Title of the Course: Biosimilar Therapeutics: Introduction Course Code: UBTH0301	L 3	T 1	P 0	Credit 4
Course Contents:				
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				**6 Hrs.**
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				**6 Hrs.**
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.)				**6 Hrs.**
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				**6 Hrs.**
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				**6 Hrs.**
Unit 6:--- Macromolecular therapeutics Central Dogma –DNA to Protein (DNA Replication, Transcription and				**6 Hrs.**

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	**L**	**T**	**P**	**Credit**
Course Code: UBTH0401	**3**	**0**	**2**	**4**
Course Contents:				
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 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				**6 Hrs.**

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 I Laboratory **Course Code:**	
Expt. 1 Vector preparations and host cell (prokaryotic / eukaryotic) transformation by vectors	
Expt. 2 Analysis of confirmation of host cell (prokaryotic / eukaryotic) transformation	

Expt. 3 Cultivation of prokaryotic hosts at shake flask level	
Expt. 4 Cultivation of eukaryotic hosts (mammalian cells) at flask level	
Expt. 5 Use of induction systems and amplification systems in culturing	
Expt. 6 Cultivation of prokaryotic / eukaryotic hosts in bioreactors	
Expt. 7 In process analysis of cells and proteins in the culture	
Expt. 8	

Title of the Course: Biosimilar Manufacturing Technology II Course Code: UBTH0501	L 3	T 0	P 2	Credit 4
Course Contents:				
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 Continuous manufacturingprocess economics				**6 Hrs.**
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.**
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 Laboratory **Course Code:**	
Expt. 1 Cell clarification from fermentation broth / cell culture by tangential filtration	
Expt. 2 Cell disruption and analysis of intracellular products	
Expt. 3 Protein purification by ion exchange chromatography	
Expt. 4 Protein purification by affinity chromatography	
Expt. 5 Protein purification by hydrophobic interaction chromatography	
Expt. 6 Protein purification by gel permeation/size exclusion chromatography	
Expt. 7 Protein concentration by ultrafiltration / diafiltration	
Expt. 8 Sterile filtration of drug substance	
Expt. 9 Demonstration of formulation of drug substance	

Title of the Course: Biosimilar Therapeutics : Characterization	L	T	P	Credit
Course Code: UBTH0601	3	0	2	4

Course Contents:

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 Bio-similarity with case study if possible In-process control strategy required to achieve required Bio-similarity for drug being developed control over host cell protein and Host cell DNA process related impurities, Microbial control strategy to make sterile product-designing various sterile filtration step, aseptic process unit operations, use of LAF etc 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 Practices(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.**
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 Therapeutics : Characterization **Course Code:**	
Expt. 1	

HPLC handling	
Expt. 2 HPLC – MS handling	
Expt. 3 SDS – PAGE handling	
Expt. 4 Protein analysis by UV and colorimetric methods	
Expt. 5 ELISA handling	
Expt. 6 Western blots handling	
Expt. 7 Process based impurities characterization	
Expt. 8 Product based impurities characterization	
Expt. 9 Product related, In process, impurity profile (impurity qualification) SOP writing (regulation based)	
Characterization publications writing drafting	

Title of the Course: Biosimilar Therapeutics : Regulatory Approval Processes Course Code: UBTH0701	L	T	P	Credit
	2	2		4
Course Contents:				
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 CTD/e-CTD contents - Contents of a dossier, quality aspects of the dossier (5 modules)				**6 Hrs.**
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 (Software) 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				**6 Hrs.**

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	

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)
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