

Clinical Trial Phases

Clinical trials are categorized into five successive phases. Each new phase is designed to build on information discovered from previous phases. The Pre-clinical phase occurs before the first phase of human testing. During the Pre-clinical phase, a drug is developed and then evaluated in cells and animals to see its potential effect on the human body. The development of a medication can take up to 18 years. The process of animal testing can take between 1.5 to 4 years. If a drug shows promise in the Pre-clinical phase, a pharmaceutical company can request permission from the Food and Drug Administration (FDA) to begin testing in humans. This is called an Investigational New Drug application (IND).

Since larger numbers of patients receive a treatment in **phase II** studies than in **phase I** studies, there is a greater chance to observe and compile side effect information. Subjects in a phase II trial may benefit from their participation if they receive an active treatment. Approximately 33% of experimental drugs, which pass phases I and II, will go on to **phase III**.

Phase I trials are concerned primarily with establishing a new drug's safety and dose range in about 20-100 healthy volunteers. How a drug is absorbed, distributed, metabolized and excreted by the human body is called Pharmacokinetics. This is determined through frequent blood draws (usually in an inpatient environment) to check for the level of drug in the blood plasma. Pharmacokinetic trials are usually considered phase 1 trials regardless of when they are conducted during a drug's development. Dosage range of a new drug is determined by administering increasingly larger doses to one or more groups of subjects, who are closely monitored for harmful side effects. The goal is to learn the maximum tolerated dose that does not produce unacceptable side effects. Phase I studies may involve risks even though an investigational drug has passed the Pre-clinical phase of testing. Phase 1 studies typically offer little or no benefit to the volunteer subjects; therefore they typically are compensated for their time and effort. Although usually conducted with healthy volunteers, phase 1 trials are sometimes conducted with severely or terminally ill patients, for example those with AIDS or cancer. A phase 1 trial takes several months to complete. About 70 % of experimental drugs pass this initial phase of testing.

Phase II studies determine the effectiveness of an experimental drug on a particular disease or condition in approximately 100 to 300 volunteers. This phase may last from several months to two years. A phase II trial answers the question, "Does Drug X improve Disease Y?" A secondary objective for a phase II trial is to ascertain therapeutic dose level and dosing frequency. This answers the questions, "What quantity of Drug X works better on Disease Y, (1 mg, 2 mg or 3 mg)?" and "Does Drug X work better on Disease Y taken once or twice a day?" Most phase II studies are randomized, which means that subjects are assigned randomly (by chance not by choice) to receive the experimental drug, a standard treatment or a placebo (harmless, inactive substance). Those who receive the standard treatment or placebo are called a control group. Randomized phase II studies are often double blind, which means that both subject and physician don't know which treatment is being used. Blinding prevents any unscientific influence on the study results that could be caused by knowledge of the treatment. In a single-blind study, only the subject is unaware of the treatment used. Since larger numbers of patients receive a treatment in phase II studies than in phase I studies, there is a greater chance to observe and compile side effect information. Subjects in a phase II trial may benefit from their participation if they receive an active treatment. Approximately 33 % of experimental drugs, which pass phases I and II, will go on to phase III.

Phase III studies are conducted at multiple centers with several hundred to several thousand patients for whom the drug is intended. Massive testing of a drug provides continued generation of data on a drug's safety and efficacy. As in phase II, most phase III studies are randomized and blinded. Phase III trials provide the bulk of information needed for the package insert and labeling of a medicine, after it has been F.D.A. approved. A drug in this phase can be studied for several years and may be one of 25-30 % that pass phases I, II and III. Once a phase III study is completed, a pharmaceutical company can request F.D.A. approval to market the drug. This is called a New Drug Application (NDA). The NDA contains all the scientific data that the company has gathered throughout the phases in all trials.