



**B.E/B.TECH DEGREE EXAMINATIONS: NOV/DEC 2023**

(Regulation 2018)

Seventh Semester

**BIOTECHNOLOGY**

U18BTT7002: Preclinical and Clinical Regulatory Affairs

**COURSE OUTCOMES**

- CO1:** Understand the regulatory aspects and ethical considerations involving human subjects
- CO2:** Understand the timelines and resources required to discover and develop new drugs in a preclinical setting
- CO3:** Demonstrate an understanding of the critical features of each stage of the preclinical drug development process
- CO4:** Classify different types of trial designs
- CO5:** Apply and demonstrate critical analysis of clinical data using statistical analysis tools
- CO6:** Identify quality parameters of clinical research report.

**Time: Three Hours**

**Maximum Marks: 100**

**Answer all the Questions: -**

**PART A (10 x 2 = 20 Marks)**

**(Answer not more than 40 words)**

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|---|-----|-------------------|
| 1. Define the role of sponsor in investigator brochure.   | CO1 | [K <sub>2</sub> ] |
| 2. Assume the human weight to be 50 kg and the animal (Dog) dose is 10mg/kg. Calculate the HED (mg/kg). Calculate the maximum recommended starting dose (MRSD) assuming the safety factor to be 10. (Given: Conversion factor for dog divide animal dose by 1.8 or multiply by 0.54). | CO2 | [K <sub>3</sub> ] |
| 3. What are the benefits and risks of participating in a clinical trial?  | CO2 | [K <sub>2</sub> ] |
| 4. Define eligibility criteria in a clinical trial.   | CO3 | [K <sub>2</sub> ] |
| 5. What is a placebo and does placebo expire?   | CO3 | [K <sub>2</sub> ] |
| 6. What is the reason behind involving healthy volunteer (generally) in phase I clinical trial?   | CO4 | [K <sub>2</sub> ] |

7. A clinical trial is designed with the requirement that 400 evaluable subjects are required to achieve the correct level of power. If it was expected that 30 percent of subjects will be non-evaluable, how many subjects should you plan to recruit? CO5 [K<sub>4</sub>]
8. Write the null hypothesis and alternate hypothesis for superiority trials. CO5 [K<sub>2</sub>]
9. What is annotated CRF? CO6 [K<sub>2</sub>]
10. Write a short note on database lock in clinical data management. CO6 [K<sub>2</sub>]

**Answer any FIVE Questions:-**

**PART B (5 x 4 = 20 Marks)**

**(Answer not more than 80 words)**

11. A consumer informed her family physician that her 5 years old daughter developed 2 episodes of vomiting and severe diarrhoea after intake of amoxicillin for the treatment of upper respiratory tract infection. The family physician discontinued amoxicillin and prescribed loperamide and ORS powder for severe diarrhoea. Write ICSR analysis tabulation for the given case. CO1 [K<sub>3</sub>]
12. Draw the schematic protocol for different types of randomizations in clinical trial. CO2 [K<sub>2</sub>]
13. A professor working on cardiac function is hoping to develop a new drug candidate. He asks a colleague who works for industry to share some data from related work. The colleague is willing to share his data ,but asks that it be kept confidential and not shared with others. The data, when it arrives, is stamped “confidential – Pre-IND” and the request for confidentiality is repeated in a cover letter. The professor submits a grant application. During scientific review, a reviewer alleges that the preliminary work section of the application contains data, which were obtained in another lab without that investigator’s knowledge or permission. What is the principle violated? Comment on the ethics in the above case. CO3 [K<sub>3</sub>]
14. Investigators wish to study the differences in patients with subtherapeutic concentrations of vancomycin via two different delivery systems. The result of this two-week study is reported below, CO4 [K<sub>3</sub>]

	Formulation A (n=55)	Formulation B (n= 62)
Subtherapeutic Vancomycin concentration	35	17

Calculate absolute risk reduction, Odds formulation A & Odds formulation B and NNT and

evaluate the formulation A and B.

15. Write on the purpose of data monitoring committee (DMC). CO5 [K<sub>2</sub>]
16. What are SAE Criteria and various outcome of SAE? CO6 [K<sub>2</sub>]

**Answer any FIVE Questions:-**

**PART C (5 x 12 = 60 Marks)**

**(Answer not more than 300 words)**

17. a) Identify the major activities that occur during the drug development and approval process of a new antidiabetic drug. CO1 [K<sub>2</sub>]
- b) Comment on preclinical research toxicology models. CO1 [K<sub>2</sub>]
18. a) Describe the history behind the development of ethics involving human subjects in clinical trials. CO2 [K<sub>2</sub>]
- b) Describe the organizational structure and list the roles of International Ethical committee review guidelines that monitors the safety and efficacy of the vaccine clinical trial process. CO2 [K<sub>2</sub>]
19. a) An investigation team has developed a thyroid drug and safety, and efficacy studies are completed in animals and humans. This thyroxine drug is to be tested in a tropical developing country with a poor health service system like Africa. Design a hypothetical cross-over design trial. CO3 [K<sub>6</sub>]
- b) Write the primary and secondary objective of above thyroxine clinical trial with consort flow diagram. CO3 [K<sub>3</sub>]
20. a) Researchers wished to assess which of two methods of managing post-operative pain following shoulder surgery was the most effective in reducing the postoperative experience for patients. The main outcome measure was the amount of patient-administered morphine used in the first 24 hours' post-operation. The effect size of interest was 7mg morphine and the population standard deviation was estimated as 10 mg, the researchers wanted to have 90 percent power to detect a difference with a two-sided significance of 0.05. Use  $Z_{\beta} = 1.282$   $Z_{\alpha} = 1.9$
- i) Calculate sample size
- b) ii) Also calculate sample size when the researcher anticipated a dropout rate of 20%. CO4 [K<sub>3</sub>]

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|-----|----|---|-----|-------------------|
| 21. | a) | Write a short note on CTD modules in clinical trial according to ICH E6 Good Clinical Practice (GCP).   | CO5 | [K <sub>2</sub> ] |
|     | b) | You are working in the drug safety department of a company and are trying to put together an adverse event report on one of your company's products. What are the minimum requirements you need to assemble a valid case in a pharmacovigilance department? | CO5 | [K <sub>2</sub> ] |
| 22. | a) | Critically evaluate the steps of discrepancy management in Clinical Data Management.  | CO6 | [K <sub>5</sub> ] |
|     | b) | Compare and contrast types of data entry in Clinical data management.   | CO6 | [K <sub>2</sub> ] |

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