects volunteers who participate in clinical trials from unreasonable and significant risk in clinical trials. FDA responds to IND applications in one of two ways:

- Approval to begin clinical trials.
- Clinical hold to delay or stop the investigation. FDA can place a clinical hold for specific reasons, including:
 - Participants are exposed to unreasonable or significant risk.
 - Investigators are not qualified.
 - Materials for the volunteer participants are misleading.
 - The IND application does not include enough information about the trial's risks.

A clinical hold is rare; instead, FDA often provides comments intended to improve the quality of a clinical trial. In most cases, if FDA is satisfied that the trial meets Federal standards, the applicant is allowed to proceed with the proposed study.

The developer is responsible for informing the review team about new protocols, as well as serious side effects seen during the trial. This information ensures that the team can monitor the trials carefully for signs of any problems. After the trial ends, researchers must submit study reports.

This process continues until the developer decides to end clinical trials or files a marketing application. Before filing a marketing application, a developer must have adequate data from two large, controlled clinical trials.