MEDICAL & PHARMACEUTICAL BIOTECHNOLOGY
(BIOT 4246)

Time Allotted : 3 hrs **Full Marks : 70**

Figures out of the right margin indicate full marks.

Candidates are required to answer Group A and any 5 (five) from Group B to E, taking at least one from each group.

Candidates are required to give answer in their own words as far as practicable.

Group – A
(Multiple Choice Type Questions)

1. Choose the correct alternative for the following: **10 × 1 = 10**

(i) The Human Leucocyte Antigen gene resides on
(a) chromosome 5 (b) chromosome 6
(c) chromosome 7 (d) chromosome 8.

(ii) Which one of the following is a chemokine?
(a) Fibroblast growth factor (b) Leukemia inhibitory factor
(c) Interleukin-8 (d) Tumor necrosis factor-α.

(iii) PNAs are used to inhibit expression of a gene at
(a) DNA level (b) RNA level
(c) protein level (d) all of the above.

(iv) Biosensors which detect production of light are known as
(a) piezoelectric biosensors (b) calorimetric biosensors
(c) optical biosensors (d) none of the above.

(v) A protein biochip is based on which of the following molecular recognition based choices?
(a) Protein ligand recognition
(b) Protein-protein recognition
(c) DNA hydridization
(d) Gene expression analysis.

(vi) A Surface Enhanced Adsorption (SEA) protein chip *typically* correlates which of the following spectral responses?
(a) Fluorescence amplification vs interlayer thickness of chip
(b) Absorbance vs wavelength
(c) Atomic force microscopy vs optical coupling of a He Ne beam
(d) all of the above.

(vii) Live, attenuated vaccines are
(a) first generation vaccines
(b) second generation vaccines
(c) third generation vaccines
(d) none of the above.

(viii) The concentration of insulin present in soluble insulin preparations (fast acting insulins) is the following:
(a) 1×10^{-9} M (b) 1×10^{-3} M
(c) 1×10^{-7} M (d) none of the above.

(ix) Cephalosporin C exhibits a mechanism of action identical to that of
(a) minocycline (b) penicillin
(c) chlortetracycline (d) doxycycline.

(x) Which of the following is a recombinant erythropoietin?
(a) Proleukin (b) Neorecormon
(c) C-GSF (d) PDGF.

Group – B

2. (a) In tabular form, represent the range of *potential impurities* and their *medical significance* that could be present in *biopharmaceutica*l products that are in the production pipeline for *parenteral administration*? How does the table establish the necessity for *extra purification steps* in the *quality control phase* of a biopharmaceutical's production?

(b) Present a flowchart for the manufacture of Betaferon, a recombinant human IFN-β, explaining the specific purposes served by the various upstream and downstream steps in the manufacturing route. How is the recombinant product structurally different from the native product? How do the final QC steps help in increasing the shelf-life of the product?

(3 + 2) + (5 + 1 + 1) = 12

3. (a) Draw a schematic diagram for the production of any patent protected erythropoietin (EPO) product paying particular emphasis to the different chromatographic steps. Explain the purpose of each of these steps.

(b) List four major classes of antibiotics along with examples, producer microoraganism and any special characteristics. What are the two major modes of beta lactam resistance?

(c) Use IFN-α and IFN-β to highlight the biological effects of these two interferons. Name two medical conditions whose symptoms are ameliorated by the use of interferons.

(3 + 1) + (3 + 2) + (2 + 1) = 12

Group – C

4. (a) Gene therapy has shown considerable success in combating some forms of Severe Combined Immunodeficiency (SCID). (i) In biological terms define SCID. (ii) Why is a retroviral vector needed in SCID? (iii) Explain the mechanism behind the treatment for ADA (adenosine deaminase) -SCID.

   (b) What does FISH stand for? What are the underlying principles of FISH? What imaging technique is used? In what areas of clinical diagnoses and medical screening has FISH found maximum applicability?

(2 + 1 + 3) + (1 + 2 + 1 + 2) = 12

5. (a) Explain how you can sort a heterogeneous mixture of biological cells using FACS.

   (b) Discuss the purposes of HLA matching.

6 + 6 = 12

Group – D

6. (a) "Many of the conditions that develop into diseases, happen because at the molecular level, there is a change in amount, function or activity of one or more proteins" Explain this statement pointwise with emphasis on the role of proteomics in human disease and drug therapy.

   (b) Name two diseases where the development of biomarkers has been especially productive. In each instance name one biomarker protein.

   (c) What are the four common immunoassay types? In which category does a sports anti-doping immunoassay fall? Name six important "wet experimental" parameters (e.g. coating buffer is one) that are important for development of an an antibody-antigen immunoassay. What are the technical factors that establish "proof of concept" in an immunoassay?

4 + 2 + (2 + 1 + 1 + 2) = 12

7. Capillary Electrophoresis's (CE) microscale nature has made it a method of choice for separation of a wide spectrum of biomolecules including amino acids, peptides, proteins and DNA fragments. Answer the following questions with respect to CE and its applications to protein separations (i) Why is a stabilising medium not needed in a capillary? (ii) Write out the equations for migration time and separation efficiency for CE; define all the terms and their significance in biomolecule separations (iii) Draw a typical capillary electrophoretograph for separation of any five random structurally related peptides. Assume the following parameters: column length 100 cm,

separation voltage 50kV, peptide detection by UV absorbance at 200 nm; assume a run time of 25-30 minutes. (iv) Give four specific examples of how CE has been successfully used for separation of biomolecules *other than* proteins or peptides.

[2 + (4 + 1) + 3 + 2] = 12

Group – E

8. (a) The clinical enzymology of liver disease often involves the measurement of serum aspartate aminotransferase. (i) What are the full names and acronyms of three other enzymes commonly used for such liver disease diagnostics purposes. (ii) Explain the mode of action for liver alkaline phosphatase enzyme. (iii) Use a labelled plot only to depict changes in serum alkaline phosphatase after complete and intermittent obstructive jaundice. (iv) Although ornithine carbamoyl transferase is exclusive to liver expression, why hasn't it been used commonly for diagnostic purposes?

   (b) Define an artificial pancreas *device system using a diagram to show its parts*. What are its three main machine components and their respective functions? What is the role of the control algorithm in this device system?

(2 + 2 + 1 + 1) + (2 + 3 + 1) = 12

9. (a) What are the classical components of a biosensor? Use a diagram to depict the working principle of a biosensor. What are the characteristic advantages of biosensors compared to conventional chemical sensors? Use a table to summarize transducer systems used in biosensor technology.

   (b) In a piezoelectric sensor, the sensor action is based on a measurement of a change in resonant frequency (Δf) of a piezoelectric crystal based upon mass changes on its surface. (i) What causes the mass changes? (ii) What is the mathematical equation representing Δf? Define the pertinent terms in the equation. (iii) Using the equation show how sensitivity is impacted significantly in a piezoelectric resonator. (iv) What are bulk piezoelectric sensors typically made of? Explain their size and configuration.

   (c) Which properties of antibodies make them excellent for development as biological analytes in biosensor technology? Other than piezoelectric crystals, what are the other two methods that are being developed that have successfully measured a signal from antibody binding and are potentially developing into next generation biosensors?

(1 × 4) + (1 × 4) + (1 + 3) = 12