Universiti Tun Hussein Onn Malaysia

UNIVERSITI TUN HUSSEIN ONN MALAYSIA

FINAL EXAMINATION
SEMESTER I
SESSION 2015/2016

COURSE NAME	:	BIOPHARMACEUTICAL TECHNOLOGY
COURSE CODE	:	BNN 40203
PROGRAMME	:	4 BNN
DATE	:	DECEMBER 2015 / JANUARY 2016
DURATION	:	3 HOURS
INSTRUCTION	:	ANSWER **FOUR (4)** QUESTIONS ONLY

THIS QUESTION PAPER CONSISTS OF **SEVEN (7)** PAGES

Q1 (a) As the general manager in a newly developed pharmaceutical company, prepare a sensible 10-year plan of the company. The plan should include strategies of the company from pharmaceutical research and development (R&D) to marketing of a product.

(10 marks)

(b) Following the R&D design, analyse **FIVE (5)** possible challenges in delivering the tasks within time given.

(5 marks)

(c) One of the widely-used technologies in pharmaceutical industry is recombinant DNA.

(i) Compare shot gun approach and the use of reverse transcriptase in getting a copy of a gene.

(5 marks)

(ii) Illustrate and describe how genes are inserted into a plasmid vector.

(3 marks)

(iii) Provide **TWO (2)** reasons of using recombinant DNA technology.

(2 marks)

Q2 (a) Aspirin (acetylsalicylic acid) is a weak acid and often used as analgesic to reduce pain and inflammation. Following synthesis and purification of aspirin, the compound undergoes formulation process in which it is chemically mixed with excipients (buffer, preservatives etc.) for the final form. One of the critical aspects in formulation is the pH, which could affect solubility and stability of the compound. pH is defined in terms of H^+ activity and as the concentration of hydrogen ion in water is very small (<1), pH is plotted as $-\log [H^+]$.

Therefore,

$$pH = -\log [H^+] \text{ or } [H+] = 10^{-pH}$$

(i) Mixture of 0.2 M aspirin and water results in a solution of pH 2.61. Determine hydrogen ion concentration in the newly-prepared aqueous solution of aspirin (assuming that $[H+]_{pure\ water} = 0$)?

(1 mark)

(ii) Calculate the equilibrium concentrations of aspirin salt and its conjugate base, and solve for ionization constant, K_a.

(3 marks)

(iii) Employing the Henderson-Hasselbalch equation and data provided below, calculate the new pH of drug solution when 0.02 moles of aspirin is dissolved in a buffer containing 50 mL of 0.5 M acetic acid ($K_a = 2.5 \times 10^{-3}$) and 100 mL of 0.5 M sodium acetate. Assume that the addition of aspirin has no effect on volume and aspirin dissociates completely.

(6 marks)

(b) Routes of administration plays an important role in drug delivery system to ensure higher chances of drug reaching its target and the most convenient and cheapest way is by oral delivery. In addition to oral, few other routes are also available.

(i) Name **THREE (3)** other routes of administration in delivering drug.

(3 marks)

(i) Discuss the advantages of these routes compared to oral administration and provide an example of compound for each route.

(6 marks)

(ii) Propose **TWO (2)** technologies in drug delivery system and based on particular example, highlight its advanced function in comparison to existing methods.

(6 marks)

Q3 (a) During pharmaceutical development, the choice of manufacturing process is a vital aspect to prevent any chemical changes of the drug and most importantly, its efficacy and effectiveness.

(i) List **THREE (3)** important physico-chemical characteristics of the finished product that must be maintained throughout developing process.

(3 marks)

(ii) Name a pharmaceutical product and identify possible chemical reactions that could alter the state of the finished product.

(4 marks)

(iii) Propose **THREE (3)** preventive measures that could be taken to avoid changes in the finished pharmaceutical drug mentioned in (ii)?

(3 marks)

(b) Granulation is one of the most important unit operations in the production of pharmaceutical oral dosage forms. This process transforms fine-powder into free-flowing and dust-free granules that are easy to compress. There are two types of granulation technique; wet granulation and dry granulation.

(i) Compare and discuss these two granulation techniques.

(5 marks)

(ii) Design a wet granulation technology and discuss its strengths and weaknesses as compared to conventional granulation method.

(10 marks)

Q4 (a) Outline **FIVE (5)** possible impurity-formation pathways during pharmaceutical development.

(5 marks)

(b) Pilot-scale batch allows preliminary investigations of a product and process on intermediate scale before a company proceeds with large production of the compound which required massive amount of money.

(i) Design and sketch block flow diagram of a pilot batch for a newly-developed pharmaceutical drug and briefly explain the process.

(10 marks)

(ii) From the sketch, identify **FIVE (5)** possible challenges in producing high quality product and determine how to solve the issues.

(5 marks)

(c) Process validation is defined as the collection and evaluation of data, from the process design stage through commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality product. There are 3 stages involve in process validation:

(i) Process design
(ii) Process qualification
(iii) Continued process verification

Discuss the activities that are taking place in all three stages of process validation.

(5 marks)

Q5 (a) Define quality assurance in pharmaceutical aspect and explain the significance of having quality assurance system in the industry.

(5 marks)

(b) Identify **FIVE (5)** good manufacturing practices (GMP) in pharmaceutical industry.

(5 marks)

(c) List **THREE (3)** potential hazards in a plant.

(3 marks)

(d) Large fire breaks out at Roche's pharmaceutical manufacturing facility. As a safety personnel in that company, outline the measures that you would take to prevent the second occurrence of this unfortunate event.

(7 marks)

(e) One of the responsibilities of a pharmaceutical company is to protect the environment. Discuss the principles and procedures that could be employed for environmental protection.

(5 marks)

- END OF QUESTION -

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$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$