BPS 2110
Assignment 1 Answers

1. Complete the following table regarding clinical trials

	Phase I	Phase II	Phase III
Goals	Safety Find max safe dose	Safety Efficacy Find effective dose	Safety Rare side effects Efficacy
Number of patients	~100	200-300	thousands
Type of patients	Healthy volunteers	patients	patients
Average time taken	< 1 year	~1 year	~1 year
Drug failure rate	30%	70%	70%

2. What are the two general types of large pharmaceutical companies? Describe their main characteristics.

- Ethical companies, discover and develop new molecular entities, very large companies that invest heavily in research
- Generic companies, market products no longer protected by patents, very large or medium companies that perform limited research focused on manufacturing

3. What is the difference between drugs in terms of drug products and molecular entities? Which is more common, and why is one much more common than the other?
   - molecular entities are the chemical substances used in pharmaceuticals. Drug products are different forms or combinations of molecular entities. These are much more common, because a drug can be sold in different doses, formulations or combinations

4. What are the 5 major phases of discovering a new drug called? Complete the following table regarding the process of producing a new drug.

Phase	Discovery	Development	Clinical trials	FDA approval	Market
Time	1 to 3 years	1 – 2 years	1-5 years	6 months to 1.5 years	unlimited
Major goals	Start with an idea and discover a new molecular entity	Turn drug candidate into a sellable product (investigational new drug)	Test IND for safety. Establish safe limits for dosing, Test for	Review data from clinical trials to ensure testing was	Make money Continue safety testing Identify

	(drug candidate)		efficacy, establish dosing, test for rare side effects	done properly, Verify that data shows clear benefit which outweighs risks	very rare side effects Find new indications
End product	Drug Candidate	Investigational New Drug	New Drug Application	Market Approval	$$$

5. What is meant by each of the following terms?
    a. Drug candidate
    - molecule identified as potential drug. Structure is kept secret by company until development is complete
    b. IND
    - Application filed with FDA asking permission to enter clinical trials. Includes pharmacology and toxicity data from animal studies as well as manufacturing information proving consistency of manufacture. Plan for clinical trials and investigator info is part of this as well.
    c. NDA
    -Application filed with FDA to enter the market. Includes full data proving safety, efficacy, dosing information and drug labeling from human clinical trials and animal experiments. Data proving sound manufacturing methods and quality controls used are included.
    d. ANDA
    -Application filed with FDA for permission to market a generic version of a drug. Data showing that the drug identity, dose, formulation, route of administration, performance and route of administration are included.

6. Why do drug companies prefer to treat chronic conditions rather than acute ones?
    -chronic conditions require long-term administration of the drug. This provides a long-term market with assured customers. Company likely to make more profits over long periods of time

7. What are the three *most common* methods of lead identification in the pharmaceutical industry?

-high throughput screening
-rational drug design
-identification of natural products

8. What characteristics make a good lead compound?
    -proven biological activity, specificity, pattern of drug-like properties, patentable, modifiable (chemistry is possible and practical)

9. What are two key difficulties associated with natural products in terms of drug development?
   -complex structures make chemical modification difficult
   -establishing supply of large amounts of drug for complex chemical structures

10. What are the advantages of using solid phase synthesis rather than solution phase synthesis?
- ease of purification
- possibility for automated methods (robots)

11. Describe how drug companies perform safety testing during drug development.
- initial tests done *in vitro* using as many biochemical and biological tests as possible
- if profile of results is consistent with a good safety profile in humans, tests are run on animals
- at least 2 species must be used, normally companies use 3 (including one primate)

12. List 4 different types of excipients and briefly explain their importance for formulation
- stabilizers (acid or base) protect drug from chemical degradation
- preservatives prevent mold or bacterial growth
- fillers ensure consistent dosing
- disintegrants help with water dissolution by forcing the components of pills apart
- binders hold solid components together in pills
- flavors mask the taste of active ingredients (many drugs are bitter)
- colors help to identify pills (important for prescription safety)
- lubricants help manufacturing by preventing pills from sticking to machinery

13. List 4 different types of formulation and provide a key advantage and disadvantage of each
- pills or caplets – oral dosing, convenient for patient
- capsules – oral dosing, convenient for patient
- liquids – oral dosing, convenient for patient
- topical cream – avoid liver, deliver drug to a specific location
- patch - avoid liver, deliver drug to a specific location, provide steady dosing over a long time period
- injectable liquid - avoid liver, avoid digestive tract (stomach), deliver drug to a specific location, provide rapid entry into the body, provide steady dosing over a long time period
- nasal spray - avoid liver, deliver drug to a specific location, provide rapid entry into the body
- eye drops - avoid liver, deliver drug to a specific location

- suppositories - avoid liver, provide rapid entry into the body, provide steady dosing over a long time period

14. What are the key parts of the Nuremburg code for research on humans? Why is it important to adopt and follow such a code?
- voluntary participation
- informed consent
- prior animal studies
- benefits outweigh risks
- qualified researchers
- no suffering (minimal)
- stop experiments if they become dangerous

15. Approximately when were the first government regulations for drugs created? Why were these rules created, and what was the major focus of the legislation?
- first rules in 1908
- rules created to ensure consumers knew what they were buying
- rules focused on labeling only, and only on listing the ingredients

16. Describe the events that lead to the creation of the FDA. What key ideas were introduced as part of the FDA's creation?
- formulation of sulfanilamide containing diethylene glycol poisoned children taking the drug
- company had not performed any safety testing at all
- drug was sold without instructions
- FDA introduced the idea of required safety testing in animals and humans
- Directions were now required on the label
- Companies would do the testing according to FDA guidelines
- FDA now started inspecting companies

17. What are the 4 key requirements for modern drug safety testing in animals? Why is each of these requirements important?
- testing in at least 2 species
- at least one species must be a primate
- must take blood samples to show drug is bioavailable (gets into the body)
- must use dose that is relevant to future human use

18. Briefly describe how agencies such as the FDA and Health Canada operate.
- safety testing done by companies
- provide full data to FDA
- FDA checks the data to ensure experiments done properly
- Approves marketing of drugs
- Companies are required to monitor the effects of their drugs in patients
- Companies required to report any difficulties to FDA
- FDA inspects drug manufacturing facilities

19. Why do you think it is important that the government does **not** perform safety testing?

- places costs of testing drugs on the consumer rather than the taxpayer
- forcing companies to spend their own money ensures that companies will only test drugs they think have a good chance of reaching market