chapter 1

Drug Definitions, Standards, and Information Sources

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Objectives

1. Define *pharmacology*.
2. Differentiate among the chemical, generic, and brand names of drugs.

Key Terms

pharmacology (făr-mă-KŎL-ŏ-jē) (p. 1)
therapeutic methods (thĕr-ă-PYŪ-tĭk MĔTH-ĕdz) (p. 1)
drugs (p. 1)
chemical name (KĔM-ĭ-kŭl) (p. 1)
generic name (jĕ-NĂR-ĭk) (p. 1)
brand name (p. 1)
over-the-counter (OTC) drugs (p. 2)
illegal drugs (ĭl-LĒ-gŭl) (p. 2)

Pharmacology (from the Greek *pharmakon*, meaning "drugs," and *logos*, meaning "science") deals with the study of drugs and their actions on living organisms. Diseases that cause illness may be treated in several different ways, which are referred to as *therapies*. The various approaches to therapy are called *therapeutic methods*. Examples of therapeutic methods include the following:

- Drug therapy: treatment with drugs
- Diet therapy: treatment with diet (e.g., a low-salt diet for patients with cardiovascular disease)
- Physiotherapy: treatment with natural physical forces (e.g., water, light, heat)
- Psychological therapy: the identification of stressors and methods that can be used to reduce or eliminate stress

Most illnesses caused by diseases require a combination of therapeutic methods for successful treatment.

Drugs (from the Dutch *droog*, meaning "dry") are chemical substances that have an effect on living organisms. Therapeutic drugs, which are often called *medicines*, are those drugs that are used for the prevention or treatment of diseases. Up until the early to mid twentieth century, dried plants were the most abundant source of medicines; thus, the word *drug* was applied to them.

DRUG NAMES, CLASSIFICATIONS, STANDARDS, LEGISLATION, AND DEVELOPMENT IN THE UNITED STATES

DRUG NAMES

All drugs have several names, which may cause confusion. When administering the prescribed drug, the spelling on the drug package must correspond exactly with the spelling of the drug ordered to ensure that the proper medicine is administered.

Each drug has three names: (1) a *chemical* name; (2) a *generic* name; and (3) a *brand* name. The chemical name is most meaningful to the chemist. By means of the chemical name, the chemist understands the exact chemical constitution of the drug as well as the exact placement of its atoms or molecular groupings.

Before a drug becomes official, it is given a generic name or common name. The generic name is simpler than the chemical name. It may be used in any country and by any manufacturer. The first letter of the generic name is not capitalized. Students are strongly encouraged to learn and refer to drugs by their generic names, because formularies (i.e., lists of medicines available through a pharmacy) are maintained by generic names. When a therapeutically equivalent drug becomes available in generic form, the generic medicine is routinely substituted for the brand-name medicine.

Generic names are provided by the U.S. Adopted Names Council, which is an organization sponsored by the U.S. Pharmacopeial Convention, the American Medical Association, and the American Pharmacists Association. The official name, which is virtually always the generic name in the United States, is the name under which the drug is listed by the U.S. Food and Drug Administration (FDA). The FDA is empowered by federal law to name the drugs for human use in the United States.

A trademark or brand name is followed by the symbol ®. This symbol indicates that the name is registered and that the use of the name is restricted to the owner of the drug, which is usually the manufacturer. Most drug companies place their products on the

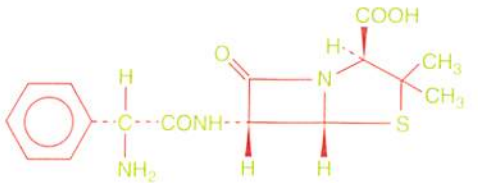

FIGURE 1-1 Ampicillin, an antibiotic.

market under brand names rather than generic names. The brand names are deliberately made easier to pronounce, spell, and remember. The first letter of the brand name is capitalized.

EXAMPLE: See Figure 1-1.

Chemical name: 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxy-lic acid, 6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-, [2S-[2α,-5α,6β(S*)]]-

Generic name: ampicillin

Brand names: Principen, Polycillin

DRUG CLASSIFICATIONS

Drugs may be classified by a variety of methods according to:

1. The *Body system* that they affect (e.g., the central nervous system, the cardiovascular system, the gastrointestinal system)
2. Their *Therapeutic use* or *clinical indications* (e.g., antacids, antibiotics, antihypertensives, diuretics, laxatives)
3. Their *Physiologic* or *chemical action* (e.g., anticholinergics, beta-adrenergic blockers, calcium channel blockers, cholinergics)

Drugs may be further classified as *prescription* or *nonprescription*. Prescription drugs require an order by a health professional who is licensed to prescribe drugs, such as a physician, a nurse practitioner, a physician assistant, a pharmacist, or a dentist. Nonprescription or **over-the-counter (OTC) drugs** are sold without a prescription in a pharmacy or in the health section of department or grocery stores. **Illegal drugs,** which are sometimes referred to as *recreational drugs,* are drugs or chemical substances used for nontherapeutic purposes. These substances are obtained illegally or have not received approval for use by the FDA. See Chapter 49 for further information about substance abuse.

SOURCES OF DRUG INFORMATION

Objectives

3. List official sources of drug standards in the United States.
4. List literature resources for researching prescription and nonprescription drugs.
5. Cite sources of credible drug information on the Internet.

Drug products made by different manufacturers or in different batches by the same manufacturer must be uniformly pure and potent. The United States Pharmacopeial Convention is a nongovernment organization that promotes public health by establishing state-of-the-art standards to ensure the quality of medicines and other health care technologies. These standards are developed by a unique process of public involvement, and they are accepted worldwide. The Convention publishes a single volume text, the *United States Pharmacopeia (USP)/National Formulary (NF),* which is revised annually. The primary purpose of this volume is to provide standards for the identity, quality, strength, and purity of substances used in the practice of health care. The standards described in the USP/NF are enforced by the FDA as the official standards for the manufacture and quality control of medicines and nutritional supplements produced in the United States. The USP/NF is also recognized by the Canadian Food and Drugs Act as an authoritative source of drug standards in Canada.

Table 1-1 lists and describes the common sources of drug information available for the professional health care provider; additional resources are described in the following sections.

PACKAGE INSERTS

Manufacturers of drugs have to develop a comprehensive but concise description of the drug, indications and precautions for clinical use, recommendations for dosage, known adverse reactions, contraindications, and other pharmacologic information relating to the drug. Federal law requires that this material be approved by the FDA before the product is released for marketing and that it be presented on an insert that accompanies each package of the product.

In 2006, the FDA adopted a new format for package inserts to help reduce medication errors and to improve patient education. The new labeling reduces practitioners' time looking for information, decreases the number of preventable medical errors, and improves treatment effectiveness and patient education. Because these labeling revisions represent considerable effort and are most critical for newer and less familiar drugs, the program applies only to relatively new prescription drug products.

Clinical Goldmine

DailyMed (see Online Resources on p. 10), which is sponsored by the National Library of Medicine, provides a database for new package inserts that is searchable by product name, indications, dosage and administration, warnings, description of drug product, active and inactive ingredients, and how the drug is supplied. See the section on p. 4 that discusses electronic databases.

Table 1-1 Sources of Drug Information for Health Care Providers

SOURCES OF DRUG INFORMATION	DESCRIPTION
USP Dictionary of United States Adopted Names (USAN) and International Drug Names	Published annually Compilation of more than 10,000 drug names Describes the criteria by which drugs are named Online version available
American Drug Index	Index of medicines available in the United States Useful for quickly comparing brand names and generic names and for checking available strengths and dosage forms
American Hospital Formulary Service, Drug Information	Contains monographs about virtually every single-entity drug available in the United States Describes therapeutic uses of drugs, including approved and unapproved uses Online version available
Drug Interaction Facts	Currently considered the most comprehensive book available about drug interactions
Drug Facts and Comparisons	Contains drug monographs that describe all drugs in a therapeutic class Monographs are formatted as tables to allow comparison of similar products, brand names, manufacturers, cost indices, and available dosage forms Online version available
ASHP's Handbook on Injectable Drugs: IV Decision Support	Collection of monographs about 349 injectable drugs with sections on available concentrations, compatibility with other drugs, dosage and rate of administration, stability, pH, and other useful information Interactive version available
Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care	Most comprehensive text available about over-the-counter medications that can be purchased in the United States Online version available
Martindale: The Complete Drug Reference	Considered one of the most comprehensive texts available for information about drugs in current use throughout the world Contains extensive referenced monographs about the international names, pharmacologic activity, and side effects of more than 5500 drugs Online subscription available
Physicians' Desk Reference (PDR)	Discusses more than 3000 therapeutic agents Divided into six sections: (1) manufacturers' index; (2) brand and generic name index; (3) product category index; (4) product identification guide; (5) product information section; and (6) dietary supplements Includes a tear-out form for the MedWatch program for use by health professionals to voluntarily report adverse effects of drugs
Natural Medicines Comprehensive Database	Scientific gold standard for evidence-based information about herbal medicines and combination products involving herbal medicines Online database available
Canadian Drug Standards	
European Pharmacopoeia *Pharmacopée Française* *The International Pharmacopoeia (Ph. Int.)* *British Pharmacopoeia* *Canadian Formulary* *The National Formulary* *Pharmaceutical Codex* *United States Pharmacopeia*	All recognized by the Canadian Food and Drugs Act as authoritative sources of drug standards
Canadian Drug Information	
Compendium of Pharmaceuticals and Specialties (CPS)	Published annually by the Canadian Pharmacists Association Comprehensive list of the pharmaceutical products distributed in Canada as well as other practical information *e-CPS* available
Patient Self-Care: Helping Patients Make Therapeutic Choices	Published by the Canadian Pharmacists Association Provides comprehensive information for health professionals and consumers about nonprescription drug products available in Canada *e-Therapeutics* available
Compendium of Self-Care Products (CSCP)	Nonprescription companion to *CPS* and *Patient Self-Care* Offers at-a-glance comparative tables for thousands of products and monographs about hundreds of commonly used nonprescription products

NURSING JOURNALS

Many specialty journals have articles about drug therapy as it relates to a specific field of interest (e.g., *Geriatric Nursing, American Journal of Critical Care*). Nursing journals such as *RN* and *American Journal of Nursing* provide drug updates and articles that discuss nursing considerations related to drug therapy and drugs. Nurses must keep in mind that the purpose of using resources like journals is for professional knowledge of current evidence-based practice changes and not as a primary source for drug information; they must be mindful of the accuracy of the information contained and should check the dates on articles to validate the currency of the information.

ELECTRONIC DATABASES

With the exponential growth of information about medicines and health, it is almost impossible to make the information available without the use of electronic databases. The U.S. National Library of Medicine provides Medline and other searchable databases at no cost. Most of the drug information sources listed in Table 1-1 are also available via electronic retrieval from libraries. Many college libraries subscribe to CINAHL, which is a cumulative index of nursing and allied health literature. These sources give nurses access to a wealth of information from sources published in the United States as well as other countries.

Databases for practitioners are also available by subscription. UpToDate, Lexi-Comp, and ePocrates are three vendors with several different packages of regularly updated information (see Online Resources on p. 10). Lexi-Comp has a particularly strong database, because the American Hospital Formulary Service is available through its portal.

The DailyMed system (see Online Resources on p. 10) was developed in collaboration with federal agencies—including the FDA, the National Library of Medicine, the Agency for Healthcare Research and Quality, the National Cancer Institute in the Department of Health and Human Services, and the Department of Veterans Affairs—to provide high-quality information about marketed drugs. DailyMed makes available to health care providers and the public a standard, comprehensive, up-to-date resource about medicines.

DRUG LEGISLATION

Objectives

6. List legislative acts that control drug use and abuse.
7. Differentiate among Schedule I, II, III, IV, and V medications, and describe the nursing responsibilities associated with the administration of each type.

Key Term

schedules (SKĔD-jūlz) (p. 4)

Drug legislation protects the consumer from false claims made by the drug manufacturer. The need for such protection is great, because manufacturers and advertisers may make unfounded claims about the benefits of their products.

FEDERAL FOOD, DRUG, AND COSMETIC ACT

The Federal Food, Drug, and Cosmetic Act of 1938 (passed on June 25, 1938, and amended in 1952 and 1962) requires the FDA to determine the safety of drugs before marketing and to ensure that certain labeling specifications and standards in advertising are met in the marketing of products. Manufacturers are required to submit new drug applications to the FDA for the review of safety studies before the products can be released for sale.

The Kefauver-Harris Drug Amendment was brought about in 1962 as a result of the thalidomide tragedy. Thalidomide was an incompletely tested drug that had been approved for use as a sedative-hypnotic during pregnancy. Fetuses exposed to thalidomide were born with serious birth defects. This amendment provides greater control and surveillance of the distribution and clinical testing of investigational drugs and requires that a product be proven both safe and effective before release for sale.

CONTROLLED SUBSTANCES ACT

The Comprehensive Drug Abuse Prevention and Control Act, which is commonly referred to as the *Controlled Substances Act*, was passed by Congress in 1970. This statute repealed almost 50 other laws written between 1914 and 1970 that related to the control of drugs. The new composite law was designed to improve the administration and regulation of the manufacturing, distribution, and dispensing of drugs that require control by the government because of their high incidence of abuse. The basic structure of the Controlled Substances Act consists of five classifications or **schedules** of controlled substances. The degree of control, the conditions of record keeping, the particular order forms required, and other regulations depend on these classifications.

Schedule I Ⓒ Drugs

1. High potential for abuse
2. Not currently accepted for medical use in the United States
3. Lack of accepted safety for use under medical supervision

Examples: lysergic acid diethylamide (LSD), marijuana, peyote, STP, heroin, hashish

Schedule II Ⓒ Drugs

1. High potential for abuse
2. Currently accepted for medical use in the United States

3. Abuse potential that may lead to severe psychological or physical dependence

Examples: secobarbital, pentobarbital, amphetamines, morphine, Vicodin, methadone, Percodan, methylphenidate

Schedule III Drugs

1. High potential for abuse but less so than drugs in Schedules I and II
2. Currently accepted for medical use in the United States
3. Abuse potential that may lead to moderate or low physical dependence or high psychological dependence

Examples: Empirin with codeine, Lortab, Fiorinal, Tylenol with codeine

Schedule IV Drugs

1. Low potential for abuse as compared with drugs in Schedule III
2. Currently accepted for medical use in the United States
3. Abuse potential that may lead to limited physical or psychological dependence as compared with drugs in Schedule III

Examples: phenobarbital, chloral hydrate, chlordiazepoxide, diazepam, flurazepam, temazepam

Schedule V Drugs

1. Low potential for abuse as compared with drugs in Schedule IV
2. Currently accepted for medical use in the United States
3. Abuse potential of limited physical or psychological dependence liability as compared with drugs in Schedule IV; because abuse potential is low, a prescription may not be required

Examples: Lomotil, Robitussin AC

Drug Enforcement Administration

The U.S. Drug Enforcement Administration (DEA) was organized to enforce the Controlled Substances Act, to gather intelligence, to train its officers, and to conduct research in the area of dangerous drugs and drug abuse. The DEA is a bureau of the Department of Justice, and the director of the DEA reports to the Attorney General of the United States. The U.S. Attorney General, after public hearings, has the authority to reschedule a drug, to bring an unscheduled drug under control, or to remove controls on scheduled drugs.

Every manufacturer, physician, nurse practitioner, physician assistant, dentist, pharmacy, and hospital that manufactures, prescribes, or dispenses any of the drugs listed in the five schedules must register biannually with the DEA. A health care provider's prescription for substances named in this law must contain the health care provider's name, address, DEA registration number, and signature; the patient's name and address; and the date of issue. The pharmacist cannot refill such prescriptions without the approval of the health care provider.

Controlled Substances in Hospitals

All controlled substances kept in stock in hospitals for unit stock must be ordered on special forms that are used to help maintain the inventory and dispersion control records of the scheduled drugs. When a nurse administers a Schedule II drug from a health care provider's order, the name of the patient, the date and time of administration, the drug administered, and the drug dosage must be entered on the controlled substances record.

Possession of Controlled Substances by Individuals

Federal and state laws make the possession of controlled substances without a valid prescription a crime, except in specifically exempted cases. The law makes no distinction between professional and practical nurses with regard to the possession of controlled drugs. Nurses may give controlled substances only under the direction of a health care practitioner who has been licensed to prescribe or dispense these agents. Nurses may not have controlled substances in their possession unless the following conditions are met: (1) they are giving them to a patient under a physician's order; (2) the nurse is a patient for whom a physician has prescribed scheduled drugs; or (3) the nurse is the official custodian of a limited supply of controlled substances on a unit or for a department of the hospital. Controlled substances that are ordered for patients but not used must be returned to the source from which they were obtained (i.e., the physician or pharmacy). Violation or failure to comply with the Controlled Substances Act is punishable by fine, imprisonment, or both as well as the possible loss of professional licensing.

EFFECTIVENESS OF DRUG LEGISLATION

The effectiveness of drug legislation depends on the interest and determination used to enforce these laws, the appropriation by the government of adequate funds for enforcement, the vigor used by proper authorities in enforcement, the interest and cooperation of professional people and the public, and the education of the public regarding the dangers of the unwise and indiscriminate use of drugs in general. Many organizations help with this education, including the National Coordinating Council on Patient Information and Education, the American Medical Association, the American Dental Association, the American Pharmacists Association, the American Society of Health-System Pharmacists, and local, county, and state health departments.

NEW DRUG DEVELOPMENT

Objective

8. Describe the process involved in developing and marketing new medications.

Key Terms

black box warnings (p. 7)
orphan drugs (ÔR-făn) (p. 8)

It currently takes an average of 8 to 15 years and more than $1 billion in research and development costs to bring a single new drug to market; health care professionals and consumers alike often have a lack of understanding about this process. The Pharmaceutical Manufacturers Association estimates that only 1 out of 10,000 chemicals investigated is actually found to be "safe and effective" and ultimately brought to the pharmacist's shelf.

The Food, Drug, and Cosmetic Act of 1938 charged the FDA with the responsibility of regulating new drugs. Rules and regulations evolved by the FDA divide new drug development into four stages: (1) preclinical research and development; (2) clinical research and development; (3) New Drug Application (NDA) review; and (4) postmarketing surveillance (Figure 1-2).

PRECLINICAL RESEARCH AND DEVELOPMENT STAGE

The preclinical research phase of new drug development begins with the discovery, synthesis, and purification of the drug. The goal at this stage is to use laboratory studies to determine whether the experimental drug has therapeutic value and whether the drug appears to be safe in animals. Enough data must be gained to justify testing the experimental drug in humans.

The preclinical phase of data collection may require 1 to 3 years, although the average length of time is 18 months. Near the end of this phase, the investigator (often a pharmaceutical manufacturer) submits an Investigational New Drug (IND) application to the FDA; this application describes all of the studies completed to date, discusses the expected safety of the drug, and explains the testing that is planned for human subjects. Within 30 days, the FDA must make a decision on the basis of safety considerations about whether to allow the human study to proceed. Only about 20% of the chemicals tested in the preclinical phase advance to the clinical testing phase.

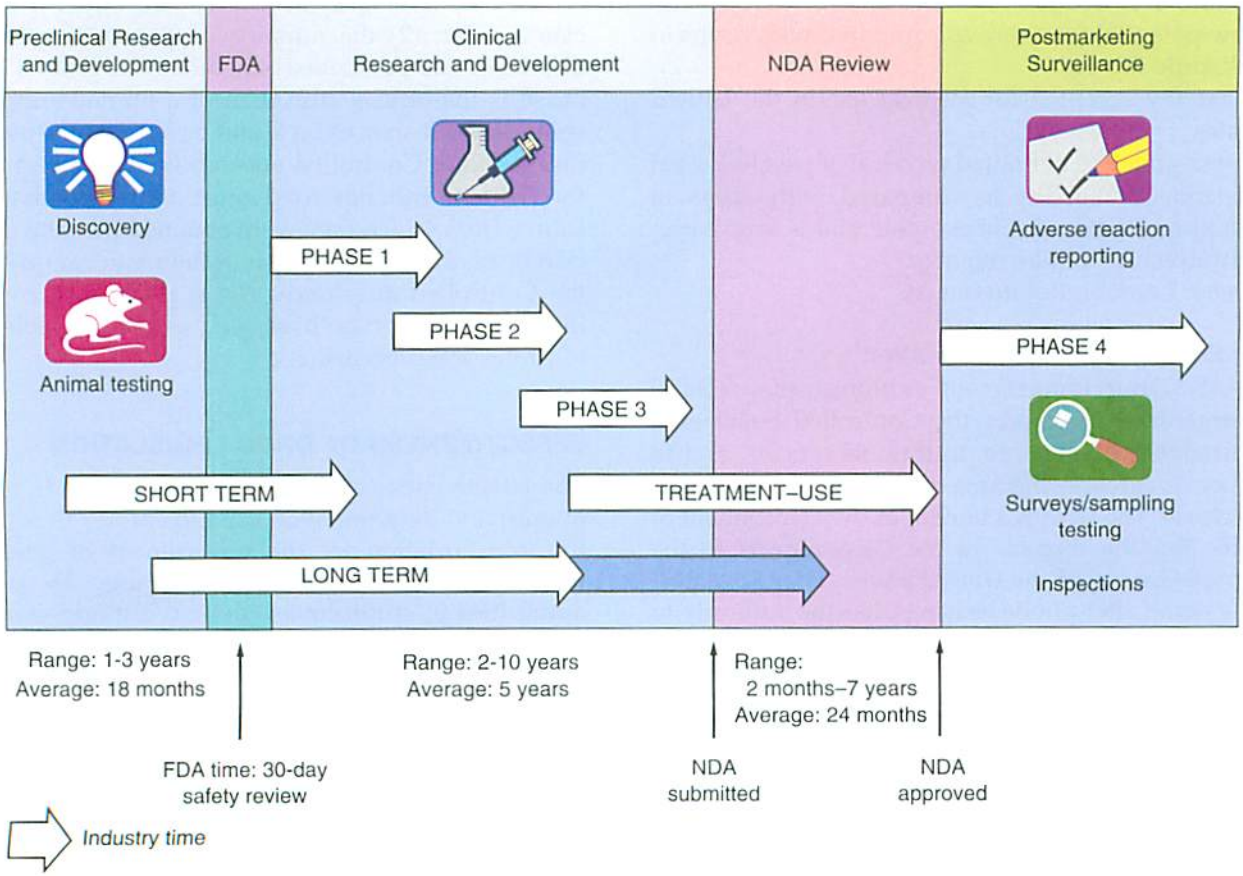

FIGURE 1-2 The new drug review process.

CLINICAL RESEARCH AND DEVELOPMENT STAGE

The stage in which humans are first tested (i.e., the clinical research or IND stage) is usually subdivided into three phases. Phase 1 studies determine an experimental drug's pharmacologic properties, such as its pharmacokinetics, metabolism, safe dosage range, potential for toxicity at a certain dosage, and safe routes of administration. The study population is comprised of normal volunteers or the intended treatment population, such as those patients for whom the standard treatments of certain cancers or dysrhythmias have been ineffective. Phase 1 studies usually require 20 to 100 subjects who are treated for 4 to 6 weeks.

If phase 1 trials are successful, the drug is moved to phase 2, which involves a smaller population of patients who have the condition that the drug is designed to treat. Studies at various dosages are conducted to determine the success rate and safety of a drug for its intended use. If successful, the drug is advanced to phase 3 trials, in which larger patient populations are used to ensure the statistical significance of the results. Phase 3 studies also provide additional information about proper dosing and safety.

The entire clinical research phase may require 2 to 10 years, with the average experimental drug requiring 5 years. Each study completed is reviewed by the FDA to help ensure patient safety and efficacy. Only one out of five drugs that enter clinical trials makes it to the marketplace. The others are eliminated because of efficacy or safety problems or a lack of commercial interest.

Fast Tracking

To expedite the development and approval of drugs for the treatment of life-threatening illnesses (e.g., acquired immunodeficiency syndrome), the FDA has drafted rules that allow certain INDs to receive the highest priority for review within the agency. This procedure is sometimes known as *fast tracking*. Additional rules allow INDs to be used for the treatment of a life-threatening disease in a particular patient—even if the patient does not fit the study protocol for the drug—when there is no alternative therapy. These cases are known as *treatment INDs*. A potentially lifesaving drug may be allowed for treatment IND status during late phase 2 studies, phase 3 studies, or after all clinical studies have been completed but before marketing approval.

Parallel Tracking

Another mechanism to make INDs available to patients with life-threatening illnesses is known as *parallel tracking*. With this procedure, an IND may be used for patients who cannot participate in controlled clinical trials and when there is no satisfactory standard therapeutic alternative. Parallel track studies are conducted along with the principal controlled clinical trials; however, unlike a controlled study, the parallel track study does not involve a concurrent control group.

Investigators and patients must realize that there may be greater uncertainty regarding the risks and benefits of therapy with agents that are in relatively early stages of testing and development. Parallel tracking is similar to the treatment IND process but allows for access to investigational agents when there is less accumulated evidence of efficacy than required for a treatment IND. A drug may be released through the parallel track mechanism when phase 2 trials have been given approval to proceed but have not necessarily been started.

NEW DRUG APPLICATION REVIEW

When sufficient data have been collected to demonstrate that the experimental drug is both safe and effective, the investigator submits an NDA to the FDA to formally request approval to market a new drug for human use. Thousands of pages of NDA data are reviewed by a team of pharmacologists, toxicologists, chemists, physicians, and others (as appropriate), who then make a recommendation to the FDA about whether the drug should be approved for use. The average NDA review takes 17 months. After a drug is approved by the FDA, it is the manufacturer's decision as to when to bring a product to the marketplace.

POSTMARKETING SURVEILLANCE STAGE

If the manufacturer decides to market the medicine, the postmarketing surveillance stage begins; this is the fourth stage of drug product development. This process consists of an ongoing review of adverse effects of the new drug as well as periodic inspections of the manufacturing facilities and the resulting products. Other studies completed during the fourth stage include identifying other patient populations for whom the drug may be useful, refining dosing recommendations, and exploring potential drug interactions.

Clinical Goldmine

Health care practitioners make a significant contribution to the knowledge of drug safety by reporting adverse effects to the FDA using the MedWatch program for the voluntary reporting of adverse events and product problems (see Online Resources on p. 10).

BLACK BOX WARNING

Although the FDA's drug-approval process is one of the most stringent in the world, a study has demonstrated the value of the ongoing safety review of medicines and the use of the MedWatch program. Of the 548 new chemical entities approved by the FDA from 1975 to 1999, a total of 56 drugs (10.2%) acquired new **black box warnings** (which indicate very serious or

potentially life-threatening problems) or were withdrawn from the market because of serious or fatal complications (Lasser et al, 2002).

The probability of a drug acquiring a new black box warning or being withdrawn from the market within 25 years of being released is estimated at 20%. Consequently, it is the responsibility of all health care professionals to constantly monitor their patients for adverse effects of drugs and to complete a MedWatch form when adverse effects are suspected. More than 200,000 MedWatch forms are filed with the FDA annually.

From a safety standpoint, prescribers, other health care practitioners, and patients should be aware that recently marketed medicines carry a risk of causing unsuspected serious adverse effects. One could make the point that there is a 90% probability that there will be no serious complications, but the devastating—and sometimes fatal—consequences cannot be ignored. When choosing medicines for treatment, it becomes important to consider whether an equally effective alternative drug is already available. At a minimum, this reduces the risk of an undiscovered adverse drug reaction, and it is often less expensive. At a maximum, the patient, his or her family, and the prescriber are saved the anguish of an avoidable adverse drug reaction.

RARE DISEASES AND THE DEVELOPMENT OF ORPHAN DRUGS

The National Organization for Rare Disorders, which is a coalition of 140 rare-disease groups, estimates that more than 6000 rare health conditions exist in about 20 million Americans. Examples of these rare diseases are cystic fibrosis, Hansen's disease (leprosy), sickle cell anemia, blepharospasm, infant botulism, and *Pneumocystis jiroveci* (formerly *Pneumocystis carinii*) pneumonia (see Online Resources on p. 10). Historically, pharmaceutical manufacturers have been reluctant to develop products that could be used to treat these illnesses. The medicines that are developed for these conditions are known as *orphan drugs,* because the manufacturers have been unable to recover the costs of the research due to the very limited use of the final product. Because no companies were willing to "adopt" the disease to complete extensive research to develop products for treatment, the diseases became known as *health orphans.*

In 1983, Congress passed the Orphan Drug Act to stimulate the development and market availability of products that are used for the treatment of rare diseases. The act defines the term *rare disease* as a condition that affects fewer than 200,000 people in the United States. The FDA's Office of Orphan Products Development (OOPD) promotes the development of products that demonstrate promise for the diagnosis or treatment of rare diseases or conditions. The OOPD interacts with medical and research communities, professional organizations, academia, and the pharmaceutical industry as well as with rare-disease groups. The OOPD administers the major provisions of the Orphan Drug Act, which provide incentives for sponsors to develop products for rare diseases.

The law provides research grants, protocol development assistance by the FDA, special tax credits for the cost of clinical trials, and 7 years of exclusive marketing rights after the product has been approved. On average, an orphan drug receives FDA approval 10 to 11 months sooner than a nonorphan drug. The act has been quite successful: more than 200 new drugs have been approved by the FDA for the treatment of rare diseases, and this has benefited several million people. Recent examples include pentamidine and atovaquone for *Pneumocystis jiroveci* pneumonia, thalidomide for Hansen's disease, zidovudine for the human immunodeficiency virus, DNase (Pulmozyme) for cystic fibrosis, and Leustatin for hairy cell leukemia.

DRUG NAMES, STANDARDS, AND LEGISLATION IN CANADA

Objectives

9. Differentiate between the Canadian *chemical* name and the *proper* name of a drug.
10. List official sources of Canadian drug information.
11. List Canadian legislative acts that control drug use and abuse.

Key Terms

Food and Drugs Act and Regulations (p. 9)
Controlled Drugs and Substances Act (p. 9)
nonprescription drugs (p. 10)

CANADIAN DRUG NAMES

OFFICIAL DRUG

The term *official drug* pertains to any drug for which a standard is described specifically in the Food and Drug Regulations or in any publication named in the Food and Drugs Act as being satisfactory for officially meeting the standards for drugs in Canada.

CHEMICAL NAME

The *chemical* name is most meaningful to the chemist. By means of the chemical name, the chemist understands the exact chemical constitution of the drug and exact placing of its atoms or molecular groupings. The chemical name is the same in both Canada and the United States.

PROPER NAME OR GENERIC NAME

The *proper* name is the nonproprietary (generic) name, which is used to identify an official drug in Canada.

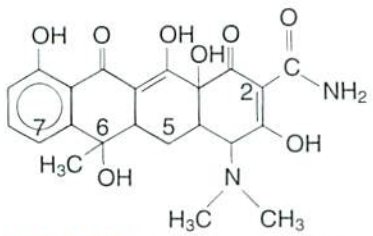

FIGURE 1-3 Tetracycline, an antibiotic.

The *generic name* is the same in both Canada and the United States.

BRAND NAME

The *brand name* (or proprietary name) is the name assigned to the drug by its manufacturer to distinguish the drug for advertisement and sale. Brand names for the same generic drug product are frequently different between Canada and the United States. See Figure 1-3 for application of terminology to drug nomenclature.

EXAMPLE: See Figure 1-3.

Chemical name: 4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11,dioxo-2-napthacenecarboxamide

Proper name: tetracycline

Official name: Tetracycline, USP

Brand names: Apo-Tetra; Nu-Tetra

SOURCES OF CANADIAN DRUG STANDARDS

The Food and Drugs Act recognizes the standards described by international authoritative books as being acceptable for official drugs in Canada (see Table 1-1).

CANADIAN DRUG LEGISLATION

FOOD AND DRUGS ACT AND REGULATIONS

The **Food and Drugs Act** (1927) and **Regulations** (1953, 1954, 1979) empower Health Canada to protect the public from foreseeable risks related to the manufacture and sale of drugs, cosmetics, food, and therapeutic devices. The legislation provides for a review of the safety and efficacy of drugs before their clearance for marketing in Canada and determines whether the medicine is *prescription* or *nonprescription*. Also included in this legislation are requirements for good manufacturing practices, adequate labeling, and fair advertising.

In Canada (as in the United States), an effort has been made to align the provincial drug schedules so that the conditions for the sale of medicines are consistent across Canada. The National Association of Pharmacy Regulatory Authorities (NAPRA) proposed a new national drug scheduling model. This model is in various stages of implementation across the provinces and territories of Canada. With the use of this model, all medicines in Canada are assigned to one of four categories.

- Schedule I: all prescription drugs, including narcotics
- Schedule II: restricted-access nonprescription drugs
- Schedule III: pharmacy-only nonprescription drugs
- Unscheduled: drugs that are not assigned to the previous categories

Schedule II drugs are available for sale directly from the pharmacist and are kept "behind the counter." Examples include insulin, pseudoephedrine, glucagon, loperamide (for children under age 12), and nitroglycerin sublingual spray and tablets (other dosage forms are schedule I). These medications are in two categories: (1) those that patients may require urgently and cannot delay taking until after an appointment with a prescriber (insulin, nitroglycerin, glucagon); and (2) those that require appropriate counseling to avoid improper use (loperamide, pseudoephedrine). Placement with a pharmacist does not allow for patient self-selection and allows for pharmacist intervention for these medications. This restriction is meant to ensure the following: (1) that patients are not self-diagnosing medically serious diseases (e.g., diabetes mellitus, angina); and (2) that patients are educated about the proper use of these drugs through appropriate counseling from the pharmacist.

Schedule III drugs are pharmacy-only nonprescription drugs. These medicines can be sold only through pharmacies and include levonorgestrel emergency contraception, diphenhydramine, child preparations of antihistamines, and the low-dose histamine-2 antagonists. It is expected that, if clients have questions, they could easily consult with a pharmacist.

Medicines that are not categorized in Schedules I, II, or III are considered to be "unscheduled" (e.g., nicotine gum and patches, acetylsalicylic acid, lower-dose ibuprofen, some lower-dosage "cough and cold" preparations) and can be sold at any retail outlet. Adequate information is available for the patient to make a safe and effective choice, and labeling is sufficient to ensure the appropriate use of the drug without professional supervision.

Drugs requiring a prescription—except for controlled drugs—are listed on Schedule F of the Food and Drug Regulations. Schedule F drugs may be prescribed only by qualified practitioners because they would normally be used most safely under supervision. Most antibiotics, antineoplastics, corticosteroids, cardiovascular drugs, and antipsychotics are Schedule F drugs.

CONTROLLED DRUGS AND SUBSTANCES ACT

The **Controlled Drugs and Substances Act** (1997) establishes the requirements for the import, production, export, distribution, and possession of substances classified as narcotics and substances of abuse in Canada. The Controlled Drugs and Substances Act

describes eight schedules of controlled substances. Assignment to a schedule is based on the potential for abuse and the ease with which illicit substances can be manufactured in illegal laboratories. The degree of control; the conditions of record keeping; assignment of penalties for possession, trafficking, and manufacturing; and other regulations depend on these classifications. Examples of schedule assignment are as follows:

- Schedule I: opium poppy and its derivatives (e.g., heroin, morphine); coca and its derivatives (e.g., cocaine), pethidine (meperidine), methadone, fentanyl
- Schedule II: cannabis
- Schedule III: amphetamines, methylphenidate, lysergic acid diethylamide (LSD), methaqualone, psilocybin, mescaline
- Schedule IV: sedative-hypnotic agents (e.g., barbiturates, benzodiazepines); butorphanol, anabolic steroids
- Schedule V: propylhexedrine, phenylpropanolamine, pyrovalerone
- Schedule VI: part I class A precursors (e.g., ephedrine, pseudoephedrine, norephedrine [phenylpropanolamine], ergotamine) and part II precursors (e.g., acetone, ethyl ether, hydrochloric acid, sulfuric acid, toluene)
- Schedule VII: cannabis resin (3 kg); cannabis (marijuana) (3 kg) (marijuana) (must be read in conjunction with Schedule II)
- Schedule VIII: cannabis resin (1 g); cannabis (marijuana) (30 g) (must be read in conjunction with Schedule II)

The Controlled Drugs and Substances Act and accompanying regulations provide for the nonprescription sale of certain codeine preparations (e.g., Tylenol No. 1 with codeine, Benylin with codeine). The content must not exceed the equivalent of 8 mg of codeine phosphate per solid dosage unit or 20 mg per 30 mL of a liquid preparation, and the preparation must also contain two additional nonnarcotic medicinal ingredients. These preparations may not be advertised or displayed, and they may be sold only by pharmacists (see previous discussion of Schedule II drugs). In hospitals, the pharmacy usually requires strict inventory control of these products as well as of other narcotics.

Requirements for the legitimate administration of drugs to patients by nurses are generally similar in Canada and the United States. Individual hospital policy determines specific record-keeping requirements on the basis of federal and provincial laws. Violations of these laws would be expected to result in fines or imprisonment in addition to the loss of professional licensing.

NONPRESCRIPTION DRUGS

The NAPRA drug schedules list three categories of **nonprescription drugs,** including Schedule II, III, and unscheduled drugs. See discussion under Federal Food and Drugs Act and Regulations (p. 9).

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- Animations
- Appendices
- Drug dosage calculators
- Drugs@FDA (a catalog of FDA-approved drug products)
- Gold Standard Patient Teaching Handouts in English and Spanish
- Interactive Drug Flashcards
- Interactive Review Questions for the NCLEX® Examination and more!

Online Resources

- DailyMed: http://dailymed.nlm.nih.gov/dailymed
- ePocrates: www.epocrates.com
- iPharmacy: http://itunes.apple.com/us/app/id348702163?mt=8&ign-mpt=uo%3D6; https://market.android.com/details?id=com.sigmaphone.topmedfree
- Lexi-Comp: http://online.lexi.com
- MedicinesComplete: http://www.medicinescomplete.com
- Medwatch: www.fda.gov/Safety/MedWatch/default.htm
- National Organization for Rare Disorders: www.rarediseases.org
- UpToDate: www.uptodate.com
- U.S. National Library of Medicine: www.nlm.nih.gov

Online Resources for Canadian Practitioners

- Canadian drug names: http://sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/drugs-drogues/lasa_premkt-noms_semblables_precomm-eng.php#def
- National Association of Pharmacy Regulatory Authorities (NAPRA) proposal for drug schedule outlines: http://napra.ca/Content_Files/Files/Schedules-Outline.pdf
- Controlled Substances and Drugs Act: From www.hcsc.gc.ca/ahc-asc/legislation/acts-lois/index-eng.php

Review Questions for the NCLEX® Examination

1. According to the U.S. Controlled Substances Act, morphine and Vicodin belong to which Schedule?
   1. I
   2. II
   3. III
   4. IV