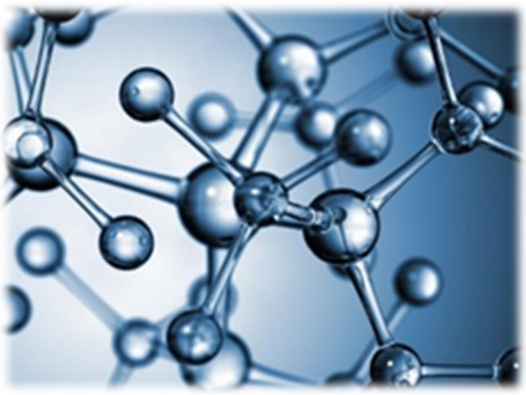


PHARMSOL NEWS

BIOSIMILARS - APPROACH FOR DEVELOPMENT

OCTOBER 2023 EDITION

PSNL/003/10/2023

Biologics are among the greatest therapeutic revolutions in the 21st century. Biologic medicines, or biologics, are large molecules or complex proteins obtained by *genetically engineering eukaryotic or prokaryotic cell lines or through biological sources such as cells or tissues*, which are used to treat or cure diseases like chronic inflammatory diseases such as Crohn's disease, rheumatoid arthritis, or psoriasis etc., Cancer therapy is also one of the key segments where Biosimilars are finding its application. This write-up attempts to give some heads-up on this vast topic

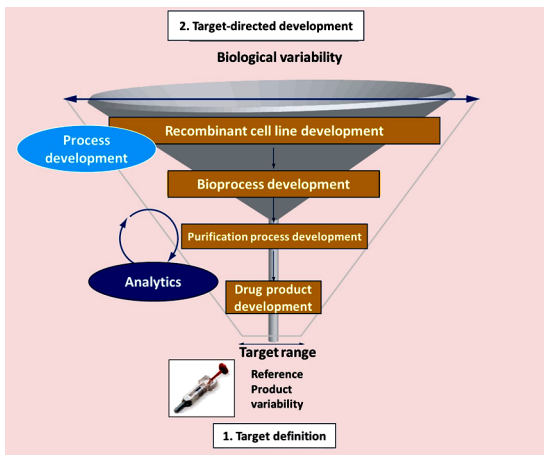
Biosimilars are biological product which are *highly similar to reference biologic* not withstanding minor differences in clinically inactive components with no clinically meaningful differences between biological product and reference.

Comparison of small molecules (Generics) & Biologics/Biosimilar

Parameter	Generics	Biologics/Biosimilars
Size	mostly small molecules (<1000 Dal)	Large protein/glycoprotein molecules (>10000 Dal)
Structure	Simple, noncomplex, well-defined structure (homogenous)	Multiple levels of structure & post-translational modifications (heterogenous)
Immuno-genicity	Generally inert	Potential to induce antibody responses
Time to market	2–3 yrs.	8–10 Yrs. (Biologics) 7–8 Yrs. (biosimilars)
Preclinical studies	No data required	Full preclinical Development (Biologicals) Abbreviated program, depending on complexity of molecule (Biosimilars)
Clinical studies	Bioequivalence studies in healthy volunteers	Phase I–III efficacy and safety studies (Biologics) Comparative PK/PD (Phase I) studies and clinical confirmation (Phase III) study in one representative indication

Development approach for Biosimilar

The goal of biosimilar development is to create a biologic drug product that is highly similar to the reference biologic product with no clinically meaningful differences in terms of safety and efficacy.



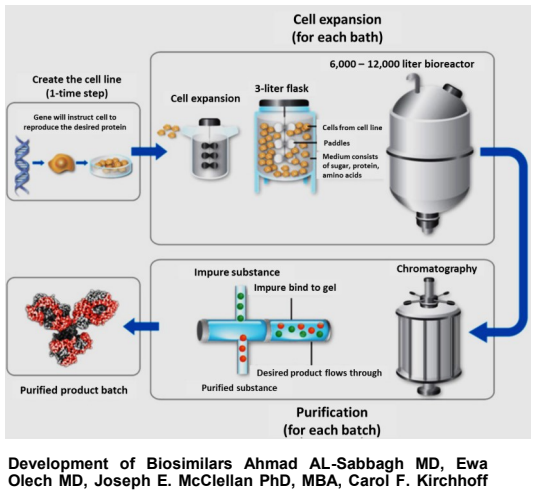
Windisch J. Int J Clin Rheumatol 2015;10(6):00–00.

Characterization of Reference product:

It is characterized to identify the product's CQAs, characteristics that affect identity, purity, biological activity, and stability of a drug. A variety of robust physicochemical and functional assays are used for this purpose. Multiple lots to be tested.

Manufacturing of desired protein:

The major steps include cell line creation, cultivation & production, isolation & purification, formulation, filling and packing in the desired configuration. State-of-the-art technology and formulation strategies are required to achieve high product purity and stability.



Development of Biosimilars Ahmad AL-Sabbagh MD, Ewa Olech MD, Joseph E. McClellan PhD, MBA, Carol F. Kirchhoff

Establishing the similarity:

Similarity is established by the ***totality of the evidence*** which includes.

1) Physico-chemical characterization
2) Biological characterization,
3) Nonclinical evaluation
4) Pharmacokinetic/ pharmacodynamic (PK/PD) data
5) Immunogenicity data, and
6) Comparative clinical studies.

Highly similar analytical and PK/PD data infer a lower likelihood of clinical differences between a biosimilar and its reference product.

Analytical Characterization:

It involves the usage of various high end analytical techniques like LC-MS, peptide mapping, NMR, Circular dichroism, Matrix-assisted laser desorption/ionization mass spectroscopy with time-of-flight analyses; MVDA: Multivariate data analyses etc. for characterization of protein's primary (i.e., amino acid sequence) and higher-order structures (i.e., secondary, tertiary, and quaternary) and enzymatic post-translational modifications (e.g., glycosylation, phosphorylation), potential variations (e.g., oxidation), and intentional chemical modifications (e.g., PEGylation sites)

Structural and functional comparison

The structure should be similar to the reference product with permitted slight differences which should not impact their intended function along with clinical safety or efficacy.

The functional comparative testing is performed to ensure that its biological activity, potency, and mechanism of action are highly like those of the reference

Market opportunity:

There are many patents of biologics which have *recently expired or near to expiry*. Development of biosimilar against those offset biologics will provide huge market potential in the future.

Conclusion

Developing a biosimilar begins with reference biologic characterization followed by customized development of manufacturing process involving many steps from cell line creation through formulation, fill and finish of the final product. Throughout these steps an iterative process of characterization and testing is used to evaluate the degree of similarity. Robust quality systems and risk assessments ensure that there is strict control over the biosimilar's quality attribute and its safety and efficacy profile.

How PharmSol can help you?

PharmSol can provide integrated and customized services for the development of Biosimilar product with focus on

- Reference product Characterization
- Physico-chemical characterization for Comparability study
- Nonclinical Testing & Clinical comparison studies and bioanalysis
- Regulatory services for Filing dossier

PharmSol

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