

# Biosimilar and Interchangeable Products: The U.S. FDA Perspective

Joe Franklin, J.D., Ph.D., Director of the Policy Staff,  
TBBS/OND/CDER/FDA.



# Disclosure Information

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*Joe Franklin*

I have no financial relationships to disclose.

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I will not discuss off label use and/or investigational use in my presentation.

# Overview of Presentation

- **Background and key concepts**
  - BPCI Act
  - Terminology
  - 351(k) Biologics License Application
  - Interchangeability
  - Biological product naming
  
- **Biosimilars program at FDA**

# **BACKGROUND AND KEY CONCEPTS**

## Background: BPCI Act

- The **Biologics Price Competition and Innovation Act of 2009 (BPCI Act)** was enacted on March 23, 2010.
- The BPCI Act created an *abbreviated licensure pathway for biological products shown to be biosimilar to or interchangeable with* an FDA-licensed reference product.
- Other provisions of the BPCI Act include:
  - An amended “biological product” definition
  - Exclusivities
  - Procedures for identifying and resolving patent disputes involving 351(k) BLAs

# “Biological Product”

The term “**biological product**” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

Section 351(i)(1) of the PHS Act.

# “Reference Product”

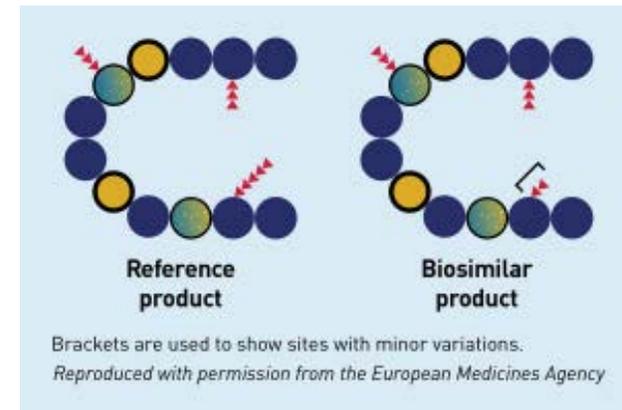
## Reference Product:

- the single biological product licensed under section 351(a) of the PHS Act against which a biological product is evaluated in an application submitted under section 351(k). Section 351(i)(4).
- An application submitted under section 351(a) of the PHS Act is a “stand-alone” application that must contain all information and data necessary to demonstrate that the proposed product is safe, pure and potent.
- In contrast, an application submitted under section 351(k) needs to demonstrate that the proposed product is biosimilar to, or interchangeable with, the reference product.

# “Biosimilar” or “Biosimilarity”

**Biosimilar** or **Biosimilarity** means:

- that 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.
- Section 351(i)(2).



# 351(k) BLA: General Requirements

A 351(k) BLA must include information demonstrating that:

- The proposed product is **biosimilar** to a reference product;
- The proposed product and the reference product utilize the **same mechanism(s) of action** for the proposed condition(s) of use -- but only to the extent the mechanism(s) are known for the reference product;
- **The condition(s) of use** in labeling for the proposed product **have been previously approved** for the reference product;
- the **route of administration**, **dosage form**, and **strength** of the proposed product are the same as those of the reference product; and
- The **facility** in which the proposed product is manufactured, processed, packed, or held **meets standards** designed to assure that the biological product continues to be safe, pure, and potent.

# “Interchangeable” or “interchangeability”

## Statutory definition:

**The term “interchangeable” or “interchangeability”—**  
—in reference to a biological product that is shown to meet the standards described in section 351(k)(4), **means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.**

Section 351(i)(3).

# Interchangeability standards

## Standards under section 351(k)(4):

- the biological product is biosimilar to the reference product;
- it can be expected to produce the same clinical result as the reference product in any given patient; and
- for a product that is administered more than once to an individual, 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 the risk of using the reference product without such alternation or switch.

# Nonproprietary Naming of Biological Products: *Four-letter suffix*



Nonproprietary names (i.e. proper names) for **biological products** should include—

—a **core name** *attached by a hyphen to an FDA-designated suffix.*

Hypothetical example: replicamab-cznm

*FDA Guidance: Nonproprietary  
Naming of Biological Products*

# Nonproprietary Naming of Biological Products: *Four-letter suffix*



**A unique suffix should be designated for each originator biological product, related biological product and biosimilar product.**

FDA is continuing to consider the format of the suffix for interchangeable biological products.

*FDA Guidance: Nonproprietary  
Naming of Biological Products*

# Nonproprietary Naming of Biological Products: *Four-letter suffix*



**Example:** for hypothetical products sharing the fictitious core name *replicamab*, the proper names would include a unique suffix:

- Originator biological product : *replicamab-cznm*
- Related biological product: *replicamab-rzbh*
- Biosimilar product: *replicamab-hixf*

*FDA Guidance: Nonproprietary  
Naming of Biological Products*



# **BIOSIMILARS PROGRAM AT FDA**

# Biosimilars Approved by FDA

- Since program inception and as of April 1, 2018, 12 companies have publicly announced submission of 23 351(k) BLAs to FDA.
- Nine 351(k) BLAs for biosimilar products have been approved.
  - Zarxio (filgrastim-sndz)
  - Inflectra (infliximab-dyyb)
  - Erelzi (etanercept-szsz)
  - Amjetiva (adalimumab-atto)
  - Renflexis (infliximab-abda)
  - Cyltezo (adalimumab-adbm)
  - Mvasi (bevacizumab-awwb)
  - Ogivri (trastuzumab-dkst)
  - Ixifi (infliximab-qbtx)

# Development-Stage Advice to Sponsors



**As of April 1, 2018,**

- **63 programs** were enrolled in the Biosimilar Product Development (BPD) Program to discuss development of **proposed biosimilar products or proposed interchangeable products**
- CDER has received meeting requests to discuss the development of biosimilar or interchangeable products for **31 different reference products.**

# FDA Biosimilars Guidance Development

1. **Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (final, 2015)**
2. **Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product (final, 2015)**
3. **Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (final, 2015)**
4. **Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants (final, 2015)**
5. **Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product (final, 2016)**
6. **Nonproprietary Naming of Biological Products (final, 2017)**
7. **Biosimilars: Additional Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (draft, 2015)**
8. **Labeling for Biosimilar Products (draft, 2016)**
9. **Considerations in Demonstrating Interchangeability With a Reference Product (draft, 2017)**
10. **Statistical Approaches to Evaluate Analytical Similarity (draft, 2017)**

# FDA's Education and Outreach Campaign for Biosimilars



- **Launched by FDA in October 2017**
- **Goals of this initiative are to increase:**
  - Understanding of biologics, reference products, biosimilars and interchangeable products.
  - Awareness of FDA's role in the biosimilar approval process.
  - Knowledge of the data and information FDA reviews/requires to determine biosimilarity.

# Biosimilars: FDA Strategic Priority

**FDA's 2018 Strategic Policy Roadmap** announced FDA's plan to launch a comprehensive program to encourage biosimilar competition.

**Goal:** to help address the high cost of medicines through the development of science-based policies that can improve competition, access, and the opportunity for patients to benefit from safe and effective, and lower cost biosimilar alternatives.

**Thank you for your attention.**

**For more information, go to  
[www.fda.gov/biosimilars](http://www.fda.gov/biosimilars)**