

# Biosimilar and Interchangeable Biological Products: Basic Concepts and Practical Resources

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# Overview



- Background and Progress To Date
  - Biosimilars Action Plan
- Introduction to Biosimilarity Concepts
  - Basics of Biosimilarity
- FDA's Approach to the Development of Biosimilars
- Using Biosimilar and Interchangeable Products
- Resources for Health Care Providers

# Learning Objectives



1. Describe how biologics differ from small molecules
2. Explain why some biologics cannot be copied exactly
3. Compare and contrast the development and approval process for new biologics and biosimilars/interchangeables
4. Recognize the differences in the statutory requirements for approval between new biologics and biosimilars or interchangeables
5. Describe and explain the resources available for health care provider to learn more about biosimilar and interchangeable products through the Purple Book and other resources.

# Background and Progress To Date

## Biosimilars Action Plan (BAP)

1. Improving the efficiency of the biosimilar and interchangeable product development and approval process
2. Maximizing scientific and regulatory clarity for the biosimilar product development community
3. Developing effective communications to improve understanding of biosimilars among patients, clinicians and payors
4. Supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition

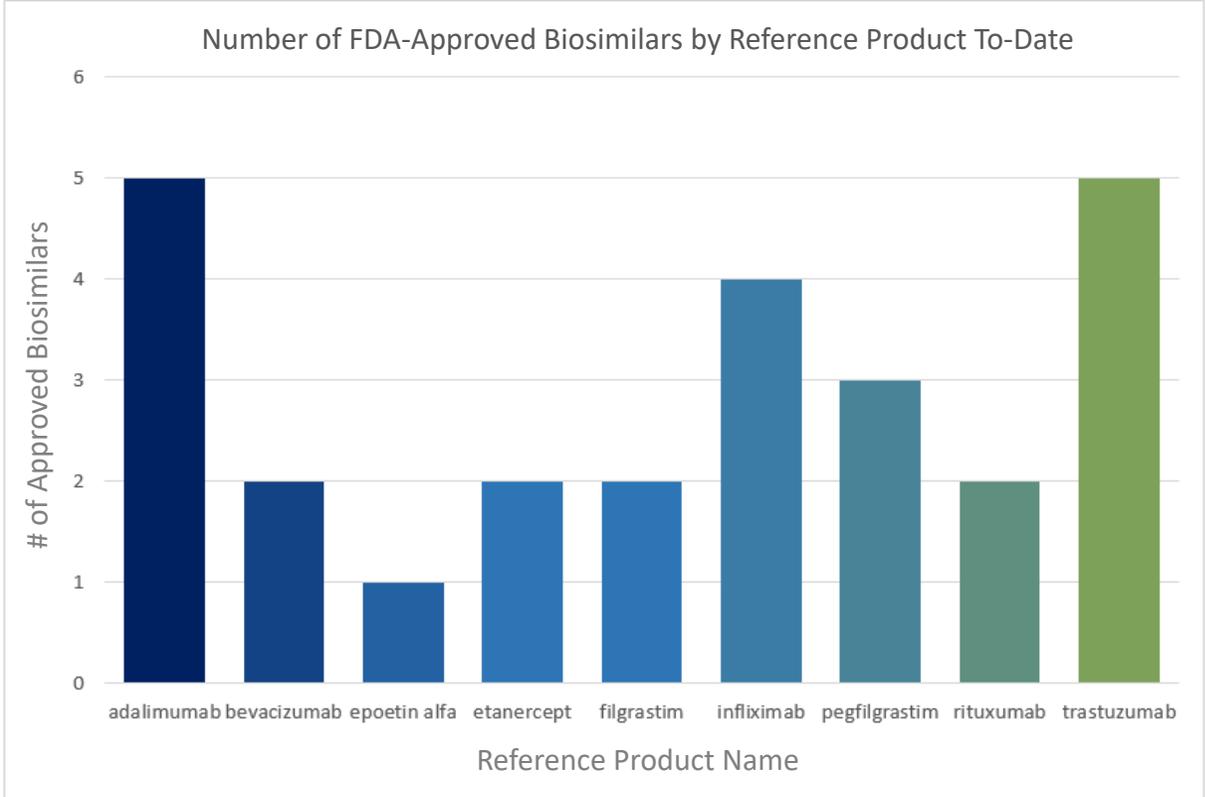
### **BIOSIMILARS ACTION PLAN:** Balancing Innovation and Competition

July 2018

# Biosimilars: 2019 Year in Review



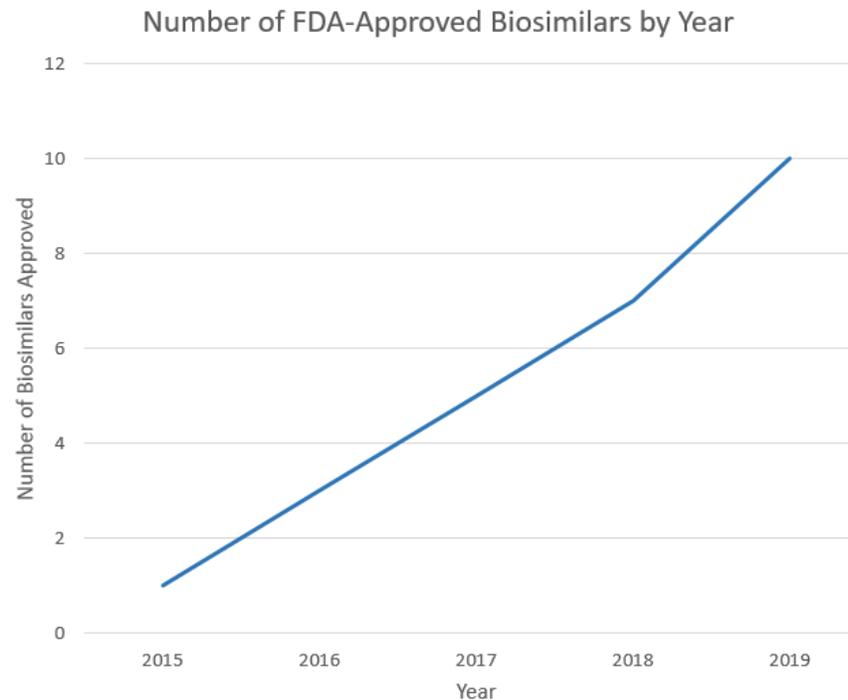
Biosimilars Approved by FDA in 2019	
<b>Ontruzant</b> (trastuzumab-dttb)	<b>Ruxience</b> (rituximab-pvvr)
<b>Trazimera</b> (trastuzumab-qyyp)	<b>Hadlima</b> (adalimumab-bwwd)
<b>Eticovo</b> (etanercept-ykro)	<b>Ziextenzo</b> (pegfilgrastim-bmez)
<b>Kanjinti</b> (trastuzumab-anns)	<b>Abrilada</b> (adalimumab-afzb)
<b>Zirabev</b> (bevacizumab-bvzr)	<b>Avsola</b> (infliximab-axxq)



# Biosimilars: 2019 Year in Review (cont.)



- As of December 2019:
  - **26** 351(k) BLAs for biosimilar products have been approved
  - **74** programs enrolled in the Biosimilar Product Development (BPD) Program
  - **12** companies publicly announced submission of **30** 351(k) BLAs to FDA
  - CDER received meeting requests to discuss the development of biosimilars for **38** different reference products



# Biosimilars: 2019 Year in Review (cont.)



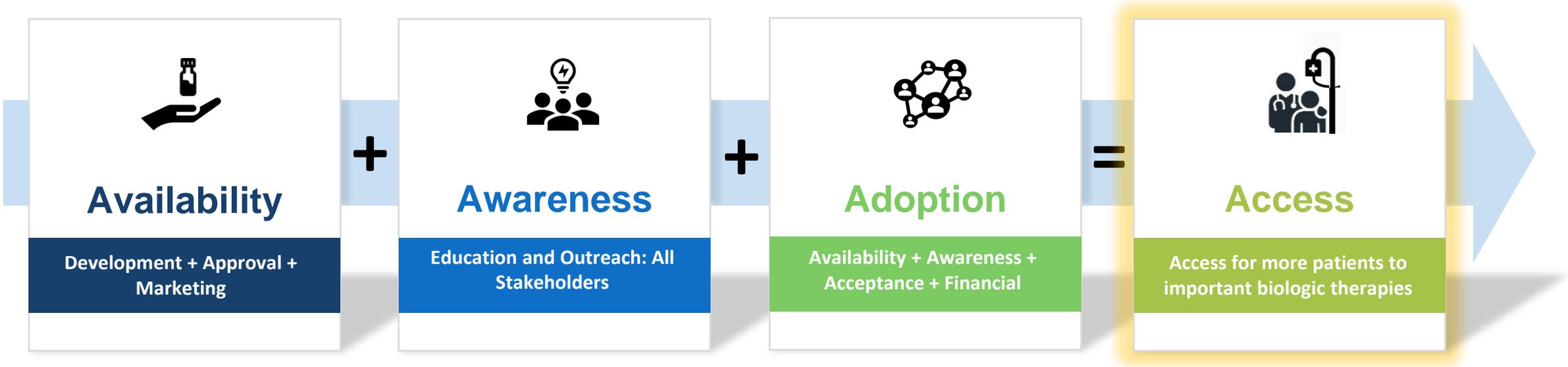
## Completed Activities

## Key In-Progress Activities

<p>Established the Office of Therapeutic Biologics and Biosimilars</p>	<p>Released Draft Guidances:</p> <ul style="list-style-type: none"> <li>- "Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations"</li> <li>- "Nonproprietary Naming of Biological Products: Update"</li> <li>- "Clinical Immunogenicity of Biosimilar and Interchangeable Insulin Products"</li> </ul> <p>Released Final Guidance:</p> <ul style="list-style-type: none"> <li>- "Considerations in Demonstrating Interchangeability with a Reference Product"</li> </ul>	<p>Released "Biosimilar Basics" for patients</p>	<p>Enhance the Purple Book</p>	<p>Develop standardized review templates specific to 351(k) BLAs</p>
<p>Published article on "Advancing biosimilar development using Pharmacodynamic (PD) Biomarkers in Clinical Pharmacology Studies"</p>		<p>Stakeholder Meetings</p>	<p>Provide product developers with information resources and development tools</p>	<p>Identify and develop additional guidances</p>
<p>Held Public Hearing on "The Future of Insulin Biosimilars"</p>		<p>Other Engagement Activities</p>	<p>Develop additional biosimilars educational resources</p>	<p>Oversee the transition of biological products</p>

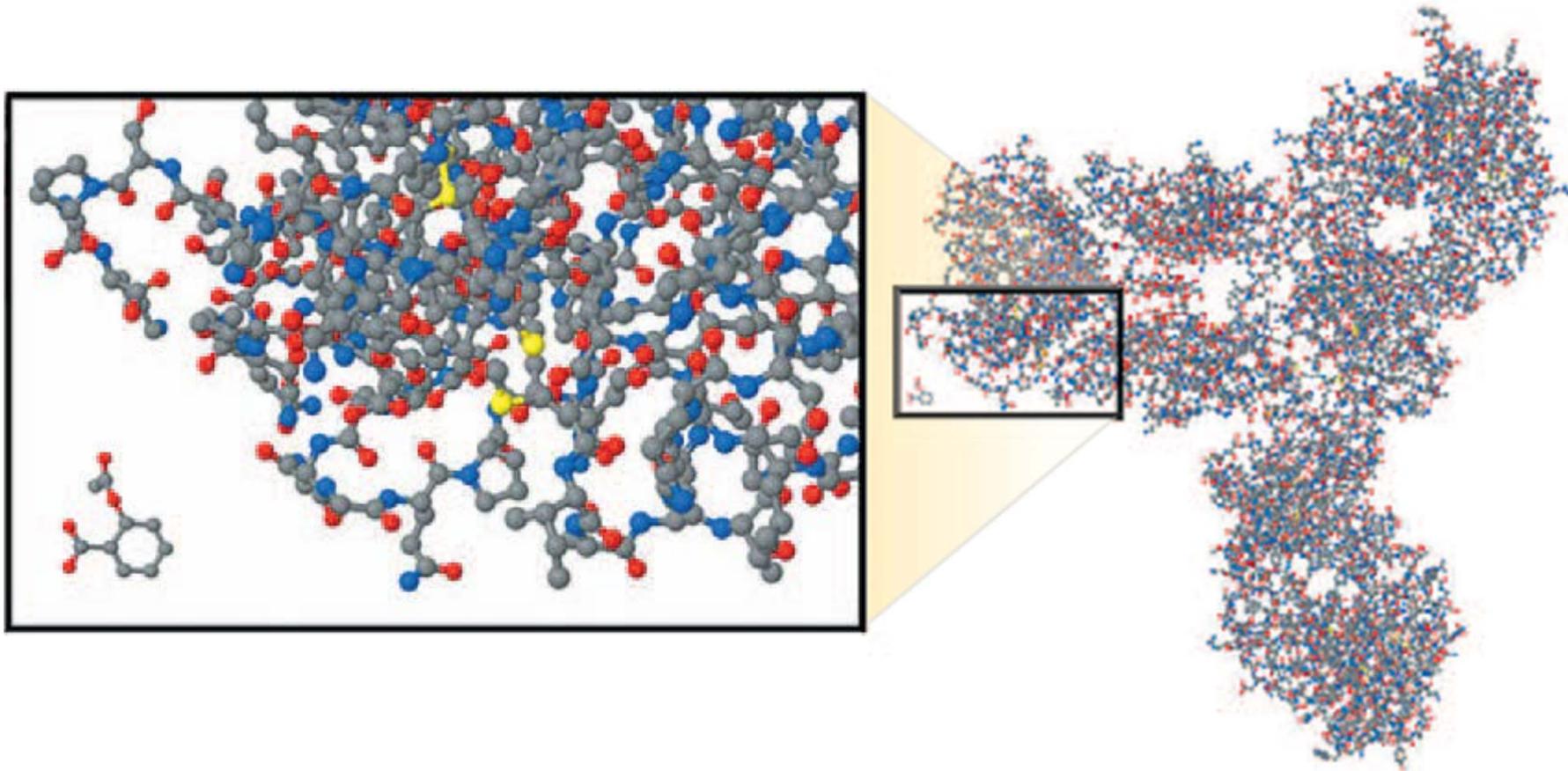


# Solving The Equation for Patient Access

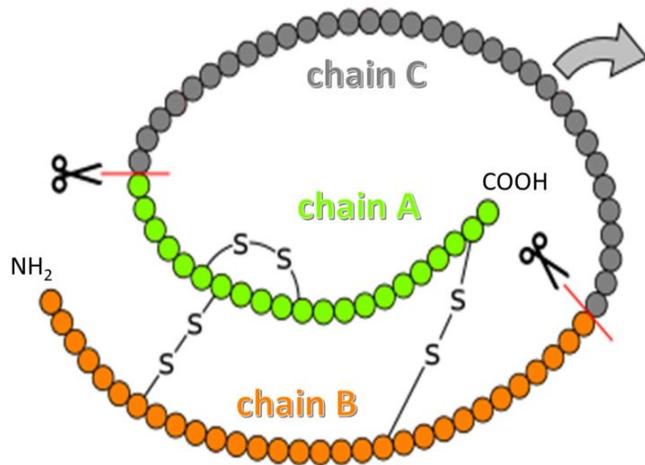


# Introduction to Biosimilarity Concepts

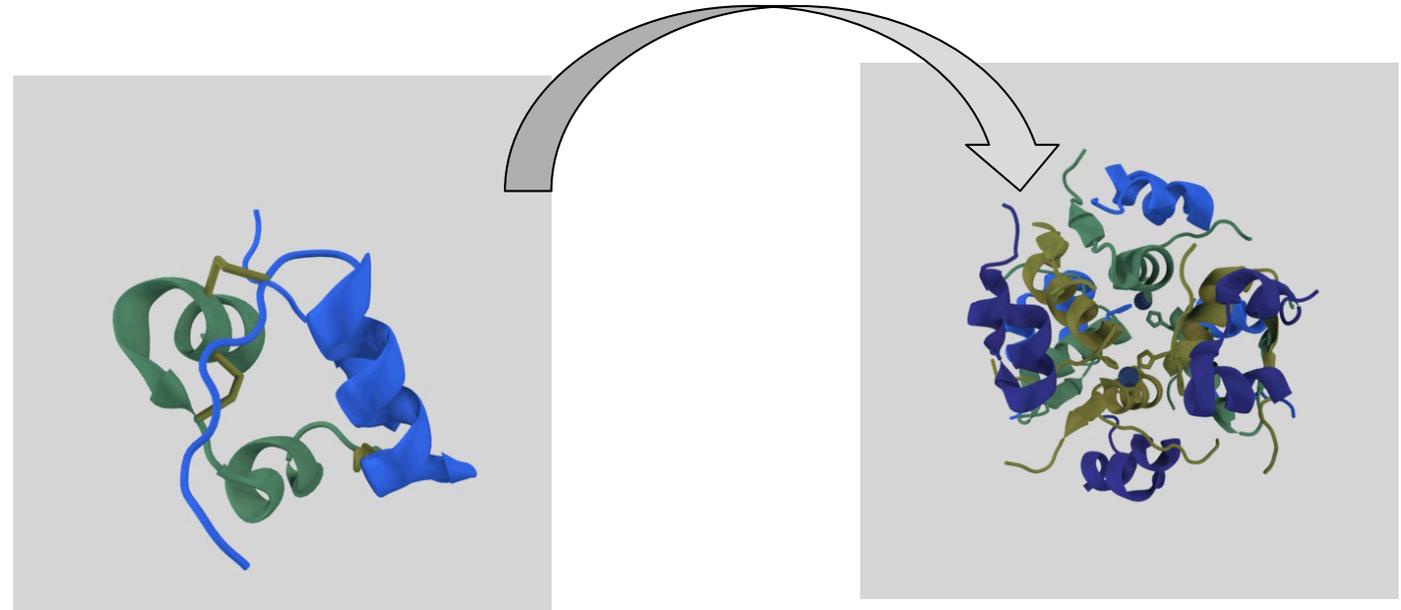
# Biologics vs. Small Molecules



# The Spectrum of Biologic Complexity: Insulin



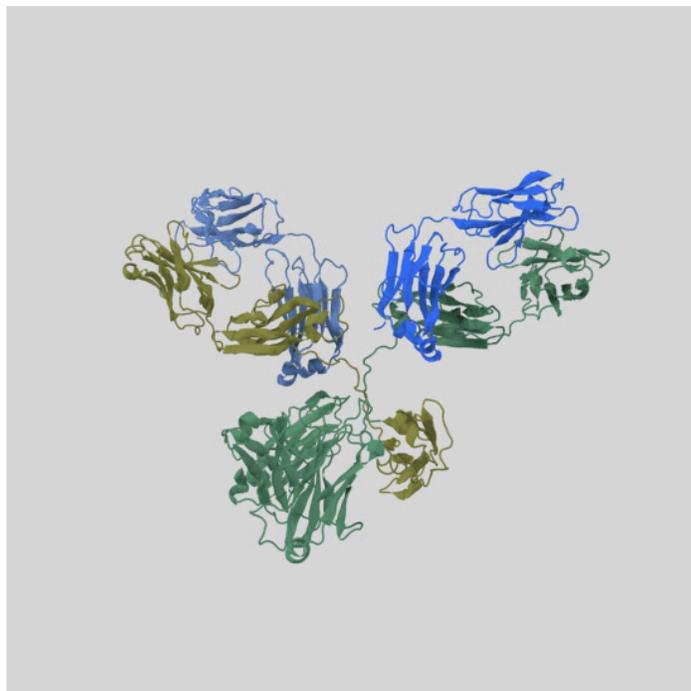
Pro-Insulin  
Chain A = Green;  
Chain B = Orange  
S-S = disulfide bridges



Insulin  
Chain A = Blue (21 aa);  
Chain B = Green (30 aa)  
Olive green = disulfide  
bridges  
Nonglycosylated

Structure: Simple  
Complexity: tendency to aggregate  
and immunogenicity

# The Spectrum of Biologic Complexity: mAbs



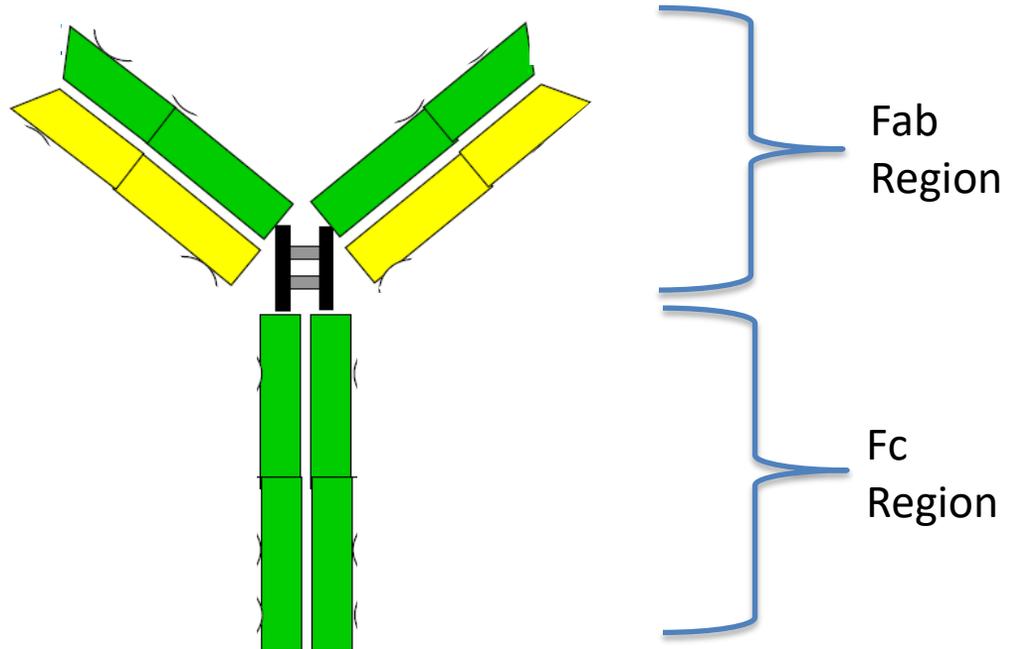
Monoclonal Antibodies  
Heavy Chain x 2 = 50 kDa  
Light Chain x 2 = 25 kDa  
Total Molecular Weight  $\approx$  150 kDa

- Structure: Complex
- Large (i.e., 150 kDa) proteins with four separate chains
- “Fab” Region: Specific antigen binding sites for specificity
- “Fc” Region: Potential additional effects on function and exposure

# The Spectrum of Biologic Complexity: Modifications



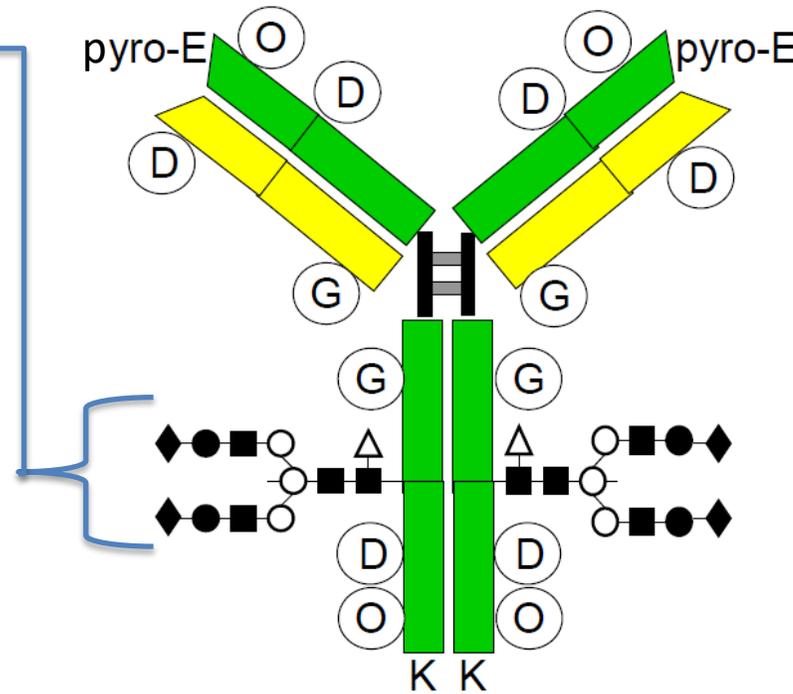
- Biosimilars and the original biologics they are referencing will have the same underlying amino acids and proteins
- So why can't they all be called "identical" or "copies"?
- "Add-ons" and modifications to certain amino acids



# The Spectrum of Biologic Complexity: Modifications



- Glycosylation, typically a variety, within certain ranges
- Result: Millions of slightly different versions of the same protein or antibody per dose or batch
- Both reference products and biosimilars contain these variations
- Biosimilars try to match the patterns and variations of the reference product

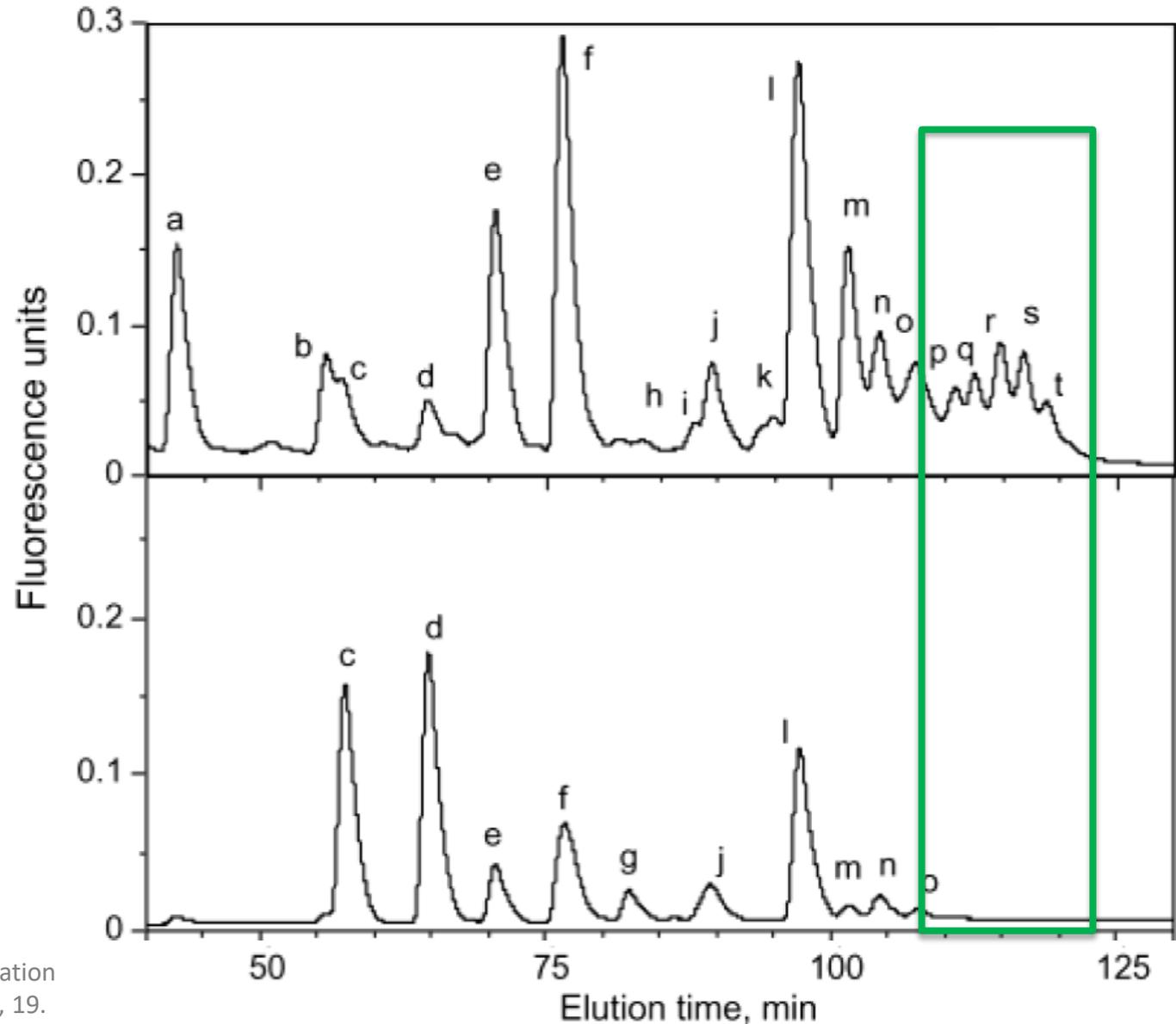


- Pyro-Glu (2)
  - Deamidation (3 x 2)
  - Methionine oxidation (2 x 2)
  - Glycation (2 x 2)
  - High mannose, G0, G1, G1, G2 (5)
  - Sialylation (5)
  - C-terms Lys (2)
- Total variants  $(9600)^2 \approx 10^8$**
- $2 \times 6 \times 4 \times 4 \times 5 \times 5 \times 2 = 9600$**

# Glycosylation Differences: Type

## Questions:

1. Will difference predispose to an immune reaction?
2. Will difference result in different exposure?
3. Will difference result in different activity?

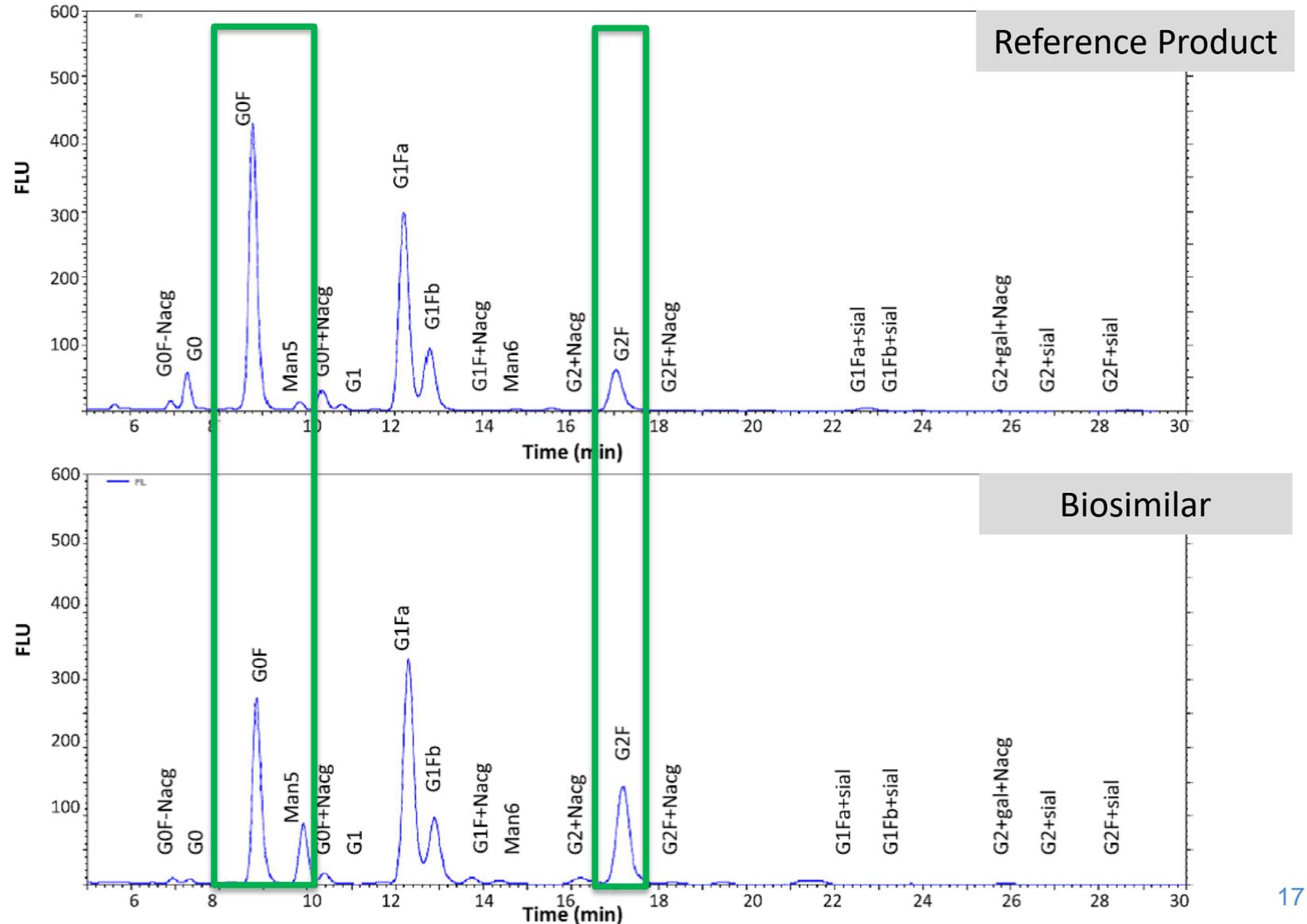


\*These graphs are for illustration purposes only and were not from pharmaceutical samples.

# Glycosylation Differences: Amount

## Questions:

1. Will difference result in different exposure?
2. Will difference result in different activity?



N-glycosylation profile analysis of Trastuzumab biosimilar candidates by Normal Phase Liquid Chromatography and MALDI-TOF MS approaches, Melo, IS et al., Journal of Proteomics 2015, 125.

# Basics of Biosimilarity



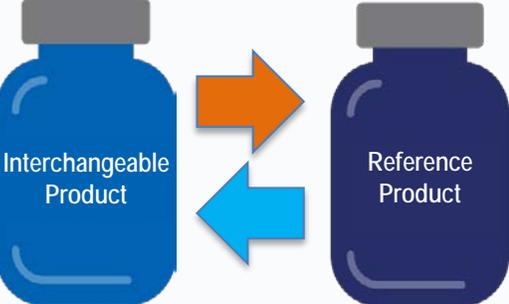
**Reference Product**

A reference product is the single biological product, already approved by FDA, against which a proposed biosimilar product is compared



**Biosimilar Product**

A biosimilar is a biological product that is **highly similar and has no clinically meaningful differences** from an existing FDA-approved reference product

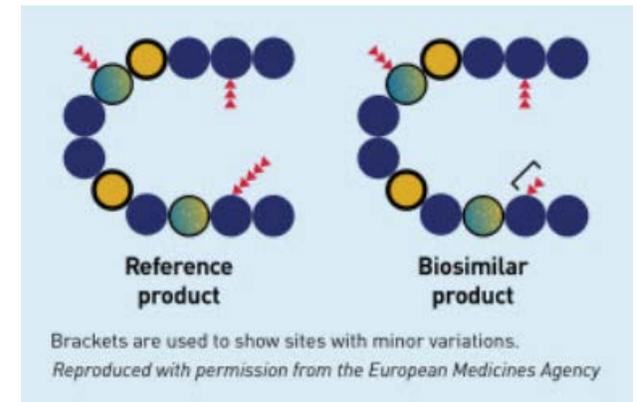


**Interchangeable Product**

An interchangeable is a biosimilar product that can be substituted for the reference product without the intervention of the prescribing health care provider

## What does it mean to be “highly similar”?

- The proposed biosimilar product is shown to be highly similar to the reference product by extensively analyzing (i.e., characterizing) the structure and function of both the reference product and proposed biosimilar.



## What does it mean to have “no clinically meaningful differences”?

- The proposed biosimilar product has no clinically meaningful differences from the reference product in terms of **safety**, **purity**, and **potency** (safety and effectiveness)

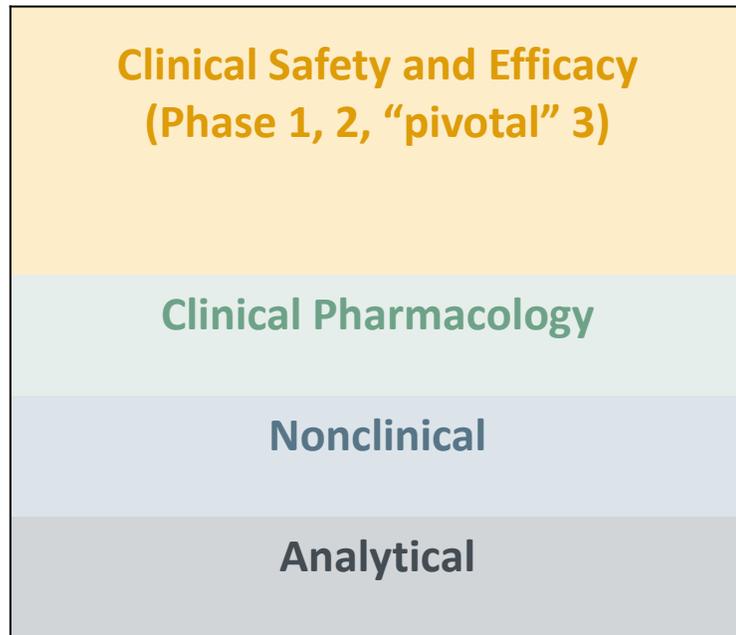
# FDA's Approach to the Development of Biosimilars

# Different Goals for “Stand-alone” vs. Biosimilar Development



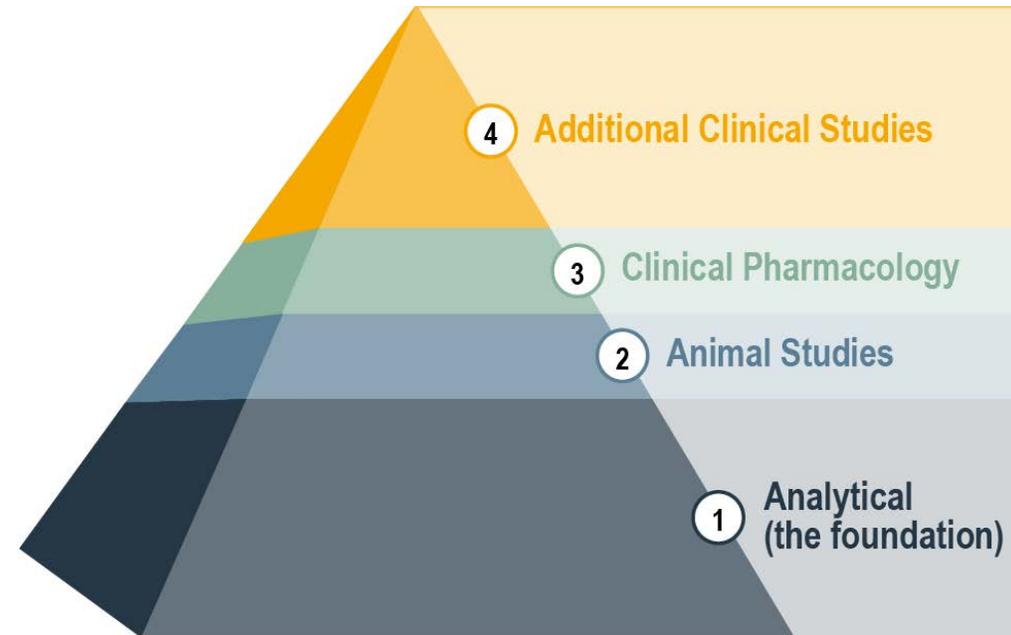
## “Stand-alone”: 351(a) BLA

Goal: To establish *de novo* safety and efficacy of a new product



## “Abbreviated”: 351(k) BLA

Goal: To demonstrate biosimilarity (or interchangeability) to a reference product

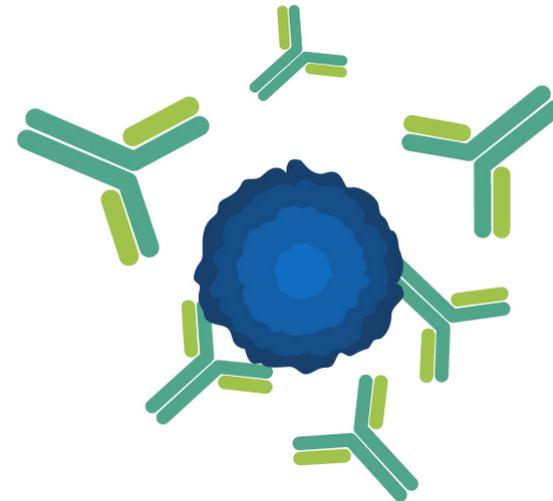
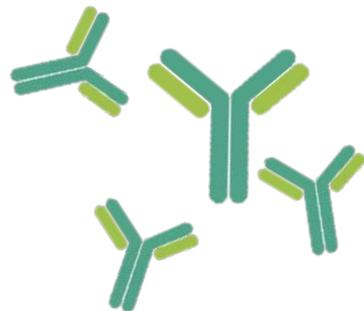


What does this difference mean from a development perspective?

# Immunogenicity

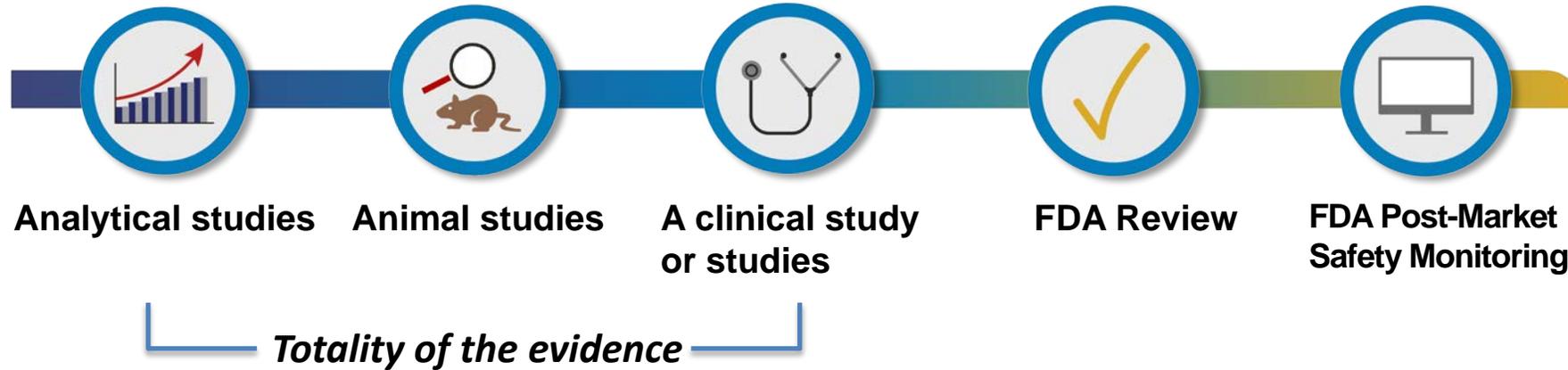


- Immunogenicity refers to the potential for the body to elicit an immune reaction in response to a biological product, which, in rare cases, may result in decreased efficacy of the product
- Biological products, including both reference products and biosimilar products, have a small risk of immunogenic response
- Biosimilar products are expected to have the same rate of immunogenic response as the reference product



# Summary

**Goal:** To establish biosimilarity between proposed product and reference product; not to re-establish safety and effectiveness.



Approval is based on the **integration of various information and the totality of the evidence submitted** by the applicant to provide an overall assessment that the proposed product is biosimilar to the reference product.

# Using Biosimilar and Interchangeable Products

# Using Reference, Biosimilar, and Interchangeable Products



- Patients and health care providers *can be confident in the **safety** and **effectiveness** of a biosimilar product* as for the reference product.
  - All approved reference products and biosimilar products meet FDA's *rigorous standards* for the indications described in product labeling.
- Once available in the U.S., states may permit a pharmacist to substitute an interchangeable product for the reference product without consulting the prescriber.

**Biosimilar & Original Biologic**

- ✓ Same benefits
- ✓ Same potential side effects
- ✓ Same strength and dosage
- ✓ Given the same way

Biosimilars are made with the same types of natural sources as the original biologic they were compared to — and **provide the same treatment benefits.**

The infographic features a smartphone-like frame on the left containing a list of four checked items. To the right, a text box explains that biosimilars use the same natural sources as the original biologics and provide the same treatment benefits. The text "provide the same treatment benefits." is highlighted in a red box.

# What to expect with a Biosimilar?



- Approved prescribing information summarizes the scientific information health care practitioners need for safe and effective use of the product.
- Labeling:
  - The Highlights Section contains a “Biosimilarity Statement” describing the biosimilar product’s relationship to its reference product
  - A biosimilar product is not required to have the same labeling as its reference product. Biosimilar product labeling may differ from the reference product labeling for a variety of reasons
  - **For specific product information, visit [Drugs@FDA](mailto:Drugs@FDA)**



# Key Takeaways



- **Fact:** FDA's high standards for approval means healthcare professionals and patients can be confident in the safety and effectiveness of a biosimilar product.
- **Fact:** Minor differences between the biosimilar and reference product are expected due to their complexity but generally do not result in clinically meaningful differences.
- **Fact:** Biosimilar labeling is not required to be the same as the reference product, but will often be similar.
- **Fact:** FDA's approval of an interchangeable biological product does not indicate a higher standard of biosimilarity.
- **Fact:** Patients and healthcare providers do not need to wait for a biosimilar product to "become" an interchangeable product (as there may be business reasons a sponsor does not seek interchangeability). Biosimilars are safe and effective, just like the reference product they were compared to.

# Resources for Health Care Providers

# Purple Book



Currently, the Purple Book is available as a PDF format on FDA.gov.



Home / Drugs / Development & Approval Process | Drugs / How Drugs are Developed and Approved / Types of Applications / Therapeutic Biologics Applications (BLA) / Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations

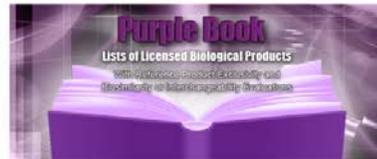
## Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations

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Therapeutic Biologics Applications (BLA)

Biosimilars

The "Purple Book" lists biological products, including any biosimilar and interchangeable biological products, licensed by FDA under the Public Health Service Act (the PHS Act).



The Purple Book includes the date a biological product was licensed under 351(a) of the PHS Act and whether FDA evaluated the biological product for reference product exclusivity under section 351(k)(7) of the PHS Act.

The Purple Book, in addition to the date licensed, also includes whether a biological product licensed under section 351(k) of the PHS Act has been determined by FDA to be biosimilar to or interchangeable with a reference biological product (an already-licensed FDA biological product). The Patient Protection and Affordable Care Act (Affordable Care

Content current as of: 11/18/2019

- CDER List of Licensed Biological Products (PDF - 217 KB) Updated: 4/21/2019
- CDER List of Licensed Biological Products (PDF - 140 KB) Updated: 11/18/2019
- More Information on the Lists

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Center for Biologics Evaluation and Research  
List of Licensed Biological Products with (1) Reference Product Exclusivity and (2) Biosimilarity or Interchangeability Evaluations to Date

BLA STN	PRODUCT (PROPE) NAME	PROPRIETARY NAME	DATE OF LICENSURE (mo/day/yr)	DATE OF FIRST LICENSURE (mo/day/yr)	REFERENCE PRODUCT EXCLUSIVITY EXPIRE DATE (mo/day/yr)	INTERCHANGEABLE/BIOSIMILAR (B)	WITHDRAWN
125296	Adenovirus Type 4 and Type 7 Vaccine, Live, Oral		01/12/2011				
102128	Albumin (Human)	Plasbumin-5; Plasbumin-20; Plasbumin-25; Albumin	0021/1942	NA	NA		
102452	Albumin (Human)	Buminate; Buminate 25N; Buminate 5N; Buminate 10N; Plasbumin	3/3/1954	NA	NA		
102893	Albumin (Human)		9/7/1975	NA	NA		
102265	Albumin (Human)	Albumin	10/1/1975	NA	NA		
102476	Albumin (Human)	Albumin	9/12/1976	NA	NA		
102892	Albumin (Human)	Albumin; Albumin-C; Albumin-20; Albumin-25	2/17/1985	NA	NA		
102895	Albumin (Human)		5/17/1989	NA	NA		
125154	Albumin (Human)		10/17/2006	NA	NA		
125284	Albumin (Human)	Infbumin	6/29/2011				
125444	Albumin (Human) Alpha Allergen: Cultural Keratins and Fibronectin in Bovine Collagen	ALBUMIND	6/19/2018				
125400		IGATU1	3/9/2012				
102174	Alpha-2-Proteinase Inhibitor (Human)	Protostat; Protostat-C	12/12/1987	NA	NA		
125208	Alpha-2-Proteinase Inhibitor (Human)	Protat; Protat NP	12/12/2002	NA	NA		
125278	Alpha-2-Proteinase Inhibitor (Human)	Zemana	1/8/2003	NA	NA		
125225	Alpha-2-Proteinase Inhibitor (Human)	Alsepa	7/12/2010				
102824	Animal Allergens, Standardized Cat Hair		7/12/1982	NA	NA		
102868	Animal Allergens, Standardized Cat Hair		9/12/1974	NA	NA		
102897	Animal Allergens, Standardized Cat Hair		9/12/1988	NA	NA		
102872	Animal Allergens, Standardized Cat Hair		9/12/1974	NA	NA		
102865	Animal Allergens, Standardized Cat Hair		12/19/1971	NA	NA		
102889	Animal Allergens, Standardized Cat Hair		9/12/1988	NA	NA		
102961	Animal Allergens, Standardized Cat Hair		9/12/1992	NA	NA		
102890	Animal Allergens, Standardized Cat Hair		3/12/1982	NA	NA		
125162	Antibiotic Immune Globulin (Human) (Source)	Antibiol	12/12/2015				
102821	Anti-toxin Vaccine (Adults)	Bot/Tetax	12/12/1975	NA	NA		
102180	Anti-thrombin Factor (Human)	Keate; Keate-Del	12/12/1974	NA	NA		
102448	Anti-thrombin Factor (Human)	Keate-Del	3/12/1994	NA	NA		
102863	Anti-thrombin Factor (Human)	Monoclonal-P; Monoclonal	9/18/1973	NA	NA		
102832	Anti-thrombin Factor (Recombinant)	Kogenate; Malsate PL; Kogenate PL	3/25/1993	NA	NA		
102875	Anti-thrombin Factor (Recombinant)	Recombinate; Bactate (Human)	12/12/1992	NA	NA		
102878	Anti-thrombin Factor (Recombinant)	ReFacto	3/6/2000	NA	NA		
125466	Anti-thrombin Factor (Recombinant)	Novaseg	10/12/2012				
125487	Anti-thrombin Factor (Recombinant), 0.35 IU/mL (pediatric)	ELCATICE	6/29/2014				
125274	Anti-thrombin Factor (Recombinant), Full Length	ECNATSE	3/16/2014				
125471	Anti-thrombin Factor (Recombinant), Clot-Specific anti...	SPINJECT	2/19/2010				
125264	Anti-thrombin Factor (Recombinant), Recombinant	ADHYNATICE	11/12/2015				
125261	Anti-thrombin Factor (Recombinant), Recombinant anti...	ant	6/29/2014				
125264	Anti-thrombin Factor (Recombinant), Plasma/Albumin Free Anti-thrombin Factor (Recombinant), Plasma/Albumin Free	SPINTECT; SPINTECT SOLUSIS	10/2/2009				
125263	Anti-thrombin Factor (Recombinant), Plasma/Albumin Free	Advate	10/2/2009	NA	NA		

## The new Purple Book database

FDA is working to digitize and expand the “Purple Book: Database of FDA-Licensed Biological Products” to:

- Improve transparency around approved biological product options
- Expand database access and functionality for users
- Advance public awareness about biosimilar products

# Purple Book Database's New Features

The future database will provide patients, payors, clinicians, and others with an accessible, easy-to-use online search engine with more information about FDA-approved biological products, including biosimilar and interchangeable biological products.

The searchable database will utilize new features tailored to different user needs, including:

- Main and advanced search options
- Auto-suggest search function
- Additional search filters
- Data download options
- Links to product labels
- Ability to show/hide sortable columns of information
- Ability to print or export search results



# Education and Outreach



- FDA is committed to developing materials and resources to improve understanding of biosimilars among patients, health care providers, and payors:
  - Engaging with health care professional and patient stakeholders
  - Developing educational materials for health care prescribers, pharmacists, and patients
  - Education is an undertaking that requires multi-stakeholder engagement
- FDA offers a variety of outreach materials for health care providers and patients:
  - Website with information for health care providers and patients
  - Health Care Professional Toolkit (4 Fact sheets, Infographics)
  - Webinars, Presentations and Articles
  - Video Series
  - Patient Materials
- Visit [www.fda.gov/biosimilars](http://www.fda.gov/biosimilars)

# Health Care Provider Materials



- Biosimilars
- Biosimilar and Interchangeable Products
- Biosimilar Development, Review, and Approval
- Prescribing Biosimilar and Interchangeable Products
- Biosimilar Product Information
- Industry Information and Guidance
- Webinars, Presentations, and Articles



## Biosimilars are safe, effective treatment options

Congress, through the Biologics Price Competition and Innovation Act (BPCI Act) of 2009, created an abbreviated licensure pathway for biological products that are demonstrated to be biosimilar to or interchangeable with an FDA-approved biological product. This pathway was established as a way to provide more treatment options, increase access to lifesaving medications, and potentially lower health care costs through competition.

### Biosimilars Action Plan (BAP)

New Educational Materials  
Learn more about biosimilars and check out our videos, fact sheets, shareable graphics, and other new resources

### FDA-approved biosimilars are safe, effective options for patients.

FDA-approved biosimilars have met the agency's rigorous standards for approval, and prescribers and their patients can count on the efficacy, safety and quality of these products.

Biological products, including biosimilars, are used to treat a wide variety of life-threatening and life-altering diseases. A biosimilar approved by FDA means rigorous standards and has no clinically meaningful differences from the reference product in terms of safety and effectiveness for the approved use. The availability of FDA-approved biosimilars in the U.S. means that patients may have access to more medications at a potentially lower price.

Visit [www.FDA.gov/biosimilars](http://www.FDA.gov/biosimilars) to learn more.

### Biological Product Definitions

**What is a biological product?**  
Biological products are regulated by the Food and Drug Administration (FDA) and are used to diagnose, prevent, treat, and cure diseases and medical conditions. Biological products are a diverse category of products and are generally large, complex molecules. These products may be produced through biotechnology in a living system, such as a microorganism, plant cell, or animal cell, and are often more difficult to characterize than small molecule drugs. There are many types of biological products approved for use in the United States, including therapeutic proteins (such as ligand), structural antibodies (such as adalimumab), and vaccines (such as those for influenza and tetanus).

**Reference Product**  
A reference product is the single biological product, already approved by FDA, against which a proposed biosimilar product is compared.

**Biosimilar Product**  
A biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.

**Interchangeable Product**  
An interchangeable product is a biosimilar product that meets additional requirements.

**What does it mean to be "highly similar"?**  
A manufacturer developing a proposed biosimilar demonstrates that its product is highly similar to the reference product by extensively analyzing its structure and function of both the reference product and the proposed biosimilar. These analyses are designed to demonstrate that the proposed biosimilar product is highly similar to the reference product. The manufacturer uses data from these comparative tests, along with other information, to demonstrate that the biosimilar is highly similar to the reference product.

**Minor differences between the reference product and the proposed biosimilar product in clinically critical components are acceptable.** For example, these could include minor differences in the excipient or buffer composition that is used in the reference product and the proposed biosimilar product. Any differences between the proposed biosimilar product and the reference product are carefully evaluated by FDA to ensure the biosimilar meets FDA's high approval standards.

**As mentioned above, slight differences (i.e., acceptable within-product variations) are expected during the manufacturing process for biological products, regardless of whether the product is a biosimilar or a reference product and are accounted for below.**

### Biosimilar Product Regulatory Review and Approval

**What is the approval process for biosimilar products?**  
An FDA-approved biological product, including reference products and biosimilar products, undergo a rigorous evaluation so that patients can be assured of the efficacy, safety, and quality of these products.

Conceptually, rather than generating the same full profile of nonclinical and clinical data as the reference product, a biosimilar product applicant may demonstrate that the proposed biosimilar product is highly similar to the reference product by using a "bridging" approach that most closely and appropriately necessary to demonstrate the safety and effectiveness. Specifically, the data and information necessary to demonstrate the safety and effectiveness of a reference product will include clinical trials for the disease indications being sought by the manufacturer.

**What data are required for approval of biosimilar or interchangeable product?**  
A biosimilar product applicant must provide data demonstrating similarity to the reference product.

**Additional studies demonstrating that the biosimilar is highly similar to the reference product, including non-clinical and clinical studies, may be required to demonstrate similarity to the reference product.**

**Additional studies, including an assessment of toxicity at a clinical study or studies sufficient to demonstrate safety and efficacy of the proposed biosimilar product, as well as the safety and effectiveness of the reference product, may be required for approval of an interchangeable product.**

**What approval standards do interchangeable products have to meet?**  
A manufacturer of a proposed interchangeable product must show that the product is biosimilar to a reference product and that it can be expected to provide the same clinical result as the reference product in any given patient. The manufacturer must also demonstrate that, for a product administered to a patient more than once, there is no additional risk or reduced efficacy if a patient switches back and forth between an interchangeable product and a reference product, compared to using reference product without switching.

### Prescribing Interchangeable Products

**Can interchangeable products be substituted for reference products by pharmacists?**  
Once interchangeable biological products are available in the United States, some states may permit a pharmacist to substitute an interchangeable product for the reference product without consulting the prescriber or a practice commonly called pharmacy-level substitution.

Many states have laws that address pharmacy-level substitution, and the specific laws vary from state to state. For information about prescription and substitution laws, check with your state pharmacy board.

**Should a health care prescriber be concerned if his/her patient receives an interchangeable product in place of the prescribed reference product?**  
Prescribers and patients can expect that the interchangeable product will have the same clinical result as the reference product. Prescribers and their patients can be assured that an FDA-approved interchangeable product has been thoroughly tested and has met FDA's high standards for approval. Meeting these standards means that health care professionals and patients can be assured of the safety and effectiveness of an interchangeable product, just as they would be for a reference product.

**Where can you find more information about interchangeable products?**  
FDA's "List of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluation," known as the "Purple Book," is an online resource for health care professionals and patients to learn more about approved biological products. The Purple Book provides information about whether a biological product is a reference product, biosimilar, or interchangeable product.

**Product-specific information, including a summary of results of the data that were used to support approval of biological product, can be found at the DrugDossier.gov. You can also visit [www.fda.gov/biosimilars](http://www.fda.gov/biosimilars).**

### Prescribing Biosimilar Products

**Can biosimilars be substituted for reference products by pharmacists?**  
When FDA carries out a scientific review of a proposed biosimilar, the evaluation does not include a determination of whether the biosimilar can be substituted for the reference product at the pharmacy. Substitution of a biosimilar for a reference product is a matter of state pharmacy law and is a decision primarily outside of FDA's regulatory purview.

Many states have laws that address substitution of biological products at the pharmacy level. It is important to note that pharmacy practices vary from state to state.

**What is the difference between receiving a reference product and a biosimilar product?**  
Patients and their physicians can expect that there will be no clinically meaningful differences between taking a reference product and a biosimilar when these products are used as intended. All reference products and biosimilar products meet FDA's rigorous standards for approval for the indications (medical condition described in product labeling). Once a biosimilar has been approved by FDA, patients and health care providers can be assured of the safety and effectiveness of the biosimilar, just as they would for the reference product.

**Where can you find more information about biosimilar products?**  
FDA's "List of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluation," known as the "Purple Book," is an online resource for health care professionals and patients to learn more about approved biological products. The Purple Book provides information about whether a biological product is a reference product, biosimilar, or interchangeable product.

**Product-specific information, including a summary of results of the data that were used to support approval of biological product, can be found at the DrugDossier.gov. You can also visit [www.fda.gov/biosimilars](http://www.fda.gov/biosimilars).**

## WHAT IS A BIOSIMILAR?

**A biosimilar is a biological product**

FDA-approved biosimilars have been compared to an FDA-approved biologic, known as the reference product. Reference and biosimilar products are:

- Large and generally complex molecules
- Produced from living organisms
- Carefully monitored to ensure consistent quality

**A biosimilar is highly similar to a reference product**

For approval, the structure and function of an approved biosimilar were compared to a reference product, looking at key characteristics such as:

- Purity
- Molecular structure
- Bioactivity

The data from these comparisons must show that the

**A biosimilar has no clinically meaningful differences from a reference product**

Studies were performed to show that biosimilars have no clinically meaningful differences in safety, purity, or potency (safety and effectiveness) compared to the reference product:

- Pharmacokinetic and pharmacodynamic studies
- Immunogenicity assessment
- Additional clinical studies as needed

Studies may be done independently or combined.

**A biosimilar is approved by FDA after rigorous evaluation and testing by the applicant**

Prescribers and patients should have no concerns about using these medications instead of reference products because biosimilars:

- Meet FDA's rigorous standards for approval
- Are manufactured in FDA-licensed facilities
- Are tracked as part of post-market surveillance to ensure continued safety

Visit [www.FDA.gov](http://www.FDA.gov) to learn more about biosimilars.

# Patient Materials

- Uses patient-friendly language and imagery
- Addresses topics, concerns, and misconceptions shown to be most important to patients
- Tested with patient advocacy organizations and with patients treated with a biologic



**Biosimilar Basics**

Biosimilars are safe and effective biologic medications for treating many illnesses such as chronic skin and bowel diseases, arthritis, kidney conditions and cancer.

Biologic medications are generally made from **natural sources** and developed using advanced science. Biosimilars are **FDA-approved** medications that are compared to another medication — the original biologic.

Biosimilars are made with the same type of natural source as the original biologic they were compared to — and **provide the same treatment benefits.**

**Benefits:** More options, More competition in the health care market, Lower costs.

Biosimilars may provide patients with **more access** to important treatments.

Biosimilars are approved by FDA after a **careful review** of data, studies, and tests. FDA monitors the **safety** and **effectiveness** of all medications after their approval.

Check for medication quality during production. Report patient safety issues.

Visit [www.FDA.gov/biosimilars](http://www.FDA.gov/biosimilars) and talk with your doctor to learn more.

U.S. FOOD & DRUG ADMINISTRATION

# Future Education and Outreach Plans



- Continue developing materials and resources for patients:
  - Videos
  - Additional infographics and graphics
  - Enhanced Social Media Strategy
- Create additional materials and resources for health care providers:
  - One-pager to address misconceptions
  - Educational curriculum/teaching resources for medical, nursing, and pharmacy schools
  - Updated Continuing Education Course
- Develop and revise materials as needed based on research/feedback

# Resources

- Visit [www.fda.gov/biosimilars](http://www.fda.gov/biosimilars) for access to all the education materials and information about biosimilar and interchangeable products
- Visit the [www.fda.gov/purplebook](http://www.fda.gov/purplebook) for information on biological products, including if products are biosimilar to a reference product
- Visit [www.fda.gov/drugsatfda](http://www.fda.gov/drugsatfda) (**Drugs@FDA**) for information on all FDA approved drug products, including labeling and review information.



# References



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# Questions?



Thank You

[www.fda.gov/biosimilars](http://www.fda.gov/biosimilars)

