



# Continuing Education



## Regulatory basics

### Learning Objectives

**Explain** the difference between prescription and nonprescription medicines, and describe the impact of generics on the pharmaceutical industry.

**Describe** key pharmaceutical legislation enacted from 1900 through the 1950s.

**Describe** key pharmaceutical legislation enacted in the 1960s and 1970s.

**Describe** key pharmaceutical legislation enacted from the 1980s through the present.

**Describe** the major elements of the PhRMA marketing code and other PhRMA-sanctioned policies.

This first article in a three-part series explains the difference between prescription and non-prescription medicines and discusses the impact of generics on the pharmaceutical industry. It also describes key pharmaceutical regulatory legislation from 1900 to the present and the major elements of the PhRMA marketing code and other PhRMA-sanctioned policies.

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**T**oday's pharmaceutical industry has been shaped by classifications and legislative measures that have evolved over the last century. The term "medicine," whether referring to a prescription or nonprescription substance, is strictly and legally defined by the Food and Drug Administration (FDA).

Prescription medicines are pharmaceutical products the FDA considers to be hypnotic or habit-forming, to have potentially harmful or toxic effects, or to be unsafe for use except under the supervision of a legally licensed prescriber (usually a physician). These medicines are legally dispensed only by pharmacists or others licensed to dispense.

Nonprescription medicines, or over-the-counter (OTC) medicines, are considered safe for self-medication and can be used without the supervision of a physician or other professional. Nonprescription product labels must conform with FDA advisory panel recommendations or proposed monograph statements.

These products may be purchased without need for a prescription. In recent years, the OTC market has grown largely because several important drugs have been changed from prescription to nonprescription status.

**Rise of generics.** A new drug usually receives three names: a chemical name (based on its structure), a generic or nonproprietary name and a trade, proprietary, or brand name (related to a specific pharmaceutical company). Very early in the life of an experimental product, the company usually obtains a patent, which is an exclusive license to produce and market its product. After the patent expires (20 years from the earliest filing date), other companies may also produce and market the product under either the generic name or different brand names.

Generics are making major inroads into the pharmaceutical industry. One major reason is that many states have enacted drug product selection laws allowing pharmacists to dispense generic equivalents of brand-name prescriptions

## RECEIVE CREDIT AND RECOGNITION

Continuing Education in *Pharmaceutical Representative* aims to provide reps with information to help them meet the needs of the people they serve and to contribute to reps' personal and professional development. Every third issue includes a self-assessment quiz covering the previous three Continuing Education articles. The quiz for this article will appear in the March issue. Reps who correctly complete the quiz and return it to the CMR Institute with a nominal handling fee will receive a completion-recognition form showing that they have successfully completed the three-part educational series and earned .25 CEU (2.5 contact hours). The CMR Institute also will send a letter of recognition to reps' managers upon completion of a quarterly series. A Certificate of Achievement will be awarded to any representative who successfully completes four quizzes or has obtained 1.0 CEU.

**Note:** The Continuing Education quizzes are not part of CMR Institute's certification program and do not count as credits toward the CMR® designation.

### About the CMR Institute:

The Certified Medical Representatives Institute is an independent non-profit educational organization established in 1966 to provide a source of professional development and certification for pharmaceutical representatives. The Institute provides an up-to-date, approved continuing education curriculum designed to expand and enhance internal company training and development in a cost-effective manner. The curriculum concentrates on providing a general knowledge base and avoids such areas as selling skills and specific product education.

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unless the prescribing physician forbids such a substitution.

The makers of brand-name drugs have devised a number of strategies to protect their market share in the face of the booming generics industry, including:

- Developing a distinctive or innovative dosage form or drug delivery method
- Developing a new salt, or ester, which may have advantages over the original form
- Obtaining a patent on a component chemical or manufacturing method
- Emphasizing bioavailability differences between their products and generics
- Acquiring or starting generics divisions
- Taking drugs to over-the-counter status themselves

## Regulations: 1900 through the 1950s

The FDA and state and federal legislatures have created numerous laws and regulations to ensure that pharmaceutical products entering the United States market are safe and effective. In addition, the pharmaceutical industry itself has developed guidelines to govern production and marketing. The following key pieces of legislation have helped to regulate the pharmaceutical industry:

**Pure Food and Drug Act and the origin of the FDA.** In 1906, Congress enacted this first federal law governing the adulteration and misbranding of food and drug products. This act banned the shipment of adulterated drugs in interstate commerce and formally recognized the U.S. Pharmacopeia and the National Formulary as official compendia establishing legal drug standards. It also forbade false and misleading claims (misbranding) about a drug's identity. The FDA was created in 1927 to oversee this law.

**Federal Food, Drug, and Cosmetic Act.** This act, passed in 1938, was designed specifically to protect the public from untested and potentially harmful drugs. It identified prohibited acts—including the introduction into interstate commerce of any adulterated or misbranded food, drug or cosmetic—and established some procedures for the premarketing clearance of new drugs. This law also defined relatively strict civil and criminal penalties for violations, including product seizures, fines and imprisonment. With amendments, the 1938 act is our current law. The Federal Trade Commission administers its drug advertising provisions, while FDA oversees the product safety and drug-labeling requirements.

**Durham-Humphrey Amendment.** This 1951 amendment to the Federal Food, Drug, and Cosmetic Act provided for the classification of two types of drugs: prescription and nonprescription. Hypnotic or habit-forming drugs, drugs with potentially

harmful or toxic effects and new drugs not proven safe for self-medication were classified as prescription medicines. They were to be dispensed only by state-licensed pharmacists upon the receipt of oral or written prescriptions from practitioners licensed to prescribe. The manufacturer's label on the original container had to bear legends or inscriptions warning, "Caution: Federal law prohibits dispensing without a prescription"; hence, they became known as "legend" drugs. Drugs not labeled with the legend were considered to be safe for use without physician supervision and could be sold over the counter without a prescription.

## Regulations: 1960s and 1970s

**Harris-Kefauver Amendments.** Passed in 1962, these amendments added a proof-of-efficacy mandate to the 1938 law and allowed FDA to specify detailed testing procedures that all companies were to follow to produce acceptable product safety and efficacy information. The Harris-Kefauver Amendments have had both positive and negative effects on the U.S. pharmaceutical industry. On the positive side, the amendments reduce the risk of unsafe or ineffective medicines reaching the

## Costs associated with compliance to the Harris-Kefauver Amendments have indirectly led to increased consolidation

marketplace. On the downside, the extensive testing requirements initially sharply reduced the annual number of new molecular entity introductions. The increased costs associated with compliance to these amendments have also led, indirectly, to increased consolidation in the pharmaceutical industry. Several very large companies dominate the market because most small companies cannot handle the high costs of R&D.

**Drug Abuse Prevention and Control Act.** In 1970, Congress passed this act to establish federal registration procedures for regulating the manufacture, distribution and dispersion of narcotics, barbiturates, amphetamines and other habit-forming substances. In 1973, the responsibility for enforcing this act fell under the newly created Drug Enforcement Administration.

The drugs controlled by this law (frequently referred to as "controlled substances") have been divided into five categories, ranging from Schedule I drugs (high potential for abuse, no currently accepted medical use and a lack of accepted safety) to Schedule V drugs (relatively low potential for abuse and development of dependence and legitimate

medical use).

**FDA OTC Drug Review.** In 1972, FDA initiated a review of the ingredients of all nonprescription medicines on the market to establish uniform standards for safety, efficacy and labeling. As a result, the FDA placed drugs in one of three categories and then issued ingredient and labeling requirements for each category.

Category I drugs were generally recognized as safe and effective, and Category II drugs were declared to be unsafe or ineffective and were removed from the market. Category III drugs required more study before their safety and efficacy could be determined, and they were allowed to stay on the market until the question was settled. Also during the OTC review, certain prescription products become nonprescription products.

### Regulations: 1980s through the Present

**Orphan Drug Amendment of 1983.** Potentially useful drugs sometimes remain undeveloped because their market is not considered large enough for a manufacturer to risk the excessive cost associated with research and development. This legislation provides developers of small market or “orphan” drugs with tax incentives, grants and patent protection privileges.

**The Hatch-Waxman Act of 1984.** This act eliminated many duplicate testing procedures previously

required of generic drug companies. It mandates that generics manufacturers file Abbreviated New Drug Applications (ANDAs) and provide data proving that their products are bioequivalent to corresponding brand-name drugs.

**Health Insurance Portability and Accountability Act of 1996.** HIPAA was passed in response to two social pressures:

- The desire for uninterrupted health insurance coverage for workers changing jobs
- A growing concern among consumers about the amount, quality and accessibility of private data in a patient’s medical records

HIPAA required the establishment of national standards for electronic healthcare transactions and measures to ensure patient privacy. Healthcare providers and pharmaceutical researchers are legally required to document that patients have been informed of their privacy rights, how their data will be used and with whom it will be shared. This law has implications for the pharmaceutical industry, since patient data is a rich source for retrospective research that could improve care, control costs and increase sales.

**Food and Drug Administration Modernization Act.** Enacted in 1997, this act is of major importance to pharmaceutical manufacturers in terms of how they conduct clinical research and file New Drug Applications (NDAs), and in terms of what healthcare representatives can say and do. It includes

## Drug Abuse Prevention and Control Act Drug categories

Categories	Potential for abuse and medical use	Examples
Schedule I	High potential for abuse; have no currently accepted medical use in the United States	LSD, heroin, marijuana, mescaline, peyote, psilocybin
Schedule II	High potential for abuse; have a currently accepted medical use in the United States; abuse may lead to severe psychological or physical dependence	Morphine, methadone, meperidine, amphetamines, secobarbital
Schedule III	Less potential for abuse than Schedule I or II drugs; have a currently accepted medical use in the United States; abuse may lead to moderate or low physical dependence or high psychological dependence	Codeine, camphorated tincture of opium, barbituric acid, glutethimide, methyprylon, ethylmorphine, dihydrocodeine
Schedule IV	Low potential for abuse relative to Schedule III drugs; have a currently accepted medical use; abuse may lead to limited physical or psychological dependence relative to Schedule III drugs	Barbital, chloral betaine, chloral hydrate, paraldehyde, phenobarbital, chlordiazepoxide, diazepam
Schedule V	Low potential for abuse relative to Schedule IV drugs; have a currently accepted medical use; abuse may lead to limited physical or psychological dependence relative to Schedule IV drugs	Elixir terpin hydrate, other cough suppressants

important initiatives relating to prescription drug user fees, off-label uses, drug economics, pharmacy compounding, risk-based regulation of medical devices, food safety and labeling, and standards for medical products.

Of significance to healthcare representatives are the initiatives to establish parameters for distributing sound and balanced information about “off-label uses” for marketed drugs, biologics and medical devices, and regulation of pharmaco-economic information in promotional material.

**Medicare Prescription Drug, Improvement and Modernization Act Of 2003.** This act established prescription drug coverage for Medicare beneficiaries, referred to as Medicare Part D. Medicare participants who want drug coverage must be enrolled in one of Medicare’s managed care plans (Medicare Advantage) that includes prescription drug coverage, or they must enroll in a prescription drug plan offered by a private insurer. These plans must be approved by Medicare and follow guidelines related to the development and conduct of formularies, pharmacy access, medication therapy management programs for patients with chronic diseases or who incur very high drug costs, and limits regarding premiums, deductibles, coinsurance and copayments. Under the MMA, negotiations with manufacturers over the cost of drug products are conducted not by the government but by the private insurers who provide the coverage.

## Industry controls

Pharmaceutical companies, individually and collectively (through trade organizations), have instituted many voluntary policies and guidelines for drug manufacturing, sales and marketing and distribution.

The Pharmaceutical Research and Manufacturers of America (PhRMA) adopted a nine-point marketing code that governs the pharmaceutical industry’s relationships with physicians and other healthcare professionals. This voluntary code emphasizes that the interactions of sales representatives with healthcare professionals should always focus on informing healthcare professionals about products, providing scientific and educational information, and supporting medical research and education.

The code allows industry representatives and others to provide occasional modest meals (but no entertainment/recreational events) in healthcare professionals’ offices in conjunction with informational presentations that provide scientific and educational benefits. Other parts of the code advise healthcare representatives that:

- Token consulting or advisory arrangements should not be used to justify compensating healthcare professionals for their time or their

## Article Summary

- The term “medicine,” whether referring to a prescription or nonprescription substance, is strictly and legally defined by the Food and Drug Administration (FDA).
- The FDA and state and federal legislatures have created numerous laws and regulations to ensure that pharmaceutical products entering the United States market are safe and effective.
- Pharmaceutical companies, individually and collectively (through trade organizations), have instituted many voluntary policies and guidelines for drug manufacturing, marketing and distribution.

travel, lodging or other out-of-pocket expenses.

- Items primarily for the benefit of patients (e.g., anatomical model for use in an exam room) may be offered to healthcare professionals if they are not of substantial value (\$100 or less).
- Noneducational items (such as pens, mugs and other “reminder” objects typically adorned with a company or product logo) are prohibited from being offered to healthcare providers and their staff.
- No grants, scholarships, subsidies, support, consulting contracts, or educational or practice-related items should be provided or offered to a healthcare professional in exchange for prescribing products or for a commitment to continue prescribing products.

In addition, member companies of PhRMA agree with and support the following practices and policies:

- Prohibiting the award of prizes, premiums and other valuable items to healthcare personnel as incentives or rewards for prescribing or dispensing certain medical products
- Requiring that samples of prescription products be distributed on written request only, with detailed recordkeeping and accountability
- Requiring appropriate documentation regarding bioavailability, bioequivalence and therapeutic equivalence
- Requiring that the name of the manufacturer appear on every prescription product label when it differs from that of the distributor
- Requiring expiration dates on all prescription drug products
- Voluntary inclusion of inactive ingredients in package labeling

The next article in the series will focus on the development and distribution of pharmaceutical products.