Biosimilars

Hot Topic: The Importance of Analytical Characterization in Biosimilar Development

Biosimilars Are Not Generic Drugs[1]

- Biologics are products produced in genetically-engineered living cells or organisms[1]
- Biosimilars are biologic medicines that are highly similar to the reference product (RP) with no clinically meaningful differences in terms of safety, purity, and potency[1,2]

	Small molecule drugs Including generics	**Biologics** Including biosimilars
Size	**Small**[3,4]	**Much larger**[1,3,4]
Structure	**Simple** and well defined[3,4]	**Complex**, with many possibilities for post-translational modification[1,3,4]
Manufacturing	Predictable chemical process; **identical copies can be made**[3]	Manufactured in a unique, living cell line; **only similar, not identical copies can be made**[3,4]
Characterization	**Easy to characterize fully**[4]	**Difficult to characterize fully**[4]
Stability	**Relatively stable**	**Often sensitive to storage and handling conditions**[4]
Immunogenicity	**Lower** potential[4]	**Higher** potential[4]

Biosimilar Manufacturers Start with Limited Knowledge of the Reference Product

- Thorough characterization of the RP is the first step in biosimilar development[1,2]
- The biosimilar manufacturer must then produce a unique cell line and develop an entirely new manufacturing process that produces a highly similar product[2]

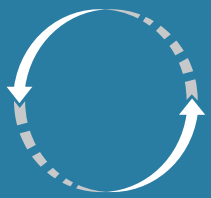
Known[3]

Protein sequence

Unknown[4]

- Cell line
- Growth media
- Method of cell expansion
- Bioreactor conditions
- Operating conditions
- Binding and elution conditions
- Formulation methods
- Reagents
- Reference standards

Analytical Characterization[1,2]



Compare structure and function to the reference product

Reference product manufacturing information is proprietary and not publicly available.[2] A biosimilar manufacturer must develop an entirely new customized process.

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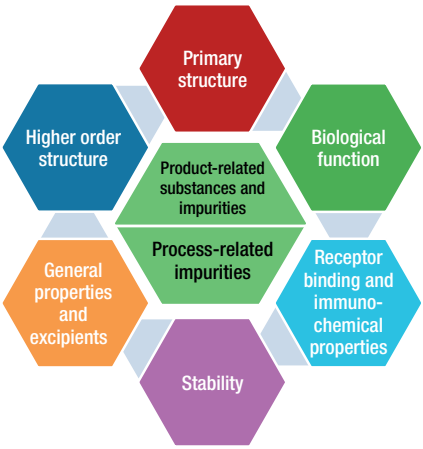
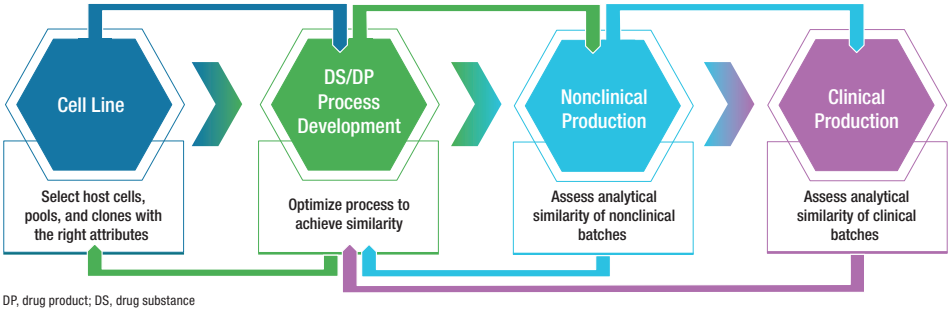
Analytical Characterization is Used to Evaluate RP Critical Quality Attributes (CQAs) in Eight Categories[5]

- Analytical characterization of the reference product identifies the CQAs[1–4]
- CQAs are specific attributes that impact pharmacokinetics, safety and efficacy[3,4]
- CQAs must be controlled within an appropriate range to ensure product quality[3]



Biosimilar Development: The Product Defines the Process

- Similarity in structure and function is established via an iterative process[1,2]



DP, drug product; DS, drug substance

- At each stage, the manufacturer evaluates analytical data and determines whether to proceed with development or conduct further optimization

Analytical similarity assessment is an iterative operation conducted throughout process development.[3,4]

References

1. FDA. Scientific considerations in demonstrating biosimilarity to a reference product. Guidance for industry, 2015. Available at: http://www.fda.gov/downloads/. 2. EMA. Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: quality issues (revision 1), 2014. Available at https://www.ema.europa.eu/documents/scientific-guideline/draft-guideline-similar-biological-medicinal-products-containing-biotechnology-derived-proteins_en-0.pdf. 3. Markus R, et al. Biodrugs 2017;31:175–87. 4. Vulto A, et al. Rheumatology 2017;56:iv14–iv29. 5. FDA. Quality considerations in demonstrating biosimilarity of a therapeutic protein product to a reference product. Guidance for industry 2015. Available at: http://www.fda.gov/downloads/. Links accessed November 2018.

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