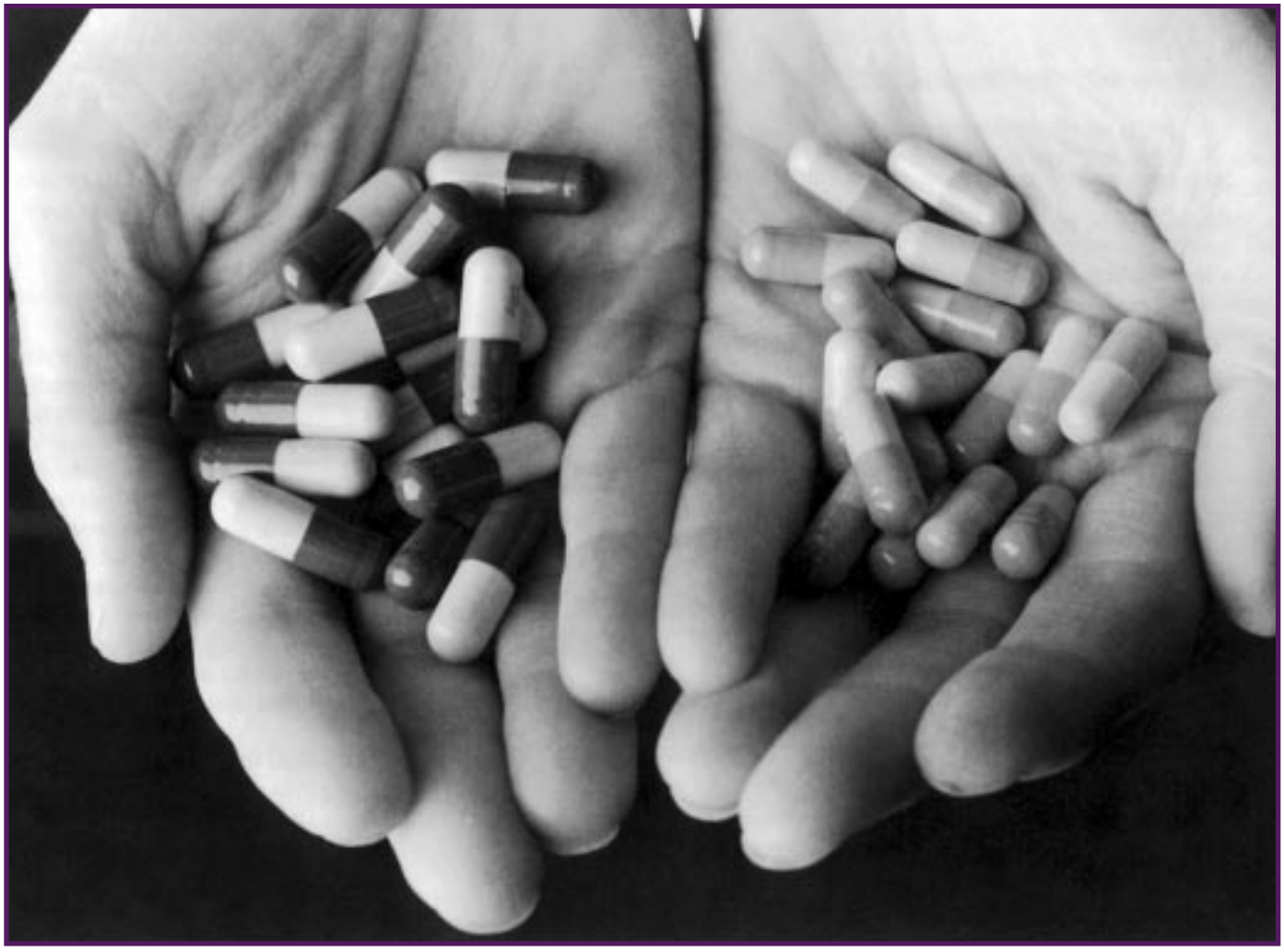
FDA Ensures
Equivalence of Generic Drugs

Drug products sold in the United States are approved by the FDA whether they are brand name or generic. "Most people believe that if something costs more, it has to be better quality. In the case of generic drugs, this is not true," says Gary Buehler, Director of FDA's Office of Generic Drugs. "The standards for quality are the same for brand name and generic products."



Despite the strict standards imposed by the FDA for approval of generic drugs, and their enforcement of these standards, a number of misconceptions about generic drugs persist (See "Myths and Facts about Generics" to the right).

New drugs, like other new products, are developed under patent protection. The patent protects the investment in the drug's development by giving the company the sole right to sell the drug while the patent is in effect. When patents or other periods of exclusivity on brand-name drugs are near expiration, manufacturers can apply to the FDA to sell generic versions.

"Much of FDA's review of generic drugs and brand name drugs is the same," Buehler explains (See "Same FDA Requirements for Brand-Name and Generic Drugs" below). There are eight major parts to the FDA's review of a firm's application to sell a generic drug:

- There must be an FDA-approved brand-name drug that is the reference for the proposed generic. The generic must have the same active ingredient or ingredients and the same labeled strength as this reference product. It must have the same dosage form—tablets, patches and liquids are examples of dosage forms. It must be administered the same way, for example, swallowed as a pill or given as an injection.
- The manufacturer must show the generic drug is "bioequivalent" to the brand-name drug (See "What Is Bioequivalence?" below).
- The generic drug's labeling must be essentially the same as that of the approved drug.
- The firm must fully document the generic drug's chemistry, manufacturing steps, and quality control measures. Each step of the process must be detailed for FDA review.

Same FDA Requirements for Brand-Name and Generic Drugs

	Brand-Name Drug	Generic Drug
For reformulations of a brand-name drug or generic versions of a drug, FDA reviews data showing the drug is bioequivalent to the one used in the original safety and efficacy testing.	✔	✔
FDA evaluates the manufacturer's adherence to good manufacturing practices before the drug is marketed.	✔	✔
FDA reviews the active and inactive ingredients used in the formulation before the drug is marketed.	✔	✔
FDA reviews the actual drug product.	✔	✔
FDA reviews the drug's labeling.	✔	✔
Manufacturer must seek FDA approval before making major manufacturing changes or reformulating the drug.	✔	✔
Manufacturer must report adverse reactions and serious adverse health effects to the FDA.	✔	✔
FDA periodically inspects manufacturing plants.	✔	✔
FDA monitors drug quality after approval.	✔	✔

Myths and Facts about Generic Drugs

MYTH: *Generics take longer to act in the body.*

FACT: The firm seeking to sell a generic drug must show that its drug delivers the same amount of active ingredient in the same timeframe as the original product.

MYTH: *Generics are not as potent as brand-name drugs.*

FACT: FDA requires generics to have the same quality, strength, purity, and stability as brand-name drugs.

MYTH: *Generics are not as safe as brand-name drugs.*

FACT: FDA requires that all drugs be safe and effective and that their benefits outweigh their risks. Since generics use the same active ingredients and are shown to work the same way in the body, they have the same risk-benefit profile as their brand-name counterparts.

MYTH: *Brand-name drugs are made in modern manufacturing facilities, and generics are often made in substandard facilities.*

FACT: FDA won't permit drugs to be made in substandard facilities. FDA conducts about 3,500 inspections a year in all firms to ensure standards are met. Generic firms have facilities comparable to those of brand-name firms. In fact, brand-name firms account for an estimated 50 percent of generic drug production. They frequently make copies of their own or other brand-name drugs but sell them without the brand name.

MYTH: *Generic drugs are likely to cause more side effects.*

FACT: There is no evidence of this. FDA monitors reports of adverse drug reactions and has found no difference in the rates between generic and brand-name drugs.

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- The firm must assure the FDA that the raw materials and the finished product meet USP specifications, if these have been set. The USP, or U.S. Pharmacopoeia, is the non-profit, scientific body chartered by Congress to set standards for drug purity in this country.
- The firm must show that its generic drug maintains stability as labeled before it can be sold. Once on the market, the firm must continue to monitor the drug's stability. The firm must show that the container and its closure system won't interact with the drug. Firms making sterile drugs must submit sterility assurance data showing microbiologic integrity of these products.
- The firm must provide a full description of the facilities it uses to manufacture, process, test, package, label and control the drug. It must certify that it complies with federal regulations about current good manufacturing practices and undergo FDA inspection of the manufacturing facility to assure compliance.
- Before FDA approves a generic drug, it usually conducts an inspection at the proposed manufacturing site to make sure the firm is capable of meeting its application commitments and to ensure the firm can manufacture the product consistently.

"Generic competition helps keep the cost of drugs down," Buehler says. "It also encourages the research based drug companies to keep finding newer and better medicines that have patent protection."

When retired federal auditor Stuart Addison went to the pharmacy, he had the pharmacist fill his prescriptions with generic drugs. "My motivation is to keep the prices down," Addison said, noting that his insurance plan helped pay for his prescriptions. "My pocketbook isn't directly affected; but, in the long run, I'm helping to keep insurance premiums down." Generic drugs save consumers an estimated $8 to $10 billion a year at retail pharmacies (according to the Congressional Budget Office). Even more billions are saved when hospitals use generics.

"FDA-approved generic drugs are bioequivalent and therapeutically equivalent to their brand-name counterparts," says Buehler. "People can use them with total confidence."

What Is Bioequivalence?

Generics are not required to replicate the extensive clinical trials that have already been used in the development of the original, brand-name drug. These tests usually involve a few hundred to a few thousand patients. Since the safety and efficacy of the brand-name product has already been well established in clinical testing and frequently many years of patient use, it is scientifically unnecessary, and would be unethical, to require that such extensive testing be repeated in human subjects for each generic drug that a firm wishes to market. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent (i.e., performs in the same manner) to the pioneer drug.

One way scientists demonstrate bioequivalence is to measure the time it takes the generic drug to reach the bloodstream and its concentration in the bloodstream in 24 to 36 healthy, normal volunteers. This gives them the rate and extent of absorption—or bioavailability—of the generic drug, which they then compare to that of the pioneer drug. The generic version must deliver the same amount of active ingredients into a patient's bloodstream in the same amount of time as the pioneer drug.

Using bioequivalence as the basis for approving generic copies of drug products was established by the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act. Brand-name drugs are subject to the same bioequivalency tests as generics when their manufacturers reformulate them.

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