NCTM
NATIONAL CENTER FOR THERAPEUTICS MANUFACTURING

Advanced Certificate in Biopharmaceutical Manufacturing

2-Week Training Cohort: December 17-21, 2018 and January 7-11, 2019

The Advanced Certificate in Biopharmaceutical Manufacturing immerses participants in a rigorous digital and hands-on training program, comprised of more than 100 hours of cGMP- and regulatory-based curricula. Subject matter includes aseptic microbial and mammalian cell processing using fixed and single-use fermentation and purification systems, regulatory compliance, quality assurance and control, process and environmental monitoring, and proper documentation and laboratory practices. Students will complete 5 self-paced online courses, then participate in 2 weeks of hands-on training at NCTM. Participants will receive **10.0 continuing education units** and a certificate of completion.

Specific learning objectives include:

- *Scientific concepts and techniques that form the groundwork for developing products and manufacturing them in the biotherapeutics industry*
- *Equipment, procedures, and preparation of the materials involved in upstream and downstream processes for manufacturing biologics*
- *Bioreactor and fermenter operations, centrifugation methods and preparation, cell lysis techniques and equipment, and filtration, chromatography skid and column preparation*
- *Optimization of cell processing and expansion*
- *Software tutorials and analytics used to evaluate upstream and downstream production*
- *Principles of aseptic techniques, sterilization, and environmental monitoring*
- *Hazards, risk mitigation, and worker and environmental safety*
- *Process documentation: laboratory notebooks, logbooks, and batch production records*
- *Standard operating procedures, regulations/regulating agencies, quality assurance and control*

***Class size is limited to the first 10 paid registrants. Program fees of $4,995/person are subsidized by grant funding through the NATIONAL INSTITUTE FOR INNOVATION IN MANUFACTURING BIOPHARMACEUTICALS; however, a registration fee of $500 must be paid upon application. Reserve your spot by emailing: Programs@NCTMmail.tamu.edu.**

ABOUT THE INSTRUCTORS

Zivko Nikolov, PhD, PE, is Director of NCTM and Associate Department Head for the Texas A&M Department of Biological and Agricultural Engineering. A Dow Chemical Professor of Bioprocess Engineering, Dr. Nikolov guides NCTM process development efforts and provides technical expertise for downstream training programs. Before joining Texas A&M in 2003, he was Vice President of bioprocess development with ProdiGene Inc., Professor at Iowa State University, and Senior Scientist at Michigan Biotech Institute.

Susan Woodard, PhD, is a Research Scientist for NCTM where she develops and delivers training in the areas of downstream biotherapeutics manufacturing and analytical testing. Dr. Woodard comes to NCTM with more than 20 years of experience working in both industry and academia. She has held positions in both analytical methods and process development at four biotechnology companies and has also worked as a bioprocess consultant.

Felipe Nicolau, PhD, is Assistant Research Engineer for NCTM wherein he performs research and training related to cell culturing and upstream biomanufacturing and bioprocessing. Prior to joining NCTM, Dr. Nicolau held various positions in R&D and production for both academia and industry. His primary research interests are in fungal biotechnology where he developed an interest in bioprocess design and safety.

Alex Wood, MBIOT, is a Research Engineering Associate for NCTM facilitating upstream bioprocessing and mammalian and microbial cell culture activities. Mr. Wood has served as lead instructor for NCTM's STEM programs and has co-developed and taught technical and continuing education related to fermentation and quality systems administration.

Online Courses to be Taken before Face-to-Face courses

NCTM ONLINE COURSE IN ORDER TAKEN	COURSE MODULES
Introduction to Pharmaceutical Manufacturing [NCTM-001] 2-hour online course This online course comprehensively discusses the fundamental elements associated with the development and manufacture of pharmaceutical products. Training modules discuss the categories of pharmaceutical products, phases of pharmaceutical discovery, development, approval, and varying manufacturing processes (chemical or biological). The curriculum also reviews regulatory agencies and their roles, current Good Manufacturing Practices (cGMP) and GXP, quality assurance and control, and finishes with an exploration of career paths within the pharmaceutical manufacturing industry.	Module 1: Pharmaceutical manufacturing basics, categories of drugs (small/large molecule), target site, drug substance/drug product, industry sectors, types of manufacturing companies (small, large, CMO)
	Module 2: Introduction to regulations, major legislation, FDA jurisdiction, FDA enforcement, Standards and Guidelines
	Module 3: Stages of the pharmaceutical development process, discovery through IND application, phase I through marketing application, FDA review through surveillance, other licensing applications
	Module 4: Manufacturing process, materials and supplies, materials management, drug production process, upstream processes (large vs. small molecule), downstream processes (large vs. small molecule), equipment, master production record
	Module 5: Current Good Manufacturing Practices (cGMP), quality system requirements, cGMP compliance overview (quality assurance and quality control), basic cleanroom requirements, dressing for cleanrooms, careers in pharmaceutical manufacturing, job skills overview
Understanding the Science of the Biopharmaceutical Industry [NCTM-002] 4-hour online course This online course provides a pragmatic study in the scientific principles of microbiology, immunology, and basic biochemistry that create the foundation for developing and manufacturing biopharmaceutical products. Curriculum covers biological macromolecules, an intensive study of infectious and non-infectious diseases, the immune system's structure and function, pathogenesis, and categories, uses, and development process of biotherapeutics and	Module 1: Biopharmaceuticals defined, history, manufacturing process, FDA mandates, structure of biological molecules, carbohydrates, proteins, nucleic acids, lipids, and their roles in biologics, infectious diseases, pathogenic organisms, viruses, bacteria, fungi and related diseases, non-infectious diseases, genetic factors vs. environmental factors
	Module 2: Immune system, innate vs. adaptive, NK cells, antigen presentation, antibodies, active vs. passive immunity, primary vs. secondary immune response, pathogenesis and routes of entry
	Module 3: Recombinant DNA technology, protein therapeutics and gene therapy, targeting activity, monoclonal antibodies, vaccine types, whole vs. partial organism, DNA, effectiveness, duration of immune memory, cost of development, biosimilars
cGMP Procedures and Documentation [NCTM-003] 4-hour online course This online course explains the expectations of and reasoning behind proper documentation protocols mandated in current Good Manufacturing Practice (cGMP) environments, like pharmaceutical production facilities. Topics include principles of data and information entry, technical writing, recording guidelines, document control, and process documentation, including laboratory notebooks, logbooks, standard operating procedures (SOPs), and batch production records (BPRs). Participants will understand the entire documentation pathway from R&D to commercialization of product, including corporate, R&D, manufacturing and qualification/validation.	Module 1: Intro to regulations in the pharmaceutical industry, Food and Drug Administration, history and legislation, current Good Manufacturing Practices (cGMP), cGMP requirements, Title 21 CFR, federal documents, FDA enforcement, correspondence for nonconformance, importance of documentation, GMP records, “documentation pyramid”, regulatory pathway of drug development, stages, measurable claims
	Module 2: Document control, legal requirements for record maintenance, features of controlled documents, system integrity, change control, recording guidelines for entering data/making corrections/signing data/reporting deviations/Corrective and Preventative Actions, reporting to FDA, identifiers and samples, internal auditing, risk levels, employee documentation and training
	Module 3: R&D documents/development protocol/records/reports/procedures, log books, Standard Operating Procedures (SOP), SOP development/types/writing/flowchart use/forms, batch records, qualification documentation/activities, validation documentation/plan
	Module 4: Fundamentals of technical writing, recording original data, data collection, making entries in lab notebook, recording laboratory procedures/inventions/ideas, attachments, referencing and blank space

Online Courses to be Taken before Face-to-Face courses

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Pharmaceutical Facility Operations [NCTM-004] 3-hour online course This online course provides an overview of pharmaceutical manufacturing facilities, including design/layout, utilities, and equipment. Participants will study clean room design, classification, and structure, and understand the many processes that are implemented to ensure a sterile environment, including practicing aseptic technique, gowning, environmental monitoring, and sanitization. Management of chemical and biological waste, sterilization techniques, and equipment maintenance and calibration are also discussed alongside the importance of validation in a pharmaceutical facility.	Module 1: Facility Design Overview (types of facilities, facility design/construction/complexities, utilities design, equipment, startup procedures, and maintenance)
	Module 2: Clean Area Design (contaminants, clean room design, clean room classifications, and controlling contamination)
	Module 3: Clean Area Operations (aseptic techniques, human and workplace contaminants, clean room supplies and storage, and environmental monitoring)
	Module 4: Sanitization and Sterilization (cleaning and disinfection, types of sanitization, reasons to sterilize, Sterility Assurance Levels, and sterilization responsibilities)
Safety in the Biopharmaceutical Industry [NCTM-005] 3-hour online course This online course covers a wide range of safety, health and environmental (SHE) issues specifically related to the pharmaceutical industry, including environmental safety, process and product safety, biosafety levels, industrial hygiene, and physical and chemical properties. Participants will receive an overview of product development stages and vaccine production, and will learn about toxicity, toxicology, drug safety and evaluation, pharmacokinetics and toxicokinetics, as well as risk assessment and analysis. Case studies, historically significant accidents, and lessons learned are incorporated throughout to provide real-life relevancy.	Module 1: Introduction to workplace safety, safety responsibilities, risks and hazards, exposure and routes, toxicity (local and systemic) and effects, types of hazards, case studies, hazardous waste and proper handling
	Module 2: Industrial Hygiene, government regulations for the pharmaceutical industry, OSHA standards 29 CFR 1910 (subpart D-J / K-Z), controlling hazards, evaluation, risk assessment, industrial hygiene controls
	Module 3: Risk Assessment, processes, Hazardous Operations Evaluations (HAZOP), risk analysis, risk evaluation, risk management
	Module 4: Basics of Laboratory Safety, biosafety defined, biosafety levels, CDC lesson, standard microbiological practices, safe storage of toxic materials, lab security, BSLs 1-3, clean benches, biosafety scenarios, case studies

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Advanced Certificate in Biopharmaceutical Manufacturing - Week 1: UPSTREAM

The Advanced Certificate in Biopharmaceutical Manufacturing immerses participants in a rigorous digital and hands-on training program, comprised of more than 100 hours of cGMP- and regulatory-based curricula. Subject matter includes aseptic microbial and mammalian cell processing using fixed and single-use fermentation and purification systems, regulatory compliance, quality assurance and control, process and environmental monitoring, and proper documentation and laboratory practices. Students will complete 5 self-paced online courses, then participate in 2 weeks of hands-on training at NCTM. Participants will receive 10.0 continuing education units and a certificate of completion.

Monday, December 17, 2018			
Start Time	**End Time**	**Activity**	**Room**
8:00	8:30	Sign In/Orientation	229
8:30	9:00	Introduction: Manufacturing Processes	229
9:00	9:30	Lab Skills: Biological Laboratory Safety Overview	
9:30	9:45	***MORNING BREAK***	
9:45	10:15	Lab Skills: Aseptic Technique on the Bench	103
10:15	11:30	Lab Skills: Aseptic Technique in the Biological Safety Cabinet	
12:00	1:00	***LUNCH BREAK***	
1:00	2:00	Cell Culture Basics: Overview	229
2:00	3:30	Cell Culture Basics: Activity - Counting of Mammalian Cells	106/103
3:30	3:45	***AFTERNOON BREAK***	
3:45	5:00	Cell Culture Basics: Activity - Passaging of Mammalian Cells	103/106
Tuesday, December 18, 2018			
Start Time	**End Time**	**Activity**	**Room**
8:30	9:45	Presenation: QA & QC	229
9:45	10:45	Gowning: Introduction to Gowning and De-gowning	229
10:45	11:00	*MORNING BREAK*	
11:00	11:30	Surface Monitoring: Activity- Surface Monitoring Overview	229
11:30	12:00	Air Monitoring: Total and Viable Air Particle Monitoring Overview and Practice	229
12:00	1:00	*LUNCH BREAK*	
1:00	1:45	Gowning: Activity- Cleanroom Gowning	114
1:45	3:30	Air Monitoring and Surface Monitoring: Activity- Air and Surface Monitoring Sample Collection	114
3:30	3:45	*AFTERNOON BREAK*	
3:45	4:30	Surface Monitoring: Activity- Surface Monitoring Sample Preparation	103
4:30	5:00	Air Monitoring: Activity- Toal Air Particle Results	103
Wednesday, December 19, 2018			
Start Time	**End Time**	**Activity**	**Room**
8:00	8:30	BioFlo 310 Fermentor: Overview	229
8:30	10:00	BioFlo 310 Fermentor: Activity - BioFlo 310 Fermentor Assembly	114B
10:00	10:15	***AFTERNOON BREAK***	
10:15	12:00	BioFlo 310 Fermentor: Activity - BioFlo 310 Controller	114B
12:00	1:00	***LUNCH BREAK***	
1:00	1:45	Culture Media Preparation: Overview (Mock BPR and Calculation)	229
1:45	2:30	Culture Media Preparation: Activity - Media Preparation	103
2:30	2:45	***MORNING BREAK***	
2:45	4:15	Culture Media Preparation: Activity - Steam & Filter Sterilization	103
4:15	4:30	Seed Culture and Cell Banking: Overview	229
4:30	5:00	Seed Culture and Cell Banking: Activity - Cultivation of Seed Culture	103
Thursday, December 20, 2018			
Start Time	**End Time**	**Activity**	**Room**
8:30	9:30	Seed Culture and Cell Banking: Activity - Inoculation of BioFlo 310 Fermentor	114B/103
9:30	10:30	Fermentation: Activity - Batch and Fed-Batch Fermentation	114B
10:30	10:40	***MORNING BREAK***	
10:40	11:40	Offline Analysis: Activity - Practice on OD, pH, and YSI analysis	114B
11:40	12:00	Offline Analysis: Activity - Sample Collection and Analysis	114B
12:00	1:00	***LUNCH BREAK***	
1:00	1:20	Offline Analysis: Activity - Sample Collection and Analysis	114B
2:00	3:00	Fermentation: Overview	229
2:30	2:50	Offline Analysis: Activity - Sample Collection and Analysis	114B
2:50	3:00	***AFTERNOON BREAK***	
3:00	3:20	Offline Analysis: Activity - Sample Collection and Analysis	114B
3:20	4:20	Advanced Bioreactors & Feeding	103
4:20	4:40	Offline Analysis: Activity - Sample Collection and Analysis	114B
4:40	5:00	Final Review	
Friday, December 21, 2018			
Start Time	**End Time**	**Activity**	**Room**
8:30	10:00	Harvest and Recovery: Activity - Harvest and Storage of Biomass	114B
10:00	10:10	***MORNING BREAK***	
10:10	12:00	Offline Analysis: Activity - Summary of Fermentation Run	114B
12:00	1:00	***LUNCH BREAK***	
1:00	1:30	Surface Monitoring: Activity- Surface Results	103
1:30	2:00	Air Monitoring: Activity- Air Monitoring Results	103
2:00	2:15	*AFTERNOON BREAK*	
2:15	2:45	Course Review and Quiz	229
2:45	3:00	Survey and Final Q/A	229

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Advanced Certificate in Biopharmaceutical Manufacturing - Week 2: DOWNSTREAM

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Monday, January 7, 2019			
Start Time	**End Time**	**Activity**	**Room**
8:00	8:30	Lecture: Quality Overview	229
8:30	9:30	Introduction to Analytical Equipment	229
9:30	10:30	Operation of Analytical Equipment	103
10:30	10:45	***MORNING BREAK***	
10:45	12:15	Operation of Analytical Equipment	103
12:15	1:00	***LUNCH BREAK***	
1:00	1:30	Overview of Protein Assays	229
1:30	2:45	Total Protein Assay: BCA	103
2:45	3:00	***AFTERNOON BREAK***	
3:00	4:30	Presentation: Protein chemistry overview	229
4:30	5:00	Review results	229
Tuesday, January 8, 2019			
Start Time	**End Time**	**Activity**	**Room**
8:00	8:45	Introduction to Downstream Processing	229
8:45	9:45	Introduction to Buffers and Molarity	229
9:45	10:00	***MORNING BREAK***	
10:00	11:45	Buffer Prep Activity	107
11:45	12:45	***LUNCH BREAK***	
12:45	1:45	Lecture: Normal Flow Filtration and Membrane Integrity Testing	229
1:45	2:30	Activity: Membrane Integrity Testing	107
2:30	2:45	***AFTERNOON BREAK***	
2:45	3:45	Demo on Single-Use Connections and Assemblies	103
3:45	4:30	Lab: Tube Sealing and Welding	103
Wednesday, January 9, 2019			
Start Time	**End Time**	**Activity**	**Room**
8:00	9:15	Primary Recovery and Clarification	229
9:15	9:45	Cell Cake Solubilization	114
9:45	10:15	Cell Lysis	229
10:15	10:30	***MORNING BREAK***	
10:30	11:45	Homogenization	114
11:45	12:00	Centrifugation of Feed Material	114
12:00	1:00	***LUNCH BREAK***	
1:00	2:00	Lecture: Tangential Flow Filtration	229
2:00	3:15	Lab: Tangential Flow Filtration with Hollow Fiber Cartridges	107
3:15	3:30	***AFTERNOON BREAK***	
3:30	4:15	Tangential Flow Filtration: Diafiltration and Sample Recovery	107
4:15	5:00	Tangential Flow Filtration: Analysis of Samples and Mass Balance Calculations	107
Thursday, January 10, 2019			
Start Time	**End Time**	**Activity**	**Room**
8:00	8:30	Lecture: Introduction to Column Packing and Qualification	229
8:30	10:00	Lab: Introduction to AKTA Pilot Chromatography System and Column Packing	107
10:00	10:15	***MORNING BREAK***	
10:15	10:45	Column Packing Activity: Column Packing Calculations	103
10:45	12:00	Unicorn Software Overview	229
12:00	1:00	***LUNCH BREAK***	
1:00	2:30	Evaluation of Column Packing Using Software and Hand Calculations	107
2:30	2:45	***AFTERNOON BREAK***	
2:45	3:15	Column Sanitization and Cleaning Lecture	229
3:15	4:15	Column Sanitization Activity	107
Friday, January 11, 2019			
Start Time	**End Time**	**Activity**	**Room**
8:00	9:00	Lecture: Introduction to Chromatography	229
9:00	9:45	Preparation of Feed Material	107
9:45	10:30	Ion Exchange Chromatography Activity: Method Preparation	107
10:30	10:45	***MORNING BREAK***	
10:45	12:00	Ion Exchange Chromatography Analysis of Results	107
12:00	1:00	***LUNCH BREAK***	
1:00	2:30	Lab: Hydrophobic Interaction Chromatography Method	107
2:30	3:00	Review Lab Results and Generate Report	107
3:00	3:15	***AFTERNOON BREAK***	
3:15	3:45	Review and Course Quiz	229
3:45	4:00	Course Survey	229