

# TYPE OF RESEARCH

## **Stage 1: Preclinical Research**

Once an experimental drug is discovered, research is conducted to help determine its potential for treating or curing an illness. This is called preclinical research. Animal studies are conducted to determine if there are any harmful effects of the drug and to help understand how the drug works. Information from these experiments is submitted to the FDA in an Investigational New Drug (IND). The FDA reviews information in an IND application and decides if it is safe to study in humans.

## **Stage 2: Clinical Research**

In Stage 2, the experimental drug is studied in humans. The studies are known as clinical trials. Clinical trials are carefully designed and controlled experiments in which the experimental drug is administered to patients to test its safety and to determine if it works to treat or cure a specific disease (effectiveness). The professional team that oversees these studies includes the pharmaceutical company, physician investigators, regulatory authorities, and committees that review the safety and ethics of the clinical trial. These groups are involved to preserve the integrity and safety of the clinical trials. The pharmaceutical companies that sponsor experimental drugs devote a great amount of time to clinical testing. Stage 2 is the most complex part of the drug approval process because of the numerous clinical trials involved and the high level of detail that is documented by the company. The four general phases of clinical research are described below.

### ***Phase 1***

The studies in Phase 1 of clinical research are generally conducted with healthy volunteers who are not taking other medicines; patients with the illness the drug will treat are not intended to be tested at this stage. Ultimately, Phase 1 studies will show how the experimental drug affects the body of a healthy individual. Phase 1 consists of a series of small studies consisting of "tens" of volunteers. Tests are done on each volunteer throughout the study to see how the person's body processes, responds to, and is affected by, the drug. Both low doses and high doses of the drug are usually studied. As a result, by the end of Phase 1, the safe dosage range in volunteers may be known. This information will determine whether the drug proceeds to Phase 2.

### ***Phase 2***

The goal of Phase 2 is to understand how the experimental drug affects people who have the disease to be treated. Phase 2 usually consists of a limited number of studies that help determine the drug's short-term safety, side effects, and general effectiveness. The studies in Phase 2 are in most cases controlled investigations, meaning they involve a comparison between the new experimental drug and a sugar pill (placebo), or perhaps between the new drug and an existing drug. This comparison helps to minimize bias in interpreting the trials. Information gathered in Phase 2 studies will determine whether the drug proceeds to Phase 3.

### ***Phase 3***

Phase 3 consists of numerous clinical trials that are used to more fully investigate the nature of the drug. These trials are different than the Phase 2 trials because a larger number of patients are studied (sometimes in the thousands) and because the studies are usually of longer duration than Phase 2 studies. Another difference is the type of patients included. Phase 3 studies can include patients who have more than one illness and are taking medications in addition to the experimental drug used in the study. Therefore, the patients in Phase 3 studies more closely reflect the general population. The information from Phase 3 forms the basis for most of the drug's initial labeling, which will guide physicians on how to use the drug.

### ***Phase 4***

Phase 4 studies are conducted after a drug is approved. Companies often conduct Phase 4 studies to more fully understand how their drug compares to other drugs. Also, the FDA may require additional studies after the drug is approved. FDA-required Phase 4 studies often investigate the drug in specific types of patients that may not have been included in the Phase 3 studies. FDA-required Phase 4 studies can also involve very large numbers of patients to further assess the drug's safety.

## **Stage 3: FDA Review and Approval**

After Phase 3, the pharmaceutical company prepares reports of all studies conducted on the drug, and submits the reports to the

FDA in a New Drug Application (NDA). The FDA then reviews the information in the NDA to determine if the drug is safe and effective for its intended use. Occasionally, the FDA will ask experts for their opinion of the drug; this occurs at Advisory Committee Meetings. These meetings are usually open to the public. If the FDA determines that the drug is safe and effective, the drug will be approved.

#### **Stage 4: Marketing**

After the FDA has approved the experimental drug, the pharmaceutical company can make it available to physicians and their patients. This is the "marketing" phase of the drug. However, research can continue. A company may also conduct research to discover new uses for the drug. Each time a new use for a drug is discovered, the drug is once again subject to the entire FDA approval process before it can be marketed for that purpose.

This process of research, testing, review, and approval helps to ensure that drugs marketed in the United States are safe and effective. Similar systems around the world provide the same assurances. There is also a process to monitor for adverse events. As a result, people everywhere can enjoy the health benefits of modern science rather than the "hit or miss" methods of old.