Choices and Challenges in developing biosimilars in the MENA region

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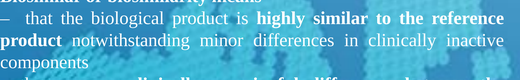
Abstract

Biosimilars are those biologics which are developed after patent expiration of innovator biopharmaceuticals. They are known as similar biologics, follow-on biologics, subsequent-entry biologics, and second-entry or off-patent biotechnology in different countries. Furthermore, they require separate marketing approval since they are not generic versions of biologics which is new in the MENA region. They establish a group of new molecules owing to a number of heterogeneities as compared to the reference innovator biologics. Moreover, this presentation will also discusses the major challenges involved in the manufacturing of Biosimilars and the required documentation on quality, safety and efficacy including comparability exercises as well as the single most important factors affecting the Biomanufacturing capacity in the region. Moreover, Biologics are one of the most important growth drivers for global pharmaceutical market but several challenges impede the way of growth of Biosimilars in the emerging markets. However, we will also take into consideration some trends that promise the bright future of Biosimilars in the MENA region. Finally, we will throw light on the regulatory guidelines of different countries especially in the MENA region and their impacts on the development of Biosimilars.

Introduction

Benta Pharma Industries Benta is one of the few biopharmaceutical facilities in the Middle East and North Africa. The company has recently launched numerous industrial projects.

- First multipurpose industrial operations sites for the pharmaceutical and the medical devices located in Dbayeh, North of Beirut, Lebanon.



Wadi El Neel Benta

- Second multipurpose industrial operations sites for the pharmaceutical and the medical devices located in Cairo, Egypt. (fully operational before the end of Q4 2015)
- Very Soon in Dubai

❑ Benta has gathered the most up-to-date comprehensive edges in the pharmaceutical industry to build a state of the art biotech facility

- the production of small and large scales therapeutic proteins derived from bacterial and mammalian cell lines (Biotech and Biosimilar products)
- Research and Development
- Quality Control area to insure the manufacturing of high quality recombinant and biological products

Biosimilars

Biosimilars

What are biosimilars?

- Legally approved subsequent versions of innovator biopharmaceutical products made by a different sponsor following patent & exclusivity expiry of the innovator product
- Manufactured using the same quality standards as the reference biologic

What is biosimilarity?

Biosimilar or biosimilarity means

– that the biological product is **highly similar to the reference product** notwithstanding minor differences in clinically inactive components

– there are **no clinically meaningful differences between the biological** product and the reference product in terms of the safety, purity, and potency of product

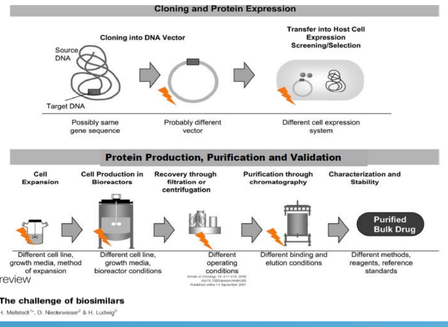
Generics and biosimilars – Is there a difference ?

Generics	Biosimilars	Same / Different
Production simple and consistent	Production complex & variable	Different
Active product always the same	Active product likely to have variation	Different
Formulations may have some variation	Formulations may have some variation	Same
Same clinical effect can be assumed	Same clinical effect cannot be assumed	Different
Regulators accept equivalence	Regulators do not accept equivalence	Different

Biosimilars/Biologics production

- Process important for biologics production
- Production process for biologics has more steps and is more complex than process for traditional drugs
- Requires significant capital investment

Manufacturing process

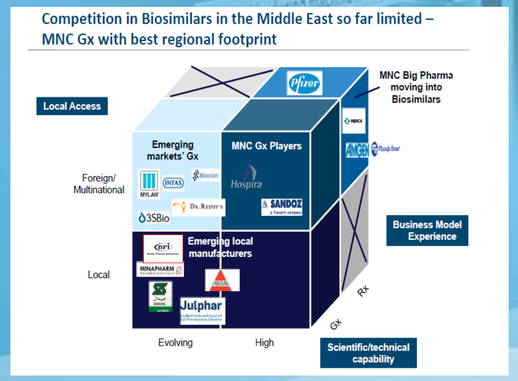


Choices and Challenges

The rising popularity of biosimilar products in emerging markets such the MENA region especially Lebanon can be explained by a number of factors:

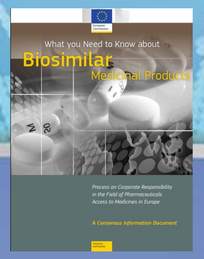
- High cost of branded biologics is placing enormous financial pressure on the national healthcare system.
- Fill in for lower-cost Biosimilars for branded biologics would help reduce government healthcare costs and minimize the financial burden of insurance companies and third-party payers.
- Lebanon and other from the MENA region are extremely dependent upon foreign biologics manufacturers and suppliers for many biologics products.
- Problems in shortages, rising drug prices, and reductions in patient access to potentially life-saving drugs.

- Advances in diagnoses, aging, fast growing populations, advances in technologies and treatment and increasing in chronic and lifestyle diseases.
- Biosimilars represent an opportunity for emerging economies such Lebanon to build domestic biologics and biotechnology capabilities which, in turn, would allow them to penetrate and more efficiently compete for a share of the global Biopharmaceutical market.



"A 2013 report from the European Commission looking at Europe's strong regulatory and commercial foundation for biosimilars found that biosimilars are helping improve competition and are thus increasing access to biologic medicines for patients"

- *"Fusion proteins and monoclonal antibodies used in cancer and autoimmune diseases are expected to form a substantial proportion of this new line of biosimilars."*



- A new report by London-based business information company **Visiongain** predicts the world biological drugs market will reach **$178.4bn in 2017**. World Biological Drugs Market 2013-2023, published in May 2013.
- *"The global market for biosimilar drugs has been forecasted to be worth **$2.445 billion this year**"*, according to a new report by British market research specialist **Visiongain**.

ex: recent approval of the biosimilar GCSF by the FDA

More than 80 % of Biologics will loose patent protection by 2019.

Biggest Challenges in Biosimilar

- We could find many challenges but some of them are common in the region, especially Lebanon:
  - Lack of governmental support (R&D credit, Grants, tax relieve, schorlarships, etc…) towards Pharma and Biopharma industries.
  - Lack of local manufacturing protection (ex: Egypt does have it)
  - "Window" limits the registration of drugs (example: Egypt and Jordan)
- Media plays an important role in the promotion of Biosimilars
- Example: Under-estimation regarding the level/expertise of people in this domain.
- Media are not emphasizing on the existence of local manufacturer and the level of their technologies
- Instability in the MENA region
  - Example: Trades are affected
- Instability in Lebanon

Impact of Regulatory Agencies

The approach for market authorization for generics cannot be extrapolated to Biosimilars

	Generics	Biosimilars
Module 1	Full	Full
Module 2	Full	Full
Module 3	Full	Full + Comparability
Module 4	Not Required	Reduced + Comparability
Module 5	BE Study	Reduced Clinical Trials + Comparability

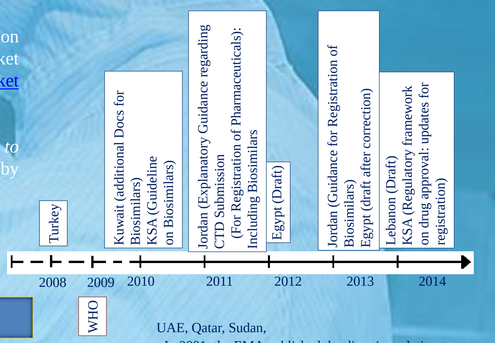
must be performed in a step-wise manner to demonstrate Biosimilarity and should be a Science based approach

- *Biosimilar regulations*

The EMA was the first Regulatory Agency to create biosimilar guidelines in 2005, swiftly followed by the first approved biosimilar products in 2006. As of December 2013, 16 biosimilar products were approved by the EMA.

- Recombinant erythropoietins (epoetin alfa, epoetin zeta)
- Recombinant granulocyte-colony stimulating factors (filgrastim)
- Recombinant human growth hormone (somatropin)
- Recombinant follicle stimulating hormone (follitropin alfa)
- Monoclonal antibodies (infliximab)

Remsima (new approval)



UAE, Qatar, Sudan,
In 2001, the EMA published the directive relating to differences in raw materials or manufacturing processes between Biosimilars and reference products

Illustration of the differences between originator and biosimilar development

In the end, both approaches provide the same level of confidence with regard to safety and efficacy of the product

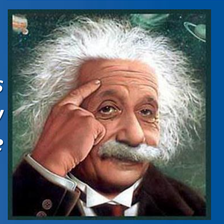
❑ What we should do

- Pharmacovigilance
- Reduce the information gap (relation between the regulators and the industry)
- USP and EP pharmacopeia
- WHO guidelines and recommendations for manufacturing and evaluating biological

❑ Future for Biosimilar

- From a scientific and regulatory perspective, the future is Bright
- Modern bioanalytical techniques are sufficiently sensitive
- The potential benefit of biosimilars in increasing patient access and reducing healthcare costs are clear.
- Biosimilars face competition from originators products
- Partnering

Conclusion



"The only source of knowledge is experience."

A learning period is important in all new activities: biosimilars are no exception

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