CHAPTER2

DRUG REGULATIONS

LEARNING OUTCOME 1

Explain the role of patent medicines in the history of pharmacology and the legislation of drugs.

Concepts for Lecture

1. In the United States and Canada laws govern all aspects of drug approval, labelling, manufacturing, marketing, and distribution.
2. Consumers expect that the drug they are taking is effective and that the label is clear and accurate.
3. Consumers expect that the drug they are taking is safe.
4. It is only since the 20th century that standards and regulations exist to protect the consumer.
5. In early America, patent medicine was widely used and available.
6. There were no laws to regulate these medicines and products could make any claim to health or cure.
7. Many patent medicines contain addictive and at times dangerous additives, such as morphine and cocaine. Such addictive additives guaranteed repeat sales.
8. Several early patent medicines have gone through drug regulation and change and are still available today.

LEARNING OUTCOME 2

Outline the key U.S. drug regulations and explain how each has contributed to the safety and effectiveness of the medications.

Concepts for Lecture

1. Drug legislation began in the 1900s to make drugs safer and more effective.
2. The first national law was the *Drug Importation Act* passed in 1848.
3. This was spurred on deaths of children in 1901 who were given a contaminated antitoxin.
4. The Biologics Control Act was passed in 1902 to regulate era, antitoxins, and blood-related products.
5. The Pure Food and Drug Act (PFDA) was passed in 1906 to control labelling of medicines.
6. The PFDA required accuracy in drug labeling.
7. In 1912 the Sherley Amendment to the PFDA addresses false therapeutic claims on drug labels.
8. The Sherley Amendment did not address the issue of proving that the drug company knew that their false claim was intentional.
9. The Harrison Narcotic Act of 1914 required prescriptions for higher doses of narcotic drugs.

10. States and the federal government have passed additional laws regulating drugs of abuse. This is covered in Chapter 8.

11. Two issues with early regulations were that the drug companies did not have to prove that the drug was effective and did not require testing before marketing.

12. After deaths in 1937 due to a contaminated drug, the Food, Drug, and Cosmetic Act (FDCA) was passed by Congress in 1938.

13. The FDCA required that drugs be tested for safety before marketing and drug labels to contain instructions for use.

14. The FDCA did not define what was considered a prescription drug.

15. In 1951 the *Durham-Humphrey Amendment* to the FDCA defined the difference between prescription drugs and over-the-counter (OTC) drugs.

16. In the late 1950s, there was a high number of birth defects from the drug thalidomide, which was prescribed to pregnant women by their physicians. Because these physicians received the drug from the manufacturer with FDA approval, the *Kefauver-Harris Amendment* to the FDCA was passed in 1962.

17. The Kefauver-Harris Amendment required that manufacturers prove their drugs safe and effective by conduction of adequate and controlled studies.

18. The Kefauver-Harris Amendment also required adverse effects be reported to the FDA and included in literature given to health care providers.

19. The Kefauver-Harris Amendment also required informed consent of those patients participating in drug research.

20. In 1966, the FDA began evaluating the effectiveness of previously approved drugs.

21. In, 1972 the FDA began reviewing over-the-counter drugs for safety and effectiveness.

22. In 1983, the *Orphan Drug Act* became law to assist with development of drugs for serious, but rare, diseases.

23. The Prescription Drug User Fee Act (PDUFA) of 1992 assessed fees from manufacturers to reduce drug review time.

24. The 1997 passage of the *Food and Drug Administration Modernization Act* reviewed medical devices and health claims for food.

25. The *Dietary Supplement Health and Education Act* of 1994 aimed to control claims of dietary supplements.

26. The *Medicare Prescription Drug Improvement and Modernization Act* of 2003 aimed to assist patients with prescription drug costs.

LEARNING OUTCOME 3

Describe how the *United States Pharmacopeia-National Formulary* (USP-NF) controls drug purity and standards.

Concepts for Lecture

1. When drugs were prepared from plants, purity and strength varied due to the ingredients and preparer.
2. Pharmacists began using formularies to list products and recipes.
3. In 1820 the U.S. Pharmacopeia (USP) was established.
4. For over 100 years, the USP and the National Formulary (NF) maintained drug standards in the United States by setting standards for drug purity and strength.
5. The USP covered drug products and the NF covered nondrug ingredients.
6. In 1975 they were merged into the USP-NF, which is published annually.
7. The USP label is found on many medications.
8. Drugs marketed in the United States must conform to USP-NF standards.

LEARNING OUTCOME 4

Evaluate the role of the U.S. Food and Drug Administration in the drug approval process.

Concepts for Lecture

1. The Food and Drug Administration (FDA) is responsible for ensuring the safety of drugs and medical devices.
2. The FDA started in 1906, making it the oldest drug regulatory agency in the world. It has eight branches.
3. The *Center for Drug Evaluation and Research* (CDER) covers drug safety.
4. The *Center for Biologics Evaluation and Research* (CBER) regulates biologic safety.
5. The *Center for Food Safety and Applied Nutrition* (CFSAN) over sees herbal products, dietary supplements, and cosmetics, but does not require testing of herbals and dietary supplements before marketing.
6. CFSAN regulates cosmetics that are not considered drugs.

LEARNING OUTCOME 5

Categorize the four stages of new drug approval.

Concepts for Lecture

1. The drug approval process in the United States was established by the FDA.
2. The drug approval process ensures drugs sold in the United States are safe and effective.
3. There are four stages to new drug approval.
4. The first stage is preclinical investigational. This is laboratory research by the pharmaceutical

company.

5. The FDA does not regulate the preclinical investigation.
6. If the preclinical investigation is positive, the company may submit an Investigational New Drug (IND) application to the FDA.
7. Once approved by the FDA, the drug can start clinical phase trials.
8. Phase 1 involves testing on 20 to 80 healthy volunteers.
9. Phase 2 involves testing several hundred patients with the particular disease for the drug.
10. Phase 3 involves a large number of patients with the disease for patient variability.
11. If the clinical phase trials are positive, the company will submit a New Drug Application (NDA) to the FDA.
12. The FDA will then approve or not approve a drug.
13. If approved, the drug can begin post marketing surveillance, which is stage 4.
14. Stage 4 looks for harmful drug effects in a large population.
15. Post marketing surveillance helps the FDA discover any serious problems. The Adverse Event Reporting System and FDA public meetings allow patients and health care providers to report problems.
16. Although more diverse populations are used to test drugs, most drugs are not tested in children and pregnant women, as these populations are not used in drug testing.
17. Off-label use is when a drug is discovered to be useful for an indication that was not approved by the FDA.
18. The FDA does not regulate off-label use. About 20% of prescription drugs are used off-label.

LEARNING OUTCOME 6

Explain the role of a placebo in new drug testing.

Concepts for Lecture

1. A placebo or inert substance is used in phase 2 of clinical drug trials.
2. The placebo serves as a control or nontreatment group.

LEARNING OUTCOME 7

Discuss how recent changes to the approval process have increased the speed at which new drugs reach consumers.

Concepts for Lecture

1. The process of developing and testing a new drug can take many years.

2. The FDA review process can take several years.
3. The estimated cost to bring a new drug to market can be over $802 million U.S. dollars.
4. Pharmaceutical companies are anxious to recoup the high expenses.
5. The public is also anxious for new medications, especially for diseases with a high mortality rate.
6. In 1992 the PDUFA was passed, which provided yearly product user fees.
7. This income allowed the FDA to restructure and hire more employees.
8. This restructuring decreased their view process by half.
9. Priority drugs now receive accelerated approval.
10. These priority drugs are for serious and life-threatening conditions.

LEARNING OUTCOME 8

Compare and contrast prescription and over-the-counter drugs.

Concepts for Lecture

1. The *Durham-Humphrey Amendment* of 1951 established the difference between prescriptions and over-the-counter (OTC) drugs.
2. A patient must have authorization, a "prescription" to receive a prescription drug.
3. Prescription drugs are considered to be potentially addictive or too harmful for self-administration. Prescription drugs require skill to administer correctly.
4. Prescription drugs allow the patient to be examined and properly diagnosed.
5. Prescription drugs allow for patient teaching and disease monitoring. Prescription drugs treat complex conditions.
6. OTC drugs do not require a prescription for a health care provider.
7. OTC drugs are safe if the patient carefully follows the instructions.
8. OTC drugs are easier to obtain.
9. Choosing the correct OTC drug can be a problem for the patient.
10. Patients may not be aware of food, drug, and herbal interactions with OTC drugs.
11. Self-treatment with OTC drugs can be ineffective.
12. Prescription drugs can undergo a review process by the FDA which can reclassify a prescription drug to be an OTC drug. In order for a prescription drug to be reclassified as an OTC drug, a high margin of safety must exist.
13. Herbal and dietary supplements are available over the counter.

14. Herbal and dietary supplements are not considered drugs. They are not subjected to the same regulatory process as prescription drugs.
15. The FDA does not test herbal and dietary supplements for safety. These products can cause side effects and interact with medications.

LEARNING OUTCOME 9

Explain how scheduled drugs are classified and regulated.

Concepts for Lecture

1. Some drugs have a high potential for dependence.
2. Some drugs are frequently abused.
3. The sale and distribution of these drugs are highly restricted.
4. Drugs with a high potential for abuse are called scheduled drugs.
5. These drugs are placed into one of five categories called schedules.
6. Dependencies and drug schedules are discussed in Chapter 8.
7. The *Comprehensive Drug Abuse Prevention and Control Act* of 1970 restricts these controlled substances.
8. The Drug Enforcement Administration (DEA) requires hospitals and pharmacies to use registration numbers to purchase these drugs.
9. Complete records must be maintained of qualities purchased and sold.
10. Drugs with the highest abuse potential have additional restrictions.
11. These restrictions may include special order forms, no telephone orders, and no refills.
12. There are strict penalties for not following the laws.

LEARNING OUTCOME 10

Describe the Canadian drug approval process and identify similarities to the drug approval process in the United States.

Concepts for Lecture

1. There are many similarities between U.S. and Canadian regulations for drugs.
2. Health Canada is the federal department and the Health Products and Food Branch (HPFB) of Health Canada is the regulatory body for health products and food safety.
3. The HPFB regulates the use of therapeutic products by directorates.
4. The Therapeutic Products Directorate (TPD) authorizes marketing of drugs and medical devices.
5. The Biologics and Genetic Therapies Directorate (BGTD) regulate biological drugs and radio

pharmaceuticals.

6. The Natural Health Products Directorate (NHPD) regulates natural products.
7. The Canadian Food and Drugs Acts is a regulatory document that specifies that drugs cannot be marketed without a Notice of Compliance (NOC) and Drug Identification Number (DIN) from Health Canada.
8. If a drug does not comply with standards set in the United States, Europe, Britain, or France, they cannot be sold, labeled, packaged, or sold in Canada.

GENERAL CHAPTER CONSIDERATIONS

1. Have students study and learn key terms listed at beginning of chapter.
2. Have students complete end of chapter exercises either in their book or on the Pearson Nursing Student Resources website.

Marginal Notes

POWER POINT SLIDES 6–11

Figure 2.1 Patent Medicines Contained a Name Brand That Clearly Identified the Product and Claimed to Cure Just about Any Symptom or Disease

Figure 2.1 Patent Medicines

SUGGESTION FOR CLASSROOM ACTIVITIES

- Discuss with students how patent medicines have "survived" over along period of time. Use examples given in the textbook such as Smith Cough Drops, Fletcher's Castoria, Doan's Pills, Vick's Vapo Rub, and Phillip's Milk of Magnesia. Why are these products still popular and widely used? What could be some of the reasons that they survived regulations?

POWERPOINT SLIDES 12–18

Table 2.1 Historical Time Line of Regulatory Acts, Standards, and Organization

Figure 2.2 USP Labels

SUGGESTION FOR CLASSROOM ACTIVITIES

- Using the time line in Table 2.1, have the students add any future regulations they believe are needed or forthcoming.

SUGGESTION FOR CLINICAL ACTIVITIES

- Have students teach assigned patients in the clinical setting what U.S. regulations ensure the safety and effectiveness of their drug therapy.

POWERPOINT SLIDES 19-20

SUGGESTION FOR CLASSROOM ACTIVITIES

- Have the students explore the USP website *(www.usp.org).* Have the students look at what type of information is available such as reference standards, healthcare quality and information, seminars, workshops, and drug safety review. Discuss how they could use this information in clinical practice.

POWERPOINT SLIDES 21–23

Figure 2.3 U.S. Food and Drug Administration

SUGGESTIONS FOR CLASSROOM ACTIVITIES

- Have the students log onto the FDA website *(http://fda.com).* Then, have the students explore the consumer links and resources. Assign a different link or resource to each student; have them give a brief summary if they thought there source would be helpful to the general patient population.

Students can choose an FDA industry link to explore. Break students into groups and assign one of the following to each group: CDER, CBER, CFSAN, MedWatch, Health Care Professional, Food Nutrition Industry, and Cosmetic Industry. Have the students report back to the group what information is available.

SUGGESTION FOR CLINICAL ACTIVITIES

- Have the students explain to their assigned patients how the FDA oversees drug products in the United States. If Internet access is available, the student can demonstrate the consumer links on the FDA website *(http://fda.com).*

POWER POINT SLIDES 24–29

Figure 2.4 Drug Development Time Line

SUGGESTION FOR CLASSROOM ACTIVITIES

- Break the students into groups, give each group one of the three phases of the clinical drug trial, have them develop a patient teaching tool to provide teaching to the patient involved in that phase of the trial. How would they explain safety, adverse effects, and patient variables?

SUGGESTION FOR CLINICAL ACTIVITIES

- If possible in your clinical setting, have the students interview either a healthcare professional or patient involved in a clinical drug trial. They should ask questions about stages and phases of the trial, preclinical investigation, goal of the trial, possible adverse effects, and patient consents and compensations. Have them report back to their clinical group what they learned in their interview. Did it change their thoughts about clinical drug trials? Why or why not?

SUGGESTION FOR CLASSROOM ACTIVITIES

- Build off the activity for Learning Outcome 5 and continue to discuss clinical drug trials. Why do some patients receive the placebo? Is there a risk with placebos? How would the patient feel about getting the placebo if the drug was very effective? Discuss the moral issues regarding controlled drug trials.

POWERPOINT SLIDES 30–32

SUGGESTION FOR CLASSROOM ACTIVITIES

- Discuss with the class which disease states could require priority drug approval. Make a list on the classroom blackboard. Ask the students then to prioritize their list. Discuss how difficult it is to decide

which disease is "more important." Discuss if the list would be different in another part of the country or world.

POWERPOINT SLIDES 19–39

SUGGESTION FOR CLASSROOM ACTIVITIES

- Discuss some of the recent drugs that have been reclassified from prescription to over the counter, such as loratadine (Claritin), cetirizine (Zyrtec), Omeprazole (Prilosec), famotidine (Pepcid), naproxen sodium (Aleve), and cromolyn sodium nasal spray (Nasalcrom). Discuss the potential for use and misuse by the consumer. Why are these drugs safer than other drugs in the same category that are still prescription drugs? Does their classification help or harm the consumer?

SUGGESTION FOR CLINICAL ACTIVITIES

- Assign the students to a patient who is prescribed a drug that is available over the counter. Have the students develop a patient teaching plan that will teach the patient how to use the drug safely and how to follow the guidelines.

SUGGESTIONS FOR CLASSROOM ACTIVITIES

- Provide the students with a list of some controlled substance medications. Have the student pick one drug and investigate its use and safety. Have them report back to the class if they think the assigned schedule is appropriate or not. Discuss the arguments presented in class.

- Refer to the DEA website for a list of controlled substances: *http://www.usdoj.gov/dea/pubs/scheduling.html*

SUGGESTIONS FOR CLINICAL ACTIVITIES

- Have the students shadow a nurse or pharmacist who prepares controlled substance medications. Have the student note the regulations in that clinical setting for recording and dispensing the drugs. Have the students report if they think the regulations are appropriate or not. What would they change, if anything?

- Refer to the DEA website about the controlled substance act: *http://www.usdoj.gov/dea/pubs/scheduling.html*

POWERPOINT SLIDES 40–46

Table 2.2 Steps for Approval for Drugs Marketed Within Canada

SUGGESTIONS FOR CLASSROOM ACTIVITIES

- Explore the Health Canada website with the students: *http://www.hc-sc.gc.ca/index-eng.php*

- Compare and contrast information found on that site against U.S. sites, such as the FDA *(www.fda.gov)* or the Centers for Disease Control *(www.cdc.gov).*

- What information is provided on the websites for healthcare professionals? What information is provided for the consumer?

- Discuss if information is easy to find and to understand. Focus on drug standards and safety.

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