

FDA's Implementation of the Legal and Regulatory Framework for Biosimilars

Sally Howard

Deputy Commissioner for Policy, Planning, and Legislation

1

What are therapeutic biologics?

Many biologics treat serious and chronic diseases:

- Monoclonal antibodies that treat cancer
- Interferons that treat autoimmune disorders (MS)
- Protein products that treat anemia
- Immunomodulators that treat inflammatory disorders.

Therapeutic biologics account for 40 percent of prescription drug spending in the U.S.

2

Biological Product Framework

- **Originator Product (Reference Product)**
 - Biologics License Application (351(a) of PHS Act)
 - Clinical trial data establishes safety and effectiveness
- **Biosimilar and Interchangeable Products**
 - Biologics Price Competition and Innovation Act (BPCI Act) Abbreviated Pathway (351(k) of PHS Act)
 - Goal: Improve patient access, encourage competition, and lower costs

3

Biosimilar or Biosimilarity

- The biological product is **highly similar** to the reference product notwithstanding minor differences in clinically inactive components; and
- there are **no clinically meaningful differences** between the biological product and the reference product in terms of the safety, purity, and potency of the product

4

Interchangeable or Interchangeability

- **Biosimilar** to the reference product;
- Produces the **same clinical result** as the reference product **in any given patient**; and
- The risk in terms of safety or diminished efficacy of **alternating or switching** between use of the product and the reference product is not greater than with repeated use of the reference product alone

5

First Biosimilar Approved in U.S.

- March 6, 2015: Zarxio (filgrastim-sndz)
 - Approved as a biosimilar to Neupogen based on review of evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data and other clinical safety and effectiveness data
 - Approved for the same indications previously approved for U.S.-licensed Neupogen (filgrastim)
 - Application discussed at a public advisory committee
 - Biosimilar only, Sandoz did not seek interchangeability
 - Nonproprietary name should not be viewed as reflective of the agency's decision on a comprehensive naming policy for biosimilar and other biological products

6

FDA Guidances for Industry

Final Guidances to Date in 2015

1. Scientific Considerations in Demonstrating Biosimilarity to a Reference Product
2. Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product
3. Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009

Draft Guidances to Date

1. Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants
2. Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product
3. Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act
4. Biosimilars: Additional Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009

7

FDA Guidances for Industry

Draft Guidances Expected in 2015

1. Labeling for Biosimilar Biological Products
2. Nonproprietary Naming for Biological Products
3. Statistical Approaches to Evaluation of Analytical Similarity Data to Support a Demonstration of Biosimilarity
4. Considerations in Demonstrating Interchangeability to a Reference Product

8

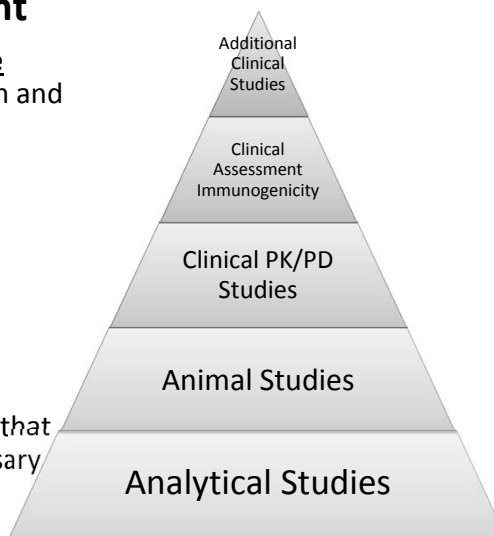
Key Concept #1: Goals of “Stand-alone” and Biosimilar Development Are Different

- The goal of “stand-alone” development is to demonstrate that the proposed product is safe and efficacious
- Drug development starts with preclinical research, moves to Phase 1, 2 and culminates in Phase 3 “pivotal” trials to show safety and efficacy
- The goal under 351(k) is to **demonstrate biosimilarity** between the proposed product and a reference product
- The goal is not to independently establish safety and effectiveness of the proposed product

9

Key Concept #2: Stepwise Evidence Development

- FDA has outlined a **stepwise approach** to data generation and the evaluation of residual uncertainty at each step
- *Totality-of-the-evidence* approach in evaluating biosimilarity
- No “one-size-fits-all” assessment. FDA may determine, in its discretion, that certain studies are unnecessary in a 351(k) application



10

Key Concept #3: Extrapolation

- FDA guidance outlines factors/issues that should be considered when providing scientific justification for extrapolation including, for example*,
 - The Mechanisms Of Action(s) in each condition of use for which licensure is sought
 - The Pharmacokinetic (PK) and bio-distribution of the product in different patient populations
 - The immunogenicity of the product in different patient populations
 - Differences in expected toxicities in each condition of use and patient population
- Differences between conditions of use do not necessarily preclude extrapolation
- A sponsor must ensure the totality of the evidence, including scientific justification for extrapolation, supports approach

*This list is a subset of the issues outlined in the FDA guidance document

11

Supporting a Robust Biosimilar Product Marketplace

External Levers

- Payor coverage
- Formularies
- Pharmacy substitution laws
- Physician/Patient uptake

12

FDA Education & Outreach

Resources

- Purple Book
- Webinars
- Dedicated Web page
- Consumer Update

Stakeholder Engagement

- In-person meetings
- Presentations at meetings
- Development of materials (e.g. ASCO Post)
- Larger Communications Planning (message testing underway)

13

Next Steps

- Continue program implementation
- Continue to issue Guidance for Industry
- Work with biosimilar applicants/manufacturers, healthcare providers, patients and other stakeholders

14