NATIONAL UNIVERSITY OF SCIENCE AND TECHNOLOGY

DEPARTMENT OF APPLIED BIOLOGY AND BIOCHEMISTRY

BACHELOR OF SCIENCE HONOURS DEGREE

THEORY: BIOTECHNOLOGY OF PHARMACEUTICAL PRODUCTS

SBB4208

MAY 2011

3 HOURS (100 MARKS)

INSTRUCTIONS

Answer Four (4) Questions. Each question carries 25 marks. Where a question contains subdivisions, the mark value for each subdivision is given in brackets. Illustrate your answer where appropriate with large, clearly labelled diagrams

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1. Aureomycin was the first tetracycline antibiotic discovered in the 1940's by Duggar of the pharmaceutical company Lederle.
   a. Describe the general chemical structure of tetracyclines. (3 marks)
   b. Explain very briefly how tetracyclines are made. (2 marks)
   c. Explain the action of tetracyclines. (7 marks)
   d. Are they bacteriocidal or bacteriostatic and why? (3 marks)
   e. Explain the mechanism of tetracycline resistance. (7 marks)
   f. Give three uses of tetracyclines. (3 marks)

2. (a) Explain the five types of vaccines approved for use: killed; live attenuated; subunit; toxoid and recombinant. (15 marks)

   (b) If you, as a Health Officer, had to develop a vaccine to protect the population of Zimbabwe against acute febrile meningococcal disease, what type of vaccine would you use? Explain your choice, taking into account that: (i) infections are often fatal in infants and are difficult to treat as antibiotics do not easily cross the blood/brain barrier; (ii) there is no widespread immunity so all healthy people less than 20 years old will need to be vaccinated to have effect; (iii) the coccus infects by contact with body fluids, usually through inhalation of droplets from coughing, but is not very infective; (iv) it contains toxic lipopolysaccharides. (10 marks)

3. You are employed to do research and development for the multinational company Betapharm that specializes in making biosimilar products to make them available for developing countries. You are tasked with isolating the erythropoietin gene, inserting it into a plasmid, amplifying the plasmid and transfecting it into a mammalian cell-line. Describe each step, what precautions you took, what testing you did and why you made the choices you did (e.g. the choice of plasmid, selection media and cell-line).

4. Recombinant human Follicle Stimulating Hormone (rhFSH) is made in CHO cells by continuous harvest fermentation. Crude diafiltered medium is stored in 50L polyethylene bags at 1-5°C. Each bag is purified to produce about 8 million International Units rhFSH of >98% purity, using five chromatography steps. Describe those five steps, explain the principle on which each step works and, from basic principles, reflect on what is achieved in each step.

5. There are five types of biotechnological production used to manufacture medicines in use: bacterial cells; plant cells; mammalian cells; human cells and transgenic animals. For each of these types of production: give an example of a therapeutic protein that would be used to produce; indicate the strengths and difficulties of the means of production; what safety issues need to be addressed.

6. As an evaluator for the Medicines Control Authority of Zimbabwe, you must prepare a report on the data submitted by a pharmaceutical company to support the registration of a new biotechnological medicine.
   a. State the legal framework on which you would base your report & decisions. (5 marks)
   b. List the five stages of manufacture on which would you report. (5 marks)
   c. Briefly describe the data you would expect to assure you of safety from viral and prion contamination. (5 marks)
   d. Name five characteristics for which every quality control test must be validated. (5 marks)
   e. Name five kinds of excipients and state their purpose. (5 marks)

END OF EXAMINATION