Chapter 51 - What are the regulatory requirements for medication approval?
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The legal standards for new medication approval, as enacted by Congress, have evolved over the past 100 years. Congress gave the FDA the authority to determine which new medications can be marketed. Through regulations, the FDA established three basic elements or hurdles necessary for the approval of new medications: safety, efficacy (sometimes referred to as effectiveness), and quality (see Chapters 48, 47 and 57).

**What are the requirements for approval in the U.S.?**
The first hurdle in the approval process is safety. Safety is determined over a medication’s life from the time of discovery and throughout its use after approval by perhaps millions of patients. Before a new medication is allowed to be given to human subjects, animal experiments must be conducted and the FDA must decide whether the medication is safe enough to test in people. The initial human studies focus on safety. If these initial studies are successful, larger studies are conducted to assess the medication’s safety and effectiveness. After a new medication is approved and then marketed to the public, safety continues to be monitored through an FDA program of post-marketing safety surveillance (see Chapter 48).

The second hurdle is efficacy, or effectiveness. The standards require a manufacturer seeking marketing approval to provide the FDA with substantial evidence of effectiveness in the form of high quality clinical trials. These trials should prove that the medication will do what the manufacturer says it will do. Typically, two high quality clinical trials show that the medication works. Replication of clinical trial results is an important scientific standard. Nothing in the FDA’s approval standards require a new medication to be more effective or safer than other products already on the market. Often new medications are approved only because they are more effective than an inactive placebo medication (see Chapter 27).

The third hurdle for approval is a guarantee that the medication is produced to high quality standards that ensure content quality, performance, and stability. The FDA deems a new medication to be safe and effective when these three requirements are met. The phrase “safe and effective” has
a regulatory definition meaning the benefits of the new medication outweigh its potential harms. This phrase does not mean that a new medication is 100 percent safe, nor does it mean it is always effective for every patient.

**Why are requirements for drug product quality so stringent?**
Medication product quality, safety and effectiveness are inseparable. For a medication to be deemed safe and effective by the FDA, the agency must be sure that consumers and prescribers will see the same effect from a medication from lot to lot and batch to batch. A medication containing too much of the active ingredient can result in an overdose. Likewise, a medication with too little of the active ingredient can be dangerous because the product is not potent enough to work properly. Natural health products, dietary supplements, and products produced or compounded by pharmacists are not inspected by the FDA and may have special risks because product quality is unknown.

**How extensive is the required documentation for a new medication?**
The documentation for safety, efficacy, and quality is voluminous, as the file may include more than 100,000 pages. Often, eight to 12 years can pass from identification of a promising chemical to FDA approval, meaning the medication does not reach the market until half of the 20-year patent period has passed.

The estimated cost of taking a medication to market has been said to be around $1 billion. This figure is derived from self-reporting by a small number of manufacturers and has not been independently verified. The amount includes costs for compounds that did not make it and the so-called “capitalized cost,” which is the projected income if the money for development had been invested in the equity market.

**What are the requirements for approval of generic medications?**
The manufacturer of a generic drug must show the FDA that the generic has exactly the same active ingredient as the brand-name product. The generic medication must be the same dosage form (tablet or capsule), the same strength and route of administration, and be approved for the same use or uses as the brand-name medication. The generic manufacturer also must show the FDA that the rate and extent of absorption of the active ingredient of the generic falls within defined limits when compared to the brand-name medication. For example, these limits for an immediate release tablet or capsule must fall within a range of 80 percent to 125 percent of the brand-name product.

Generic medication manufacturers must comply with the same manufacturing standards required for brand-name products to ensure a consistent effect from lot to lot and batch to batch.
Key messages

✔ Prescription drugs are among the most regulated products in the U.S.
✔ Approved drugs must be safe and effective for their intended use.
✔ The FDA requirements for drug quality are very stringent.
✔ The documentation for approval of a new drug is extensive and costly.