Exam Date & Time: 09-Sep-2021 (02:00 PM - 05:00 PM)

MANIPAL ACADEMY OF HIGHER EDUCATION

Manipal Academy of Higher Education, Manipal MPharm Theory End-Semester Examinations.

Pharmacological and Toxicological Screening Methods II [PHA-MPL202T]

Marks: 75 **Duration: 180 mins.**

SECTION - A

Answer all the questions.

Answer the following (10 marks x 5 = 50 marks)

1) How do we grade ADRs based on their severity? Classify and explain the different types of ADRs with suitable examples. Describe photosensitivity reaction and the type of allergic response. What type of ADR can safety pharmacology predict? (2 + 4 + 3 + 1) (10)

2) Compare and contrast various repeated dose oral toxicity guidelines of OECD. (10)

3) Why was GLP created? List out its objectives, advantages and disadvantages. What are the practices we need to develop while setting up a GLP testing lab? (2 + 2 + 6) (10)

4) A series of new molecules were evaluated for anti-diabetic activity by a pharmacological team. Now the desired molecules are to be taken up for the regulatory toxicity. The Head of the Research wing invited you to audit the pharmacological data generated and set criteria for selecting the compounds to be considered for safety assessment. What would be your approach on this? (4 marks). How would you plan for the safety pharmacological studies for these compounds? (6 marks) (10)

5) Elaborate the characteristic features of the rat vaginal smear and how it can be used to improve the chances of plug formation during mating? Discuss the phases of animal fertility testing as per ICH guidelines. Clarify the distinction between IND-enabling toxicology and safety pharmacology studies (4 + 4 + 2) (10)

SECTION - B

Answer all the questions.

Answer the following (5 marks x 5 = 25 marks)

6) As a team leader you are presenting to the Head of your organization to conduct a chronic toxicity of a test compound which can potentially be an IND based on the OECD guidelines 452. However, the Vice-President of the organization comments that the study needs to be fastened for IND approval and recommends you go as per ICH guidelines with adaptations from OECD 453. How do think these modifications will meet the time frame and improve the quality of your work. (5)

7) List the importance of guidelines in regulatory toxicity studies. Explain the four steps in toxicity assessment of chemicals that includes hazard identification, dose-response and exposure assessment and risk characterization (2 + 3) (5)

8) How do we perform in vitro genetic toxicity testing for chromosomal abnormality? (5)

Describe the relevance of mammalian alkaline comet assay? (3 + 2)

9) A new chemical entity (NCE) intended to be used as an analgesic and anti-inflammatory was tested for chronic toxicity studies in dogs. At a dose of 50 mg/kg, 2 out of 5 dogs in the group showed decreased urine output after 3 months of treatment. Subsequently, the observer could identify swelling in the dog's hind limbs. The study director ordered for haematological and biochemical examination of blood samples. The blood report showed increase in serum creatinine and urea levels. What type of toxicity the NCE could have resulted in these dogs? Justify your answer. What further measures can be taken to confirm the target organ toxicity? (5)

10) Write a short note on cardiovascular safety studies recommended by ICH guidelines. (5)

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