
# State of Biosimilars and Generics 2023

Access! AAM Annual Meeting
February 14, 2023

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U.S. FOOD & DRUG ADMINISTRATION

# Disclosures

- No financial disclosures

- This presentation represents the views of the speaker and not necessarily those of FDA

# Innovation and Access

- Meeting Public Health Needs
- Facilitating Approvals
- Regulatory Science Drives Policy
- FDA Guidance
- Inspections Post-COVID
- Other Priorities

# Generic Drugs and Patient Impact

**Generic drugs increase access**

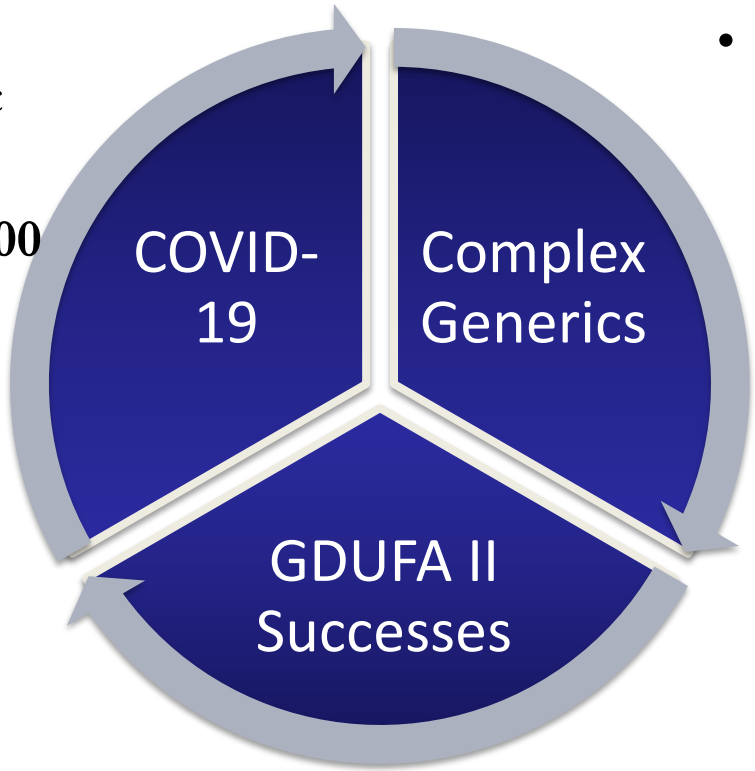
- More treatment **choices**
- More **competition**
- Lower **cost**

- In 2021, generic drugs generated **$365 billion** in savings
- The top three conditions that generated savings for patients by using generics instead of the brand alternative are:
  - **$96.7** billion for patients diagnosed with heart disease
  - **$59.7** billion for patients suffering from mental illness
  - **$56.7** billion for persons living with diabetes
- The average copay for brand-name drugs is **$56.12**; the average generic copay is only **$6.16**.
- Generics represent only **3%** of total health care spending.

AAM U.S. Generic & Biosimilar Medicine Savings Report, 2022

# GDUFA II Highlights

- Prioritized assessment of **COVID-19** generic drug submissions:
  - **More than 1700 COVID-related approval actions**
  - **100+** original ANDAs




- **4,792 Abbreviated New Drug Applications** (ANDAs) approved or tentatively approved, including
  - **490 first generics**
  - **553 complex generics**

- **Pre-ANDA Program**
- **Product-Specific Guidances**
- **GDUFA Science and Research Program**
- **Controlled Correspondence**



*Data as of 10/12/22*

# BIOSIMILARS

# Timeline of Biosimilar and Interchangeable Biosimilar Approvals

Biosimilars

Interchangeable Biosimilars

**2015**

03/06/15
**Zarxio (filgrastim-sndz)**

**2016**

04/05/16
**Inflectra (Infliximab-dyyb)**
08/30/16
Erelzi (etanercept-szzs)
09/23/16
**Amjevita (adalimumab-atto)**

**2017**

04/21/17
**Renflexis (Infliximab-abda)**
08/25/17
Cyltezo (adalimumab-adbm)
09/14/17
**Mvasi (bevacizumab-awwb)**
12/01/17
**Ogivri (trastuzumab-dkst)**
12/13/17
Ixifi (infliximab-qbtx)

**2018**

05/15/18
**Retacrit (epoetin alfa-epbx)**
06/04/18
**Fulphila (pegfilgrastim-jmdb)**
07/20/18
**Nivestym (filgrastim-aafi)**
10/30/18
Hyrimoz (adalimumab-adaz)
11/02/18
**Udenyca (pegfilgrastim-cbqv)**
11/28/18
**Truxima (rituximab-abbs)**
12/14/18
**Herzuma (trastuzumab-pkrb)**

**2019**

01/18/19
**Ontruzant (trastuzumab-dttb)**
03/11/19
**Trazimera (trastuzumab-qyyp)**
04/25/19
Eticovo (etanercept-ykro)
06/13/19
**Kanjinti (trastuzumab-anns)**
06/27/19
**Zirabev (bevacizumab-bvzr)**
07/23/19
**Ruxience (rituximab-pvvr)**
07/23/19
Hadlima (adalimumab-bwwd)
11/04/19
**Ziextenzo (pegfilgrastim-bmez)**
11/15/19
Abrilada (adalimumab-afzb)
12/6/19
**Avsola (infliximab-axxq)**

**2020**

06/10/20
**Nyvepria (pegfilgrastim-apgf)**
07/06/20
Hulio (adalimumab-fkjp)
12/17/20
**Riabni (rituximab-arrx)**

**2021**

7/28/21
**Semglee (insulin glargine-yfgn)**

09/17/21
**Byooviz (ranibizumab-nuna)**

10/15/21
Cyltezo (adalimumab-adbm)

12/17/2021
Yusimry (adalimumab-aqvh)

Rezvoglar (insulin glargine-aglr)

**2022**

02/2022
**Releuko (filgrastim-ayow)**
04/2022
**Alymsys (bevacizumab-maly)**
5/26/2022
**Fylnetra (pegfilgrastim-pbbk)**
09/01/22
Stimufend (pegfilgrastim-fpgk)
09/27/22
Vegzelma (bevacizumab-abcd)
12/13/22
Idacio (adalimumab-aacf)

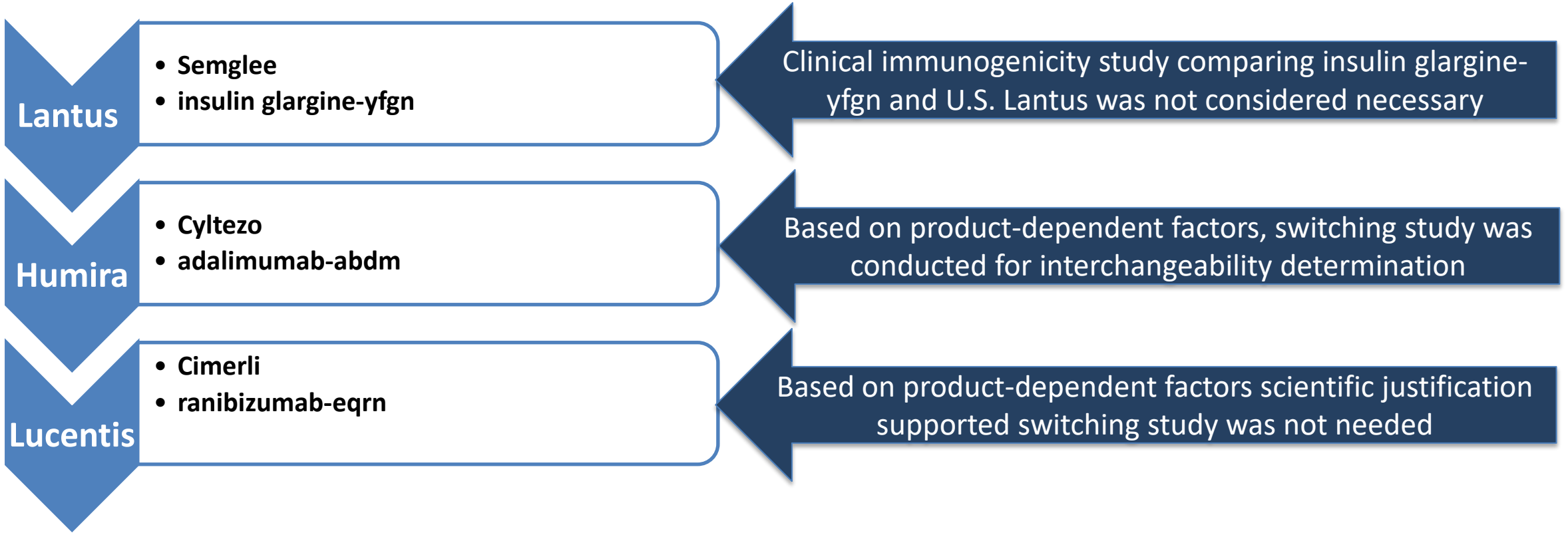
08/2/2022
**Cimerli (ranibizumab-eqrn)**

**40 Approved**

**27 Currently marketed**

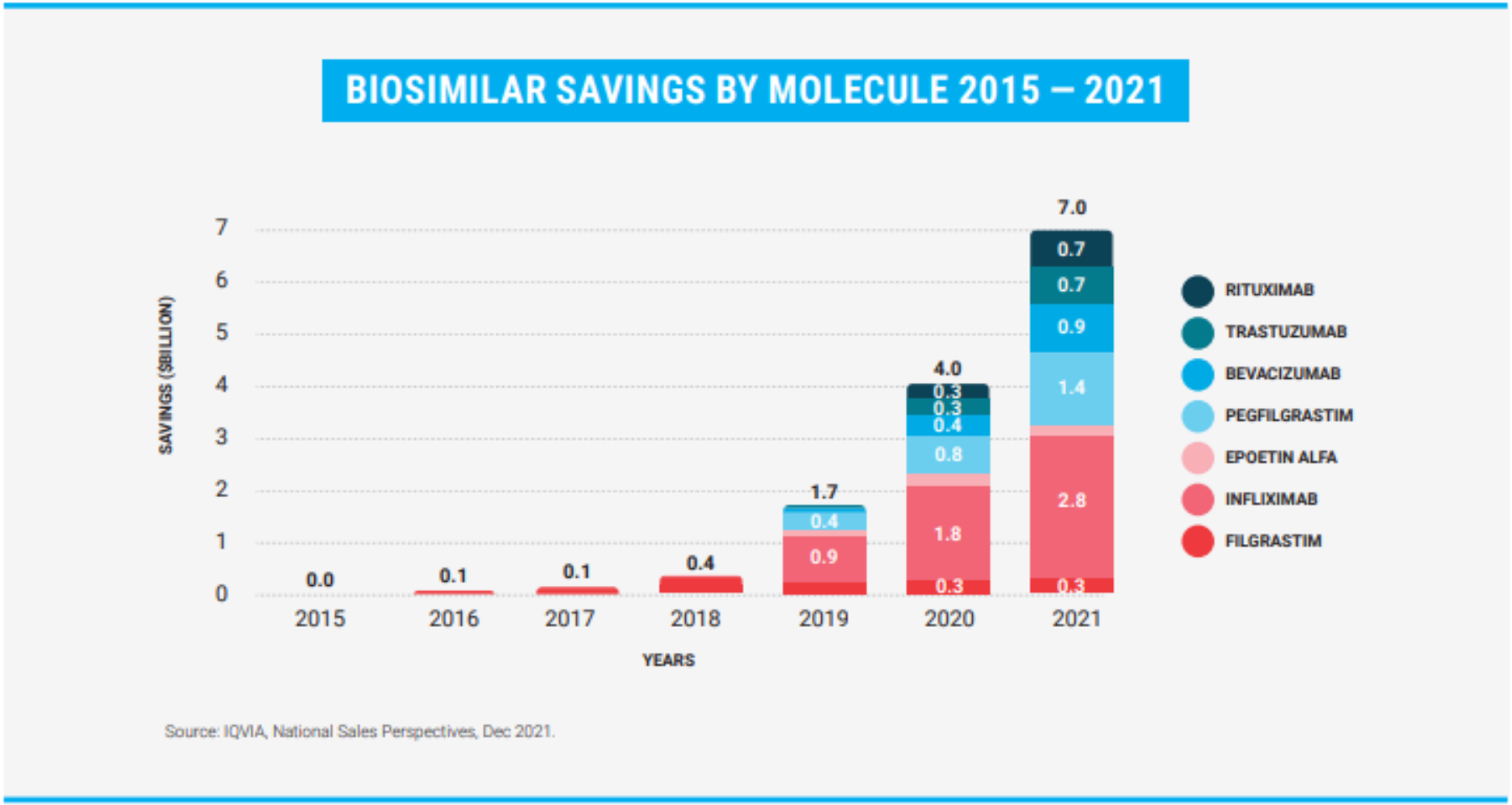
https://www.fda.gov/drugs/biosimilars/biosimilar-product-information

# Interchangeable Biosimilars



# Biosimilar Savings Totaled $7 Billion in 2021

SINCE 2015, BIOSIMILARS HAVE GENERATED $13.3 BILLION IN SAVINGS




Source: IQVIA, National Sales Perspectives, Dec 2021.

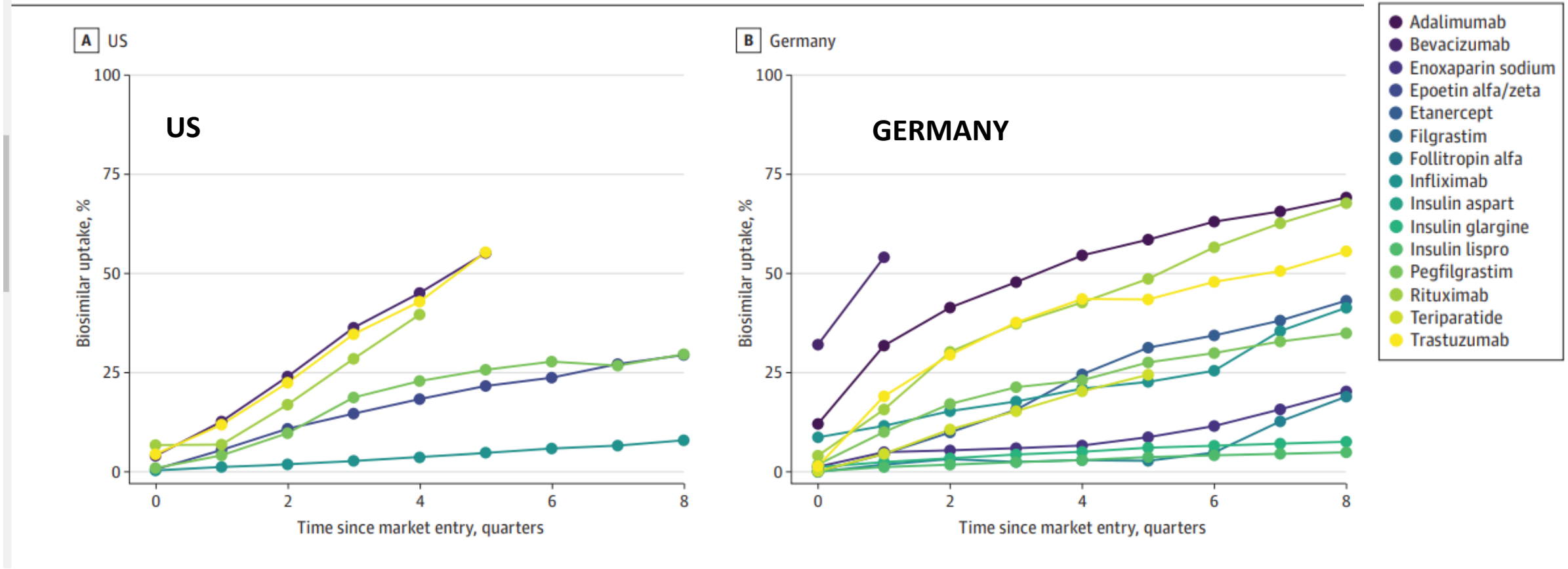
SOURCE: AAM / THE U.S. GENERIC & BIOSIMILAR MEDICINES SAVINGS REPORT 2022

Original Investigation | Health Policy

# Comparison of Uptake and Prices of Biosimilars in the US, Germany, and Switzerland

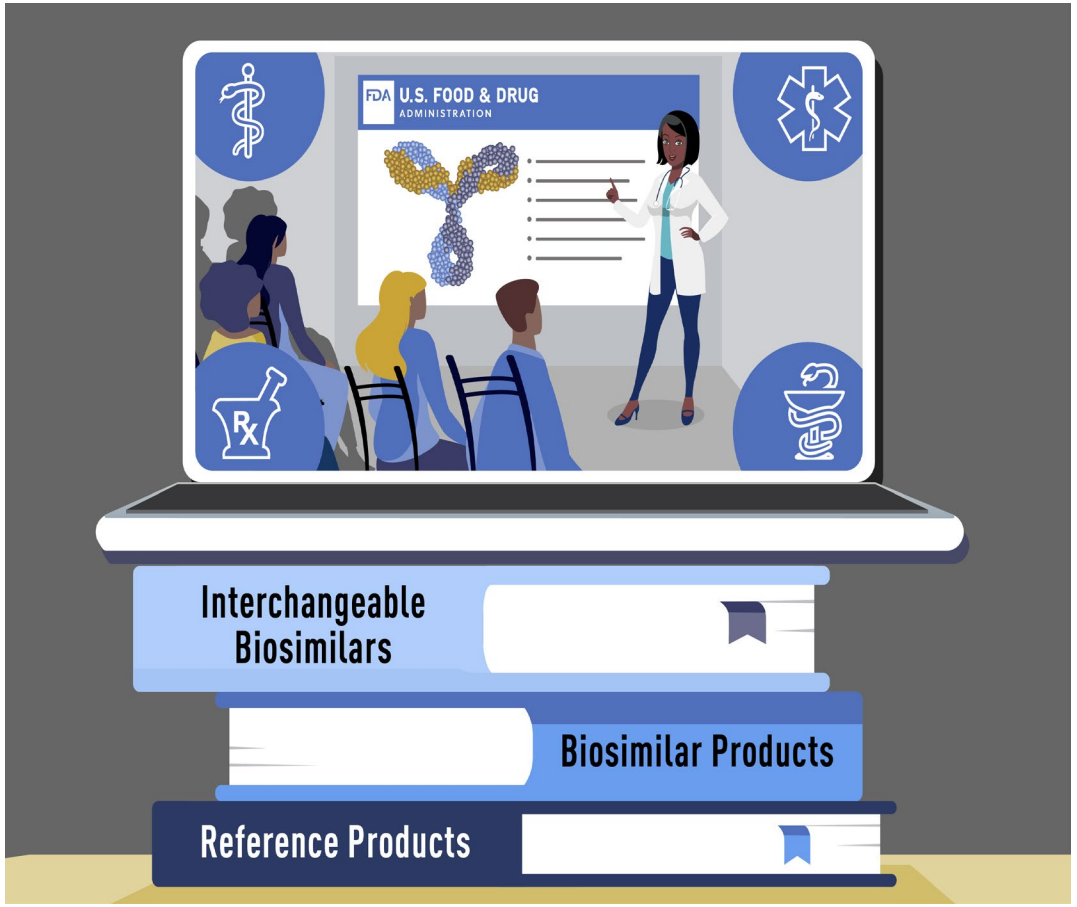
David L. Carl, MSc; Yannic Laube, BA; Miquel Serra-Burriel, PhD; Huseyin Naci, PhD; Wolf-Dieter Ludwig, MD; Kerstin N. Vokinger, MD, JD, PhD, LLM

Figure 1. Uptake of Biosimilars in the US, Germany, and Switzerland



# Curriculum for Healthcare Professional Programs

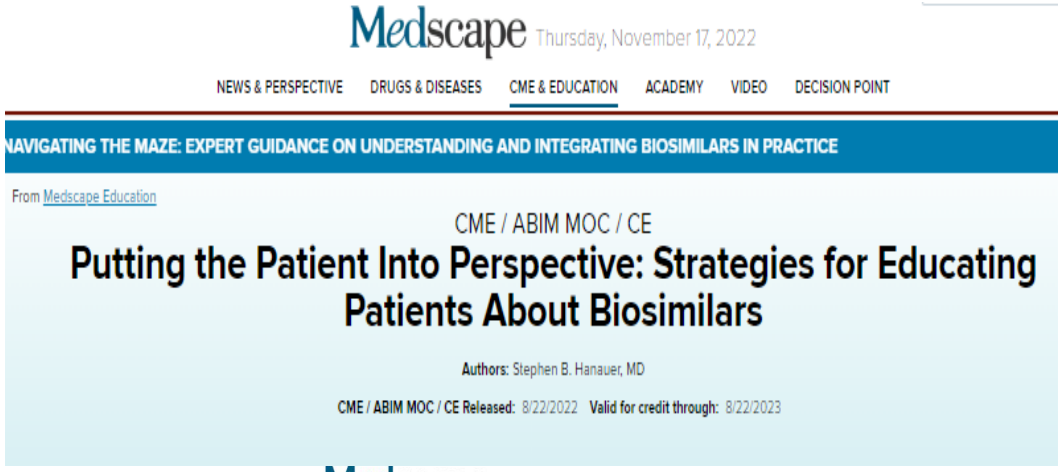
- The Biosimilar Curriculum Toolkit contains multiple types of materials to help faculty integrate biosimilars and interchangeable products into the education and professional training of healthcare students.
- Goal is to increase knowledge and real-world application of concepts among students in healthcare degree programs (Medicine, Nursing, Physician Asst./Assoc., and Pharmacy).
- Materials are designed to meet a variety of needs and are divided into 2 levels of content.

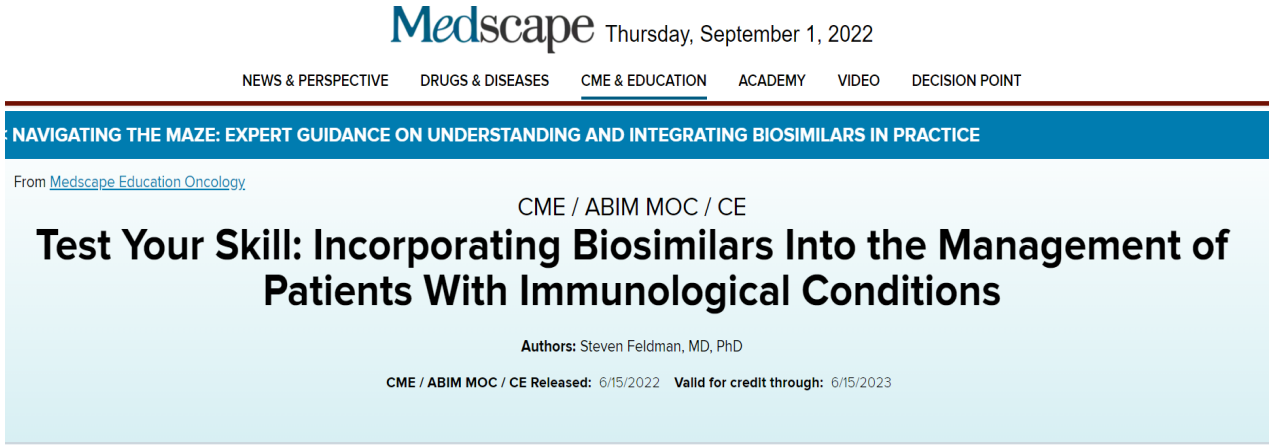


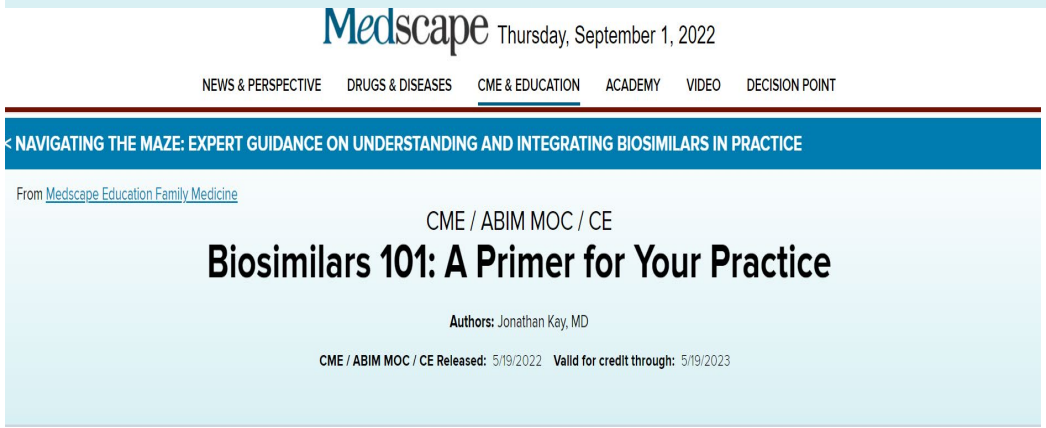

https://www.fda.gov/drugs/biosimilars/curriculum-materials-health-care-degree-programs-biosimilars

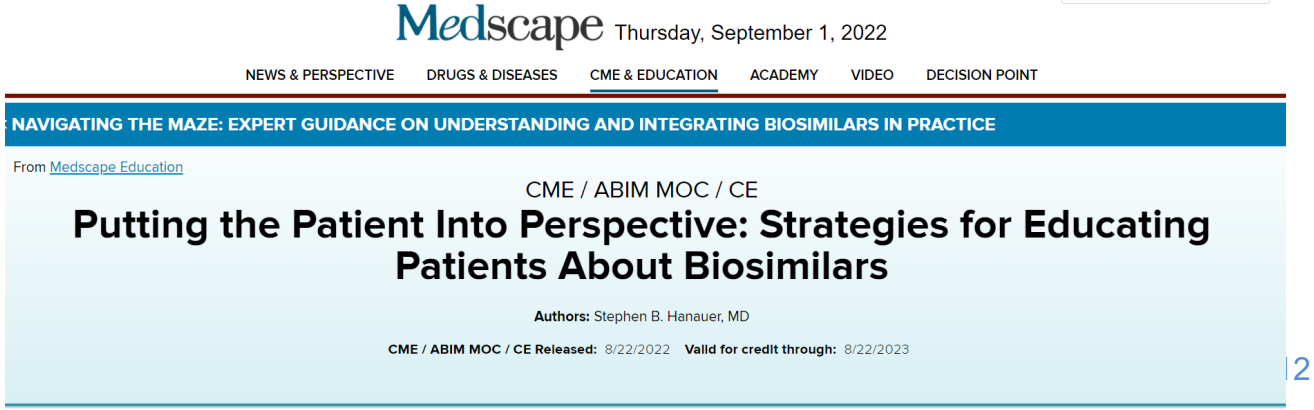
# Medscape Continuing Education

FDA is supporting the development of a series of continuing education (CE) courses through Medscape about biosimilar and interchangeable products. This includes 4 courses in 2022 and a dedicated website for the content.



# FDA Biosimilar Materials for Patients



# FDA Biosimilar Materials in Spanish




Artículos en español

- Alimentos y Bebidas
- Cosméticos
- Dispositivos Médicos
- Dispositivos que Emiten Radiación
- Fraude en la Salud
- Medicamentos
- Nutrición
- Productos de Tabaco
- Productos Veterinarios
- Salud de la Mujer
- Salud Infantil
- Vacunas, Sangre y Productos Biológicos

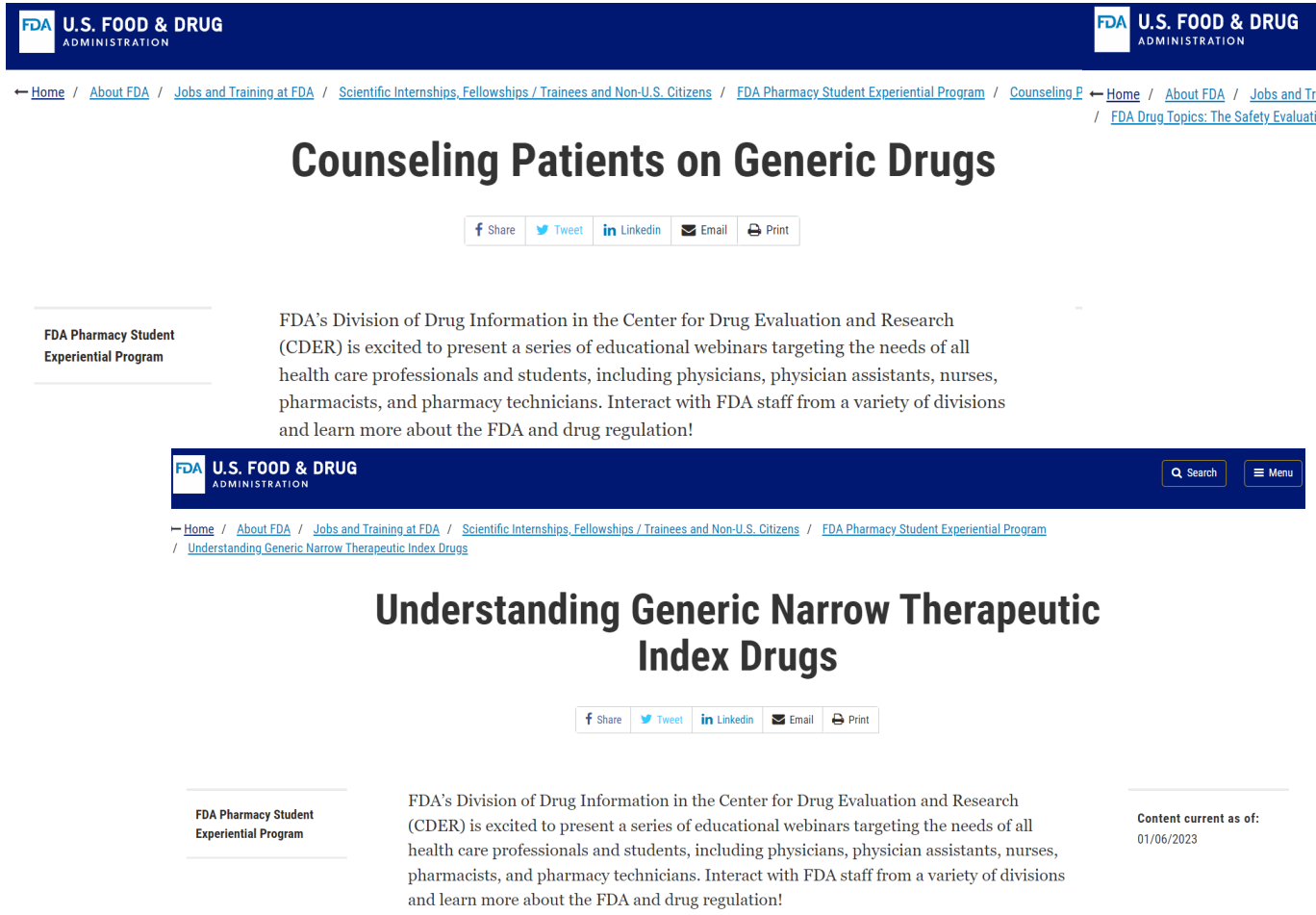
English

La Administración de Alimentos y Medicamentos de los EE.UU. (FDA, por sus siglas en inglés) ha aprobado medicamentos biosimilares para tratar enfermedades como el cáncer, la enfermedad de Crohn, la colitis, la artritis reumatoide, la psoriasis y otras.

Pero, ¿qué son los medicamentos biosimilares y biológicos intercambiables? Para

# Division of Drug Information (DDI) Continuing Education

In 2022 FDA supported a series of educational webinars on **generic drug topics** targeting the needs of all health care professionals and students, including physicians, physician assistants, nurses, pharmacists, and pharmacy technicians. More than 2,400 health care professionals attended these webinars live, including those from countries like Canada, Germany, Nigeria, and many more!



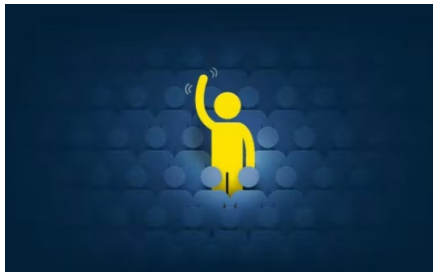

# GDUFA and BsUFA III

# Advancing Earlier Cycle Approvals- GDUFA III

Reduce Review cycles by maximizing each cycle –
Imminent approval/ goal date extensions as appropriate

Facilitate Pre-submission Facility Correspondence Pathway


- ✓ Expand options for advice after a complete response letter (CRL) by **adding to scope of controlled correspondence**
- ✓ **Post-CRL scientific meetings** in certain cases
- ✓ Opportunities to communicate when **changes in product-specific guidances that impact ongoing bioequivalence studies**



New goals around responses to **suitability petitions** to facilitate development of new ANDAs for a different route of administration, strength, dosage form, or one different active ingredient in a fixed-combination drug product from a reference listed drug

# BsUFA III: Advancing Access through Streamlined Review

- Introduces **new supplement categories and timelines** to expedite the review of supplements.

- Includes **faster review timelines** for safety labeling updates and labeling updates to add or remove an indication where FDA does not need to review efficacy data.

# Supplements

- Enhancements to the supplement categories and timelines

| Category | Goal | Letter |
|---|---|---|
| **Category A** (original and resubmitted)<br>Safety labeling updates | **3 months** of the receipt date<br>FY2023: 70%, FY2024: 80%, FY2025-2027: 90% | Within **60 calendar days** of receipt, FDA will issue a letter acknowledging receipt of the submission and provide a date for FDA to take action.<br>FY2023-2027: 90% |
| **Category B** (original and resubmitted)<br>Adding an indication w/o new data sets<br>**Category C** (original and resubmitted)<br>Removing an approved indication | **4 months** of the receipt date<br>FY2023: 70%, FY2024: 80%, FY2025-2027: 90% | |
| **Category D** (original and resubmitted)<br>Adding an indication w/ new data sets (other than efficacy) | **6 months** of the receipt date<br>FY2023: 70%, FY2024: 80%, FY2025-2027: 90% | |
| **Category E** (original)<br>Adding an indication w/ efficacy data sets<br>**Category F** (original)<br>Seeking initial determination of interchangeability | **10 months** of the receipt date<br>FY2023-2027: 90% | Within **74 calendar days** of receipt, FDA will issue a filing letter.<br>FY2023-2027: 90% |
| **Category E** (resubmitted)<br>**Category F** (resubmitted) | **6 months** of the receipt date<br>FY2023-2027: 90% | |

# BsUFA Meeting Management

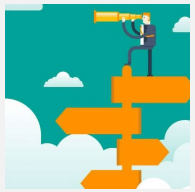
- Modifies the **Biosimilar Initial Advisory meeting so preliminary comparative analytical data is no longer required to meet with FDA.**

- Introduces a **new Biosimilar Product Development meeting type: Type 2a, focused on a narrow set of issues**.
  - No more than two issues and associated questions, requiring input from no more than three disciplines or review divisions.

- Consistent with PDUFA VII, introduces a new **follow-up opportunity for sponsors** to submit clarifying questions after meetings or WROs to ensure sponsor's understanding of FDA feedback.

# Science Drives Policy

# GDUFA Science and Research



enables FDA to be proactive in addressing future challenges

enables FDA to be adaptive to emergent challenges

facilitates patient access to modern medicines

# Product-Specific Guidance

| | |
|---|---|
| **Nusinersen sodium intrathecal solution** | • First PSG for this class of oligonucleotide drugs<br>• Provided recommendations on assessing pharmaceutical equivalence and bioequivalence for this complex product |
| **Vasopressin solution** | • GDUFA research was critical to facilitating the generic development of this life-saving medication |
| **Exenatide subcutaneous suspension (1&2)** | • For the first time recommended two in vivo pharmacokinetic BE study options for this diabetes medication |

# Generic Drug User Fee Amendment (GDUFA) Science and Research Priority Initiatives for 2023

1. Develop Methods for Generics to Address Impurities such as Nitrosamines

2. Enhance the Efficiency of BE Approaches for Complex Active Ingredients

3. Enhance the Ef4. Enhance the Efficiency of BE Approaches for Complex Routes of Delivery

4. Improve Efficiency of BE Approaches for Complex Dosage Forms and Formulations

5. Enhance the Efficiency of BE Approaches for Complex Drug-Device Combination Products

6. Improve the Efficiency of BE Approaches for Oral and Parenteral Generic Products

7. Facilitate the Utility of Model-Integrated Evidence (MIE) to Support Demonstrations of BE

- https://www.fda.gov/media/162554/download

# Enhancing Approval of Complex Generics

- **New goal for completion of product specific guidances (PSGs) for complex products**
- Establish new teleconference/meeting when PSG impacts ongoing bioequivalence studies

**Enhance Communications around Review**

- **Focus Pre-submission meetings** on key issues for review and assure review team participates
- Create option for more **enhanced scientific mid-cycle meeting** with goal of resolving more substantive issues within a single review cycle
- Establish **new post-CRL scientific meeting** to facilitate subsequent cycle approval

**FDA Approves First Generic of Symbicort to Treat Asthma and COPD**

**FDA Approves First Generic of Restasis**

# Regulatory Science – BsUFA III

# Regulatory Science – BsUFA III

- Pilots a BsUFA regulatory science program broadly applicable to biosimilar and interchangeable biological product development. Project goals should not be specific to a product or product class.

- **Two demonstration projects:**
  - Advancing the Development of Interchangeable Products
  - Improving the Efficiency of Biosimilar Product Development

- **Stakeholder engagement:**
  - Includes a public meeting on or before Oct. 2025 to review progress and solicit input on future priorities
  - In advance of the meeting, FDA will issue an interim report on project progress
  - Publish final summary report on pilot outcomes in FY2027

- **Deliverables:**
  - Publish a comprehensive strategy document within 12 months of completing the projects


# Released January 25, 2023
# Comments Due April 5, 2023

The Roadmap:

- highlights scientific areas where advancement is expected to impact science-based recommendations and regulatory decision making.

  1) Increasing the accuracy and capability of analytical (structural and functional), and chemistry, manufacturing, and controls (CMC) characterizations

  2) Developing alternatives to and/ or reducing the size of studies involving human participants

Researchers, both external and internal to FDA, should use this roadmap to guide research proposals, collaborations, and other efforts as they seek BsUFA III research funding

# Regulatory Science: Recent Research Awards

## Improving the Efficiency of Biosimilar Development

- **Assessment of the performance of Multi-Attribute Method (MAM) vs conventional Quality Control (QC) methods** (USP Pharmacopeia)
- **Platform for reliable characterization and evaluation of comparability of biosimilar drug products in lyophilized and liquid formulations** (National Institute for Pharmaceutical Technology and Education)
- **Systematic Analytical Characterization of Innovator and Biosimilar Products with the Focus on Post-translational Modifications** (University of Michigan – Ann Arbor)

## Advancing the Development of Interchangeable Products

- **CHO protein impurity immunogenicity risk prediction for improving biosimilar product development and assessing product interchangeability** (Epivax)
- **Improving the Efficiency of Regulatory Decisions for Biosimilars and Interchangeable Biosimilars by Leveraging Real-World Data** (Academy of Managed Care Pharmacy)

# Regulatory Science – Next Steps

- New Funding Announcement to open Winter 2023
- Provide comments on research road map docket by April 5th
- Interim report and public meeting on or before Oct 25, 2025 (as outlined in commitment letter)
- Visit the biosimilar research website - Biosimilars | Science and Research | FDA


# GUIDANCE DEVELOPMENT

# Recent Generic Guidances

Controlled Correspondence Related to Generic Drug Development
Guidance for Industry
***DRAFT GUIDANCE***

Statistical Approaches to Establishing Bioequivalence
Guidance for Industry

Sameness Evaluations in an ANDA — Active Ingredients
Guidance for Industry

Failure to Respond to an ANDA Complete Response Letter Within the Regulatory Timeframe
Guidance for Industry

# BsUFA Guidance Updates

## Guidance for labeling of interchangeable products (9/30/2023)

- Draft biosimilar labeling guidance may be updated to include interchangeable products

## Guidance for formal meetings with industry (9/30/2023)

- 2018 draft guidance on meetings with industry can be updated

## Guidance on classification of new supplement types (9/30/2023)

- Work is currently underway

## Best practices in communications (12/31/2023)

- Workshop on Best Practices in Communication held on 5/11/2022.
- Report received from Eastern Research Group (ERB) currently under review

## Guidance for device/presentations/CC for interchangeables (9/30/2025)

# INSPECTIONS

- FDA has conducted domestic inspections at standard operational levels since **October 2021**
- FDA resumed foreign facility surveillance inspections in **March 2022**
- FDA continues to **leverage a variety of tools** for facility assessment, including remote assessments and MRAs

# Optimized Approach for Regulatory Oversight Tools to Better Protect Public Health

**Conducting Remote Regulatory Assessments**

**Questions and Answers**

**Draft Guidance for Industry**

*Today, the FDA is releasing a draft guidance on the expanded use of remote regulatory assessments (RRAs) and how the FDA generally intends this tool, once finalized, to be incorporated consistently across all FDA-regulated products beyond the current COVID-19 public health emergency.*

July 2022

## BsUFA Commitment Letter

On or before **September 30, 2023, FDA will issue draft guidance on the use of alternative tools to assess manufacturing facilities named in pending applications (e.g., requesting existing inspection reports from other trusted foreign regulatory partners through mutual recognition and confidentiality agreements, requesting information from applicants, requesting records and other information directly from facilities and other inspected entities, and, as appropriate, utilizing new or existing technology platforms to assess manufacturing facilities**). The guidance will incorporate best practices, including those in existing published documents, from the use of such tools during the COVID-19 pandemic.

# Update on GDUFA III DMF Enhancements

- **Section VI E of the Commitment Letter: DMF Review Prior to ANDA Submission**
- FDA implemented a DMF prior assessment process for on October 1, 2022
- FDA provided the following additional support to stakeholders for this new process:
  - Draft Guidance: ***Review of Drug Master Files in Advance of Certain ANDA Submissions Under GDUFA issued October 3, 2022***
  - Stakeholder Education: **Q&A at the SBIA DMF Workshop: GDUFA III Enhancements and Structured Data Submissions on November 30, 2022**
- Initial projections were that at least 80 DMFs would qualify for prior assessment annually with the actual number *contingent on industry submitting a valid request to the DMF.*
- For the first quarter *only 1* DMF Prior Assessment request was received, and none have been granted.

# Trends in Biosimilar Inspections

- **Lower rate of alternative facility assessment approaches**
  - Facilities are generally new to biotechnology products or processes
- **Inspection may still be necessary for risks that are unique to biologic products**
  - Cell line being used is new to the facility (e.g., if a facility has limited experience with mammalian cell culture)
  - Manufacturing process is novel or has manufacturing operations unfamiliar to the facility
- **Continue to see inspection challenges with sites with prior inspectional and marketing history that are seeking first BLA approval**
  - Occurring even on repeat inspections
- **Encourage industry to focus efforts on understanding FDA expectations for biologics manufacturing and increasing quality of operations to support biologics approvals**

- 
Priorities
1.
2.
3.

# National Strategy for a Resilient Public Health Supply Chain

JULY 2021

https://www.phe.gov/Preparedness/legal/Documents/National-Strategy-for-Resilient-Public-Health-Supply-Chain.pdf

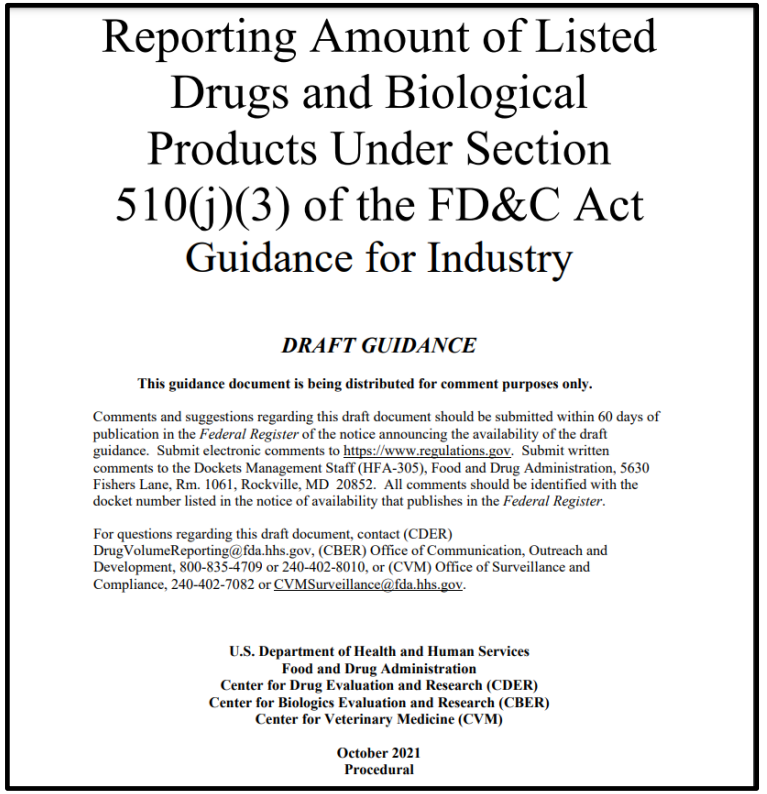
**Maintain end-to-end public health supply chain visibility:** Supply chain visibility is critical to the U.S. Government's ability to anticipate, prepare for, and respond to potential disruptions, particularly during a public health emergency. The U.S. Government is prepared to implement new supply chain situational awareness capabilities and authorities as well as establish a rhythm of regular supply chain illumination, analysis, and mapping. Expanding current supply chain visibility into critical public health and other all-hazard-scenario supplies requires 1) identifying and prioritizing the list of critical medical supplies/products for a pandemic response, and 2) prioritizing mapping and analysis of those products' supply chains, to include raw materials, components, manufacturers, distributors, and end users. Visibility should also extend to stockpiles, including federal, SLTT, and private-sector stores. These capabilities will allow the U.S. Government to identify vulnerabilities, predict and prevent supply chain disruptions, and mitigate risks.

**Sub-objectives: 1. Establish deep U.S. Government visibility into the medical supply chain through end-to-end supply chain data access—to include U.S. Government supply chain data—in a centralized HHS-managed technology platform that can be tied to epidemiological data.**

# Enhanced Focus on Supply Chain Surveillance

**Driven by the response to the COVID-19 pandemic, FDA expanded its drug shortage program to include supply chain surveillance that:**

- Integrates FDA data to help assess risk to critical medicines aiming for earlier detection and response to supply disruptions
- Used to inform a multimodal, cross-government response to shortages
- We are enhancing this system by investigating additional data sources and advanced analytics through a phased process to expand coverage to additional products
  - Integrating CARES amount reporting
  - Collaborating with the HHS Supply Chain Control Tower



Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act

Guidance for Industry

***DRAFT GUIDANCE***

**This guidance document is being distributed for comment purposes only.**

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) DrugVolumeReporting@fda.hhs.gov, (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010, or (CVM) Office of Surveillance and Compliance, 240-402-7082 or CVMSurveillance@fda.hhs.gov.

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**
**Center for Biologics Evaluation and Research (CBER)**
**Center for Veterinary Medicine (CVM)**

**October 2021**
**Procedural**

# Building Resiliency Requires Quality Manufacturing

- Prior to COVID-19 the majority of shortages were due manufacturing issues
- We continue to see problems at facilities, many of which manufacture older sterile injectables used for acute/ICU care, oncology, parenteral nutrition and ophthalmic drugs
- How do we do better?

# Efforts to Support Quality Manufacturing (Cont.)

- **Quality Management Maturity (QMM) – optimizes manufacturer's early detection of major variability**
  - quality management maturity (QMM) is achieved when drug manufacturers successfully integrate business and manufacturing operations with quality practices and technological advancements to optimize product quality, enhance supply chain resiliency, mitigate drug shortages, and drive continual improvement

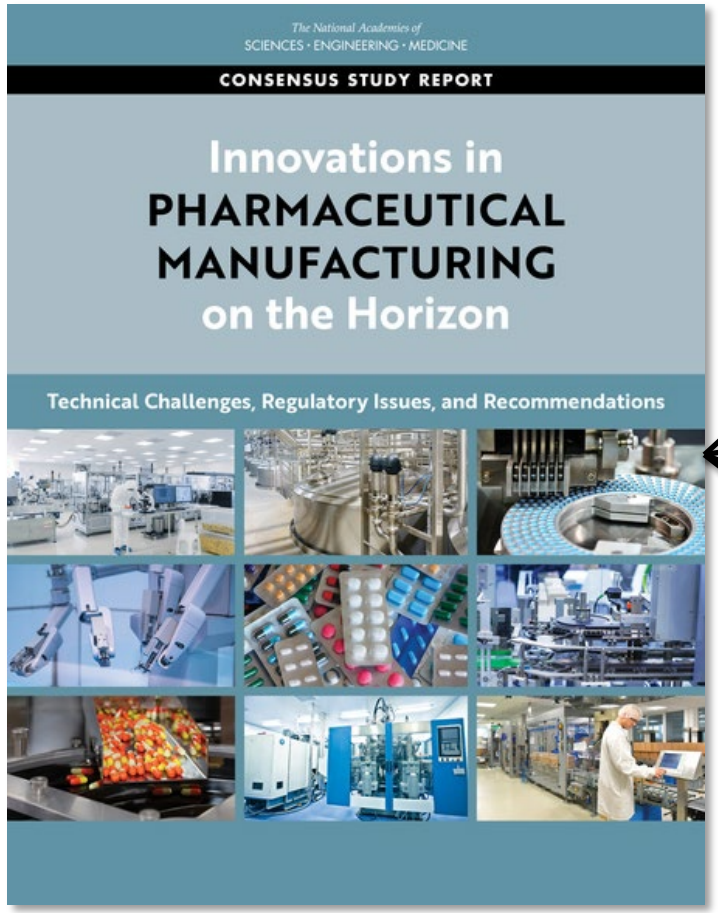
- **Recent FDA Actions**
  - Published a White Paper on QMM
  - Convened a QMM Public Workshop (2,000 global attendees)
  - Published peer-reviewed journal articles on:
    - Quality Benchmarking Study (based on collaboration with D&B and University of St. Gallen)
    - Lessons Learned from QMM Pilots (Domestic FDF and Foreign API)
  - Held an FDA Advisory Committee Meeting
    - Voted unanimously in favor of CDER establishing a QMM program that will incentivize adoption

# Efforts to Support Quality Manufacturing

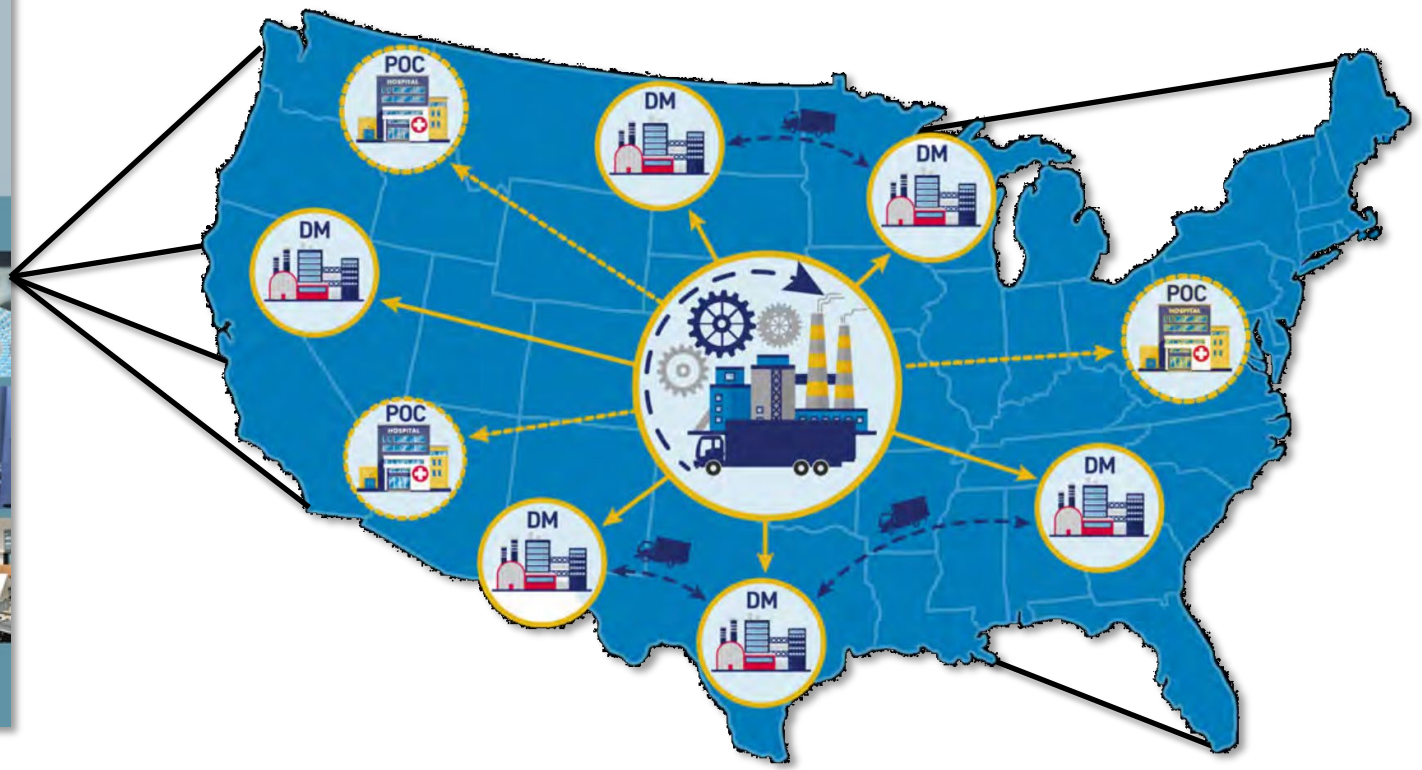
- Adoption of advanced manufacturing is one strategy to improve U.S. drug supply chain resilience.

  - CDER's Emerging Technology Program
    - Held over 150 FDA-industry meetings on advanced manufacturing technologies
    - Approved 18 applications under ETP
    - Collaborates with international regulatory counterparts in developing requirements
    - Under the Product Development Science Program, funded more than 60 intramural and extramural research projects in advanced manufacturing

# **FRAME: F**ramework for **R**egulatory **A**dvanced **M**anufacturing **E**valuation




**INTEGRATED, FLEXIBLE, AND DISTRIBUTED**




*NASEM *Innovations in Pharmaceutical Manufacturing on the Horizon: Technical Challenges, Regulatory Issues, and Recommendations* (2021)

# FRAME Engagements

- **Distributed and point-of-care manufacturing discussion paper in Federal Register** (now)
  - 60 days for public comment
- **FDA/PQRI distributed and point-of-care manufacturing public workshop** (November 14-16, 2022)
- **Artificial intelligence discussion paper in Federal Register** (TBD)

# Dispelling the Myths of AM

- **The use of AM is not mandated by FDA**
  - FDA approves drugs if they comply with standards, regulations, and laws
  - Benefits of using AM in some, but not all, instances
- **AM is not just for innovator companies**
  - Multiple developers of generics have engaged with CDER's ETP
- **Generic drug companies are not required to implement AM because an innovator company has done so**
  - Specification criteria are based on patient relevance and not on process capability
- **AM applications have not taken longer to review and approve…**

# NITROSAMINES

# FDA Guidance – Control of Nitrosamine Impurities in Human Drugs (Sept. 2020, Revised Feb 2021)

**3 Steps**

1. Assess the risk of nitrosamine impurities (complete by March 31, 2021)
2. Conduct confirmatory testing when there is a risk identified
3. Report changes implemented to prevent/reduce nitrosamines (complete before October 1, 2023)

*FDA may request an expedited risk assessment, confirmatory testing, or other regulatory action based on information available to the Agency

# FDA Update on Possible Mitigation Strategies (Nov 2021)

- Nitrosamine Drug Substance-Related Impurities (NDSRIs)
  - Incorporating antioxidants (e.g., propyl gallate) in formulations may significantly inhibit the formation of NDSRIs
  - Formation of nitrosamines typically occurs under acidic conditions; thus, incorporating excipients in formulation design that modify the micro-environment to a neutral or basic pH should in principle inhibit formation

- FDA encourages manufacturers to consider these as well as other innovative strategies to reduce the formation of NDSRIs to acceptable levels in drug products.
  - FDA will consider meeting requests, as appropriate, to discuss innovative mitigation strategies with prospective applicants or manufacturers.

# Final Thoughts

- Medicines only work if patients have access
- The generic and biosimilar industries have made outstanding contributions to public health by increasing access and affordability
- Access requires resilience which includes quality manufacturing
- We look forward to continuing to innovate with you to maintain a robust generic and biosimilar market

# Thank You!

# &

*The talented staff in the*

*Office of Therapeutic Biologics and Biosimilars*

*Office of Generic Drugs*

*Office of Pharmaceutical Quality*