



*Making Medicines Affordable*

## **FDA Public Hearing: Approval Pathway for Biosimilar and Interchangeable Biological Products**

### **Comments by the European Generic medicines Association (EGA)**

**Joerg Windisch, PhD  
Vice-Chair of EGA's Biopharmaceuticals Group**

**FDA White Oak Campus, Silver Spring, MD  
November 2-3, 2010**

---



*Making Medicines Affordable*

## **Vast Experience**

- **Enormous experience** of EGA members - up to 15 years in biosimilars and much longer in biologics in general
  - EGA Members have **pioneered biosimilars** and market them in the EU (since 2006), Japan, Canada, Australia, the US (FD&C Act products only), and many other countries
  - Biosimilars have been **used in the EU** (and the US for FD&C Act products) without safety or potency issues **for more than 4 years**
  - Biosimilars are gaining **significant market share**
  - EGA and its members worked closely with the European Medicines Agency, European Commission, Health Canada, PMDA, TGA, and WHO on establishing high regulatory standards for biosimilars and highly **appreciate the opportunity to now also work with the FDA**
-



Making Medicines Affordable

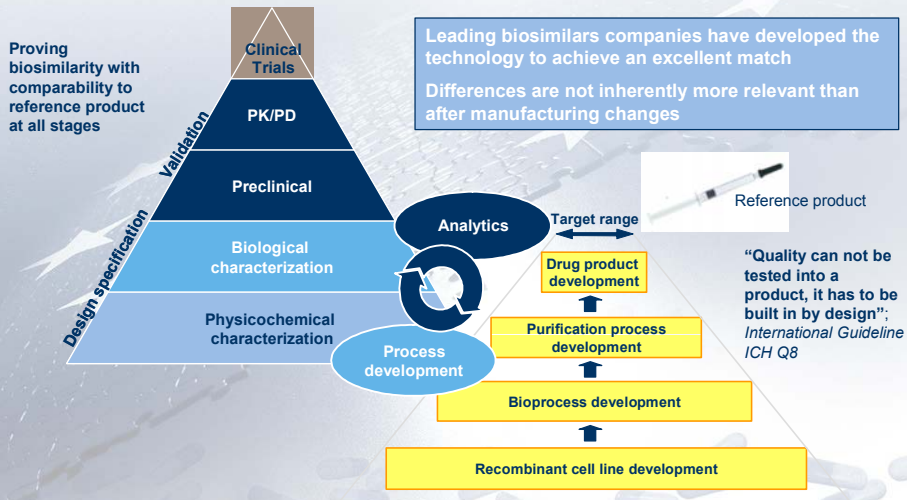
# A. Biosimilarity

- High degree of similarity is key
  - To justify abbreviated non-clinical and clinical programs
  - To extrapolate between indications
  - To allow interchangeability
  - To gain acceptance by patients and the healthcare community
- Scientific principles of biosimilarity are the same as for comparability
  - Similarity/differences in product attributes are what matters to safety and potency, not the manufacturing processes per se
  - Variability of reference product defines “goalposts”
- Products can be engineered to match the reference product



Making Medicines Affordable

# A. Biosimilars must be Systematically Engineered to Match the Reference





Making Medicines Affordable

## A. Biosimilarity, Q1

*... factors ... in determining whether the biological product is highly similar?*

The criteria for the comparison of the purity profile of the biosimilar candidate and the reference product should be based on

Understanding batch-to-batch and historical **variability of the reference** product

**Classification** of the product variants into **product-related substances or impurities** (ICH Q6B)

Level of **understanding** of the relevance of **subtle differences** on safety/efficacy (ICH Q5E)

5



Making Medicines Affordable

## A. Biosimilarity, Q2+3

*... factors ... to assess ... differences?*

- The nature of **differences** should be fully elucidated analytically
- The potential **impact of differences** should be assessed based on existing knowledge and specifically conducted investigations
  - Extent of difference (how different, how much)
  - Information from literature
  - Presence in products other than reference product
  - Characterization in bioassays and immunological assays
- In most cases, the above studies should clarify the relevance of differences

*... range of ... differences ... consistent with ... “highly similar”*

- Decision to be taken based on evaluation of clinical relevance
- **FDA reviewers** should be given **discretion** to decide, in consultation with the sponsor, on the acceptability of differences based on current scientific knowledge on a case-by-case basis

6



Making Medicines Affordable

## C. Patient Safety and Pharmacovigilance

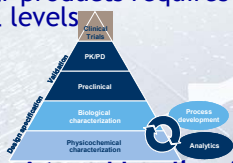
- We acknowledge that the US already has the REMS system
- There is no need for a separate system for biosimilars
- Under the TAS Action Plan we fully support
  - the collaboration of EC/EMA/FDA on product specific Risk Management initiatives
  - further convergence of Risk Management formats and
  - the FDA/EMA collaboration on biosimilars
- We believe that **different nonproprietary names**, prefixes, or suffixes will **not be necessary** since all **biologics can be clearly identified** based on the following parameters:
  - Product name
  - Manufacturer/NDC Number
  - Lot number

7



Making Medicines Affordable

## D. Use of Supportive Data Global Development: The Issue

- Development of biosimilar products requires comparison to a reference products at all levels
- 
- Reference products are **registered locally** with health authorities in different jurisdictions, and are thus, **legally, 'different' products despite being identical with regard to purity, safety, and potency**
  - While many countries have recently established legal frameworks and regulatory pathways for biosimilars, most **require** that the comparison occurs against „their“ **national reference product** or are silent about this issue
  - This would mandate the performance of **separate, full development programs** for each country
  - This is **unnecessary, unethical** (duplication of preclinical and clinical studies), and **uneconomical**

8

## D. Use of Supportive Data

### Global Development is a Must

- Reference products are **often the same** or highly similar in different countries, even though licensed under different jurisdictions
  - Often, **documentation** is available in the public domain, confirming that the products are the same
  - **Comparability** of reference products of one original manufacturer from different highly regulated countries (US, EU) can be clearly established by stringent analytical and functional studies
- Under these premises it **should not** be required to **duplicate** preclinical and clinical studies for each country/region

## D. Use of Supportive Data: Demonstrating Comparability of Reference Products

US	EU	Requirements
√	√	rigorous physicochemical and biological comparison with reference product of different regions
case by case	case by case	↓ if no conclusive information available that US and EU products are the same or if different formulation used in US: rigorous comparative non-clinical or clinical phase I PK/PD studies with reference product of different regions
√		↓ comparative clinical phase III studies with reference product from <u>one</u> region only (US <u>or</u> EU)

Leverage „EC-FDA Medicines Regulation Transatlantic Administrative Simplification“



*Making Medicines Affordable*

## Summary

- **EGA welcomes the establishment of a pathway in the US and the opportunity to work with the FDA**
  - **Biosimilars have been used safely in the EU (and the US for FD&C Act products) for more than 4 years**
  - **A high degree of similarity is the prerequisite for abbreviated clinical programs, extrapolation of indications, and interchangeability**
  - **Such a high degree of similarity can be achieved by target-directed, iterative process development**
  - **Global development should be allowed based on documentation of sameness or demonstration of comparability of reference products, and is key to ensuring affordability and patient access.**
- 



*Making Medicines Affordable*

**Thank you**

**[www.egagenerics.com](http://www.egagenerics.com)**

---



*Making Medicines Affordable*

# Acronyms

- EGA-European Generic medicines Association
- EU-European Union
- EMA-European Medicines Agency, EU
- FDA-Food and Drug Administration, US
- PMDA-Pharmaceuticals and Medical Devices Agency, Japan
- TGA-Therapeutic Goods Administration, Australia
- WHO-World Health Organization
- PK/PD-Pharmacokinetic/Pharmacodynamic
- ICH-International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
- ICH Q8-Pharmaceutical Development
- ICH Q6B-Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
- ICH Q5E-Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process
- TAS-Transatlantic Administrative Simplification
- NDC-National Drug Code
- REMS-Risk Evaluation and Mitigation Strategies