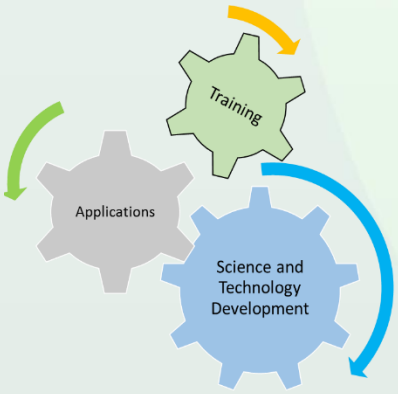
Centre of Excellence Biopharmaceutical Technology

DEPARTMENT OF BIOTECHNOLOGY
Ministry of Science & Technology
Government of India

A warm welcome to Centre of Excellence Biopharmaceutical Technology!

The **Centre of Excellence for Biopharmaceutical Technology (CBT)** was established at IIT Delhi in 2015 by the Department of Biotechnology, Government of India, in recognition of the importance of Biotechnology for India, particularly that of producing **affordable biotech therapeutics**.

The vision of CBT is to deliver innovation in biopharmaceutical technology to effectively address the challenges faced by the Indian biotech industry and thereby assist in the "**Make in India**" initiative by making India the **global hub** of manufacturing economical, safe and efficacious therapeutics.



CBT aspires to achieve this tall objective by providing a foundation of scientific and technology development to create **novel technologies**, engage with the biotech industry to **translate** these into applications, and finally to offer short term training courses to industry, academia, and regulatory agencies to facilitate **creation of an ecosystem** that delivers **affordable biotech therapeutics** to India and to the world.

CBT is bringing forth a **world class training program** that brings together leaders from across the world to come together and share the best practices and cutting edge technologies on a diverse set of topics:

Empowering Regulatory Leaders in India	**Driving Rapid Biologics Development**	**Design of Experiments**
Data Analytics and Statistics for Risk Assessment during Drug Development	**Mechanistic Modelling Of Biopharmaceutical Unit Operations**	**Host Cell and Process Related Impurity Analysis & Glycan Analysis**
Multivariate Data Analysis for Bioprocessing Data	**Advantages of CE in the characterization of mAbs**	

Prof. Anurag S. Rathore
Coordinator, CBT, IIT Delhi

Prof. James Gomes
Co-Coordinator, CBT, IIT Delhi

Day 1- December 10, 2019

Parallel Sessions			
Session-1 Empowering Regulatory Leaders in India- Validation and Monitoring during large scale Manufacturing of Bio Therapeutics (8:30 am to 5:30 pm)	**Session-2** Driving Rapid Biologics Development – From Cell Line Development to Commercial Manufacturing (8:30 am to 6:00 pm)	**Session-3** Data Analytics and Statistics for Risk Assessment during Drug Development (8:30 am to 6:00 pm)	**Session-4** Mechanic Modelling and Control of Biopharmaceutical Unit Operations (8:30 am to 6:00 pm)

Day 2- December 11, 2019

Parallel Sessions			
Session-5 Empowering Regulatory Leaders in India- Good Manufacturing Practices (GMP) (8:30 am to 5:45 pm)	**Session-6** Advantages of Capillary Electrophoresis Techniques Characterization of Monoclonal Antibodies and Related Products (8:30 am to 6:00 pm)	**Session-7** Design of Experiments (8:30 am to 6:00 pm)	**Session-8** Host Cell and Process Related Impurity Analysis and Glycan Analysis of Biotherapeutics (8:30 am to 5:30 pm)

Day 3- December 12, 2019

Parallel Sessions	
Session-9 Empowering Regulatory Leaders in India- Good Clinical Practices (GCP) (8:30 am to 6:00 pm)	**Session-10** Multivariate Data Analysis for Bioprocessing Data: Concepts & Case Studies (8:30 am to 6:00 pm)

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Empowering Regulatory Leaders in India
(10th-12th December 2019)

Description: Regulatory approval is the desired endpoint of all development and commercialization activities in the biopharmaceutical industry. A critical aspect of similar biologics development is having comprehensive regulatory guidelines. Indian regulatory authorities published the Guidelines on Similar Biologics in 2012 with a revision in 2016. This proposed three-day course aims to strengthen our regulators and the industry on some of the key aspects of biopharmaceutical product development and commercialization. Validation and Monitoring during Large Scale Manufacturing of Bio therapeutics, Good Manufacturing Practices (GMP) and Good Clinical Practices (GCP) will be the focus of this course. The audience is expected to consist primarily of Indian regulators and other stakeholders that play a key role in the approval process. Limited participants from the Indian biotech industry will also be accommodated.

OUTLINE

DAY 1 Validation and Monitoring during Large Scale Manufacturing of Biotherapeutics

08.30-09.00:	Breakfast
09.00-10.00:	Inaugural session
10.00-11.00:	Issues related to large scale manufacturing of biotherapeutics ***(Sadettin Ozturk, Mass Biologics, US)***
11.00-11.15:	Break
11.15-12.15:	Analytical method validation ***(EK Lee, Hanyang University, South Korea)***
12.15-13.15:	Process validation ***(Krunal Mehta, Amgen US)***
13.15-14.00:	Lunch
14.00-14.45:	Viral clearance validation ***(Krunal Mehta, Amgen US)***
14.45-15.45:	Cleaning validation ***(Akundi Sriram, Biocon)***
15.45-16.00:	Break
16.00-17.00:	Process monitoring ***(Krunal Mehta, Amgen US)***
17.00- 17.30:	Discussion & wrap up


Sadettin Ozturk


EK Lee


Krunal Mehta

DAY 2 Good Manufacturing Practices (GMP)

08.30-09.00:	Breakfast
09.00-09.30:	Introduction to GMP & c-GMP regulations ***(Akundi Sriram, Biocon)***
09.30-10.15:	Premises and Facility Design and Warehousing ***(Sankar B., Biocon)***
10.15-10.30:	Break
10.30-11.15:	Equipment, maintenance and calibration ***(Sankar B., Biocon)***
11.15-12.15:	Validation, qualification and change control ***(EK Lee, Hanyang University, South Korea)***
12.15-13.15:	Lunch
13.15-14.15:	Quality Control – GLP ***(EK Lee, Hanyang University, South Korea)***
14.15-15.15:	People and training ***(Narendra Chirmule, SymphonyTech Biologics)***
15.15-15.30:	Break
15.30-16.30:	Quality risk management ***(TBD)***
16.30-17.30:	Documentation, records and data integrity ***(EK Lee, Hanyang University, South Korea)***
17.30-17.45:	Discussion & wrap up


Akundi Sriram


Sankar B.


Narendra Chirmule

DAY 3	**Good Clinical Practices (GCP)**
08.30-09.00:	Breakfast
09.00-10.00:	An update on recent guidelines of GCP and clinical trials (DCGI) and role of ethics committee ***(Narendra Chirmule, SymphonyTech Biologics)***
10.00-10.45:	IND/IMPD & informed consent ***(TBD)***
10.45-11.00:	Break
11.00-12.00:	Adverse Events & Drug Accountability ***(Narendra Chirmule, SymphonyTech Biologics)***
12.00-13.15:	Post Drug Approval and Monitoring Simulation ***(TBD)***
13.15-14.00:	Lunch
14.00-15.30:	Electronic systems and data management ***(Ravindra Khare, Symphony Technologies)***
15.30-15.45:	Break
15.45-16.45:	Preparing for FDA inspections ***(TBD)***
16.45-17.45:	Collecting, managing and reporting clinical study data ***(Ravindra Khare, Symphony Technologies)***
17.45-18.00:	Discussion & wrap up

Narendra Chirmule

Ravindra Khare

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Driving Rapid Biologics Development – From Cell Line Development to Commercial Manufacturing (10th December 2019)

Description: Cell culture technology has advanced significantly over the last few decades and is now generally considered a reliable, robust and relatively mature technology. A range of monoclonal antibody-based therapies are currently produced using cell culture methods in large scale manufacturing facilities that produce products for both commercial use and clinical studies. The robust implementation of this technology requires optimization of a number of variables, including:

a. Cell line development with cell lines capable of producing the required molecules at high productivities that ensure low operating cost
b. Cell bank manufacture and characterization together with the support for developing structural biology, physicochemical and bioanalytical (binding and potency) analytics
c. High throughput and scalable bioreactor culture conditions that achieve both the requisite productivity and meet product quality specifications
d. Appropriate on-line and off-line sensors capable of providing information that enhances process control
e. Good understanding of culture performance at different scales to ensure smooth and faster scale-up.
f. Process development, scale-up and process characterization and validation that enable robust operation and ensures compliance with current regulations

OUTLINE

08.30-09.00:	Breakfast
09.00-10.00:	Inaugural session
10.00-10.30:	Biologics ǀ Biosimilar market overview (interactive session) ***(Ravin Mehta, Sartorius Stedim India)***
10.30-11.00:	General overview and trends in product development ***(Ravin Mehta, Sartorius Stedim India)***
11.00-11.15:	Break
11.15-11.45:	Driving rapid biologic development – from cell line to clinic ***(Ravin Mehta, Sartorius Stedim India)***
11.45-12.45:	Strategies for studying cell culture development ***(Mark Smales, University of Kent, UK)***
12.45-13.30:	Toolbox for intensified bioprocessing in upstream applications to reduce cost ***(Deepak Vengovan, Sartorius Stedim India)***
13.30-14.30:	Lunch
14.30-15.30:	Accelerating the process scale-up and process characterization studies (interactive session) ***(Sadettin Ozturk, Mass Biologics, US)***
15.30-15.45:	Break
15.45-16.30:	Qualification of raw materials and cell substrates for biomanufacturing ***(Annu Uppal, US Pharmacopeia, India)***
16.30-17.15:	Hands-on exercises with bioreactor simulation tool ***(Deepak Vengovan, Sartorius Stedim India)***
17.15-18.00:	Discussion and wrap up


Ravin Mehta


Mark Smales


Deepak Vengovan


Sadettin Ozturk


Annu Uppal

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Data Analytics and Statistics for Risk Assessment during Drug Development
(10th December 2019)

Description: Over the past three decades, development of biotherapeutics has revolutionized innovation in medicines. The field has made major advances in developing recombinant technologies for clone development, cell culture and purification technologies, formulation and devices, pre-clinical pharmacology and clinical trial designs. The industry encompasses various aspects of approaches, including proteins, cells and genes as drugs. Drug development is at a turning point in human medicine. Efficiency and Quality compliance are critical to achieve innovation and affordability. This comprehensive course will provide an in-depth overview of the basics and multi-dimensional nature of drug development utilizing technology, statistical and quality considerations. The course also provides the current trends and future challenges in the field with case studies.

OUTLINE

08.30-09.00: Breakfast
09.00-10.00: Inaugural session
10.00-11.00: An introduction to the drug development and risk assessment
(Narendra Chirmule, SymphonyTech Biologics)
11.00-11.30: DOE & hypothesis testing (statistical concepts)
(Ravindra Khare, Symphony Technologies)
11.30-11.45: Break
11.45-12.30: Defining the unmet need: disease pathology; and design of drugs
(Narendra Chirmule, SymphonyTech Biologics)
12.30-13.00: Analysis of variance, Regression analysis (statistical concepts)
(Ravindra Khare, Symphony Technologies)
13.00-13.45: Lunch
13.45-14.30: Pharmacology & Toxicology
(Narendra Chirmule, SymphonyTech Biologics)
14.30-15.00: Precision, Accuracy (statistical concepts)
(Ravindra Khare , Symphony Technologies)
15.00-15.45: Process Development & Manufacturing
(Anurag S. Rathore, IITD)
15.45-16.00: Break
16.00-16.30: Robustness, Sampling, Stability specifications (statistical concepts)
(Ravindra Khare , Symphony Technologies)
16.30-17.15: Clinical trials and regulatory approval process
(Narendra Chirmule, SymphonyTech Biologics)
17.15-17.45: Trend Analysis, Comparability, Management of change (statistical concepts)
(Ravindra Khare , Symphony Technologies)
17.45-18.00: Risk assessment summary and conclusions (Discussion & wrap Up)


Narendra Chirmule


Ravindra Khare


Anurag S. Rathore

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Mechanistic Modelling and Control of Biopharmaceutical Unit Operations
(10th December 2019)

Description: In the current paradigm of implementation of Quality by Design (QbD) for production of biopharmaceutical products, there is renewed interest in mechanistic modelling of the unit operations that are typically utilized in these production processes. The biotech industry uses empirical models at present, owing to the complexity of these unit operations. However, the superiority of mechanistic modelling over empirical modelling with respect to robustness and accuracy is widely accepted. This course will aim to present approaches towards mechanistic modelling of key bioprocess unit operations. Both theoretical approaches as well as experimental validation of the approach will be presented. These models can be used for process optimization, process characterization, and process scale-up.

OUTLINE

08.30-09.00:	Breakfast
09.00-10.00:	Inaugural session
10.00-10.30:	Role of mechanistic modelling in bioprocess development ***(Anurag S. Rathore, IITD)***
10.30-11.00:	CFD based mechanistic modelling of bioreactor ***(Shital Joshi, Ansys)***
11.00-11.15:	Break
11.15-12.00:	Case studies in CFD modelling of a reactor ***(Venkataramana Runkana, TCS)***
12.00-12.30:	Case study in CFD modelling of bioreactor ***(Jayati Sarkar, IITD)***
12.30-13.00:	Mechanistic modelling of bioreactor – lump parameter model ***(Leelaram Santharam, IITD)***
13.00-14.00:	Lunch
14.00-14.30:	Mechanistic modelling of acoustic wave separator ***(Shantanu Banerjee, IITD)***
14.30-15.00:	Mechanistic modelling of continuous UF and DF ***(Garima Thakur, IITD)***
15.00-15.30:	Mechanistic modelling of process chromatograph ***(Anamika Tiwari, IITD)***
15.30-15.45:	Break
15.45-16.15:	Mechanistic modelling for surge tank management ***(Nikita Saxena, IITD)***
16.15-17.15:	Process Control ***(Anders Johansson, Applied Materials)***
17.15-18.00:	Discussion and Wrap-up


Anurag S. Rathore


Shital Joshi


V. Runkana


Jayati Sarkar


Anders Johansson

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Advantages of Capillary Electrophoresis Techniques Characterization of Monoclonal Antibodies and Related Products (11th December 2019)

Description: Monoclonal antibodies (mAb) are the backbone of many biotherapeutic drugs. In the drug development process, from clone selection to release and stability, characterization of the antibody is crucial for an in-depth understanding of its structural integrity. In recent years capillary electrophoresis (CE) has been demonstrated to be a powerful and versatile separation technique for the characterization of biologics. This comprehensive course will provide an in-depth overview of the basics of CE techniques and hands-on sample analysis of purity and glycans. This course will also cover a brief introduction of sheath-less CESI MS technology.

OUTLINE

Prashant Dour

Sagar Amberkar

08.30-09.00:	Breakfast
09.00-10.00:	Recent advances in the use of Capillary electrophoresis for biopharmaceutical analysis ***(Prashant Dour, Application Manager, SCIEX)***
10.00-10.45:	CE SDS analysis of purity and heterogeneity (theory) ***(Sagar Amberkar, Application Specialist, SCIEX)***
10.45-11.00:	Break
11.00-12.00:	**Case Study 1-** Harnessing the power of electrophoresis and chromatography (***Ramesh Kumar, IITD***)
12.00-13.00:	CE SDS analysis of purity and heterogeneity (lab session I) (***Sagar Amberkar, Application Specialist, SCIEX)***
13.00-14.00:	Lunch
14.00-14.30:	Glycan Analysis of monoclonal antibodies using CGE (theory) (***Prashant Dour, Application Manager, SCIEX)***
14.30-15.30:	Glycan Analysis of monoclonal antibodies using CGE (lab session II) (***Sagar Amberkar, Application Specialist, SCIEX)***
15.30-16.00:	Break
16.00-16.45:	Characterization of biologics using CESI-MS ***(Prashant Dour, Application Manager, SCIEX)***
16.45-17.30:	**Case Study 2:** Identification of HCP in process using LC-CE-MS & LC-MS/MS ***(Rohan Shah, IITD)***
17.30-18.00:	Discussion & wrap up

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Design of Experiments
(11th December 2019)

Description: Quality by Design (QbD) and Design Space estimation, initiated by ICH, are moving to the phase of establishing standardized procedures and definitions within biopharmaceutical companies. The challenge is to extract a statistically useful description that matches the flexibility and risk control described in the ICH Q8 guidelines. Design of Experiments (DOE) is required for a good and reliable Design Space description. However, most of the set-points derived from DOE are overoptimistic and do not consider risk of failure. A design space can be an irregular multidimensional region or a strict Proven Acceptable Range (PAR) for Critical Process Parameters (CPP's). This course will present the fundamentals of DOE and illustrate how to derive a multidimensional Design Space. Hands-on exercise is an integrated part of the course which let you experience how DOE and Design space estimation are carried out.

OUTLINE

08.30-09.00: Breakfast

09.00-10.15: Introduction to DOE
(Vaibhav Patil, Sartorius Stedim India)

10.15-10.30: Break

10.30-11.00: Role of DOE in biopharmaceutical development
(Anurag S. Rathore, IITD)

11.00-12.30: DOE for screening and hands-on exercises
(Vaibhav Patil, Sartorius Stedim India)

12.30-13.00: **Case Study:** DOE based screening of media components
(Rishabh Mishra, IITD)

13.00-13.45: Lunch

13.45-14.15: **Case Study:** DOE application for optimization of Acoustic Wave Separation
(Shantanu Banerjee, IITD)

14.15-14.45: **Case Study:** DOE application for optimization of crystallization of a pharmaceutical API
(Manu Garg, Sun Pharma)

14.45-16.15: DOE for optimization and hands-on exercises
(Vaibhav Patil, Sartorius Stedim India)
- DoE based optimization of a fermentation process
- DoE based designing a chromatographic medium for protein purification

16.15-16.30: Break

16.30-17.30: Find robust set-point for design space using DOE and Monte Carlo simulations; DOE on stability testing ***(Vaibhav Patil, Sartorius Stedim India)***

17.30-18.00: Discussion and wrap up

Vaibhav Patil

Anurag S. Rathore

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Host Cell and Process Related Impurity Analysis and Glycan Analysis of Biotherapeutics
(12th December 2019)

Description: Analytical characterization is the backbone of establishing comparability, arguably the most critical step in development and commercialization of biotherapeutic products. Major advancements have occurred in the past few years with respect to both development of novel, high resolution analytical tools as well as of novel approaches. Of these, arguably the most significant is the emergence of mass spectrometry as the tool of choice for identification and quantification of a biotherapeutic. In this course, we will showcase some of the most challenging applications of this tool with the aim to demonstrate the power and dexterity of this tool.

OUTLINE

08.30-09.00:	Breakfast
09.00-09.45:	Extractables and Leachables Frontiers: analytical solution by mass spectroscopy using database and SW workflows in single-use systems ***(Chander Mani, Agilent Technologies)***
09.45-10.15:	Determining elemental impurities in biopharmaceuticals using USP/ICH Methodology by ICP-MS ***(Vinay Jain, Agilent Technologies)***
10.15-10.30:	Break
10.30-11.00:	Analysis of Extractable/Leachable compounds from generic liquid drug formulation using GC/MSD systems ***(Praveen Arya, Agilent Technologies)***
11.00-11.45:	Identification and quantification of HCP impurities in biopharmaceuticals (***Mark Smales, University of Kent, UK)***
11.45-12.30:	Rapid N-linked glycan profiling for biotherapeutics ***(Debdip Ghosh, Agilent Technologies)***
12.30-13.30:	Lunch
13.30-14.00:	Biologics N-linked glycan analysis from sample preparation to data analysis ***(Saurabh Nagpal, Agilent Technologies)***
14.00-14.45:	Analytical Quality by Design approach in glycan method development ***(Sreelakshmy Menon, Agilent Technologies)***
14.45-15.30:	Workflows for amino acid and cell culture analysis in spent media ***(Debdip Ghosh, Agilent Technologies)***
15.30-15.45:	Break
15.45-16.15:	**Case Study-** Biocomparability of N-Glycan between innovator & in-house produced mAb using instant PC ***(Rohan Shah, IIT D)***
16.15- 17.15:	Bioreactor cell culture Monitoring by LC/MS ***(Ashish Pargaonkar, Agilent Technologies)***
17.15- 17.30:	Discussion & Wrap Up


Chander Mani


Vinay Jain


Praveen Arya


Mark Smales


Debdip Ghosh


Saurabh Nagpal


Sreelakshmy Menon


Ashish Pargaonkar

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Multivariate Data Analysis for Bioprocessing Data: Concepts and Case Studies (12th December 2019)

Description: Biopharma and biotech manufacturing today involves larger and larger masses of data. Correct management of these data can give us valuable insights to process development as well as production, help us understand the progress of a batch and also point us in the right direction to troubleshoot. By applying state-of-the art data analysis technologies in the biopharma production the time for fault detection and diagnosis in production can be significantly reduced. In one recent example, a company identified the cause of a cell culture problem about a month earlier than it otherwise might have. For that biologic product, making the fix early and not losing that month saved $2.4 million. The course will present fundamental theory and practice of Multivariate Data Analysis (MVDA) within the framework of PAT to improve quality and throughput, as well as hands-on exercises on how MVDA should be used in process development and production

OUTLINE

08.30-09.00: Breakfast

09.00-10.30: Introduction to MVDA ***(Vaibhav Patil, Sartorius Stedim India)***
Principal component analysis (PCA)
- Explanation
- Score plot & loading plot
- Diagnosis of observations, variables and model

Vaibhav Patil

10.30-10.45: Break

10.45-11.30: Role of MVDA in biopharmaceutical development ***(Anurag S. Rathore, IITD)***

Anurag S. Rathore

11.30-12.30: Hands on exercises (***Vaibhav Patil, Sartorius Stedim India)***
- Main steps of data analysis with SIMCA
- **Case study:** Multi-scale cell culture data overview
- **Case study:** Raw material characterization – Particle size distribution

12.30-13.15: Lunch

13.15-13.45: **Case Study**: Use of MVDA for analysis of proteomic data ***(Shantanu Banerjee, IITD)***

13.45-15.00: Partial least squares (PLS) and orthogonal partial least squares (OPLS) (***Vaibhav Patil, Sartorius Stedim India)***
- **Case study:** Blend uniformity and developing calibration model in spectroscopy.

15.00-15.30: Break

15.30-17.00: How to build batch models (***Vaibhav Patil, Sartorius Stedim India)***
- Batch evolution model & batch level model
- **Case study:** Modelling an upstream cell culture process for process monitoring and control

17.00-17.30: **Case Study:** Analysis of manufacturing data ***(Vishwanath Hebbi, IITD)***

17.30-18.00: Discussion and wrap up