

GUIDE TO DRUG DEVELOPMENT AND APPROVAL

This information was developed by Gilead Sciences, a biopharmaceutical company. We are grateful for permission to reprint the material. Before a new drug can be prescribed for patient use, it must first be approved by the U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER). CDER is responsible for overseeing the testing and development of new drugs and new drug uses, and for ensuring that the methods used in drug development are both safe and effective.

CDER does not actually test new drugs. That responsibility falls to the company or institution developing the drug, also known as the "sponsor." Before a new treatment can be approved by the FDA, a sponsor must extensively test the new drug and submit the data collected to CDER for review. Throughout the development and testing process, CDER scrutinizes everything from the design of the drug's clinical trials to the nature of side effects to the manufacturing conditions under which it will be produced and packaged.

Preclinical Testing

Before approaching the FDA for permission to test a new drug in humans, the sponsor must first analyze the drug in the lab and thoroughly test it in animals to make an initial determination about its safety and effectiveness. These preclinical trials are the first step in the development and approval of a new treatment. Preclinical trials mark the end of the road for the vast majority of experimental drugs. According to industry research, only one out of every 1,000 potential new drugs proceeds from preclinical to clinical trials.

Investigational New Drug Applications (IND)

If preclinical trials are successful, the sponsor can submit an Investigational New Drug Application (IND) to the FDA. This document includes the results of the preclinical testing and proposes a "protocol" for clinical trials—a detailed plan of how the sponsor will test the drug in humans.

Each protocol is reviewed both by CDER and a local Institutional Review Board (IRB), an independent panel of scientists and other experts that has the authority to approve, change or reject research designs. Before the clinical trial can proceed, both CDER and IRB must determine that the research protocol is sound and that the sponsors will take appropriate steps to inform trial participants of any risks and make every effort to protect participants from harm.

Clinical Trials

There are four stages or "phases" of clinical studies, the human trials required for a drug to be considered for approval.

Phase I

The primary goal for Phase I trials is to evaluate the safety of the drug and determine how the drug behaves in the body (also known as pharmacokinetics). These initial clinical tests help to identify a drug's most frequent side effects when used for relatively short periods of time (days to weeks). Phase I trials often investigate the drug's effects at several dose levels and typically involve a relatively small number of participants (generally between 20 and 100). Roughly 70% of the drugs that make it this far successfully navigate Phase I trials.

Phase II

Phase II trials are designed to provide evidence for effectiveness—whether the drug provides a benefit against a certain disease or condition. Safety continues to be evaluated, and short-term side effects are also studied. Phase II studies generally last from several months to two years and involve anywhere from a few dozen to several hundred subjects. About one-third of drugs that enter Phase II trials proceed to the next phase.

Phase III

These large-scale studies involve larger groups of participants and generally last from one to five years. Phase III trials gather additional information about safety and effectiveness by studying how the drug affects different populations in different dosages and examining how it interacts with other drugs. Roughly 30% of drugs that enter Phase III trials go on to seek FDA approval.

Phase IV

These "post-marketing" studies take place only after the drug being tested has been approved by the FDA. Phase IV trials may be used to evaluate long-term safety and efficacy of the drug, to explore alternate uses for a treatment or its effects on other patient populations.

New Drug Application (NDA)

Before the FDA will consider approving a new drug for marketing in the United States, the sponsor must file a New Drug Application (NDA), a document that tells the entire "life story" of a drug's development. The NDA includes detailed analyses of the results of each preclinical and clinical trial, information about how the drug works and behaves in the body, as well as information about how the drug will be manufactured.

Once a sponsor files an NDA, the FDA has 10 months (six, if the drug is a new compound for the treatment of a very serious illness) to review the application. The FDA may then reject the application outright, return it to the sponsor as incomplete or approve the drug as a treatment for a specific condition.

Sources: FDA, PhRMA, WebMD.com, AIDSmeds.com, New Mexico AIDS Infonet and AIDSinfo.nih.gov.