Drug Design, Testing, Manufacturing, and Marketing

Course
Practicum in Health Science-Pharmacology

Unit VII
Career Preparation and Employability

Essential Question
Why is quality control important in pharmaceutical services?

TEKS
130.205
1(G)
2(A)(B)
3(A)(C)(D)(E)
7(A)(B)(C)

Prior Student Learning
None

Estimated time
3 hours

Rationale
An understanding of how pharmaceutical agents are discovered and developed as well as an extensive knowledge of drug nomenclature is essential for the health care professional to provide quality health care.

Objectives
Upon completion of this lesson, the student will be able to:

- Describe drug nomenclature
- Understand how drugs are discovered and developed
- Differentiate between chemical, generic, and trade/brand names of drugs
- Identify the approval process for drug/new pharmaceutical agents by the FDA

Engage
Have students brainstorm the following questions:

- How are pharmaceutical drugs discovered, and how are they named?
- How do computers facilitate drug design?

Key Points
I. Nomenclature – Critical for safety reasons
   A. Chemical name
      1. molecular structure of the drug
      2. distinction from all other drugs
   B. Generic name
      1. pharmaceutical company and USANC (United States Adopted Names Council) together determine
      2. some generic groups of drugs may have similar spelling to reflect chemical similarity. Examples: all of the following are members of the benzodiazepine classification, used to treat anxiety
         a. diazepam Valium
         b. lorazepam Ativan
         c. halazepam Paxipam
         d. oxazepam Serax
         e. prazepam Centrax
   C. Trade name or brand name is selected by the manufacturer once FDA gives approval for drug to be marketed
      1. brand name is registered trade mark
      2. also known as proprietary name
      3. only original manufacturer has right to advertise and market drug under this name
      4. in general particular spelling of brand name proposed by
manufacturer for several reasons
a. manufacturers not held to specific linguistic standard – spelling not always as expected by phonetic rules
b. simplify generic name, retaining phonetic sound; e.g.,
   *pseudoephedrine – Sudafed*
   *haloperidol – Haldol*
   *ciprofloxacin – Cipro*
c. indicate disease to be treated; e.g., Azmacort to treat asthma, Rythmol to treat cardiac dysrhythmia
d. indicate the source of the drug
   *Premarin – pregnant mare’s urine*
e. indicate the action of the drug
   Elavil – to elevate depressed mood,
   Asendin – to help patients to ascend from depression
f. indicate several drugs in combination
   Serpasil, Apresoline, and Esidrix combine to form Ser-Ap-Es
g. indicate frequency of administration
   Spectrobid – to be taken bid or twice daily
h. indicate duration of action
   Slow-K – potassium in slow release form
i. indicate drug strength
   Bactrim *DS* – double strength dose
j. indicate amount of active ingredient
   *Tylenol # 3* - 30 mg codeine
   *Tylenol # 2* - 15 mg codeine
k. reflect manufacturer’s identity
   Wyeth-Ayerst: Wycillin – antibiotic
   Wygesic – analgesic
   Wytensin – antihypertensive

II. Drug Design – time consuming and expensive process; thousands of chemicals evaluated before receiving FDA approval. New drugs discovered in two ways
A. New chemical substance discovered in environment
   1. soil samples
   2. plants/animals
   3. minerals
   4. microbes

B. New chemical derived from molecular manipulation of existing drug
   1. semisynthetic
   2. totally synthetic
   3. slight molecular changes may significantly change original drug
      a. absorption
         i. penicillin G derived from mold *Penicillium chrysogenum* is destroyed by stomach acid and cannot be administered
orally

ii. Ampicillin, semisynthetic penicillin derived by changing nucleus through adding chemicals to penicillin during fermentation stage, not destroyed by stomach acid

b. metabolism
c. half-life
d. side effects
e. action

C. Methods of Designing

1. old method of designing new drug tedious
   a. trial and error
   b. intuition
   c. molecular models from wood and wire

2. new method by using computers
   a. can process hundreds of variables in chemical structure in fraction of time
   b. identify chemicals probably not successful in treating disease
   c. saves time and money in testing phase
   d. can study any molecule rotating in three dimensions

3. recombinant DNA technology
   a. gene splicing
   b. genetic engineering
   c. represents recent advance in drug development
   d. aided by computer design
   e. use of enzymes
   f. remove DNA chemically from one organism and transplant DNA into different organism
      o Recipient organism directed by new DNA to produce particular substance
      o Humulin (human insulin) first recombinant DNA drug approved by FDA (1982)

III. Drug Testing, Manufacturing, and Marketing -- regardless of method of design, drugs must be thoroughly tested by manufacturer according to FDA specified guidelines to determine effectiveness and safety

A. In vitro testing – Latin in glass, done in laboratory in glass tubes and Petri dishes

B. In vivo testing – Latin in living, carried out in humans and animals

C. Animal phase: evaluate for
   1. toxic effects
   2. side effects
   3. addiction
   4. cancerous tumors
   5. fetal deformities
   6. also calculate therapeutic index (ti – reflects relative margin of safety between dosage that produces
a. therapeutic effect  
b. toxic effect  
7. not always reliable indicator how well drug will work in humans, e.g., Penicillin  
a. few side effects even in relatively high doses in humans  
b. toxic in animals even in small doses  
8. at conclusion of animal phase manufacturer applies to FDA for permission to test on humans  

D. Three phases of human testing  
1. Phase I: Healthy volunteers to  
a. study safe dose range  
b. evaluate side effects  
c. establish correct dosage  
d. also study  
   o Absorption  
   o Metabolism  
   o Excretion of drug  
e. want ads in classifieds of large cities recruiting volunteers  
f. informed consent mandatory  
g. volunteers monitored and given medical examinations  
2. Phase II: Drug given to experimental patients with disease intended for eventual therapy to determine therapeutic effect  
3. Phase III: Several hundred or thousand ill patients  
a. treatment exactly in the way it will eventually be used clinically once approved by FDA  
   o Dosage  
   o Route of administration  
b. upon completion manufacturer submits all documentation to FDA and awaits approval  

IV. FDA Regulations  
A. Monitors quality of both generic and brand name drugs manufactured by all pharmaceutical companies  
1. generic and related trade name drugs must contain exactly same active drug ingredients  
2. must be administered in exactly the same way  
3. variations among manufacturers are permitted for  
a. inert ingredients (fillers and binders)  
b. preservatives  
c. antioxidants  
d. buffers  

B. Evaluate new drug based on manufacturer’s recommendation  
C. Consider risk versus benefit ratio  
D. Can take more than one year before approval or rejection given
E. Once approved by FDA manufacturer cannot change
   1. ingredients
   2. manufacturing process
   3. labeling
   4. packaging
   5. dosage

F. indicated uses may be expanded with further clinical trials; examples:
   1. Inderal (propranolol)
      a. approved 1967 for hypertension
      b. 1979 to treat migraine headaches
   2. Indocin (indomethacin)
      a. initially approved for treatment of arthritis and gout
      b. 1985 approved for premature infants to close ductus arteriosus
to avoid surgery

V. Drug Patents – requested when a new drug is discovered or designed
   A. All companies protected by patent on new drugs
   B. Length of 17 years including the testing process
   C. No other company can manufacture or market identical drug during
      that time
   D. When patent expires any pharmaceutical company can manufacture
      1. under original generic name
      2. under new brand name selected by manufacturer
   E. Original brand name can only be used by original manufacturer

VI. If generic drug manufactured by several companies may be listed under
    several brand names, e.g. ampicillin
    1. Omnipen - Wyeth-Ayerst
    2. Policillin - Bristol
    3. Principen - Squib
    4. Totacillin - Beecham Labs

VII. Drug Withdrawals and Recalls
    A. Post-Marketing Surveillance – An approved drug is not guaranteed
       to stay on the market indefinitely, Drug companies and the FDA
       continue to monitor the effectiveness and safety of approved drugs.

    B. Healthcare professionals and consumers can report adverse events
       concerning drugs through MedWatch, the FDA’s safety information
       and adverse event reporting system on the internet.

    C. If a drug is associated with adverse effects, the FDA may elect to
       have the drug company expand existing warning labels to include new
       information rather than withdrawing.

    D. The FDA can remove (recall) certain batches of drugs due to
       manufacturing defects (e.g., Drug does not remain stable until its
E. It is the responsibility of the manufacturer to notify the physicians, hospitals, and pharmacies of a drug recall.

F. Once notified of a recall it is the responsibility of physicians, hospitals, and pharmacies to dispose of recalled lots of drugs as per policy.

Activity
I. Create a drug/pharmaceutical agent. Give it a chemical, generic, and trade name. Must give an indication for use, dosage, form and side effects. And, create a picture of their drug & container. See guidelines.

II. Write and perform a public service announcement demonstrating the approval process for the new drug/pharmaceutical agents by the FDA. (See HOSA PSA event guidelines)

III. Debate the availability and access of new pharmaceutical agents to clients with AIDS, diabetes, or indigent people.

IV. Complete the FDA Web Search.

V. Show any of the following movies:
   Medicine Man
   Awakenings – (Awakenings Questions provided)
   Lorenzo’s Oil
   * Remember to follow your school district policy for viewing movies

Assessment
Quiz: Drug Design, Testing, Manufacturing, and Marketing
Project Rubric
PSA HOSA rubric
Movie questions

Materials
www.fda.gov/drugs
www.accessdata.fda.gov/scripts/cder/
http://www.fda.gov/Safety/MedWatch/default.htm
www.hosa.org
Key - Quiz: Drug Design, Testing, Manufacturing, and Marketing
Computers with Internet access
HOSA Biomedical Debate Guidelines
HOSA PSA Guidelines
Movies and questions:
   Medicine Man
   Awakenings
   Lorenzo’s Oil
   * Remember to follow your school district policy for viewing movies
Accommodations for Learning Differences
For reinforcement, the student will research the Internet and other sources to trace research, design, and approval process for any one pharmaceutical agent.

For enrichment, the student will write a proposal to be submitted to the FDA for a pharmaceutical agent that has just been discovered.

National and State Education Standards
National Health Science Cluster Standards
Foundation Standard 2: Communications
Healthcare professionals will know the various methods of giving and obtaining information. They will communicate effectively, both orally and in writing.
Accountability Criteria
2.1 Concepts of Effective Communication
2.11 Interpret verbal and nonverbal communication.
2.12 Recognize barriers to communication.
2.13 Report subjective and objective information.
2.14 Recognize the elements of communication using a sender-receiver model.
2.15 Apply speaking and active listening skills.
2.3 Written Communication Skills
2.31 Recognize elements of written and electronic communication (spelling, grammar, and formatting).

TEKS
130.205(c)(1)(G) implement scientific methods in preparing clinical case studies
130.205(c)(2)(A) accurately describe and report information, according to facility policy, observations, and procedures;
130.205(c)(2)(B) demonstrate therapeutic communication skills to provide quality care
130.205(c)(3)(A) demonstrate proficiency in medical terminology and skills related to the health care of an individual;
130.205(c)(3)(C) describe the steps necessary for entrepreneurship in a free enterprise system;
130.205(c)(3)(D) develop new problem-solving strategies based on previous knowledge and skills; and
130.205(c)(3)(E) evaluate performance for continuous improvement and advancement in health science.
130.205(c)(7)(A) interpret knowledge and skills that are transferable among health science professions;
130.205(c)(7)(B) plan academic achievement for advancement in the health science industry; and
130.205(c)(7)(C) analyze emerging technologies in the health science industry.

Texas College and Career Readiness Standards
Cross Disciplinary
I. Key Cognitive Skills
A. Intellectual curiosity
1. Engage in scholarly inquiry and dialogue
D. Academic behaviors
1. Self-monitor learning needs and seek assistance when needed.
C. Critical listening
1. Understand and interpret presentations (e.g., speeches, lectures, informal presentations) critically.
b. Listen to a lecture and write down questions that require clarification, either by consulting the lecturer or other students.
c. Listen to a lecture and connect the new information with previously studied topics.
E. Technology
1. Use technology to gather information.
a. Use the Internet or other appropriate technologies to post survey questions on an assigned topic.
II. Foundational Skills
A. Reading across the curriculum
1. Use effective pre-reading strategies.
B. Writing across the curriculum
1. Write clearly and coherently using standard writing conventions.
C. Research across the curriculum
1. Understand which topics or questions are to be investigated.
8. Present final product.
a. Use appropriate media for presentation of research results.
b. Document sources using a standard format appropriate to the subject area.
Creating a Drug/Pharmaceutical Agent Guidelines

You will create a drug/pharmaceutical agent.

- Give it a chemical, generic, and trade name.
- Give an indication for use, dosage, form and side effects.
- Create a picture of the drug and container.
## Project Rubric

**Student:** ________________________  **Date:** ___________________________

<table>
<thead>
<tr>
<th>Scoring criteria</th>
<th>4. Excellent</th>
<th>3. Good</th>
<th>2. Needs Some Improvement</th>
<th>1. Needs Much Improvement</th>
<th>N/A</th>
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<tbody>
<tr>
<td>Clearly/effectively communicates the main idea or theme.</td>
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<td>Reflects application of critical thinking.</td>
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<td>Information clearly provided in an organized and thoughtful manner.</td>
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<td>Strong examples used to describe the theme or objective.</td>
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<td>Illustrations follow a logical reasoning.</td>
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<td>Each image and font size is legible to entire audience.</td>
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<tr>
<td>No spelling, grammatical or punctuation errors.</td>
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**NOTE:** N/A represents a response to the performance which is "not appropriate."
1. List and describe 10 recent drug or medical device recalls. See www.fda.gov/drugs.

2. List 10 different FDA approved drug products. See www.accessdata.fda.gov/scripts/cder/.
Drug Design, Testing, Manufacturing, and Marketing Quiz

1. By what names can a drug be known?
   a.____________________________________
   b.____________________________________
   c. ____________________________________

2. Match the following (not all choices apply):
   A. _____ diazepam    1. Paxipen
   B. _____ lorazepam    2. Valium
   C. _____ halazepam    3. Centrax
   D. _____ oxazepam    4. Serax
   E. _____ prazepam    5. Ativan
                     6. Prozac
                     7. Atarax

3. List 5 (five) reasons for manufacturers to propose brand names for their products:
   1. __________________________________________________________________
   2. __________________________________________________________________
   3. __________________________________________________________________
   4. __________________________________________________________________
   5. __________________________________________________________________

4. By which two ways are new drugs discovered?
   _________________________________________________________________
   _________________________________________________________________

5. Describe Phase I of human testing of new drugs.

6. What is meant by tests that are performed \textit{in vitro}?

7. What is meant by tests that are performed \textit{in vivo}?

8. Explain \textit{Post Marketing Surveillance}.

9. What is \textit{MedWatch}?

10. How long is a drug patent good for?
KEY - Drug Design, Testing, Manufacturing, and Marketing Quiz

1. chemical
generic (nonproprietary)
trade name (brand name; proprietary)

2. A  2
   B  5
   C  1
   D  4
   E  3

3. (any 5):  indicate disease to be treated
   simplify generic name
   indicate source of drug
   indicate action of drug
   indicate several drugs in combination
   indicate frequency of administration
   indicate duration of action
   indicate drug strength
   indicate amount of active ingredient
   reflect manufacturer’s identity

4. a. new chemical substance discovered in environment
   b. completely new chemical derived from molecular manipulation of existing drug

5. **Phase I:** Researchers test a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects. Studies assess the safety of a drug or device. *This initial phase of testing, which can take several months to complete,* usually includes a small number of healthy volunteers (20 to 100), who are generally paid for participating in the study. The study is designed to determine the effects of the drug or device on humans including how it is absorbed, metabolized, and excreted. This phase also investigates the side effects that occur as dosage levels are increased. About 70% of experimental drugs pass this phase of testing.

6. *In vitro* testing – Latin *in glass*, done in laboratory in glass tubes and Petri dishes
7. *In vivo* testing – Latin *in living*, carried out in humans and animals
8. Drug companies and the FDA continue to monitor the effectiveness and safety of approved drugs.

9. **MedWatch** is the FDA’s safety information and adverse event reporting system on the internet.

10. 17 years including the testing process.
Awakenings Movie

Answer the following questions with a short answer.

1. What caused the brain damage to the "frozen" people in the film?

2. Why do you think Lucy could keep walking when the pattern on the floor continued?

3. How was music important to the "frozen" people?

4. What kind of music "worked?"

5. Do you think Dr. Sayer is justified in experimenting with drugs on his patients before research was conducted to find out how the drugs would affect the people?

6. What do you think would have happened if the patients had died as a result of the drug treatments?

7. Discuss whether or not you felt the L-Dopa should have been discontinued.

8. Had you been one of the patients, would you want to continue using L-Dopa?

9. Would you want a family member to continue using L-Dopa?

10. Why did Dr. Sayer have to stop using the drug L-Dopa on the "frozen" patients?
11. The cost of administering the L-dopa to 15 patients was $12,000 (US) in 1969. Why are new drugs so expensive? What justifies their price if they are not even proven?

12. What do you make of the way the funding was generated for the experiments? Should the kind of research we see in AWAKENINGS be funded by private donors?

13. After the therapeutic effects of the L-dopa no longer seem to be working for Leonard and his Parkinsonian condition worsens dramatically, he says to Dr. Sayer: “Sometimes I’m not a person, just a repertoire of tics. …This isn’t me.” What does Leonard mean by this? Is his personhood really under threat from this disease? In what way(s)?

Opinion Questions

14. The title of this movie was Awakenings. During the movie, Leonard said, "... You didn't awake a thing, you woke a person." That was just one awakening. I believe that Dr. Sayer, the nurses and Leonard’s girlfriend also “awoke” during this movie. Choose one of these characters and explain why they also awoke.

15. During the first part of the movie, Lucy stops when the pattern on the floor stops. When Doctor Sayer paints in the pattern, Lucy goes to the window instead of the drinking fountain. What did Doctor Sayer realize when he said, "She’s looking out the...?" From this scene and others in the movie, what did you learn about how you should treat others?

16. Once Lucy realizes that she is no longer young, she said “I can't imagine being older than 22. I've no experience at it. I know it's not 1926. I just need it to be.” What happens to her and the other patients in the movie would be like you going to sleep today, and waking up on your 45th birthday. What would this be like?

17. When Dr. Sayer was trying to communicate with Leonard using an Ouija board, Leonard gave him the library code for the following poem: “His gaze is from the passing of bars so exhausted, that it doesn't hold a thing anymore. For him, it's as if there were thousands of bars and behind the thousands of bars no world. The sure stride of lithe, powerful steps, that around the smallest of circles turns, is like a dance of pure energy about a center, in which a great will stands numbed. Only occasionally, without a sound, do the covers of the eyes slide open-. An image rushes in, goes through the tensed silence of the frame- only to vanish, forever, in the heart. "Why was this poem important to Leonard?