MEDICAL AND PHARMACEUTICAL BIOTECHNOLOGY
(BIOT 3221)

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) Diagnostic fluids recognized by non –invasive biosensor is
(a) Sweat (b) Saliva (c) Blood (d) Both (a) & (b)

(ii) Biosensors which detect changes in mass is known as
(a) Piezoelectric Biosensors (b) Calorimetric Biosensors
(c) Optical Biosensors (d) None of the above.

(iii) Thermistors are used in
(a) Potentiometric Biosensors (b) Amperometric Biosensors
(c) Optical Biosensors (d) Calorimetric Biosensors.

(iv) First liver enzyme to rise in the blood when the bile duct gets obstructed is
(a) Alkaline phosphatase (b) Lactate dehydrogenase
(c) Gamma-glutamyltransferase (d) Alanine transaminase.

(v) Vancomycin acts by forming a complex with multiple points of contact to which of the following terminal residues of the peptidoglycan?
(a) D-alanyl D-alanine (b) L-alanyl D-alanine
(c) L-alanyl L-alanine (d) D-alanyl D-Lactate.

(vi) The process of using the patient's own adipose tissue to extract the stem cells is known as
(a) Harvesting (b) Separation
(c) Activation (d) Treatment.

(vii) Which of the following DOES NOT constitute a test on a potential new drug in the preclinical phase of drug development?
(a) Pharmacokinetic profile (b) Pharmacodynamic profile
(c) Bioequivalence and bioavailability (d) Global tolerance.

(viii) Hypoxia stimulates enhanced EPO production. Which of the following conditions induce hypoxia?
(a) Blood loss (b) Increased haemoglobin oxygen affinity
(c) Decreased renal blood flow (d) All of the above.

(ix) Upon ligand binding, cell surface receptors move laterally to be capped and internalized. *Leishmania*, a protozoan parasite, can use several receptors on macrophages to get internalized. One of them is Toll-like receptor 2 (TLR 2) that binds lipophosphoglycan on *Leishmania*. Once internalized, the parasite is destroyed in the phagolysosome. Which of the following treatments of *Leishmania*-infected macrophages,will result in lowest parasite number in macrophages?
(a) Membrane cholesterol-depleting drug , β-methyl cyclodextrin (β-MCD)
(b) Ammonium chloride that increases lysosomal pH
(c) Both (β-MCD) and ammonium chloride
(d) Anti-TLR antibody.

(x) Which of the following does not represent a clinical trial type?
(a) Factorial design (b) Cross over design
(c) Hybrid design (d) Teratogenicity profile.

Group- B

2. (a) Using one example in each category, show how recombinant DNA technology has assisted in the generation ofengineered therapeutic proteins. Your answer should correlate the type of changes that have been engineered with the corresponding medical advantages.
[(CO1&CO2)(Understand-analyze/IOCQ)]

(b) "The bulk of biopharmaceuticals that are in current therapeutic use are produced by genetic engineering using multiple recombinant expression systems". Using this statement as your template, answer the following questions (i) what are the two major recombinant protein systems in use? Name one example each of a biopharmaceutical for the two major expression systems (ii) what are the specific advantages of using E.coli as a recombinant protein expression system? Which advantage is the most relevant? Briefly state two disadvantages of using *E coli* cells as a biopharmaceutical producer. Which one of these disadvantages complicates downstream processing for the purified therapeutic protein? Explain your answer.
[(CO2)(Remember-Understand/LOCQ)]

(c) List 3 different proteins *of potential/actual therapeutic interest* that have been expressed at laboratory scale in transgenic plants. Why were plants originally considered to be suitable as recombinant therapeutic protein producers? Cite two specific disadvantages that have emerged with the use of plant-based expression systems. [(CO1)(Remember-Understand-LOCQ)]

3 + 6 + 3 = 12

3. (a) In the development cycle of a large molecule pharmaceutical/biopharmaceutical where does the pharmacokinetic (PK) profile determination fit in? What are the typical measurement variables in the determination of the PK profile for a

therapeutic drug? What are two important characteristics of a drug that are established from its PK profile? [(CO1)(Remember-understand/IOCQ)]

(b) What are the types of interferons? How does interferon signal transduction happen? Use a table to identify minor and major potential adverse side effects of interferons. What is the most significant impact of this in terms of an interferon's maximum the rapeuticdose? [(CO1)(Understand/LOCQ)]

(c) Using one example, illustrate the role that intelligent data mining and cell based assays could play in distinguishing pharmacodynamic endpoints of the activity profile of a biopharmaceutical versus a small molecule pharmaceutical. [(CO2)(Understand-Analyse/IOCQ)]

4 + 4 + 4 = 12

Group - C

4. (a) Illustrate the two pathways by which the DNA vaccine works. [(CO4)(Illustrate/HOCQ)]

(b) Justify the statement "Prochymal, was approved for the management of acute graft-vs-host disease in children who are unresponsive to steroids." [(CO4)(Justify/HOCQ)]

8 + 4 = 12

5. (a) Examine pharmacogenetics, taking the CYP450 gene as an example. [(CO4)(Examine/IOCQ)]

(b) Illustrate the process of inhibiting the gene expression with the help of Intrabodies. [(CO4)(Illustrate/IOCQ)]

6 + 6 = 12

Group - D

6. (a) In the production process of a biopharmaceutical how can the following steps be utilized (i) essential nucleotide coding (ii) use of inclusion bodies (iii) ultrafiltration. Use an appropriate example. [(CO1&CO2)(Understand-analyse/IOCQ)]

(b) (i) In a typical protein-protein interface of area 1800$(A^0)^2$, how many intermolecular hydrogen bonds would you expect to be formed? How many fixed water molecules would you expect to find in the interface? How are these parameters relevant in the characterization of a protein-based drug? (ii) If you were separating a therapeutic protein from tissue and there are proteinaceous impurities that you were trying to separate from the pure product protein, use an ideal *properly labelled* chromatogram of Intensity vs Elution parameter to represent this situation. Assume there are three separate proteinaceous impurities. Interpret the diagram if there was a less than ideal separation profile for this biopharmaceutical. [(CO4) (Understand, Interprete/LOCQ,HOCQ)]

6 + (3 + 3) = 12

7. (a) Use a labelled flowchart to represent the complete steps involved in the production of purified recombinant insulin. [(CO1)(Illustrate/IOCQ)]

(b) Alpha-antitrypsin is abiomarker identified with emphysema/chronic obstructive pulmonary disorder (COPD). In general, what are the characteristics that a protein like alpha-antitrypsin must possess to make it ideal as a serum biomarker. Cite two techniques that would be suitable for detection of this protein biomarker. [(CO3)(Analyze, Remember/IOCQ,LOCQ)]

(c) What are the specific product development reasons for validation of an immunoassay? If you were designing and developing a clinical biosensor what are the immunoassay validation characteristics that are relevant for this purpose? Give one example for the latter. [(CO4)(Analyse/HOCQ)]

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

Group - E

8. (a) Illustrate the process of detecting glucose in a sample with the help of Amperometric Biosensor? [(CO5)(Illustrate/HOCQ)]

(b) Analyze the role of diagnostics kits. [(CO6)(Analyze/IOCQ)]

7 + 5 = 12

9. (a) Name a diagnostic enzyme that is used to detect liver disorder. State it's principle of action in our body. Write down the assay by which you can detect it in blood. [(CO6)(Understand/LOCQ)]

(b) Discuss the applications of biosensor in defence. [(CO5)(Discuss/IOCQ)]

(1 + 3 + 3) + 5 = 12

Cognition Level	LOCQ	IOCQ	HOCQ
Percentage distribution	25	47.92	27.08

Course outcomes (CO):

At the end of this course students will be able to:

1. Understand and apply principles and practices of drug development of biopharmaceuticals (e.g. insulin, interferons, EPO); pharmaceuticals of biological origin (e.g. corticosteroids) and microbial origin (e.g. antibiotics) including synthesis, biological and therapeutic characteristics (e.g.PK/PD profiles) of such molecules.
2. Understand the methodological and technological differences between formulation, delivery and post-production quality control of biopharmaceuticals versus small molecule pharmaceuticals.
3. Understand the process of discovery, technological developments and subsequent applications of monoclonal antibodies, DNA/RNA based diagnostics and protein based biomarkers.
4. Understand principles and applications of the following topics with relevance to disease therapeutics: vaccines, gene therapy, proteomics techniques in drug development.
5. Understand the principles of fabrication, operation and clinical applications of biosensors.
6. Understand and apply principles of enzymology for applications in microclinical diagnostics in kits and biochips.

*LOCQ: Lower Order Cognitive Question; IOCQ: Intermediate Order Cognitive Question; HOCQ: Higher Order Cognitive Question