Advanced Class Outline

Key Elements for Specifications, Method Validation, Comparability, and Stability of Biotechnology/Biosimilar Products

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This class is designed to follow the Introductory course, but it may be a stand-alone class for attendees with experience in aspects of biotechnology. Details will be presented on technical issues in designing and executing specific critical analytical studies. Practical examples will be provided as illustration for key studies. Ample time will be allowed for discussion designs and outcomes. Finally, tips on suitable generation of internal study reports and the presentation of data in regulatory dossiers will be given. 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. **Managing Stage-Specific Specifications for Biotech/Biosimilar Products**

    a. Why do biotechnology products have different specification requirements versus traditional chemical products for comparability, product quality and consistency, and shelf life determination?
    b. What four main elements are critical for establishing reliable, meaningful product specifications for biotech and biosimilar products?
    c. What are the specification considerations for product-related heterogeneity in biotechnology products?
    d. What is the basis for specifications on product and process related impurities?
    e. How much detail is required on impurities and degradants at each phase of product development?
    f. What are the key points to include in the Justification of Specifications for drug substance and drug product?

2. **Biotech Analytical Methods: Specific Examples of Method Lifecycle Studies**
    a. What goes into a written procedure for characterization/comparability methods?
    b. What goes into a written procedure for QC release and stability methods?
    c. What are practical examples of typical non-compendial method qualification and validation studies?
    d. What are practical examples of typical compendial method verification studies?
    e. What are practical examples of method tech transfer studies?
    f. What are practical examples of method bridging studies?

3. **Design and Execution of Forced Degradation Studies for Biotech/Biosimilar Products**
    a. How do comprehensive, systematic forced degradation studies differ from ICH accelerated or stress stability studies, and why?
    b. What kinds of physical and chemical forced degradation studies are applicable to biotech/biosimilar products?
    c. When should various forced degradation studies be conducted during product development and after product approval?

d. Where do data from accelerated, stress and forced degradation studies go in the product regulatory dossier sections at each phase of development?
e. What are the typical experimental designs for accelerated, stress and forced degradation studies (chemical and physical) for biotech/biosimilar products?

4. Development and Validation of Process-Specific Host Cell Protein (HCP) Assays

a. Why are HCPs the most challenging analytical impurities for biotechnology process development and product quality and consistency?
b. What has changed over the last few decades in assessment of HCPs, and why are they of special interest for biosimilar products?
c. When are commercial HCP ELISA kits acceptable for use, or not, and why?
d. What are current and emerging experimental designs for generating and validating custom immunoreagents for HCP ELISAs?
e. How are ELISAs just one part of a total HCP characterization and control strategy for biotechnology/biosimilar processes and products? What are the other parts?

5. Design and Execution of Analytical Comparability Studies for Biotechnology and Biosimilar Products

a. What are critical technical aspects of assessing biotechnology product comparability?
b. How do comparability studies performed for developmental continuity differ from demonstration of analytical biosimilarity?
c. What are key elements of conducting a biotechnology product comparability or analytical biosimilarity study?
d. How do you strategically select among the collection of analytical methods for comparability/biosimilarity vs release/stability testing?
e. How do you establish acceptance criteria for the conclusion of 'comparable' for a biotech product?
f. How do you establish acceptance criteria for the conclusion of 'analytical biosimilarity' for a biosimilar product?

6. Reference Standards and Materials for Biotechnology/Biosimilar Products

a. What are some of the types and uses of biotechnology reference standards and materials?
b. How do they differ from small molecule reference standards?
c. What is the 'tiered approach' to establishing a master reference standard and qualifying working reference standards?
d. How is biotechnology product reference standard stability monitored?
e. What tests should be done to bridge new lots of reference standards and materials?
f. What are the current and emerging considerations when using a national or international reference standard for your product?