

RESEARCH NOTE**● New Drug Development—
How Are New Drugs Tested**

What happens when you or a family member is seriously ill? If you're lucky, a drug is available to treat the illness or disease. A streamlined Food and Drug Administration approval process now allows new drugs that offer the promise of saving lives to reach the market faster.

Drug Studies Include Four Phases

Before a new drug can be sold, its sponsor—a pharmaceutical company, a research organization, or a public or private agency—must first conduct studies to show that the drug is safe and effective. The results of these studies are submitted to the Food and Drug Administration (FDA) for approval. If the FDA determines that the drug is both safe and effective, the drug may then be approved for sale. The FDA currently requires drugs to be tested in four phases, each designed to answer specific questions about the drug.

Is the drug safe to use on humans? During Phase I, investigators seek to answer questions about how the drug is absorbed and excreted by the body and seek to discover what effects (including short-term side effects) various doses of the drug have on the body. Investigators also determine the minimum effective dosage, the amount of the drug that is effective yet does not produce undesirable side effects. Phase I testing involves only a few individuals, usually healthy volunteers.

Does the drug work? If Phase I testing does not reveal unacceptable safety problems, Phase II testing can begin. Investigators look to see if the drug is effective in treating the disease or condition for which it is intended.

Researchers also seek to discover if the drug has short-term side effects. These side effects may be very harmful, so it is important to know exactly what they are before many people use the drug.

How effective is the drug? By the time a drug reaches Phase III, researchers have shown that the drug does have a therapeutic effect. Phase III tests involve large numbers of people (usually several hundred individuals) who have the condition against which the drug is effective. These tests measure the extent of the drug's effectiveness and help determine what fraction of the population is helped by the drug. In some cases, Phase III testing may also examine the consequences of long-term use of the drug. After the drug has gained FDA approval, Phase IV studies evaluate the drug's long-term effectiveness. Phase IV studies are sometimes referred to as post-marketing studies. Phase IV studies obtain information from large numbers of individuals who are using the drug as directed by their physicians.

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How Are New Drugs Tested** *continued***Accelerated Studies Speed Drug Availability**

Testing a new drug from Phase I to Phase IV can take more than ten years. When a new drug offers hope to patients with otherwise untreatable, life-threatening diseases, new FDA guidelines can provide access to the drug before it has received full FDA approval. In each case, the benefits of early use must be carefully weighed against the threat of potential dangers, and patients using the drug must be carefully monitored. If the drug is found to be ineffective or dangerous, it can then be removed from the market.

Technique**Experimental Design**

Before a new drug study can begin, the Food and Drug Administration must approve its experimental design. The study must include two groups of individuals: a group that receives the drug and a control group that does not. Instead of taking the medication containing the drug, the control group is instead given a placebo (*pluh SEE boh*). The placebo is identical to the medication in every way except one—it does not contain the drug.

To ensure valid results, drug studies are often conducted as double-blind studies. In a double-blind study, neither the doctors nor the patients know who receives the drug and who receives the placebo. Double-blind studies eliminate bias, the tendency of individuals to lean towards a particular conclusion based upon what they know. The removal of bias reduces the likelihood that a positive drug response could be due solely to a patient's wishful thinking.

Applications: Knowledge of experimental design is required by research scientists in many areas.

Users: Medical researchers, biostatisticians, marketing researchers

Analyzing the Issues**1. Why is it important that a new drug be thoroughly tested?**

Research the use of the drug thalidomide in Europe in the early 1960s. For what purpose was the drug prescribed? What happened when the drug was taken by pregnant women? How do the consequences of thalidomide use support the need for drug testing?

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2. When a new drug is tested, should all test participants be given the drug?

If a potential new drug is known to improve survival, should Phase II tests omit the use of placebos? Use references available in the library or research an on-line database to find information supporting your viewpoint. Write a report summarizing the benefits and drawbacks of using placebos.

3. Are study participants informed of potential risks and benefits?

By law, before individuals can participate in a drug study, they must give their informed consent, indicating that they are willing participants and that they understand the purpose of the study. What facts do you think participants in a new drug study should know before they agree to participate in the study?

4. How does the cost of drug testing influence which drugs are developed?

The Orphan Drug Act passed by the United States Congress in 1983 has helped to ensure that certain drugs will be developed and brought to market. What is an “orphan drug”? How did the Orphan Drug Act encourage pharmaceutical companies to develop orphan drugs?