Question Paper

Exam Date & Time: 13-May-2023 (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 -S3]

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

SECTION - A

Answer all the questions.

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

1)	Based in Japan, a research organization proposes to develop a new OECD test guideline for the assessment of biological products for specific use in humans. Describe the requirements to consider the proposal and the steps involved to introduce the same. (3+7)	(10)
2)	As a team leader you are presenting to the Head of your organization to conduct a chronic toxicity of a test compound based on the OECD guideline 452 which can potentially come to the market for human usage. However, the Vice-President of the organization comments that the study needs to be hastened and recommends following ICH guidelines with adaptations from OECD 453. How do think these modifications will help the study meet the time frame and improve the quality of the work? A new chemical entity (NCE) intended to be used as an analgesic and anti-inflammatory agent was tested for chronic toxicity studies in dogs. At a dose of 50 mg/kg, 2 out of the 5 dogs in the group showed decreased urine output after 3 months of treatment. Subsequently, the observer could also identify swelling in the dog's hind limbs. The Study Director ordered for haematological and biochemical examination of blood samples. The report showed increase in serum creatinine and urea levels. What type of toxicity could the NCE have resulted in these dogs? Justify your answer. What further measures should be taken to confirm the target organ toxicity? (6+4)	(10)
3)	Elaborate the characteristic features of a rat's vaginal smear based on the phases of its oestrus cycle. Illustrate the study design for pre- and post-natal testing in animals and explain its significance. (4+6)	(10)
4)	Explain the minimum CNS safety pharmacology studies needed for regulatory submission.	(10)
5)	What are the emerging technologies for alternative animal testing? Describe any two with merits and demerits. (3+4+3)	(10)

SECTION - B

Answer all the questions.

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

6)	A new chemical entity (NCE) intended to be used as a sedative and hypnotic was tested for sub-acute toxicity in rodents. This compound at a dose of 200 and 400 mg/kg caused lethargy and decreased food consumption from day 14 to 28. In NCE group, 6 out of 10 rats showed decreased RBC, WBC, Hb, platelet count, plasma protein and elevated levels of serum transaminases. The remaining 4 rats showed elevation in serum creatinine and blood urea nitrogen. What are the target organs that might be affected by the NCE? How can histology of various organs confirm the toxicity to the target organs?	(5)
7)	Write a short note on the *in vitro* genotoxicity test to assess chemicals that induce gene mutations by base substitutions or frameshifts.	(5)

8)	Write about hERG assay.	(5)
9)	Frame the study design for assessing the toxicokinetics of a compound.	(5)
10)	Explain the scope of saturation kinetics in toxicology with an example.	(5)

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