KOLHAPUR INSTITUTE
OF TECHNOLOGY'S
COLLEGE OF
ENGINEERING
(AUTONOMOUS),
KOLHAPUR

Proposed Structure for
B.Tech in Biotechnology Engineering (As Per NEP)

(To be implemented w.e.f Academic Year 2024-25)

Department of Biotechnology Engineering
KIT's College of Engineering(Autonomous) Kolhapur

06/06/2024
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B. Tech. (Hons.) in Biosimilar Technology

Sr. No.	Course Code	Course Name	L	T	P	Hrs./ Week	Credits	Evaluation Scheme		
								Component	Marks	
									Max	Min for Passing
1	UBTHN0351	Biosimilar Therapeutics : Introduction	3	1	0	4	4	ESE	100	40
2	UBTHN0451	Biosimilar Manufacturing Technology-I	3	1	0	4	4	ESE	100	40
3	UBTHN0551	Biosimilar Manufacturing Technology-II	3	1	0	4	4	ESE	100	40
4	UBTHN0651	Biosimilar Therapeutics: Characterization	3	1	0	4	4	ESE	100	40
5	UBTHN0751	Biosimilar Therapeutics: Regulatory Approval Processes	2	0	0	2	2	ESE	100	40
		Total:				**18**	**18**	**Total Marks: 500 TotalCredit:18**		

Title of the Course: Biosimilar Therapeutics: Introduction **Course Code:** **UBTHN0351**	**L**	**T**	**P**	**Credit**
	3	**1**	**-**	**4**

Course Description: This course describes the biosimilar industry scenario with their departments and biosimilar therapeutics modalities

Course Objectives:

1. To introduce the biopharmaceutical industry scenario
2. To describe industry departments and work profiles
3. To explain basics of drug discovery development with biosimilar therapeutics modalities

Course Outcomes:

CO	**After the completion of the course the student will be able to**	Bloom's Taxonomy level
CO1	Classify biopharmaceutical industry based on the functionality with their product classes	2
CO2	Describe the functions of the different departments in biopharmaceutical industry	3
CO3	Illustrate the layout and design of biopharmaceutical industry facility	3
CO4	Outline drug discovery, development and manufacturing process along with its regulatory aspects	4

CO-PO-PSO Mapping:

COs	**POs**									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	1									
2										
3										
4										

Assessments:

End Semester Examination (ESE) having 100% weightage

Assessment	**Marks**
ESE	100

Unit 1:--- Introduction to Biopharmaceuticals

Synthetic/chemical drugs/medicines versus Biotechnology based drugs/medicines, Technology based differences, Biopharmaceutical drugs classes with examples of molecules (Antibodies, Insulin, Growth factors, Clotting factors, Enzymes, Peptides, Vaccines, RNAi based drugs, Cell and Gene therapy products etc.) Roles of Biopharmaceutical molecules in human systems , Need for production of Biopharmaceutical molecules

Unit 2:--- Biopharmaceutical Industry

Difference between recombinant technology based drugs, biologics and biosimilars, Historical perspectives, Market Scenario, Future career scopes in India and abroad, Type of industries like

manufacturing , raw material providers, contract research based etc. and their role

Unit 3:--- Industrial divisions and operations

Different divisions in industries (Inventory, Raw material, Upstream and Downstream processing, Research and Development, Quality control, Quality assurances, Regulatory Affairs, Business Development, Sales and Marketing etc.) Role of each divisions and interconnections Process economics/ Economics

(Humira, Avastin (Rituximab), Herceptin , Insulin, t-PA, EPO, Covid vaccine etc.)

Unit 4:--- Biomanufacturing facility

General Layouts, Concept of Cleanroom, Types of Cleanrooms, Pharmaceutical Cleanroom Classification, Basis of Cleanroom Standards, Federal Standard 209E/IS0 standards- ISO14000-1, Design of Turbulently Ventilated and Ancillary Cleanrooms (Air supply, High efficiency air filters, Air movement within a turbulently ventilated Cleanroom, Room pressurization and air movement control between rooms, Load pattern study, Construction materials and finishes) Ancillary Clean Rooms (Clothing change area, Material transfer area, Containment Rooms), Cleanroom testing and monitoring, Cleaning validation, Area validation

Unit 5:--- Drug discovery, development and manufacturing : An overview

Concept of life cycle of a drug, Drug discovery process (Impact of genomics and related technologies upon drug discovery, Pharmacogenomics), Drug development process (Pre-clinical studies, PK and PD studies, Toxicity studies, Role and remit of regulatory authorities), Drug manufacturing process

Unit 6:--- Macromolecular therapeutics

Central Dogma –DNA to Protein (DNA Replication, Transcription and Translation),
Protein therapeutics (Protein structure of drugs and functional relationship, Types of drugs - Holoproteins, modified proteins, fusion proteins, peptides) , Nucleic acid therapeutics, Cell therapeutics, Pharmacopial extracts from USA, EU

Textbooks:

1. Understanding Biopharmaceuticals: Manufacturing and Regulatory Issues by Grindley, Jill E. Ogden (CRC Press)
2. Pharmaceutical Biotechnology, 2nd Ed. By Crommelin D.J.A. , Sindelar R. D ,Bernd Meibohm (Springer)
3. Pharmaceutical Biotechnology by Gary Walsh (Wiley)

References:

1. Pharmaceutical Biotechnology by O. Kayser, R. H. Muller (Wiley - VCH)
2. Handbook of Pharmaceutical Biotechnology by Jay P Rho, Stan G Louie (Haworth Press.)

Title of the Course: Biosimilar Manufacturing Technology I Course Code: UBTHN0451	L	T	P	Credit
	3	1	-	4

Course Description: This course describes the upstream processing for the production of biosimilar modalities including cell engineering, cell cultivations , bioreactor technologies.

Course Objectives:

1. To explain gene manipulation basics
2. To illustrate protein expression and controls
3. To explain bioreactor technologies with quality by design concept

Course Outcomes:

CO	After the completion of the course the student will be able to	Bloom's Taxonomy	
		level	Descriptor
CO1	Recall gene manipulation basics	1	Remembering
CO2	Illustrate different expression host genotypes with their expression and regulation	2	Understanding
CO3	Explain cell culture basics and the bioreactors used for biosimilar manufacturing	2	Understanding
CO4	Summarize quality by design aspects in biomanufacturing process	2	Understanding

CO-PO-PSO Mapping:

COs	POs												PSOs		
	1	2	3	4	5	6	7	8	9	10	11		1	2	3
1	2														
2	2	2	2		1						1				1
3	2										1				
4	1		2								1			1	

Assessments:

End Semester Examination (ESE) having 100% weightage

Assessment	Marks
ESE	100

Unit 1:--- Gene Manipulation Basics Types of vectors (Expression and Cloning vectors), Different elements of vectors and their uses, Gene Cloning : PCR, Restriction Digestion, Ligation, Transformation etc. Primer Designing, alternative cloning methods apart from traditional method	**6 Hrs.**
Unit 2:--- Host expression systems Different expression hosts with history and genotypes Prokaryotes - *E.coli* DH5 alpha , *E.coli* BL21A1, *E.coli* BL21DE3 etc. Eukaryotes – Yeast hosts like *Pichia pastoris* , Mammalian hosts like CHOK1, CHO DuxB11, CHO DG44, NS0, SP02 cell line etc.	**6 Hrs.**
Unit 3:--- Protein Expression and Regulation	**6 Hrs.**

Protein Expression in Prokaryotes and Eukaryotes, Operon systems (lac, trp operon etc.) and their use, IPTG induction system, DHFR-MTX based selection and amplification system, GS based selection and amplification system, Post translational modifications like glycosylation and its importance in Biosimilar context	
Unit 4:--- Basic of cell cultures Microbial cell cultivations, Media and sterilization, Anchorage dependent and independent cell lines, Cell culture techniques (Master cell bank, Working cell bank, vial revival, cell passaging), Cell bank preservation, Generation number calculation, Cell culture media (Serum based media, Serum free adaptation), Introduction of gene in cells (Electroporation, lipofection etc.)	**6 Hrs.**
Unit 5:--- Bioreactor Technologies Shake flasks, Small scale glass bioreactors, wave bioreactors, single use/disposable bioreactors , perfusion cultures , Mode of culturing – Batch, Fed batch, Continuous Operating systems of Bioreactors (SCADA, DCS , PLC etc.), Agitation and aeration (top driven and bottom driven agitation, design and types of impellers) impacts on kLa, H/D ratio, In process analysis (Cell density , cell growth and quality of protein)	**6 Hrs.**
Unit 6:--- Quality by Design aspects Terminologies in QbD (Process characterization, Critical quality attributes, critical process parameters, Failure mode effect analysis), Design of Experiment (DoE), Multivariate Data Analysis	**6 Hrs.**

Textbooks:

1. Understanding Biopharmaceuticals: Manufacturing and Regulatory Issues by Grindley, Jill E. Ogden (CRC Press)
2. Pharmaceutical Biotechnology, 2nd Ed. By Crommelin D.J.A. , Sindelar R. D ,Bernd Meibohm (Springer)
3. Pharmaceutical Biotechnology by Gary Walsh (Wiley)

References:

1. Pharmaceutical Biotechnology by O. Kayser, R. H. Muller (Wiley - VCH)
2. Handbook of Pharmaceutical Biotechnology by Jay P Rho, Stan G Louie (Haworth Press.)

Title of the Course: Biosimilar Manufacturing Technology II Course Code: UBTHN0551	L	T	P	Credit
	3	1	-	4

Course Description: This course describes the downstream processing for the production of biosimilar modalities including cell separations , product purifications, formulations, filling and packaging and brief of clinical trials

Course Objectives:

1. To explain product purification technologies
2. To describe formulations and packaging
3. To introduce concepts of clinical trials

Course Outcomes:

CO	After the completion of the course the student will be able to	Bloom's Taxonomy	
		level	Descriptor
CO1	Outline general purification platforms for biosimilars	2	Understanding
CO2	Illustrate different unit operations used in purification of biosimilars	2	Understanding
CO3	Summarize the concepts of formulation, filling, packaging and stability of biosimilars	2	Understanding
CO4	Explain clinical studies of biosimilars	2	Understanding

CO-PO-PSO Mapping:

COs	POs												PSOs		
	1	2	3	4	5	6	7	8	9	10	11		1	2	3
1	2				2								1		
2	2	2	1	1	1								1		
3														2	2
4															1

Assessments:

End Semester Examination (ESE) having 100% weightage

Assessment	Marks
ESE	100

Unit 1:--- Primary processing of microbial / cell cultures General platforms used in protein purifications - Sequence of steps with objectives to be followed in Microbial and Mammalian Molecules Purification, Objectives of each purification step, Cell separation by Clarification (Direct flow filtration, Tangential flow filtration) Centrifugation (batch and continuous mode) , Cell disruptions for intracellular products	**6 Hrs.**
Unit 2:--- Purification processes Chromatographic product capture processes using Affinity chromatography, Ion Exchange Chromatography, Hydrophobic Interaction chromatography, Multi-modal chromatography, Size exclusion chromatography etc., Viral clearance, Ultrafiltration/Diafiltration	**6 Hrs.**

Continuous manufacturing process economics	
Unit 3:--- Formulation and Filling Importance and types of excipients in formulation of drug substance, Types of formulations for Biosimilar drugs Different membrane technologies for purifications, Buffer exchange, Concentration adjustments for liquid forms, Crystallization/Drying for solid forms, Sterile filtration of final drug substance, Sterile filling /terminal sterilization of drug product (Dose design during filling)	**9 Hrs.**
Unit 4:--- Stability Stability studies of drug substances (Accelerated, Long term, Stress , Photostability) Stability studies of drug product after packaging	**3 Hrs.**
Unit 5:--- Drug product packaging Types of packaging based on Drug Delivery System **(**Pre-filled syringe (lyophilized powder with sterile WFI) , Vial, Cartridge, Medical devices (Pen assembly) etc.) (Container closure)	**6 Hrs.**
Unit 6:--- Clinical Trials Concepts of non-clinical animal trials and clinical trials on human volunteers (Phase I, II, III, IV clinical trials), Guidelines and Case studies	**6 Hrs.**

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1. Understanding Biopharmaceuticals: Manufacturing and Regulatory Issues by Grindley, Jill E. Ogden (CRC Press)
2. Pharmaceutical Biotechnology, 2nd Ed. By Crommelin D.J.A. , Sindelar R. D ,Bernd Meibohm (Springer)
3. Pharmaceutical Biotechnology by Gary Walsh (Wiley)

References:

1. Pharmaceutical Biotechnology by O. Kayser, R. H. Muller (Wiley - VCH)
2. Handbook of Pharmaceutical Biotechnology by Jay P Rho, Stan G Louie (Haworth Press.)

Title of the Course: Biosimilar Therapeutics : Characterization **Course Code: UBTHN0651**	**L**	**T**	**P**	**Credit**
	3	1	-	**4**

Course Description: This course describes analytical characterization of biosimilar therapeutics.

Course Objectives:

1. To explain product and process-based impurities and their characterization techniques
2. To describe cGMP requirements

Course Outcomes:

CO	**After the completion of the course the student will be able to**	Bloom's Taxonomy	
		level	Descriptor
CO1	Illustrate the process and product based impurities in biopharmaceutical industry	2	Understanding
CO2	Connect the biosimilar characterization techniques (biosimilarity assessment) for in-process quality control	4	Analyzing
CO3	Illustrate bio-assay based techniques for pharmacokinetic and pharmacodynamic studies of biosimilars	2	Understanding
CO4	Summarize cGMP requirements for biomanufactruring, validations and bio-waste treatment	2	Understanding

CO-PO-PSO Mapping:

COs	**POs**												**PSOs**		
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**		**1**	**2**	**3**
1	1													2	
2	1													2	2
3	1													1	
4	1														3

Assessments:

End Semester Examination (ESE) having 100% weightage

Assessment	**Marks**
ESE	100

Unit 1:--- Drug Characterization Primary and secondary structure analysis (Amino acid analysis, Peptide mapping, N-terminal sequencing) , Tertiary and quaternary structure analysis, Electron microscopy, NMR, Isoelectric point estimation, Biosimilarity assessment protocols Characterization of process and product based impurities using different HPLC systems, Mass Spectrometry, UV based analysis, Electrophoresis, Blotting techniques etc. , Quality control of finished goods Organic Volatile Impurity (OVI) analysis	**6 Hrs.**

Unit 2:--- Analytical Similarity and In-Process control Analytical Similarity,/Bio-similarity exercise and In-process control strategy 1. Bio-similarity with case study if possible 2. In-process control strategy required to achieve required Bio-similarity for drug being developed I) control over host cell protein and Host cell DNA process related impurities, II) Microbial control strategy to make sterile product-designing various sterile filtration step, aseptic process unit operations, use of LAF etc III) Control over product related impurities or product degredents, product isomer/variants etc. Analytical similarity and in-process control strategy is very essential in Biosimilar application	**6 Hrs.**
Unit 3:--- Pharmacokinetics and Pharmacodynamics Studies ADME studies of Biosimilars, Bioavailability and bioequivalence concepts, Immunogenicity and allergenicity testing, Toxicity testing, Bioassays (ELISA, Cell based assays), Estimation of association dissociation constants Guidelines , monographs	**6 Hrs.**
Unit 4:--- cGMP Requirement for Manufacturing, Quality control,Warehouse, Utility and other support areas ICH Q7 , Good Documentation Practice(ALCOA), Data Integrity	**6 Hrs.**
Unit 5:--- Validation/Qualification Process Validation, Cleaning validation , Equipment Qualification and Software Qualification, Analytical Method Validation, Water system Qualification , Area/HVAC Qualification	**6 Hrs.**
Unit 6:--- Bio-wastes management and treatments, Decontamination, Environmental health and safety HAZOP, Rules and regulations RCGM, IBSC, Pollution board, Green tribunal	**6 Hrs.**

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2. Pharmaceutical Biotechnology, 2nd Ed. By Crommelin D.J.A. , Sindelar R. D ,Bernd Meibohm (Springer)
3. Pharmaceutical Biotechnology by Gary Walsh (Wiley)

References:

1. Pharmaceutical Biotechnology by O. Kayser, R. H. Muller (Wiley - VCH)
2. Handbook of Pharmaceutical Biotechnology by Jay P Rho, Stan G Louie (Haworth Press.)

Title of the Course: Biosimilar Therapeutics : Regulatory Approval Processes **Course Code: UBTHN0751**	**L**	**T**	**P**	**Credit**
	2	-	-	**2**

Course Description: This course describes analytical characterization of biosimilar therapeutics.

Course Objectives:

1. To explain product and process-based impurities and their characterization techniques
2. To describe cGMP requirements

Course Outcomes:

CO	**After the completion of the course the student will be able to**	Bloom's Taxonomy	
		level	Descriptor
CO1	Summarize regulatory frameworks for biosimilar industry	2	Understanding
CO2	Outline the regulatory guidelines and submissions in biosimilar industry	2	Understanding
CO3	Recall IPR and business development aspects in biosimilar industry	1	Remembering

CO-PO-PSO Mapping:

COs	**POs**											**PSOs**			
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**		**1**	**2**	**3**
1											1				2
2											1				2
3											1				2

Assessments:

End Semester Examination (ESE) having 100% weightage

Assessment	**Marks**
ESE	100

Unit 1:--- Overview of Regulatory framework Expectations in terms of data required for a biosimilar approval (totality of evidence), Types of submissions (DMF, IND, CTA, BLA, MAA etc.) Guidelines available on FDA and EMA websites , BPCI Act, USFDA, EMEA, CDSCO	**6 Hrs.**
Unit 2:--- Biosimilar Approval Pathways Regulatory approval pathways (from submission to approval) for the major regulatory agencies like FDA, EMA, PMDA (for ICH countries and non-ICH countries) , Functions of different agencies, Post approval changes (types of variations that can be filed for FDA, EMA, PMDA).	**6 Hrs.**
Unit 3:--- ICH and WHO guidelines Key guidelines that are specific to biosimilar development	**6 Hrs.**

CTD/e-CTD contents - Contents of a dossier, quality aspects of the dossier (5 modules)	
Unit 4:--- Case studies of approvals Approval pathways, Contents of module 3 of the dossier, Challenges faced during biosimilar development	**6 Hrs.**
Unit 5:--- IPR aspects Patenting agencies , types of patents Concepts of IP, Role of IP department , Agencies, Patents (data analysis , patentability , filing process) Freedom to operate, trademarks	**6 Hrs.**
Unit 6:--- Business Development Basics of Business Planning (Market mapping, Sales forecasting, Prioritization), Sales planning, Customer profiling, Call planning, In clinic effectiveness, KOL/KBL relationship management, Product messaging, identify the gaps in the current pipeline for new products and keep a watch on the competitor products. Distribution management, process flows in manufacturing, supply chain, research & development and quality functions at a broad level, escalation matrix for reporting identified issues, expiry and sales returns Benchmark company data with competitor presence/ market trends - sources for gathering information and understanding rising trends in market, data extraction, and interpretation analysis techniques from systems, market research techniques	**6 Hrs.**

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