efficacy. Since 1962, however, newly developed drugs have been extensively tested before being marketed for general use. The drugs are carefully evaluated at each step. Testing usually proceeds if there is evidence of safety and effectiveness but may be stopped at any time for inadequate effectiveness or excessive toxicity. Many potential drugs are discarded and never marketed; some drugs are marketed but later withdrawn, usually because of adverse effects that become evident only when the drug is used in a large, diverse population.

Testing and Clinical Trials

The testing process begins with animal studies to determine potential uses and effects. The next step involves FDA review of the data obtained in the animal studies. The drug then undergoes clinical trials in humans. Most clinical trials use a randomized, controlled experimental design that involves selection of subjects according to established criteria, random assignment of subjects to experimental groups, and administration of the test drug to one group and a control substance to another group.

In Phase I, a few doses are given to a few healthy volunteers to determine safe dosages, routes of administration, absorption, metabolism, excretion, and toxicity. In Phase II, a few doses are given to a few subjects with the disease or symptom for which the drug is being studied, and responses are compared with those of healthy subjects. In Phase III, the drug is given to a larger and more representative group of subjects. In double-blind, placebo-controlled designs, half the subjects receive the new drug and half receive a placebo, with neither subjects nor researchers knowing who receives which formulation. In crossover studies, subjects serve as their own controls; each subject receives the experimental drug during half the study and a placebo during the other half. Other research methods include control studies, in which some clients receive a known drug rather than a placebo, and subject matching, in which clients are paired with others of similar characteristics. Phase III studies help to determine whether the potential benefits of the drug outweigh the risks.

In Phase IV, the FDA evaluates the data from the first three phases for drug safety and effectiveness, allows the drug to be marketed for general use, and requires manufacturers to continue monitoring the drug's effects. Some adverse drug effects may become evident during the postmarketing phase as the drug is more widely used. Several drugs have been withdrawn in recent years, partly or mainly because of the increased postmarketing surveillance. Critics contend that changes enacted to streamline the approval process have allowed unsafe drugs to be marketed; proponents claim that the faster review process helps clients with serious diseases to gain effective treatment more quickly.

The FDA has increased efforts to monitor marketed drugs more closely in recent years, especially for their adverse effects. One such effort involves contracts with some commercial companies that provide access to databases containing information on the actual use of prescription drugs in adults and children. Examples of information include how long nonhospitalized patients stay on prescribed medications, which combinations of medications are being prescribed to patients, and the use of prescription drugs in hospitalized children. Individual patients are not identified in these databases.

Food and Drug Administration Approval

The FDA approves many new drugs annually. In 1992, procedures were changed to accelerate the approval process, especially for drugs used to treat acquired immunodeficiency syndrome. Since then, new drugs are categorized according to their review priority and therapeutic potential. "1P" status indicates a new drug reviewed on a priority basis and with some therapeutic advantages over similar drugs already available; "1S" status indicates standard review and drugs with few, if any, therapeutic advantages (ie, the new drug is similar to one already available). Most newly approved drugs are "1S" prescription drugs.

The FDA also approves drugs for OTC availability, including the transfer of drugs from prescription to OTC status, and may require additional clinical trials to determine safety and effectiveness of OTC use. Numerous drugs have been transferred from prescription to OTC status in recent years and the trend is likely to continue. For drugs taken orally, indications for use may be different, and recommended doses are usually lower for the OTC formulation. For example, for OTC ibuprofen, which is available under its generic and several trade names (eg, Advil) in 200-mg tablets and used for pain, fever, and dysmenorrhea, the recommended dose is usually 200 to 400 mg three or four times daily. With prescription ibuprofen, Motrin is the common trade name and dosage may be 400, 600, or 800 mg three or four times daily.

FDA approval of a drug for OTC availability involves evaluation of evidence that the consumer can use the drug safely, using information on the product label, and shifts primary responsibility for safe and effective drug therapy from health care professionals to consumers. With prescription drugs, a health care professional diagnoses the condition, often with the help of laboratory and other diagnostic tests, and determines a need for the drug. With OTC drugs, the client must make these decisions, with or without consultation with a health care provider. Questions to be answered include the following:

1. Can consumers accurately self-diagnose the condition for which a drug is indicated?
2. Can consumers read and understand the label well enough to determine the dosage, interpret warnings and contraindications and determine whether they apply, and recognize drugs already being taken that might interact adversely with the drug being considered?