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Swaying biosimilars market

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ABSTRACT

Biosimilars are having massive demand in future in order to provide good quality therapy for human well-being. Biosimilars also pronounced as biologics / biopharmaceuticals / follow-on biologics / subsequent entry biologics (SEB's) with the statement of a biopharmaceutical drug deigned to have active properties similar to one that has previously been licensed. As per WHO biosimilars are defined as "a bio therapeutic product which is similar in terms of quality, safety and efficacy to an already licensed referenced bio therapeutic product". Biosimilars can relieve the financial burden on healthcare systems and expand patient accessibility. This review embraces the significance, regulatory consideration, available regulatory guidelines and current market scenario on biosimilars.

Keywords: Bio therapeutics, biosimilars, follow-on-biologics, subsequent entry biologics.

INTRODUCTION

A biosimilar is defined as a biologic that is already authorized for use. Here the biologic can be a medicinal substance derived from living organisms such as bacteria or yeast. These biologics can be smaller molecules or complex heavy chained molecules. Examples for biosimilars include Epoetin, g-csf, insulin, somacropin. For a biosimilar to be approved it must possess similarities with the reference medicine. Biosimilars generally exhibit high molecular complexity, and may be quite sensitive to changes in manufacturing process[1].

They do have easy access for approval process the European regulatory authorities adapted approval process to authorize subsequent versions of previously approved biologics, termed as "similar biological medicinal products" by thorough demonstration of comparability of the similar products[2]. In US the FDA suggested a new legislation required for approval on 17th march 2009 called the pathways for biosimilars act also states that, advances in current state-of-the art analytical methods enhance the likelihood that a product will be highly similar to another product by better targeting the original product's physicochemical and functional properties[3]. Further series of public meetings held on biosimilars the FDA gained the authority to approve biosimilars as a part of patient protection and affordable care act. The experimental data of a biologics should produce and contributes the same clinical results without any potential immunogenicity[4]. The BPCI Act was written into law which has given FDA the authority to approve biosimilars products. Based on this

definition we would interpret that a biological medicine is biosimilars to a reference biological medicines if it is highly similar to the reference in safety, purity and potency (in the EU, the sponsors should The European medicines agency and FDA regulations indicates that biosimilarity does not imply interchangeability[5].

Regulatory consideration for biosimilars products:

The variations in regulatory impacts globally, as in Canada does not support automatic substitution. In UK and Belgium recommend prescribing by brand name to avoid substitutions. Spain and Germany prohibit automatic substitution. In Ireland, Poland and Portugal have no clear position. In japan substitutions should be avoided during the pharmacovigilance study period. The global market of biosimilars expand and biosimilars become more complex, it is very essential to ensure clarity in prescribing regulations and make uniform for global practice to get a therapeutically important biosimilars[6].

Available regulatory guidelines

There is no single uniform international guideline for biosimilars. Rather, there is a dichotomy of a highly regulated and a less regulated registration pathway[7].

1. Highly regulated approval pathways

i) European Medicine Agency (EMA)

The announcement of the initial "guidelines on similar biological medicines" in 2005, the EMA has continued to be at the forefront of legislation governing biosimilars and a standard for regulatory authorities in other countries.

ii) US Food and Drug Administration (FDA)

In 2009, US congress released the Biologic Price Competition and Innovation Act (BPCIA) as part of Patient Protection and Affordable Care Act, which empowered the FDA to identify an abbreviated approval pathway for biosimilars.

iii) The Canadian food and drug regulatory agency (Health Canada)

Subsequent entry biologics are tested as a new drug submission. Direct submission or interchangeability is not permitted and guidance is for specific classes only.

iv) The Australian therapeutic goods administration (TGA)

TGA has adopted the European guideline for approval of biosimilars. Because biosimilars will be assessed on a case by case basis, a pre submission meeting with the TGA is encouraged for manufacturers to determine data requirements.

2. Less regulated regulatory pathways

In some countries, approval criteria for copies of original biologics are less stringent, to accelerate their potential for cost savings. The less rigorous comparative assessments in these countries have seen them referred to as a biopharmaceutical not subjected to regulatory approval. However the guidelines for them are relatively vague.

China: State Food and drug Administration (SFDA) regulates the biosimilars law, states that a biosimilars product must be registered and approved as new biological products.

India: in contrast, Indian regulation do not have a defined biosimilars of a biology that have been on the market for more than four years undergo an abbreviated approval pathway, whereas biosimilars of newer biologics must register as a new product.

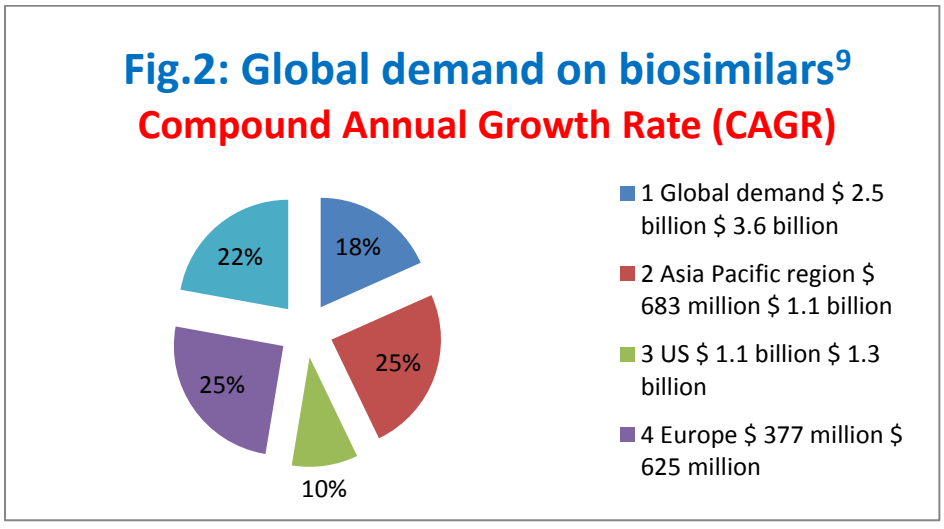
Current status of biosimilars

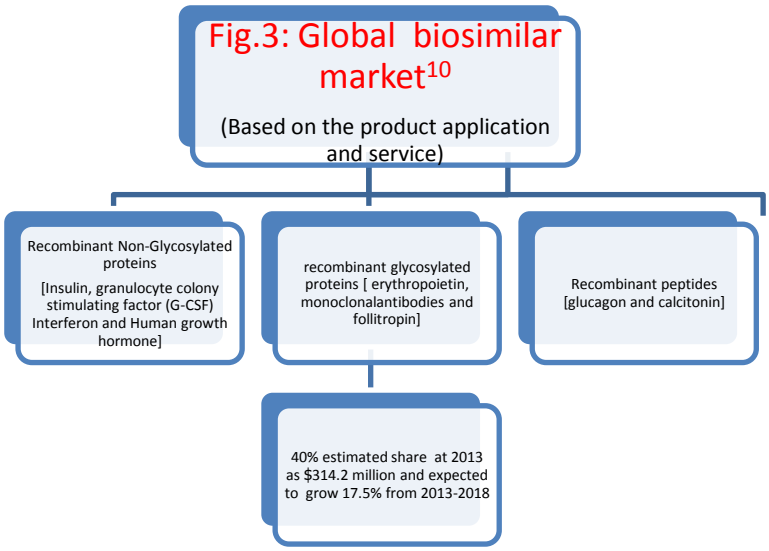
Wellesley, Mass – According to a new technical market research report, Biosimilars: Global markets (BIO090A) from BCC research, the global demand for biosimilars totally nearly $ 2.5 billion in 2011 and should reach $ 3.6 billion in 2016, a compound annual growth rate (CAGR) of 7.7% over the five year period[8].

Fig.1: Current status of biosimilars in global market[9]

Table.1: Global demand on biosimilars[9]

S.No	Area	Year 2011	Year 2016	Compound Annual Growth Rate (CAGR)
1	Global demand	$ 2.5 billion	$ 3.6 billion	7.7%
2	Asia Pacific region	$ 683 million	$ 1.1 billion	10.3%
3	US	$ 1.1 billion	$ 1.3 billion	4.1%
4	Europe	$ 377 million	$ 625 million	10.6%
5	Rest of the world	$ 335 million	$ 522 million	9.3%





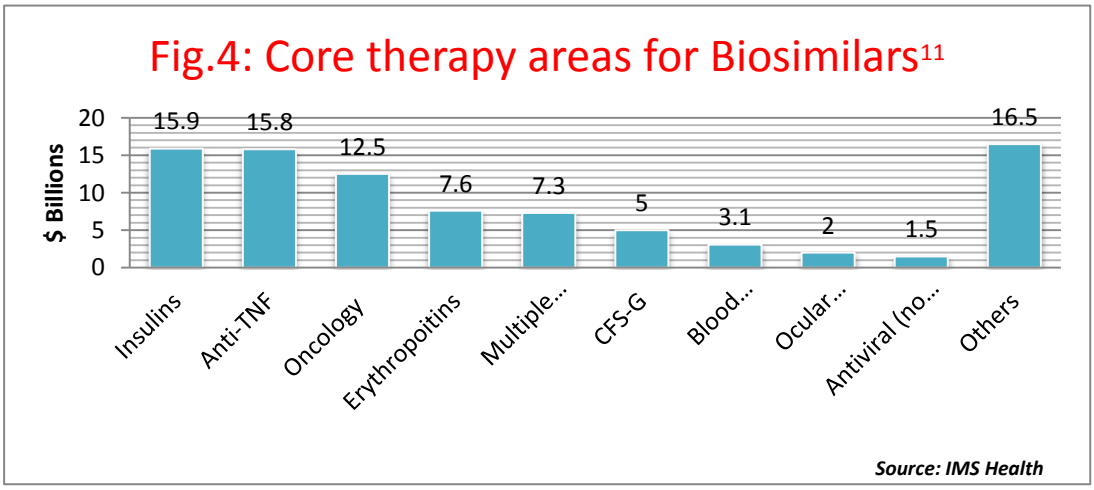


Fig.5: Biosimilars products market

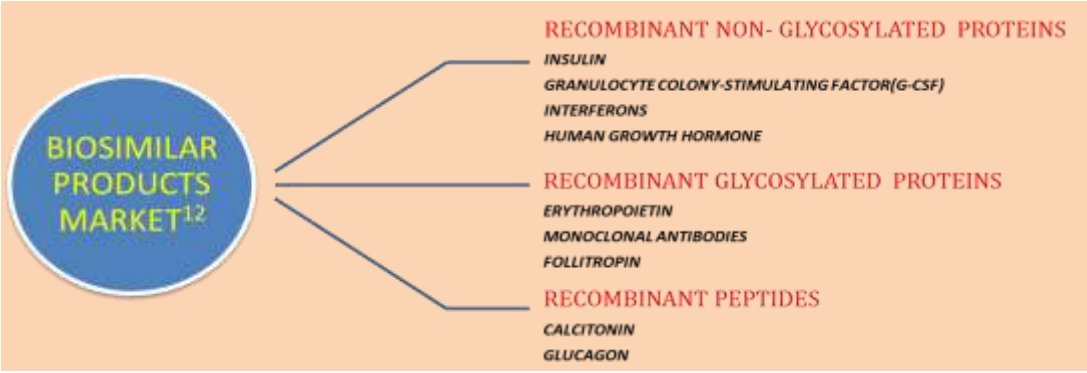


Table.2: Expressions of different research areas[13, 14]

S.NO	Area of research / compounds	Significance	Outcome
1	Insulin:	To treat anaemia associated with kidney disease and cancer therapy	Fierce competition from large generics.
2	Granulocyte colony-stimulating factor(G-CSF):	It stimulates the production of white blood cells, Hence used in the treatment of neutropenia. Significant demand in the field of oncology and hematology	Low price and faster market penetration is expected.
3	Interferons	Stimulate macrophages and natural killer cells thus eliciting anti-viral response. Also active against tumors.	Interferon alpha and beta biosimilars are under development.
4	Human growth factor:	A protein-based peptide hormone that stimulates growth, cell production and regeneration in humans	Somatotropin biosimilars are experiencing high demand; there is less competition in the high biosimilars space.
5	Erythropoietin:	To treat anaemia associated with kidney disease and cancer therapy	Fierce competition from large generics
6	Monoclonal antibodies:	Monoclonal antibodies are mono specific high-molecular weight proteins indicated for various diseases	These are the most awaited market segment with immense opportunity. Fierce competition is expected.
7	Follitropin:	in vitro fertilization drug Gonal-F, which contains recombinant follicle stimulating hormone (FSH), which helps egg development in the ovaries	There are currently no biosimilars of follitropin alfa available on the European market.

Biosimilars market in India

In India currently there are 10 Biotechnology companies involved in the field of biosimilars. There are about 40 Biosimilar products that are available in Indian market. By far, Dr. Reddy's is the Biosimilar player in the Indian market.

Table 3: Indian Companies in Biosimilars Market[15]

Indian Company	Biosimilar Product
Dr Reddy's Lab	Grafeel, Reditux, Cresp
Intas	Neukine, Neupeg, Intalfa, Epofit
Shantha Biotech / Merieux Alliance	Shanferon,Shankinase,Shanpoietin
Reliance Life Sciences	ReliPoietin, ReliGrast, ReliFeron, MIRel
Wockhardt	Wepox, Wosulin
Biocon	Eripro, Biomab, Nufil, Myokinase, Insugen

The cost involved in the development of Biosimilars in India can be between 10-20 million USD due to legislation and environment in the country. Also Biosimilars in India need not undergo phase I/ II studies but phase III is a mandatory step and minimum 100 patients are needed for this study. Thus they can be launched at 25-40% lesser price than the originator too.

Sales figures of Indian Biosimilars in 2008 were recorded to be 200 million USD and looks promising for the upcoming years too as market for 2012 has been forecasted to 580 million USD, which means a CAGR of +30%[15].

Why should biosimilars be considered?

The cost of treatment with biosimilars is much less than that of the innovator drugs. They usually cost 20-25% less than the original products because of reduced clinical trials.

They have comparable quality, safety and efficacy.

They don't have to be proved for each and every indication.

There is no requirement of clinical trails

The profit margin for biosimilar drugs is comparatively higher than that of the traditional generic drugs.

Limitations of biosimilars:

- Cost of development of biosimilars is higher than chemical based generics.
- These are less stable and increasing the stability requires special handling.
- They have a shorter half-life.
- Mostly they do not have pharmacopoeia monographs.
- Their production requires a high capital investment, equipment's and the cost of manufacturing is also high.
- Immunogenicity can be affected by various factors like manufacturing processes and impurities.

CONCLUSION

Biosimilars are expected to rapidly increase market share and economic relevance as more biologics reach patent expiry. Despite various challenges biosimilars will flourish in the near future due to the increasing financial burden on global healthcare system. Product specific guidelines for biosimilars to overcome this problem.

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