Molecular Medicine Ireland

EDUCATION & TRAINING
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Molecules to Medicines: How Biopharma Delivers; 10-11 November 2010
Location: Royal College of Surgeons in Ireland, 123 St Stephens Green, Dublin 2

Lecture Course: Wednesday 10 November (1000 - 1700)

1000	**Introduction**
	DISCOVERY Dr Jonny Finlay (Pfizer)
1005	**Introduction to the business of discovering biopharmaceuticals**
1055	*Coffee/Tea*
1115	**Current biopharmaceutical product candidates and a look into next generation technologies**
	DEVELOPMENT Dr Patrick Gammel (Pfizer)
1205	**Cell line development**
1255	*Lunch break (lunch will be provided)*
1340	**Process development**
	MANUFACTURING Dr Paul Dillon (Pfizer)
1430	**Introduction to the science and technology of biopharmaceutical manufacturing**
1520	*Coffee/Tea*
1540	**Focus on the application of molecular technologies in manufacturing environments**
1630	**Discussion & round up**

Abstracts

DISCOVERY

- Introduction to the business of discovering biopharmaceuticals
- Current biopharmaceutical product candidates and a look into next generation technologies

Dr Jonny Finlay (Principal research scientist, Pfizer)

The Biotech industry was launched in 1982 when the US Food and Drug Administration approved Humulin, a recombinant form of human insulin genetically-engineered to be produced in E. coli. From humble beginnings less than 25 years ago, the Biotech industry has expanded steadily over the years with over 80 recombinant DNA products approved by the FDA to date. Today, the collection of Biotech products includes secreted factors, fusion proteins, monoclonal antibodies and other products.

The Pharmaceutical industry, working in close collaboration with academic institutions, research organizations and medical centers, has developed advanced tools and technologies to enable Biotech drug discovery. These technologies involve molecular and cellular biology techniques, protein structure/function technologies, protein engineering, in vitro assays and animal models. This session will describe how the Pharmaceutical industry adapts such diverse tools to the discovery of biotech drugs, how projects are shepherded through the complexity of pharmaceutical product development, how scientific innovation and creativity are utilized and how the risk of drug discovery is spread over multi-pronged strategies.

Suggested Reading

Walsh, G. (2003). Biopharmaceutical benchmarks – 2003. Nat. Biotechnol. 21, 865-870. PubMed Entry

Gill, D.S. and Damle, N.K. (2006). Biopharmaceutical drug discovery using novel protein scaffolds. Curr Opin Biotechnol. 6, 653-658. PubMed Entry

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DEVELOPMENT

- Manufacturing cell line development
- Process development and characterization

Dr Patrick Gammell (Scientist, Pfizer)

The Biotechnology industry has changed dramatically since the first FDA approval for insulin in 1982. The earliest recombinant protein products, including insulin, growth hormone and coagulation factor VIII, were replacements for naturally-occurring endogenous human proteins that were already available as existing products from alternative sources, including human pituitaries and plasma. The technologies used for the production of these early products leveraged heavily off the available “academic” expression platforms (host cells, vectors and media formulations) and the high potency of many of these early products (hormones, growth factors and enzymes), enabled relatively low-yielding process to be commercially viable.

The past 20-years has seen much change in the types of biotechnology products being made and a trend towards high-dose chronic administration, particularly for antagonist antibody products. As a result, the biotechnology manufacturing process has undergone considerable “industrialization” with a drive towards significantly improved expression levels, process yields and ease of product administration, with shorter process development timelines. In addition, much effort and attention has been paid to improving the quality of production process, particularly with regard to product consistency and viral/TSE safety – a significant improvement over the early human tissue – and plasma-derived products.

This session will describe the major elements and considerations in the development of a typical manufacturing process and highlight some of the current and future challenges.

Suggested Reading

Kelley, B.D. (2001). Bioprocessing of therapeutic proteins. Curr. Opin. Biotech. 12, 173-174 PubMed Entry
Wurm, F.M. (2004). Production of recombinant protein therapeutics in cultivated mammalian cells. Nat. Biotechnol. 22, 1393-1398 PubMed Entry
Therapeutic Proteins, Methods and Protocols (2005). Smales, C.M. and James, D.C., Eds. Humana Press.

MANUFACTURING

Dr Paul Dillon (Senior Scientist, Pfizer)

Introduction to the science and technology of biopharmaceutical manufacturing
The contribution of biopharmaceuticals to medicine has grown rapidly from an early start as complex mixtures of protein preparations extracted from tissue to today's highly purified proteins produced from cell culture. Early biopharmaceuticals were often replacement proteins such as cytokines or growth factors that were used to supplement a deficiency that contributed to the disease process. The recombinant proteins in use today have a variety of modes of action and are used to tackle a wide range of diseases. The proteins available now are often specifically targeted against identified proteins in the circulatory system and impact disease by binding molecules such as mediators of inflammation or by marking tumour cells for destruction. Together with a major impact on a number of serious disease states, these new medicinal products have had significant commercial success with sales of non-vaccine biopharmaceuticals exceeding €37BN in 2004.
This new generation of medicines has been enabled by breakthroughs in a number of areas in science and technology. Apart from the huge explosion of knowledge in biology which has revolutionized the Discovery and Development processes, advances in cell culture technology, bioprocess technology and protein characterization have provided the platforms on which stable, reliable and economical manufacturing systems have been established.
The course will introduce participants to the biotechnology industry and review its recent history. This session will present an overview of biopharmaceutical manufacturing and discuss facility design and operation. The participants will see how the various technologies operate in the plant and how they are used in the various unit operations as well as in the supporting functions such as technical support and analytical laboratories. The course will also examine the interrelationships on a manufacturing site and look at how the process of manufacturing a batch involves a wide range of participants.

Focus on the application of molecular technologies in manufacturing environments
A unique feature of the production of biopharmaceuticals, distinct from medicines produced by chemical synthesis, is the use of living cells as the primary unit of production of the active ingredient. This feature and the relative complexity of the molecules produced by living organisms creates a need and an opportunity to utilize modern molecular techniques in the operation and control of biopharmaceutical processes. In the upstream area of the process, where cell growth and protein production occurs, a sound understanding of cell biology and physiology allows scientists and engineers to monitor and control the growth of cells and manage their production of recombinant proteins.
Building on the work carried out by Development colleagues, manufacturing technologists carefully manage bioreactor processes to ensure optimal conditions for growth and protein purification. Later,

in the downstream area, where the protein is captured and purified, a sound knowledge of the physicochemical characteristics ensure that conditions here are similarly managed to maintain maximum output and quality. All of the critical processes in a plant manufacturing biopharmaceuticals should be validated, usually operated under significant automated control and should not require frequent intervention. However, natural variability can occur in biological systems and the investigative scientists who support the plant will utilize a range of modern technologies to solve problems in routine manufacturing or to support planned changes. This course will outline some of the approaches that are taken and use a number of case studies to show how this work is carried out.

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Walsh, G. (2003). Biopharmaceutical benchmarks – 2003, Nat. Biotechnol. 21, 865-870. PubMed Entry