

Introductory Class Outline

Analytical Considerations and Laboratory Operations for Biotechnology/Biosimilar Products

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This class will present the major analytical and stability concepts that distinguish the production and testing of biologically-derived from chemical, small molecule pharmaceutical products. It provides a comprehensive top-down overview of how analytical elements come together in regulatory dossiers, which drives the nature and timing of key studies. Key points in current and emerging concepts of method lifecycle management will be discussed. Finally, practical elements of laboratory quality practices and GMP laboratory operations – where all analytical data are generated - will be provided. All attendees will be given a USB drive containing over 200 current and draft global regulatory and quality guidance documents associated with the development and commercialization of biotech and biosimilar products.

1. Current and Emerging Biotechnology/Biosimilars CMC Regulatory Requirements

- a. What sets of world-wide regulations detail CMC analytical study requirements for biotechnology/biosimilar products?
- b. What are the 10 (or 11 if biosimilar) non-negotiable CMC characterization, comparability, release specification and stability data packages required for a biotechnology-based product?
- c. What are some of the current CMC 'hot buttons' for biotechnology analytical and stability studies that are of increasing regulatory concern for chronic deficiencies in product dossiers?
- d. What are the current analytical questions for global development of biosimilar products?
- e. How should the required CMC analytical and stability studies be staged during the product development lifecycle?
- f. Which of these elements have the most critical project planning considerations based on their time and material requirements for biotechnology/biosimilar products, and why?

2. Analytical Test Method Requirements for Biotechnology Products

- a. How do regulators and inspectors categorize analytical test methods?
- b. What are the commonly used and currently expected analytical methods for various types of biotechnology products (eg Mabs, vaccines, GT vectors, ADCs, etc...)?
- c. Why do biotech products require orthogonal methods for physiochemical characteristics as well as functional potency assays?
- d. What is the difference between methods used for characterization and comparability studies vs release and stability testing?
- e. What are some of the typical performance aspects of analytical method technologies widely used with biotechnology/biosimilar products?

3. Biotech Analytical Methods: Development, Qualification, Validation, Tech Transfer and Bridging

- a. Which analytical test methods have to be validated, and by when?
- b. What is the difference between method validation and method 'qualification'?
- c. How can you tell if method qualification or validation studies have been designed correctly for each analytical technology and intended use?
- d. What should you do to tech-transfer analytical methods from one lab to another?

- e. What should you do to make changes in release and stability analytical methods over time?
- f. What are the current expectations for generating and maintaining method lifecycle document packages?
- g. How can you separate tracking of method performance from product performance to monitor each method's state of control?

4. Overview of Biotech/Biosimilar Product Stability Studies and Stability-Indicating Method Validation

- a. What are the requirements for biotech product stability studies during development and post approval?
- b. What is required to qualify vs validate methods that are claimed to be stability-indicating?
- c. Why can't shelf life dates be extrapolated from accelerated stability data for biotech/biosimilar products?
- d. What are the critical elements to include in sound stability protocols for drug substance and drug product?
- e. What are the current expectations for extractable/leachable studies for biotech/biosimilar product container/closure interactions?
- f. What are the emerging expectations for subvisible and visible particle determination for biotech/biosimilar products throughout shelf life?

5. Lab Quality Practices from R&D to GxP

- a. What are the key similarities and differences among the current compliance expectations for GxP testing labs?
- b. What are the emerging expectations for lab quality practices for R&D labs, and how do they align with the principles of ICHQ10?
- c. What are the 6 key regulatory/compliance information packages expected from biotech/biosimilar analytical groups from R&D through GMP?
- d. What are the most common factors associated with biotech/biosimilar analytical method failures in QC labs?
- e. What are the current 'best practices' for OOS investigations for biotech/biosimilar analytical laboratories?
- f. What are the current Data Integrity expectations for GxP and R&D laboratories?

6. Laboratory Pre-Approval Inspection and General GMP Audits

- a. What are the two major objectives of PAI audits for regulatory agency product approval?
- b. What are some of the key CMC reports and documentation covered in a PAI inspection?
- c. What are the goals of laboratory GMP inspections, and how do they differ from manufacturing GMP inspections?
- d. What are the significant laboratory operational elements covered in GMP laboratory inspections for product release testing?
- e. What are the significant laboratory operational elements covered in GMP laboratory inspections for product stability testing?
- f. How should you handle the remediation of inspection observations?