CONCEPT

Biologics Comparability and Biosimilars: ICH Q5E Protocols, CQAs and Tiered Statistics

23 – 27 May 2027
Dammam - Eastern Province five-star



Biologics Comparability and Biosimilars: ICH Q5E Protocols, CQAs and Tiered Statistics

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Introduction:

Biologics comparability decides whether a cell line, site, scale or purification change can reach patients without new clinical studies, yet many change packages arrive with unranked quality attributes, acceptance criteria set after the data and statistics that cannot separate process drift from real difference. This Core Concept course trains CMC, quality, regulatory and process development teams to plan comparability exercises under ICH Q5E principles and to run biosimilar analytical similarity assessments against a reference product. Participants finish with a Comparability Protocol for a case process change.

Course Objectives:

- Rank critical quality attributes of a biologic by impact on activity, pharmacokinetics, immunogenicity and safety using ICH Q9 risk tools
- Classify manufacturing changes by comparability risk and define the extent of pre- and post-change testing each one requires
- Design a comparability protocol under ICH Q5E principles with lot selection, analytical panel, acceptance criteria and decision rules
- Assign quality attributes to statistical tiers and apply equivalence testing, quality range and graphical comparison to lot data
- Judge when stability, non-clinical or clinical bridging data are needed to close residual uncertainty
- Assemble analytical similarity and comparability evidence into a dossier section and a post-approval change plan under ICH Q12

Target Audience:

- CMC leads responsible for change control strategy and module 3 quality content for biologic products
- Quality assurance managers responsible for approving manufacturing changes and comparability conclusions
- Quality control and analytical development managers responsible for characterisation panels and method suitability
- Regulatory affairs managers responsible for post-approval variations and biosimilar submissions
- Process development and MSAT managers responsible for scale, site and process changes on biologics lines
- Biosimilar development managers responsible for reference product sourcing and similarity programmes

Course Outline:

Day 1: Biologics Variability and the Comparability Question

- Heterogeneity of Monoclonal Antibodies and Recombinant Proteins: Glycoforms, Charge and Size Variants
- Process Sensitivity Map: Cell Line, Culture Conditions, Purification and Formulation Effects on Quality
- Comparability Versus Biosimilarity: Same-Manufacturer Change Versus Reference Product Comparison
- Totality of Evidence and Stepwise Approach Concepts
- Change History Review Template for an Existing Biologic Portfolio

Day 2: Critical Quality Attributes, Risk Ranking and ICH Framework

- ICH Q5E Principles: Scope, Highly Similar Standard and Adverse Impact Test
- ICH Q6B Specification Philosophy Versus Characterisation Beyond Release Testing
- CQA Criticality Scoring Matrix: Impact and Uncertainty Scores Under ICH Q9
- Change Classification Grid: Cell Bank, Scale, Site, Raw Material, Column Resin and Formulation Changes
- ICH Q12 Established Conditions and Post-Approval Change Management Protocols

Day 3: Comparability Protocol Design and Analytical Characterisation Toolbox

- Protocol Architecture: Objective, Pre-Change and Post-Change Lot Selection and Sample Sizing
- Primary and Higher-Order Structure Methods: Peptide Mapping, Intact Mass and Spectroscopic Profiles
- Purity and Impurity Methods: Size Exclusion, Charge Variant, Glycan and Host Cell Protein Assays
- Potency and Functional Assays: Binding, Cell-Based Bioassay and Effector Function Panels
- Forced Degradation and Side-by-Side Stress Profiling of Pre- and Post-Change Material

Day 4: Tiered Statistics, Stability Comparability and Bridging Decisions

- Tier 1 Equivalence Testing: Two One-Sided Tests and Equivalence Margin Setting
- Tier 2 Quality Range Approach: Mean Plus or Minus k Standard Deviations and Lot Count Effects
- Tier 3 Graphical and Qualitative Comparison of Profiles and Chromatograms
- Stability Comparability Under ICH Q5C: Degradation Rates, Real-Time and Accelerated Slopes
- Bridging Decision Tree: Residual Uncertainty, Non-Clinical Studies and Clinical Pharmacokinetic Data

Day 5: Case Work: Analytical Similarity Exercise and Comparability Protocol

- Case: Biosimilar Analytical Similarity Assessment Against Multiple Reference Product Lots
- Case: Out-of-Range Glycan Attribute Investigation and Justification Record
- Dossier Presentation: Comparability Summary Tables and Conclusion Statement
- Comparability Protocol Build for a Site Transfer and Scale-Up Case
- Protocol Presentation and Challenge by a Mock Assessor Panel

Skills You Will Gain:

- CQA Criticality Assessment
- Manufacturing Change Classification
- Comparability Protocol Authoring
- Analytical Panel Selection
- Equivalence Margin Justification
- Stability Slope Comparison
- Bridging Study Decision Logic
- Similarity Evidence Presentation

Why Attend This Course:

- Leave with a Comparability Protocol for a case process change ready to adapt to your own product
- Defend tier assignments and acceptance criteria before lot data are generated, not after
- Work through a biosimilar similarity exercise on multi-lot reference data rather than reading about it
- Compare change-control and similarity practice with peers from innovator, biosimilar and contract manufacturing organisations

Conclusion:

A process change on a biologic is acceptable only when the evidence shows no adverse impact on quality, safety or efficacy. The week moves from product heterogeneity and process sensitivity, through CQA risk ranking, change classification, ICH Q5E, Q6B and Q12, to protocol design and the characterisation toolbox. It then covers tiered statistics, stability comparability and bridging decisions, and closes with a biosimilar analytical similarity exercise and a Comparability Protocol for a case process change for each participant.