GUJARAT TECHNOLOGICAL UNIVERSITY

Bachelor of Engineering
Subject Code: 3160416
Subject name: Biosimilars technology
Semester VI

Type of course: Open Elective

Prerequisite: Advanced Molecular biology, Cell Biology, Biochemistry, Basics of IPR

Rationale: The subject aims to acquaint the students with the application of biotechnology to the pharmaceutical industry. The subject introduces the students with a requirement of skills that they may use to get employed in the biopharmaceutical industry.

Teaching and Examination Scheme:

Teaching Scheme			Credits	Examination Marks				Total Marks
				Theory Marks		Practical Marks		
L	T	P	C	ESE(E)	PA (M)	ESE (V)	PA(I)	
3	0	0	3	70	30	0	0	100

Course Contents:

Sr. No.	Topics	Teaching Hours	Module Weightage
1	**UNIT I: Introduction to Biopharma** Generics in Biopharma, definition of biologics, biosimilars, super biologics, differences between chemical generics and biosimilars, The developmental and regulatory challenges in biosimilar development, Prerequisites for Biosimilar development, Biosimilar market potential.	**7**	**15.5**
2	**UNIT II: Types of biosimilar drugs** Peptides, proteins, antibodies, Enzymes, Vaccines, Nucleic acid based therapies (DNA, RNA, etc), Cell based therapies (including stem cells)	**5**	**11.1**
3.	**UNIT III: Process pipeline for Recombinant protein biosimilar:** Searching for candidate biosimilar with patent search and Nucleotide database, Choice of elements of gene of interest: Restriction Enzyme recognition sites, kozak sequence, start codon, codon optimized gene sequence, termination signal, secretion signal. Selecting a Vector, cloning cassete into vector and expansion of construct, Trasnfection in to selected host cell line (CHO, BHK, NS0, SP2/0, HEK 293), Clone selection and Expansion, Research cell bank, Mother cell bank and Working cell bank. Upstream optimization: Media and feed optimization, KLa, Growth characterization, production parameters. Downstream optimization:	**14**	**31.1**

	Size exclusion, ion exchange, HIC, **mixed-mode**, and affinity chromatography. Analytics/ cGMP requirements: HCP (Host cell protein) and hcDNA (host cell DNA) determination, End of Production Cell Bank (EPC), Genetic stability of cell line, Bulk harvest testing for contaminants, Formulation of final product		
5.	**UNIT IV: Bioequivalence studies** Immunogenicity & allergenicity of biosimilars; factors affecting immunogenicity -structural, post-translational modifications, formulations, impurities, Biological activity:antibody based and whole cell assays, Safety studies, manufacturing and formulation methods for biosimilars; types of bioequivalence (average, population, individual), experimental designs & statistical considerations for bioequivalence studies (Non-replicated designs –General Linear Model, Replicated crossover designs), introduction to "ORANGE BOOK" & "PURPLEBOOK".	**11**	**24.4**
6.	**UNIT V: Case studies** Cell based Biosimilars, gene therapy and CAR-T cells:Case study of KYMRIAH, Erythropoietin, growth hormone, Adalimumab (Humira) biosismilars	**8**	**17.7**

Suggested Specification table with marks (Theory):

Distribution of Theory Marks					
R Level	**U Level**	**A Level**	**N Level**	**E Level**	**C Level**
5	10	10	10	15	0

Legends: R=Remembrance**; U**= Understanding**; A=** Application**; N** = Analyze**;E** = Evaluate; **C** = Create and above Levels **(Revised Bloom's Taxonomy)**

Note: This specification table shall be treated as a general guideline for students and teachers. The actual distribution of marks in the question paper may vary slightly from above table.

Reference Books:

1. https://www.biooutsource.com/wp-content/uploads/2016/03/Biosafety-Technical-Booklet.pdf
2. Rasmussen, S. K., Næsted, H., Müller, C., Tolstrup, A. B., & Frandsen, T. P. (2012). Recombinant antibody mixtures: production strategies and cost considerations. *Archives of biochemistry and biophysics*, *526*(2), 139-145.
3. Liu, C., & Morrow Jr, K. J. (Eds.). (2016). Biosimilars of Monoclonal Antibodies: A Practical Guide to Manufacturing, Preclinical, and Clinical Development. John Wiley & Sons.
4. Rodriguez-Cartagena, L. G., Bowles, B. S., Kurani, S. S., Windebank, A. J., Kenderian, S. S., & Greenberg-Worisek, A. J. (2018). Chimeric Antigen Receptor T-Cells: Successful Translation of the First Cell and Gene Therapy From Bench to Bedside. *Clinical and translational science*, *11*(6), 537.

GUJARAT TECHNOLOGICAL UNIVERSITY

Bachelor of Engineering
Subject Code: 3160416

Course Outcome:

After learning the course, the students should be able to:

Sr. No.	CO Statement	Marks % Weightage
CO-1	To evaluate the difference between generic drugs, biosimilars and different types of biosimilars	20
CO-2	To apply the knowledge gained from molecular biology to clone development for biologics/ biopharma peptide	40
CO-3	To analyze various reports regarding biosimilar characteristics of a candidate molecule and evaluate its performance.	30
CO-4	To get infer barriers that may be encountered before launching a biosimilar.	10

List of Open Source Software/learning website:

Students can refer to video lectures relevant to subject, available on the websites, including NPTEL.
Students can refer to the CDs which are available with some reference books.