

Details of BTFS Domains

A. Fermentation and Bioprocess:

Probiosys, Bengaluru

St. Aloysius College, Mangaluru (Mangalore)

Fermentation and Bioprocess:

Introduction:

The term “Biopharmaceutical” refers to drugs that have unique qualities in the way that they are derived and manufactured as opposed to traditional drug products. Biopharmaceuticals are protein-based (including antibodies), nucleic acids (DNA, RNA or antisense oligonucleotides) used for therapeutic or in vivo diagnostic purposes and are produced from genetically altered microorganisms or may come from blood or blood plasma products (usually referred to as biologics). The first such substance approved for therapeutic use was biosynthetic human insulin made via recombinant DNA technology.

Nowadays almost all the biopharmaceutical products are manufactured commercially through various fermentation routes using genetically engineered microorganisms like *E.coli*, yeast, mammalian cell and insect cell culture, maintaining various regulatory compliances since these products are marketed in regulated markets of different countries. The present domain Fermentation and Bioprocess comprehensively deals with theoretical and practical aspects of upstream and downstream of Biopharma manufacturing processes keeping cGMP in mind.

Description: In the present BTFS curriculum, the domain Fermentation and Bioprocess has been divided into four modules viz. Upstream Process, Downstream Process, Biopharma Facility Engineering and Regulatory affairs. This domain deals with the production of therapeutic proteins using different expression systems as well as high cell density fermentation including media selection, preparation and sterilisation, fermenter functional design, sterilization in place and sterilization process validation, fermenter inoculation and maintenance of different fermentation parameters, scale up of fermentation process, fermenter harvest and cleaning process validation. For animal cell culture, media preparation and sterilization by filtration, sub-culturing, suspension culture and monitoring, monitoring of bioreactor cultures. In downstream processing, familiarization with chromatography equipment, column packing methods, column equilibration, and operation of tangential flow filtration as well as its cleaning and sanitation, dead end filtration will also be part of the curriculum. In addition, regulatory requirements of different countries and cGMP requirements for the production area of biopharmaceuticals will also be covered in the present domain.

Application: Pharmaceutical proteins produced via fermentation in transgenic microbes or mammalian cell culture systems provide economical systems for production of therapeutic

proteins. Fermentation systems can be scaled up to produce quantities of pharmaceuticals that are difficult or impossible to produce via traditional methods.
In

addition rapid growth rate and high productivity, higher product content per unit of cells, the process occupy little land area, production is independent of seasonal variations and climatic conditions has added advantages to the fermentation process. Some of the Biopharma products are produced commercially through fermentation routes are - Human insulin, Streptokinase, Erythropoietin, Hepatitis B Vaccine, Human growth hormone, Interleukin, GCSF, GMCSF, Alfa-Interferon, Gamma Interferon etc.

Biopharma Industries: Biocon, Serum Institute of India, Panacea Biotech, Reliance Life Sciences, Shantha Biotechniques, Indian Immunologicals, Bharat Biotech, Cadila Health Care, Intervet India, Intas Biopharma, Eli Lilly, Hafkine Biopharma, Glaxo Smith Kline, Novo Nordisk etc.

Future Prospects: In the fastest growing Biotech Industry, Biopharmaceuticals consist of about 62% of the \$3 billion generated by the Biotech Industry in financial year 2009/10. According to the 9th Biospectrum-ABLE Biotech Industry Survey 2011, the industry has grown by 21.5%, slightly less than \$4 billion in financial year 2010/2011

B. Cellular and Molecular Diagnostics:

Manipal Life Science Center, Manipal
The Oxford College of Science, Bengaluru (Bangalore)

Cellular and Molecular Diagnostics of diseases is a rapidly growing translational area that bridges discoveries in molecular pathogenesis by basic scientists and the application of these discoveries in useful clinical assays.

Description: Diagnosis of diseases, either human or veterinary has evolved over the past decades. With the advances in translational technologies, diagnostic industries have been growing rapidly, integrating recent advances in genomics and proteomics into their arsenal. This is in addition to currently practiced traditional pathological, immunological, biochemical, cellular and molecular diagnostics of number of diseases. In this ever growing field, there is immediate need for trained personnel who are not only equipped with knowledge to understand the relevance of diagnostic tests, but are also able to handle the sophisticated equipment used in the modern diagnostic laboratories. Biotechnology Finishing School concept precisely wished to address this lacunae to facilitate growth of this important sector of biotechnology.

Scope and Application: Currently, there is a need for human resource to cater to the needs of diagnostic industries to adapt, discover, develop and translate various diagnostic tests which are in use. It is envisaged that there will be a continued and growing demand for rapid, reliable and high-throughput, cost-effective diagnostic tests in future. The Biotechnology finishing school is designed to fill this void by creating fully trained manpower who able to face the challenges that are encountered in any diagnostic industry. These include industries who manufacture diagnostic products and the service providers who undertake cellular and molecular diagnostic at the primary, secondary and tertiary sites. The curriculum of the Biotechnology Finishing School in Cellular and Molecular diagnostics consists of hands-on training in routine as well as state of the art technologies with a sound background on principles and practices of each technology.

With the sophisticated facilities acquired and built specifically for this, finishing schools have the required personnel, manpower and the knowledge to train future generation of workforce to cater to the needs of diagnostic industries. It is also envisaged that there

will be an intense interaction with the diagnostic industries and their constant input and feedback is expected to benefit the trainees.

C. Pre-clinical, Clinical Research, Biostatistics and Data Management:

Maharani Lakshmi Ammanni College for Women, Bengaluru
(Bangalore) PES Institute of Technology, Bengaluru (Bangalore)

Pre-clinical, Clinical Research, Biostatistics and Data Management:

INTRODUCTION

Clinical Research is a systematic study for new drugs in human subjects to generate data for discovering or verifying the Clinical, Pharmacological (including pharmacodynamic and pharmacokinetic) or adverse effects with the objective of determining safety and efficacy of the new drug.

Clinical Research is conducted in 4 Phases which are *Phase I trials, Phase II trials, Phase III trials, Phase IV trials*.

Clinical Research Industry - A Global & Indian Perspective

The projected market of global pharmaceutical is US\$ 427 billion and Research & Development cost is estimated at US\$ 60-65 billion annually. India has become a signatory to TRIPS. Consequently, a new patent law has come into effect from January 2005. The new keyword for the pharmaceutical industry after recession is innovation & cost reduction and to introduce new drugs, clinical trials in low cost destination are mandatory. The clinical trials that have been conducted in India till date have gone well. For majority of the studies, patient enrollment is a key advantage. This helps compress the development timeline and data quality is excellent. Numerous audits in India are a testimony to level of quality. And data from clinical study in India have been successfully filled with international regulatory agencies. The potential realized at present is a fraction of the possible in India. Consistent with WTO guidelines effective from 2005, India will also offer 10-year tax concessions on revenue to companies making Research & Development (R&D) investments here. These incentives are expected to substantially increase R&D activities of both multinational and domestic biopharmaceutical companies.

Analysts projects that clinical trial outsourced market in India is forecasted to grow at a CAGR of over 30% during 2010-2012 to around US\$ 600 Million by 2012. With this anticipated growth, India will become one of highest growing clinical trial destinations in the world.

Various Types of Clinical Trials being conducted in India:

Trials are on for drug which is indicated for reduction of mortality in adult patients and can be used for sepsis. Clinical Trials have already been held on more than 600 patients for human insulin and insulin. Clinical Trials are being conducted on oncology and developing a new molecule for lung cancer.

Clinical trials are on 300 patients on a new malaria 'cocktail' drug that combines chloroquine (to which Indian malarial strains have developed resistance) and azithromycin, an antibiotic. Clinical Trials are also being conducted for drugs to treat osteoporosis, breast cancer and schizophrenia involving new drugs and therapies for treatment of different variants of blood cancer and colorectal diseases. The trials in

India are mostly in different areas like oncology, endocrinology, traumatology, sports, medicine, pulmonary diseases, paediatric diseases, and infectious diseases. The largest Clinical Trial outside US for a drug delivery device has been conducted in India.

Major players in Clinical Research in India: The major global players that have started operations in India are Quintiles, Paraxel, Icon, Wyeth, BMS, Novartis, Novo- Nordisk, GSK, Pfizer .There are now quite Indian CROs who are involved in CR and CDM operations such as TCS, CTS, Clinigene etc.

D. Protein Expression and Scale-up:

JSS College of Arts, Commerce & Science, Mysooru (Mysore)

Protein Expression and Scale-up: GENERAL INTRODUCTION

Proteins are instrumental in all biochemical transformations that occur in any living system. They perform diverse functions such as transport, transformation, stimulation, regulation, stabilization and host of other functions. The information for the protein structure is stored in genes (DNA). Any change in DNA structure can result in the structural changes in proteins. There genetic diseases due to mutations in genes are known. There are diseases due to by destruction of certain cells. To help ameliorate genetic defect and infectional destructions of cells that produce specific proteins, isolation of a specific gene and its expression is important. To make it commercially available like the productions of insulin, scale-up of the process is important.

DESCRIPTION: Traditional strategies for recombinant protein expression involve transfecting cells with a DNA vector that contains the template and then culturing the cells so that they transcribe and translate the desired protein. Typically, the cells are then lysed to extract the expressed protein for subsequent purification. Both prokaryotic and eukaryotic *in vivo* protein expression systems are widely used. The selection of the system depends on the type of protein.

Bacterial protein expression systems are popular because bacteria are easy to culture, grow fast and produce high yields of recombinant protein. However, multi-domain eukaryotic proteins expressed in bacteria often are non-functional because the cells are not equipped to accomplish the required post-translational modifications or molecular folding. Also, many proteins become insoluble as inclusion bodies that are very difficult to recover.

Mammalian *in vivo* expression systems usually produce functional protein, but the yield is low, cost of production is high and mammalian cell culturing is time-consuming. In addition, *in vivo* systems are not conducive to either high throughput protein synthesis or expression of proteins that are toxic to host cells.

Cell-free protein expression is the *in vitro* synthesis of protein using translation compatible extracts of whole cells. In principle, whole cell extracts contain all the macromolecular components needed for transcription, translation and even posttranslational modification. These components include RNA polymerase, regulatory protein factors, transcription factors, ribosomes, and tRNA. When supplemented with cofactors, nucleotides and the specific gene template, these extracts can synthesize proteins of interest in a few hours.

APPLICATION

1. Production of hormones – Insulin
2. Production of proteins for constituting physiological fluids such as blood
3. Production of commercially important enzymes
4. Mutation analysis
5. Genetic variation and detection
6. Enzymatic activity analysis
7. Molecular diagnostics
8. Post-translational modification analysis

MAJOR INDUSTRIES AND TOP PLAYERS IN INDIA

1. Serum Institute of India
2. Biocon Pvt Ltd
3. Panacea Biotech
4. Shantha Biotechnics
5. Novozymes South Asia
6. Advanced Enzyme Technologies
7. Dr. Reddy's Lab

FUTURE PROSPECTS: The production of recombinant proteins has great potential as effective tool for research and commercial biotechnology. During the last few years, there has been an increasing interest in the field of gene regulation and protein synthesis in different systems that may be used as a novel approach for production of some important therapeutic drugs or proteins.

Recent improvements/developments in this area have significantly increased its utility and enabled various groups to explore the possibilities of production of recombinant proteins, which can be directly or indirectly used for various pharmaceuticals, nutraceuticals and therapeutic purposes.

Commercial production of proteins is required in the development of drugs, pharmaceuticals, nutraceuticals and enzymes of commercial importance.

E. Nutraceuticals and Food Processing:

Padmashri Institute of Management & Sciences, Bengaluru (Bangalore)

Nutraceuticals and Food Processing: The term “nutraceutical” is defined as any substance that may be food or part of a food that provides medical benefits including the prevention and treatment of diseases. Nutraceuticals include isolated nutrients, dietary supplements, diets, genetically engineered designer foods, herbal products, processed products, such as cereals, soups and beverages.

Globally nutraceutical market is growing at the rate of 7 % and the market is estimated to cross US \$ 177 billion by the year 2013. The United States, Europe and Japan dominate the global market, with the combined share estimated at about 85%. The

Asia-Pacific market is expected to record exceptional gains in coming years, buoyed by its rising economic prosperity especially Chinese and Indian markets. Indian nutraceutical market is estimated to be USD one billion and has been growing much faster at 18 per for the last three years, mostly driven by functional food and beverages categories. However, the latent market in India is two to four times the current market size and is between USD two to USD four billion with almost 148 million potential customers, (FICCI - Ernst & Young study titled „Nutraceuticals - Critical supplement for building a healthy India).

The recent trend and logical progression noticed is convergence of health and food industry.

FOOD PROCESSING: India is the world's 2nd largest producer of food. Food processing industry is one of the largest industries in India ranking 5th in terms of production, consumption, export and anticipated growth. Domestically, the spending on food and food products amounts to 21% of India's GDP and constitutes the largest portion of the Indian consumer's spending. With rapid expansion of the processed food industry, there is going to be a huge increase in demand for professionally skilled manpower. The Industry aims to grow at a rate of 40% of the current market size by 2015, to touch USD 258 billion by 2015.

For both the industries, the major bottleneck hampering the growth is the availability of skilled manpower in various roles within the industry. In fact, of late, shortage of skilled workers has emerged as a critical factor to achieve the projected growth targets and become globally competitive. For the want of skilled manpower, industry spends most of the time to train and equip the human resource with basic skill set, needed at various functions in the Industry. FICCI estimates show that this accounts to the total monetary loss of approx. 1 billion for food processing companies alone. This is a very alarming situation for the growth of food processing industry and needs to be addressed.

Clearly understanding the need for studying the closely related industry in a holistic and comprehensive manner, an unique Advanced Post-graduate Diploma program in Nutraceutical and Food Processing course is offered under Biotechnology Finishing School. Both being a specialized segment and highly interdisciplinary, the course content has been developed keeping in mind the industry demand with more focus on research, latest technology and innovations, cost effective technology and packaging solutions with a futuristic outlook.

F. Plant Genetic Transformation, Genome, Seed and Marker Analysis:

Dayanandsagar Institution, Bengaluru
(Bangalore)

Plant Genetic Transformation, Genome, Seed and Marker Analysis:

Plants are valuable source of food, fodder, fuel and fiber. The demand for their products is ever increasing globally as well as locally. Techniques used in regenerating whole plants from small tissue or plant cells under controlled conditions are broadly referred to as plant tissue culture. Plant tissue culture, or the aseptic culture of cells, tissues, organs and their components under defined physical and chemical conditions *in vitro*, is an important tool in both basic and applied studies as well as in commercial application.

Plant tissue culture is based on the principle of "Totipotency" It is the natural ability of plant cells to regenerate into cells, embryos, shoot or roots. It also refers to the *in vitro* cultivation of plants, seeds, tissues, organs, embryos, single cells, protoplasts on nutrient media under aseptic conditions. It owes its origin to the ideas of the German scientist, Haberlandt, at the beginning of the 20th century. It was the availability of these techniques that led to the application of tissue culture to broad areas of cell behavior, plant modification and improvement, pathogen-free plants and germplasm storage, clonal propagation, and products mainly secondary metabolite formation, starting in the mid-1960s. Cell cultures have remained an important tool in the study of basic areas of plant biology and biochemistry and have assumed major significance in studies in molecular biology and agricultural biotechnology.

The advantages of tissue culture techniques for rapid multiplication of plants, limited requirement of mother plants, Uniformity of planting material, Disease-free planting material, Improved production, Independent of season and environmental conditions. It can also be used to establish cell lines for production of secondary metabolites of commercial importance.

Some of the successfully tissue cultured plants are Banana, pineapple, strawberry, Sugarcane, potato, Turmeric, ginger, vanilla, cardamom, Aloe vera, geranium, stevia, patchouli, bamboo, eucalyptus and populus sps.

Agri based Companies: Nuziveedu Seeds, Rasi Seeds, Mahyco, Metahelix, Ankur Seeds, Krishidhan Seeds Monsanto, Ajeet Seeds, JK Agrigenetics, Bayer CropScience, Nath Seeds, Bayer Crop Science, Sami laboratories, Cadila Healthcare, Avesthagen, Indo-American Hybrid Seeds, Sri Ramco Biotech, MSR Biotech, K.F.Biotech, Rishi Herbals, Lakshmi Biotech, Labland Biotech.

Future Prospects: The fastest growing sector, BioAgri, has increased its market share in the last five years – from less than five percent to over 14 percent in the 2011 industry revenue. The BioAgri market clocked total revenue sales of `2,480 crore in 2010-2011 as against Rs. 1,936 crore in 2009-2010. This accounts for 14.38 percent of the total biotech revenues.

G. Bioinformatics and Rational Drug Design:

Maharani Lakshmi Ammanni College for Women, Bengaluru (Tumkur)
(Bangalore) Siddaganga Institute of Technology, Tumkur

Bioinformatics and Rational Drug Design:

Bioinformatics heralds beginning of new era in the most complex and challenging world of life sciences research that has witnessed dramatic increase in the data volume with the novel application of computational skills and statistical methods for analysis and for modelling. Bioinformatics is the answer for better and faster progress in research. Bioinformatics with the use of advanced computational technologies allows us to gather, store, analyze, integrate and represent genetic information effectively. It

Bioinformatics is associated typically with massive databases of gene and protein structure and function. It also does comparative analysis using remote computer access.

Exponential growth of biological data requires huge amount of storage space and high speed interpretation. This is possible only by computers. Studies on genomes have brought in a surge of information and that is growing every day. The data also needs to be interpreted as in DNA chips and microarrays. Speed computational cataloguing and retrieval of this information has become pertinent in all fields be it medical literature, understanding metabolic pathways, interpreting protein 3D structure, study of phylogeny, pharmacogenetics, drug designing, comparative genomics or agriculture.

Management of these complex datasets is becoming a bottleneck to scientific advances.

By giving a global perspective, Bioinformatics can play a pivotal role for biologists.

Scope of bioinformatics: - Improvement in drug designing to suit individual needs, through personalized genomic medicine using clinical informatics.

- Microbial genome research for Bio fuel and environmental clean up

- More accurate risk assessment by gene mapping
- To be able to analyze data in forensics
- Yield better crops
- To improve economy by all the above

Various Industrial giants are involved making this dream a reality. Industries like GVK Biosciences, MNCs like IBM, Biocon, Dr. Reddy's labs.-DAC, GlaxoSmithKline Pharmaceuticals are actively involved.

H. Plant Tissue Culture and Micro-propagation:

MM Arts & Science College, Sirsi

St. Aloysius College, Mangalooru (Mangalore)

Plant Tissue Culture and Micro-propagation:

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I. Bioprocessing & Microbial Technology:

Department of Biotechnology,
University of Gulbarga (GU) - Gulbarga

Introduction:

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Description: In the present BTFS curriculum, the domain Bioprocessing & Microbial Technology has been divided into four modules viz. Upstream Process, Downstream Process, Biopharma Facility Engineering and Regulatory affairs. This domain deals with the production of therapeutic proteins on using different expression systems as well as high cell density fermentation including media selection, preparation and sterilisation, fermenter functional design, sterilization in place and sterilization process validation, fermenter inoculation and maintenance of different fermentation parameters, scale up of fermentation process, fermenter harvest and cleaning process validation. For animal cell culture, media preparation and sterilization by filtration, sub-culturing, suspension culture and monitoring, monitoring of bioreactor cultures. In downstream processing, familiarization with chromatography equipment, column packing methods, column equilibration, and operation of tangential flow filtration as well as its cleaning and sanitation, dead end filtration will also be part of the curriculum. In addition, regulatory requirements of different countries and cGMP requirements for the production area of biopharmaceuticals will also be covered in the present domain.

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