SAQ Paper 2016

1

a) Define oral bioavailability. **(1 mark)**
b) List 4 factors that can influence the oral bioavailability of a drug. **(2 marks)**
c) Define elimination half-life. **(1 mark)**
d) Describe what is meant by volume of distribution. **(2 marks)**
e) Describe how elimination half-life relates to volume of distribution and clearance. **(2 marks)**
f) The mean steady state volume of distribution for a drug is 105 litres. What does this tell you about the drug? **(2 marks)**

2

a) What is a biosimilar? **(2 marks)**
b) Briefly describe 8 key principles (the "biosimilar approach") that should be considered when developing a biosimilar in the European Union. **(8 marks)**

3

a) Briefly describe the types of data / information that are needed from non-clinical studies to support a phase I first in human study for a new chemical entity (NCE). **(8 marks)**
b) List 4 additional types of non-clinical data that are (or maybe) needed to support a marketing authorisation application for this NCE. **(2 marks)**

4

a) Briefly describe the 3 legal classifications of medicinal products in the United Kingdom (UK). **(2 marks)**
b) What are the criteria that must be met for a product to be available without a prescription in the UK? **(6 marks)**
c) Briefly describe 2 sections of the Summary of Product Characteristics (SmPC) that may be impacted when a product moves from prescription to non-prescription status. **(2 marks)**

5 A 45 year old man with lung cancer is participating in a double blind, randomised phase 2b clinical trial with 2 arms. Patients either receive a small molecule experimental drug (Drug Z) in combination with cisplatin or matched placebo plus cisplatin. The patient develops pulmonary symptoms culminating in a diagnosis of Interstitial Lung Disease (ILD) and is admitted to the Intensive Care Unit. **(10 marks)**

Briefly describe the factors you would consider to determine the likelihood that the experimental drug (Drug Z) contributed to the development of this patient's ILD.

6 Give advantages and disadvantages of conducting first time in human trials in healthy volunteers. **(10 marks)**

7 Unusual results were identified in 2 subjects (A and B) when the pharmacokinetic (PK) data from a phase I trial were analysed.

The trial was a randomised, double-blind, cross-over of 3 independent study periods, with an appropriate washout period between each study period. Subjects received active drug in two of the study periods and matching placebo in one period.

Trial supplies were dispensed by a qualified (unblinded) Trials Pharmacist at the study site on the day of attendance for each study period. Both subjects (A and B) were recruited late into the study and so their attendance for their first study period was at the same time that the rest of the trial subjects were attending for their second dosing period.

- Subject A had PK data consistent with active dosing in all 3 study periods.
- Subject B had PK data consistent with active dosing in only 1 study period.

It was suspected that the unblinded trial Pharmacist at site, in error, dispensed study period 2 medication instead of study period 1 for these two subjects for their first study period and then correctly dispensed study periods 2 and 3 at subsequent visits.

a) List 5 groups who may need to be informed by the Sponsor of this issue and for each group briefly explain why. **(5 marks)**

b) List 4 different "analysis sets" you could define for the data you have. **(2 marks)**

c) Given the usual objectives of a phase I trial, which 2 of the analyses sets (you have listed above) could be considered the most important? **(1 mark)**

d) With respect to the Corrective Actions and Preventive Actions (CAPA) relevant to the involvement of the Trials Pharmacy in the dispensing of study period medication, briefly describe the underlying principles of the CAPA. **(2 marks)**

8 a) Briefly describe why we perform
   i. A superiority study.
   ii. A non-inferiority study.
   iii. An equivalence study. **(3 marks)**

b) What do you understand by the non-inferiority margin? **(1 mark)**

c) A non-inferiority study was performed with a new drug (X) versus a licensed reference drug (Y). The non-inferiority margin for relative risk (RR) on all-cause mortality (the primary endpoint) was 1.30

Draw a diagram* to illustrate the position of the 95% confidence interval for the RR result for the following scenarios:
   i. Test drug (X) is non-inferior to reference (Y).
   ii. Test drug (X) meets the criteria for non-inferiority but the reference drug (Y) is better. **(6 marks)**
   iii. Test drug (X) does not meet the criteria for non-inferiority and the reference drug (Y) is better.
   iv. Test drug (X) is superior to reference (Y).
   v. The result is inconclusive (neither X nor Y is superior and the criteria for non-inferiority are not met).

**** you need only draw one diagram, but please clearly label each scenario***

9 Drug A is the UK "standard of care" treatment for a chronic disease state. Your company has licensed a new Drug B. You conduct a Cost Effectiveness Analysis (CEA) of Drug B compared to Drug A in this disease, for submission to the National Institute for Health and Care Excellence (NICE).

For parts a) to d) answer the following questions, which relate to some possible differing outcomes of this CEA:

a) What Health Economic word is used to describe the situation where Drug B is found to be less costly and more effective than Drug A? **(1 mark)**

b) If your new drug (Drug B) is found to be more effective than Drug A, and the Incremental Cost Effectiveness Ratio (ICER) of Drug B is £60,000:
   i. Give 2 possible explanations for this result of Drug B compared to Drug A **(2 marks)**
   ii. What would this result be likely to mean, in terms of whether NICE recommends use of Drug B? **(1 mark)**

c) If your new drug (Drug B) is found to decrease the quality of life for patients, but the Cost Effectiveness Ratio (CER) of Drug B compared to Drug A is below that for Drug A:
   i. Give 2 possible explanations for this result **(2 marks)**
   ii. What would this result be likely to mean, in terms of whether NICE recommends use of Drug B **(1 mark)**

d) If your medicine has a similar effectiveness as Drug A, but has an ICER at a level that is unable to be approved by NICE, give one action a company might take, without reducing the list price, which may allow the medicine to receive a positive recommendation from NICE. **(1 mark)**

e) Other than CEA, list 2 other forms of health economic analysis used by governments to decide whether to fund a medicine. **(2 marks)**

10 **You are launching a new medicine in the UK and your company wishes to have a promotional stand at a meeting only attended by UK Physicians.**

a) Briefly describe 7 key considerations that are required to ensure compliance with all relevant codes of practice. **(7 marks)**

b) Following a complaint by a delegate at the conference, the promotional stand was found to be in breach of the UK ABPI Code of Practice as it had promoted an indication for the medicine that is not approved in the UK. List 6 potential sanctions that can be imposed upon a company. **(3 marks)**