Poster P308

BioAgilytix

Biosimilar Pathways: Optimized CMC Analytical Solutions for Seamless Comparability and Compliance

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BACKGROUND

The development of biosimilars demands an optimized Chemistry, Manufacturing, and Controls (CMC) analytical strategy aligned with both FDA and/or EMA expectations. Robust comparability studies remain the cornerstone of approval, requiring orthogonal structural, functional, and stability testing to demonstrate high similarity to the reference product. Success hinges on a disciplined approach: *must do* activities include sourcing region-specific reference material, applying orthogonal characterization, and early regulatory engagement; *to do* activities include stress testing and risk-based justification of minor differences; while *do not do* pitfalls include over-reliance on single assays, assuming "similar" equals "identical," or neglecting region-specific requirements.

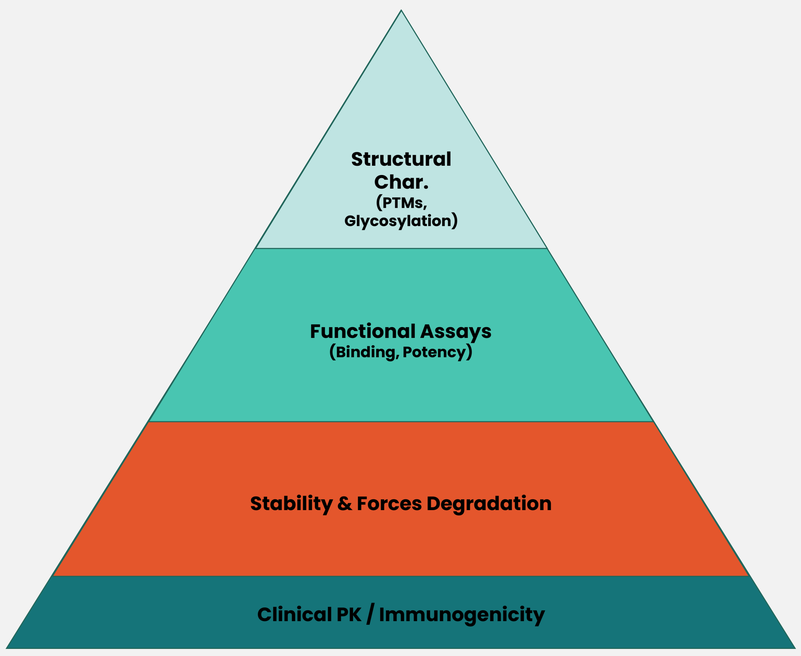


Figure 1: Totality of Evidence Framework. Orthogonal methos across all tiers → build confidence in similarity

TOTALITY-OF-EVIDENCE

The demonstration of biosimilarity is based on cumulative data and evidence. Some of the data are more impactful than others and drive MUST and DO NOT objectives, while others provide additional support or demonstrate a more general acceptance of the product as a market-worthy biologic. Some of these MUST and DO NOT attributes are listed below.

MUST Do:
- Clear demonstration of similarity across multiple orthogonal assays
- Benchmarking against region-specific reference standards, minimal of 3 x 3 comparability
- Access to state-of-the-art platforms (MS, NMR, bioassays)
- Knowledge of and access to supporting information and assays (not CGAs)

DO NOT do:
- Reliance on singular assays
- Assuming "similar" equals "identical"
- Neglecting region-specific requirements

RISK-BASED ASSESSMENT

It is important to understand that now all testing and supporting data are of equal importance in the similarity assessment. The potential for variance between biosimilar and innovator will be viewed differently by regulators. Typically, critical structural and efficacy attributes that may impact the clinical effectiveness of the product should be evaluated first. A progressive approach can then be followed to allow for early assessment of the probability of success or risk of a negative outcome.

Table 1: Risk-Based Assessment Matrix

Structural	Glycosylation differences	Charge variants	Same expression system
Functional	Reduced potency	Binding affinity shift	Comparable potency
Stability	Accelerated degradation	Excipient changes	Same formulation
Clinical	Unexpected Immunogenicity	PK variability	Well-matched PK

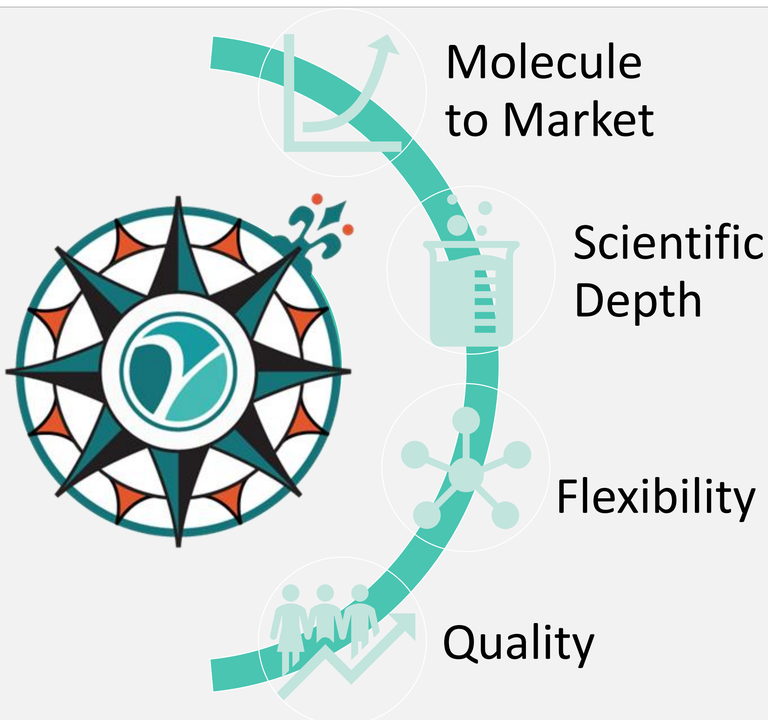
High Risk ----------→ Low Risk

REGULATORY ENGAGEMENT

- Guideline on similar biological medicinal products 2014 EMA
- Guideline on similar biological medicinal products containing monoclonal antibodies – non-clinical and clinical issues EMA
- Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues 2015 EMA
- 2018 BAP Activity Summary of Accomplishments April 2024
- Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations FDA
- Questions and Answers on Biosimilar Development and the BPCI Act (Revision 2) FDA
- New and Revised Draft Q&As on Biosimilar Development and the BPCI Act (Revision 3) FDA

ASSAY PARAMETER	PLATFORM
Primary Structure, Peptide Mapping, Intact Mass	LC/MS, CE, HPLC
Post Translational Modifications	CLS, CE_LIF, HPLC
Glycosylation Profile	LC/MS, UPLC, CE
Charge Variants	IEF, icIEF, IEX-HPLC
Size Variants / Aggregates	SEC-HPLC, SEC-MALS, DLS
Purity	CE-SDS, RP-HPLC, RP-UPLC, SEC-HPLC
Process Related Impurities (HCP, HC DNA, Residuals)	ELISA, PCR, LCMS, HPLC
Target Binding	ELISA, Flow Cytometry, SPR
Receptor Binding (Fc Region, Effector Function	Non-Cell (SPR)
Cell-Based Potency Assays (Proliferation, Inhibition, Reporter Gener, ADCC, CDC, Neutralization	ELISA, Flow Cytometry, MSD, Cytation, LSMS, qPCR, ddPCR

Table 2: List of analytical characterization assay parameters BioAgilytix can support for your biosimilar program.



CRO PARTNERSHIP EXPECTATIONS

Leveraging a global CMC analytical CRO ensures scalable solutions, region-specific compliance, and efficient execution of comparability programs.

BioAgilytix, is that global CMC analytical CRO, we can support sponsors with these challenges by providing end-to-end analytical solutions, harmonized assay platforms, and regulatory-informed strategies that streamline comparability packages covering any combination of the assays listed in Table 2.

Where we meet your needs with our capabilities:
- End-to-end analytical services (molecule → market)
- Scientific depth across modalities
- Ability to scale as needs change.
- Harmonized global quality systems

Remember
Similar ≠ Identical