UNIVERSITY COLLEGE LONDON

University of London

EXAMINATION FOR INTERNAL STUDENTS

For The Following Qualification:-

M.Eng.

Biochemical Eng E187: Bioprocessing of New Medicines

COURSE CODE	:	**BENGE187**
UNIT VALUE	:	**1.00**
DATE	:	**16-MAY-03**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

TURN OVER

Answer ***THREE QUESTIONS.*** **Only the first three answers given will be marked.**
ALL questions carry a total of ***25 MARKS*** *each, distributed as shown* [ ]

1.

Researchers at UCL discovered that in cancer cells co-expression of genes Onc and Lyt is associated with solid tumor regression. Animal models of various types of cancers indicated that the genes could be used therapeutically when expressed transiently at very high levels. Considering that repeated doses are likely to be required:

(a) Outline 3 key aspects that will need to be considered when choosing a delivery vector. [9]
(b) Outline a typical manufacturing process for a replication-deficient virus. Could a replication-deficient virus be used for this application? Give reasons. [8]
(c) Describe the features that a non-viral vector should have in order to be used for delivery of Onc and Lyt. [8]

2.

The results of a recent review of FDA Biological license approvals (BLAs) are shown in Table 1. BLAs products are categorised on the basis of product application, and subcategories for each product application include bioreactor type, process feeding design and medium type. In the Table, "tissue culture" refers to tissue engineered medical products and "speciality" to specialised culture systems, for example multilayer stacked plates.

Numerical summary of BLA products generated in mammalian cell-culture systems, 1996–2000*.

Recombinant therapeutics			Vaccines			Diagnostics			Tissue culture		
13			3			4			1		
Stirred-tank	Speciality	Unknown	Stirred-tank	Speciality	Unknown	Stirred-tank	Speciality	Unknown	Stirred-tank	Speciality	Unknown
9	0	4	0	1	2	0	1	3	0	1	0
Batch/ fed-batch	Perfusion	Unknown	Batch/ fed-batch	Perfusion	Unknown	Batch/ fed-batch	Perfusion	Unknown	Batch fed-batch	Perfusion	Unknown
6	3	4	1	0	2	0	1	3	0	0	1
Serum-free	Serum-containing	Unknown	Serum-free	Serum-containing	Unknown	Serum-free	Serum-containing	Unknown	Serum-free	Serum-containing	Unknown
6	1	6	0	2	1	2	1	1	0	1	0

*BLA products are categorized on the basis of product application, and subcategories for each product application include reactor type, process feeding design and medium type. Source: www.fda.gov.

TABLE 1

CONTINUED

(a) Explain possible reasons for the trends observed with regards to bioreactor type, feeding design and medium type for each of the products. [15]
(b) What issues need to be considered when using serum-containing media for manufacturing i) diagnostics and ii) tissue engineered products. [10]

3.

Write short notes on:

(a) the differences and similarities of bacterial vs. mammalian cells for production of recombinant therapeutics. [5]
(b) the importance of cell banking in development and manufacture. [5]
(c) the automation of culture systems for autologous cell therapy applications. [5]
(d) the processing of monoclonal antibodies produced in transgenic plants [5]
(e) the significance of using microwells for process development. [5]

4.

As a biochemical engineer you have been asked to make recommendations on the future manufacturing routes for an important class of therapeutic antibodies that are currently reaching the 2nd clinical phase. Explain, under what circumstances you would choose:

1- microbial fermentation
2- mammalian cell culture
3- transgenic animals and plants [25]

END OF PAPER