

A Short Course on Regulatory Affairs with emphasis on Biopharmaceutical Drug Substances and Products, including Biosimilars

THE BACKGROUND TO THIS COURSE

Biologicals

Biologics

Biotechnologicals

Biopharmaceuticals

Biological medicines

Biosimilars

Biogenerics

Similar biological medicinal product

Some of the above words or phrases have the same meanings and some do not! People often use them rather loosely as if they were interchangeable terms. Whilst there can be considerable overlap in such designations, there are differences which can be important in the pharmaceutical industry and to understanding regulatory matters in particular.

In our course we will show you how legislation, guidelines and pharmacopoeias can inform you about what is required and how you can build your Clinical Trial [(CT) or Investigational Medicinal Product (IMP)] and Marketing Authorisation (MA) dossiers in order to gain approval from the authorities.

At the moment you may not know the answers to some short questions given below but one of the key objectives of the course is to ensure that soon you will know and understand.

What is an innovator product?

What is a biosimilar product?

What makes a biological/biotechnological product different from non-biological ones?

We will tell you in lay terms and in regulatory terms.

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You will become familiar with the relevant Articles in EU legislation affecting pharmaceuticals and then to know why and how biologicals and biological medicines are treated differently from non-biologicals. There are many official guidelines to help you both to interpret the meaning of the law when developing a biological medicine and to compile acceptable IMP and MA dossier applications. We will help you in these tasks.

Scientific and medical writing is an important skill to have if you are working in regulatory affairs and it is vital to understand what is required legally, scientifically and in terms of presentation.

Although huge challenges face the innovators of 'small molecule' drugs that are usually synthetic organic compounds, or sometimes semi-synthetic ones, they may be even greater for the 'biological' innovator. Understanding the regulatory demands on these different products is critical to success and important to know about during product development.

Based on the maxim for biologicals that 'process defines product', both an in-depth understanding of and complex control systems for the manufacturing process for biologicals are vital to both industry and the authorities.

There is enormous diversity both in the types of manufacturing process used and in the nature of the starting materials for these processes, which is not surprising when you consider examples of product types such as recombinant proteins, hormones, growth and coagulation factors, monoclonal antibodies, vaccines.

Genetic engineering as well as cell- and tissue-culture technologies is often involved and raises further complex issues. Manufacturing procedures may involve extraction from microbial cells or human and animal tissues such as blood, or natural, hybridised or otherwise-modified tissue cells. The use of genetically-modified animals such as goats, rabbits and hens is a recent development. Biological active ingredients are usually very expensive to produce, especially if recombinant-cell technology is used.

The size and complexity of the active molecules used in biological/ biotechnological products means that Analytical Development work is challenging. It is necessary to characterise the active molecule, to validate and monitor various in-process control stages in manufacture and purification, to establish stability and shelf life and storage conditions, to set chemical and microbiological specifications and to verify and maintain successful impurities control for the end-product.

Process development aims for higher yield and output of materials of potential commercial interest. These can be achieved by improvements to and scaling up of cell-fermentation production systems and higher handling capacity in various downstream-processing methods. Such changes to manufacturing detail are of obvious concern to regulatory staff in industry and in competent authorities alike because of their possible impact on the consistency of the product obtained. They require extensive and often complex validation to provide reassurance of consistency, quality, safety and efficacy, not only during clinical trials but also when the product has been approved. They require multi-disciplinary expertise.

There are different legal and scientific requirements, which you might need to know about, for MA application dossiers for 'small molecule' generics as distinct from

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'biosimilars'; the latter being sometimes known as 'biogenerics' or 'similar biological medicinal products'.

Do you understand the meaning of 'comparability' when linked with the world of biopharmaceuticals? It is a key component of your application and can be very costly and time-consuming to demonstrate.

Efficacy in relation to the therapeutic objective for the end product is outside the remit of our course but numerous regulatory issues with pharmaceutical (CMC) and non-clinical (toxicological and immunological) dimensions will be discussed. Immunological issues often loom large and need very careful investigation.

Another subject common to all biological and biotechnology products but again of huge potential diversity concerns the potential for serious contamination. Preventing and removing contamination threats or realities are areas of critical interest, especially to the authorities, for ensuring the quality and safety of biological medicines.

Formulation work intended to produce stable, bioavailable, convenient, safe and efficacious medicinal products may be more demanding for biological products containing proteins or other macromolecules than it is for conventional medicines. It is usually critical to maintain the tertiary structures or shapes of biological active ingredients throughout manufacture, formulation and product shelf-lives to ensure efficacy and safety.

Attention will be paid in the course to appropriate product documentation (Summary of Product Characteristics, labelling texts and package leaflet), which is needed by the healthcare professional and/or patient especially when there are special requirements for storage, reconstitution or dilution prior to administration.

Overall, biopharmaceuticals are a major and growing focus of the pharmaceutical industry's activities with global annual sales of prescription biotechnologicals in excess of \$90 billion. If you are developing or thinking of developing a regulatory or allied career in this field, our course will be of great help and interest to you.

AGENDA

(Not the precise running order and may be subject to some changes)

INTRODUCTION AND WELCOME

- WHAT ARE BIOLOGICAL MEDICINAL PRODUCTS?
Lay terms, legal terms, legislation, guidelines, pharmacopoeias

BIOLOGICAL MACROMOLECULES AND PRINCIPLES OF THEIR QUALITY CONTROL

- SCIENTIFIC ISSUES
History and product evolution, chemical and structural types, manufacturing approaches, analytical demands, medicinal product diversity

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- **EUROPEAN UNION (EU) REGULATORY PROCEDURES**
Legal requirements and interpretation through guidelines and other publications from the European Medicines Agency (EMA), the European Directorate for the Quality of Medicines & Healthcare (EDQM) and the International Conference on Harmonisation (ICH)
- **WHO INVOLVEMENT**
Official nomenclature, establishment of reference standards and their provision and correct use in bioassays and immunoassays, for expression of activity and other purposes

PREPARING CONTENT FOR THE QUALITY MODULES 2.3 and 3 OF THE COMMON TECHNICAL DOCUMENT (CTD)

- **DRUG SUBSTANCE AND DRUG PRODUCT** Key issues about the Quality Overall Summary and the CTD 'Quality' Body of Data (Module 3)
- Source of materials and establishment of cell banks
- Culture and fermentation
- Characterisation of recombinant and other materials
- Analytical issues and specifications
- Biological and immunological issues for characterisation and control
- Consequences of a manufacturing change and understanding about comparability
- Stability issues: Special considerations for biologicals compared to 'small molecules' drug substances, choice of and influence of excipients including biological excipients, maintenance of molecular structure, compatibility
- Numerous examples including deficiencies

PREPARING CONTENT FOR THE NON-CLINICAL MODULES 2.4 and 4 OF THE CTD

- **HOW DO BIOLOGICS DIFFER FROM CONVENTIONAL SMALL-MOLECULE DRUGS?**
Small-molecule drugs versus biotechnology products, nonclinical testing guidelines (ICH M3/S6), manufacturing and specification issues, trans-species conservation and choice of pharmacologically relevant species, dealing with main types of pharmtox studies, recent regulatory developments

BIOLOGICAL CONTAMINATION

- **MAJOR POTENTIAL PROBLEMS** TSE, viruses, bacteria and mycoplasma in source materials and those used in production (culture media)

BIOSIMILARS

- **EXAMINING NONCLINICAL, CLINICAL AND QUALITY ASPECTS** Highly similar objectives, bridging nonclinical and clinical studies, establishing safety and efficacy with multi-disciplinary approaches

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WHO SHOULD ATTEND

Delegates are likely to be from the pharmaceutical and biotechnology industries and working mainly in analytical, regulatory, Quality Assurance or management roles. The course is suitable for people new or relatively new to regulatory affairs as well as for more experienced staff looking to broaden or update their knowledge about regulatory affairs and biologicals.

SPEAKERS

The trainers will be Professor Derek Calam, Mr Paul Fleming, Dr Mark Richardson, Dr Mike Robertson and Dr David Snodin who collectively have many years of experience within UK, European and WHO institutions, the pharmaceutical industry and have reviewed numerous MAAs.

WHAT'S INCLUDED

High-quality, carefully-structured training, accommodation for one night, one breakfast, two lunches and a conference dinner, daytime in-course refreshments, a substantial delegates manual to reinforce the learning experience and a certificate of attendance [14h Continuing Professional Development (CPD)]
*extra night(s) bookable if required, subject to availability

Conference package fee:
£995 + VAT

Booking form:
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