FACULTY OF PHARMACEUTICAL MEDICINE
of the Royal Colleges of Physicians of the United Kingdom

DIPLOMA IN PHARMACEUTICAL MEDICINE PART 2 EXAMINATION
19 OCTOBER 2015

SHORT ANSWER QUESTIONS - INSTRUCTIONS TO CANDIDATES

1. **Two hours and 30 minutes** are allowed for answering this paper.
   Allow 15 minutes for each question.

2. **Answer all 10 questions.**
   You do not have to answer the questions in numerical order.

3. We strongly advise you to **write your answers as brief notes / bullet points**, not in the form of essays.

4. Each **question is worth 10 marks.**

   Where questions have more than one part, the number of marks available for each part is shown.

   The number of marks shown for each part should be taken as a guide to the relative extent of the answer required.

   For some questions, a full answer will require more points to be given than the number of marks available because some questions are marked in increments of 0.5 marks.

   Where a specific number of answers are requested, you can provide more and they will be marked, however you cannot score more than the maximum mark for that part of the question.

5. Complete the **front cover of the answer book** with your last name, forename(s), candidate number and signature.

6. **Begin each question on a new page and write only on one side.**
   Please do not write outside the margins of the pages.

7. **On each page of your answer book**, write your candidate number, the question number and the page number:

   e.g. candidate 12 starting his second page in answer to question 5 would complete the answer book page as:

Candidate No:	*12*	Short Answer Questions	Question No:	*5*	Page No:	*2*

8. When the Invigilator announces the end of the session, please stop writing **immediately** and stay in your seat until we've collected the question paper, your answer book and any other notes you have made.

SAQ Paper 2015

1 You are the Principal Investigator of a First in Human study with a new small molecule. List the types of data you would expect members of a dose escalation committee to review prior to each dosing step, and indicate the rationale for each data type. **(10 marks)**

2 a) *In vitro* studies suggest your new drug is a CYP3A4 substrate. Describe how the significance of this can be evaluated in humans. **(7 marks)**

b) CYP3A4 substrate status could impact on the decision to continue development of your new drug. Describe 3 key factors which should be taken into account when deciding whether to continue clinical development of this new drug. **(3 marks)**

3 Define the terms listed below and draw a typical dose response curve for each.

a) Full Agonist **(2 marks)**

b) Partial Agonist **(2 marks)**

c) Inverse Agonist **(2 marks)**

d) Competitive Antagonist **(2 marks)**

e) Non-competitive Antagonist **(2 marks)**

4 Your company is planning to launch a product which is a potent teratogen. You need to include a pregnancy prevention programme into your European Union Risk Management Plan.

a) Describe the elements that you could include within the pregnancy prevention programme. **(6 marks)**

b) Describe how you could demonstrate to the regulatory authorities that the measures you put in place have been effective once the product is on the market. **(4 marks)**

5 a) What is the definition of a counterfeit medicine? **(1 mark)**

b) List 6 potential consequences of counterfeit medicines. **(3 marks)**

c) List 3 factors that are associated with an increased likelihood that a product will be counterfeited. **(3 marks)**

d) Describe 3 steps a drug manufacturer can take to decrease the risk of counterfeiting. **(3 marks)**

6 You are considering whether to include study sites from developing countries in your clinical trial. What factors would you consider in making your decision? Describe 10 factors, covering a broad range of topics **(10 marks)**

7 Describe 10 considerations when choosing an active rather than placebo comparator in pivotal phase III study designs. **(10 marks)**

8 The Association of the British Pharmaceutical Industry Code of Practice requires certain materials and activities to be certified on behalf of the company.

a) What is the reason for certification of promotional materials? **(2 marks)**

b) Apart from promotional materials give two further examples of types of materials or activities that require certification. **(1 mark)**

c) Give two examples of materials or activities, outside of clinical research, that do not require certification. **(1 mark)**

d) Summarise the key aspects necessary for ensuring compliance with certification requirements? **(6 marks)**

9 <u>Regarding Statistical Error</u>

a) In the context of testing drug A on mortality in a placebo controlled study, give the "Null Hypothesis". **(1 mark)**

b) In the table below, there are cells labelled W,X,Y,Z. If you could replace these letters using just one of the three terms "*Correct decision*", "*Type I error*" or "*Type II error*" indicate what term should be given to each letter. **(2 marks)**

	Accept Null Hypothesis	Reject Null Hypothesis
Null Hypothesis is true	W	X
Null Hypothesis is false	Y	Z

c) Which letter could be considered the "Regulator's Risk" and why? **(1½ marks)**

d) Which letter could be considered the "Sponsor's Risk" and why? **(1½ marks)**

Regarding missing data

e) List 2 reasons why missing data is of concern in a clinical trial. **(1 mark)**

f) List 3 ways to handle missing data in an Intention to Treat analysis for continuous data. **(1½ marks)**

g) List 1 way to handle missing data in an Intention to Treat analysis for binary data (e.g. dead or alive). **(½ mark)**

h) To assess the impact of missing data, what would you ask your statistician to do? **(1 mark)**

10 Monoclonal antibodies (mAbs) possess a number of characteristics that distinguish them from small molecules/new chemical entities (NCEs).

Copy and complete this table, listing in a few words in each column, the typical characteristic of mAbs and NCEs. An example ("molecular weight") is given for you. **(10 marks)**

Note:
- You only need to complete 10 of the 12 rows in the table
- This question refers to general statements, not the odd exception

Typical Characteristic	NCEs	mAbs
Molecular weight	Small (<1000 Da)	Large (150-180 kDa)
Species specificity		
Immunogenicity risk		
Route of metabolism		
Duration of action / half-life		
Route of administration		
Toxicity (on/off target)		
Bioequivalence		
Production costs		
Targets		
Blood brain barrier permeability		
Produced in		
Manufacturing/starting materials		