Your Roll No.....

JAMIA HAMDARD

M.Sc TOXICOLOGY SEMESTER III EXAMINATION, JANUARY 2023

Paper: Pre-clinical Toxicology for Drug Development

Paper Code: MTX-DCE – 302

Time: 1.5 hours **Maximum marks: 37**

QUESTION 1.Very briefly explain importance of the following: **[1X7=7 MARKS]**

a. DRF
b. LLNA
c. CPCSEA
d. MABEL
e. Thalidomide
f. NDA application
g. LD10

QUESTION 2. Answer any 3 of the following: **[3X5=15 MARKS]**

a. Discuss justification of conducting animal toxicity tests in risk assessment of medicines for humans.
b. Discuss the use of RABBITS in toxicity studies in drug development.
c. Describe toxicity study requirements as described in New Drugs & Clinical Trial Rules 2019 for medicines which alter the development of children.
d. Toxicity data required for conduct of Phase II efficacy and safety clinical Trials of new chemical entity in male and female patients.
e. List the laboratory test requirements to be fulfilled in 90-day repeat dose subchronic toxicity study.

QUESTION 3. Answer any 3 of the following: **[3X5=15 MARKS]**

a. Human peripheral lymphocytes cultured *In Vitro* in presence of eprosartan mesylate at 2000µg/ml with metabolic activation increased structural aberration at 24hour post treatment. This concentration exhibited cytotoxicity, with mitotic index reduced by 94%. Eprosartan without metabolic activation did not increase structural aberration at any concentration. What is your interpretation? What studies will you plan to assess the risk caused by eprosartan.
b. Describe the tests suggested by New Drugs & Clinical Trial Rules 2019 to reduce and refine animal use in the drug development process.
c. In a reproductive toxicity study in Sprague-Dawley rats, Eprosartan was administered to all rats orally by gavage for 105-108 days at dose levels of 0, 30, 100, 1000mg eprosartan/kg/day. Mortality and clinical signs of toxicity was observed in one male in the 30mg/kg/day dose group died prior to dosing on day 48. No deaths occurred at the two higher doses. What other data will you examine to ensure that eprosartan can safely be given to men?

d. Identify the NOAEL of CBD using the data provided in question 3c. Considering the rat-to-human conversion factor is 0.08 and dog-to-human conversion factor as 0.541, describe the step-by-step approach to calculate the Maximum Recommended Starting Dose (MRSD) in 60 kg man using safety factor of 1/10.

e. A single IV dose of 100 mg/kg administered over 20 minutes was the NOAEL for rats in an acute toxicity study with plazomicin, an aminoglycoside. Mortality, clinical signs of toxicity and nephrotoxicity was observed at 150 and 200 mg/kg. Pivotal studies of 14 and 28 days repeat doses were conducted with plazomicin in rats and dogs. Mild anemia in rats, but not in dogs, and renal toxicity was observed. Discuss.

-:The End:-