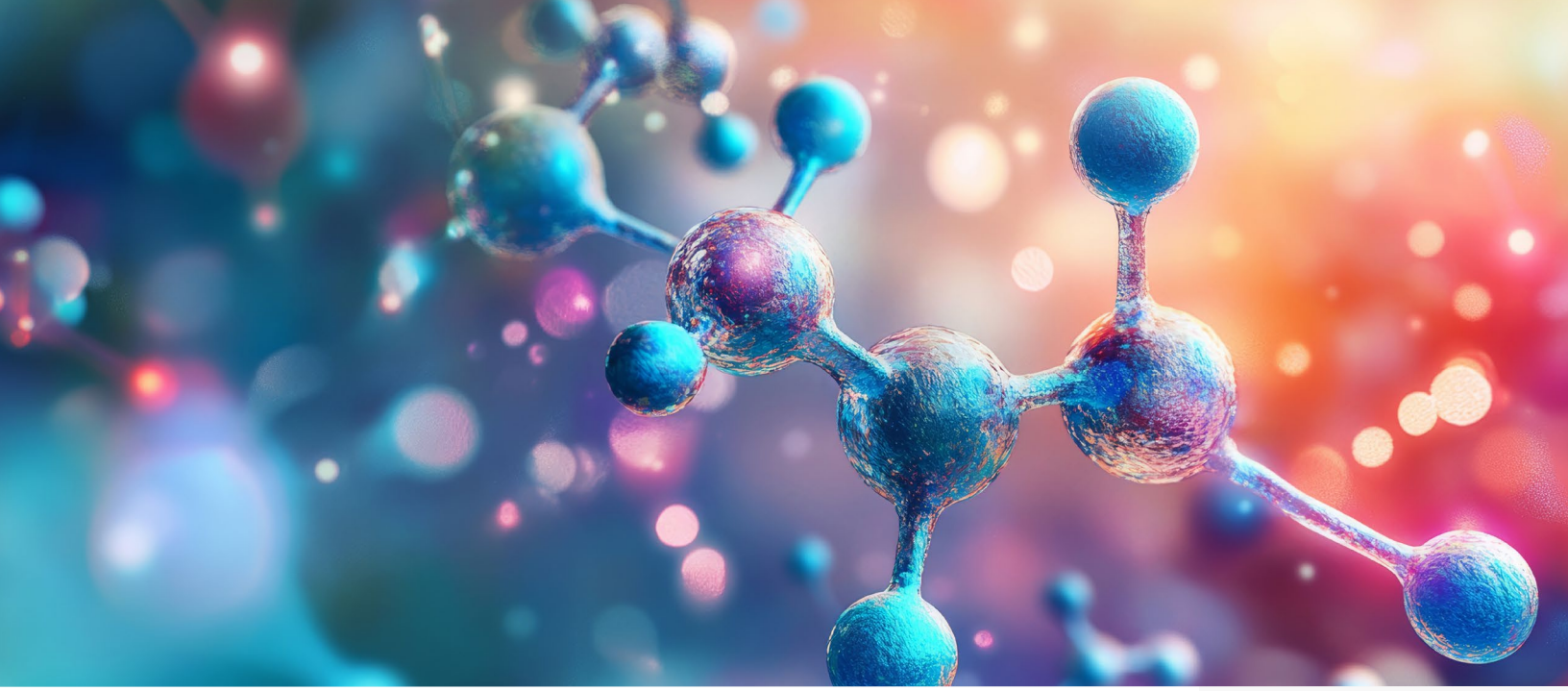
U.S. FOOD & DRUG ADMINISTRATION

BsUFA III Future Needs for the Development of Interchangeable Products

POST–WORKSHOP STRATEGY DOCUMENT

2026

Contents



Introduction and Background

Biosimilar and Interchangeable Biosimilar Products

The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) created an abbreviated licensure pathway for biological products that are demonstrated to be "biosimilar" to or "interchangeable" with a Food and Drug Administration (FDA)-licensed biological product.[1] This pathway was established as a means to provide patients with more treatment options, increase their access to lifesaving medications, and potentially lower health care costs through competition. [2]

The development of biosimilar biological products (also referred to as "biosimilars" or "biosimilar products") is grounded in the comparison of a proposed biosimilar product to an FDA-licensed biological product, referred to as the "reference product". Manufacturers generate the data needed to demonstrate a product meets the statutory standard for biosimilarity through detailed analytical (structural and functional) characterization and clinical studies, as appropriate.[3] Specifically, for the FDA to license a biosimilar product, the proposed biosimilar must be "highly similar to" and have "no clinically meaningful differences in safety, purity, and potency" from its reference product.[4] As such, the goal of a biosimilar development program is to demonstrate biosimilarity between the proposed biosimilar product and the reference product, not to independently establish safety or effectiveness of the proposed biosimilar product.

Along with demonstrating biosimilarity, a sponsor may request an "interchangeable" designation (a biosimilar product that receives an "interchangeable" designation is referred to as an "interchangeable product," "interchangeable biosimilar," or "interchangeable biosimilar product") from the FDA, which may allow pharmacists to substitute the biosimilar product for the reference product without consulting the prescribing health care provider, subject to state pharmacy law. To meet the standard for interchangeability, an applicant must provide information to show that the proposed

product is “biosimilar”; “can be expected to produce the same clinical result as the reference product in any given patient”; and for a product administered more than once to an individual, switching between the proposed interchangeable biosimilar product and the reference product does not increase safety risks or decrease effectiveness compared to using the reference product without such switching between products.[3] As of August 2026, FDA has licensed (approved) 89 biosimilar products, 42 of which were designated as interchangeable.[5]

Current Challenges of Interchangeable Biosimilar Development and Adoption

Despite the statutory and regulatory structure set in place for interchangeable biosimilar product development and approval, manufacturers and stakeholders have faced significant obstacles that span regulatory, economic, and implementation domains. Historically, from a regulatory perspective, manufacturers were expected to demonstrate both biosimilarity and interchangeability through extensive analytical and clinical studies, as appropriate, to provide evidence that switching between products poses no additional risk. However, the data needed to demonstrate interchangeability have evolved based on FDA’s experience and the body of evidence and information generated by FDA and other regulatory agencies on the utility of switching studies. Market access also presents challenges to interchangeable development, as anticipated cost savings have not fully materialized due to rebate structures and formulary positioning, while physician and patient hesitancy to adopt biosimilars persists despite interchangeable designations. Lastly, the complex reimbursement landscape, with varying insurance policies and state substitution laws, may further complicate the interchangeable biosimilar product development and adoption landscape. To help address these challenges, FDA has committed to ongoing educational efforts supporting the understanding, development, and adoption of biosimilars and interchangeable biosimilars.

Biosimilar User Fee Act (BsUFA)

The third authorization of the Biosimilar User Fee Act (Fiscal Years (FY) 2023–2027) (BsUFA III) includes a commitment for FDA to hold, on or before October 31, 2025, a scientific workshop on the development of interchangeable products to help identify future needs (e.g., guidance, research).[6,7] In addition, FDA agreed to issue this draft strategy document, within 12 months following the public workshop, for public comment. This post-workshop report provides a summary of the scientific workshop held on September 19, 2025, and the comments we received to public docket following the workshop and fulfills the BsUFA III commitment of developing a strategy document that identifies future goals and priorities related to FDA’s biosimilar and interchangeable scientific programs.

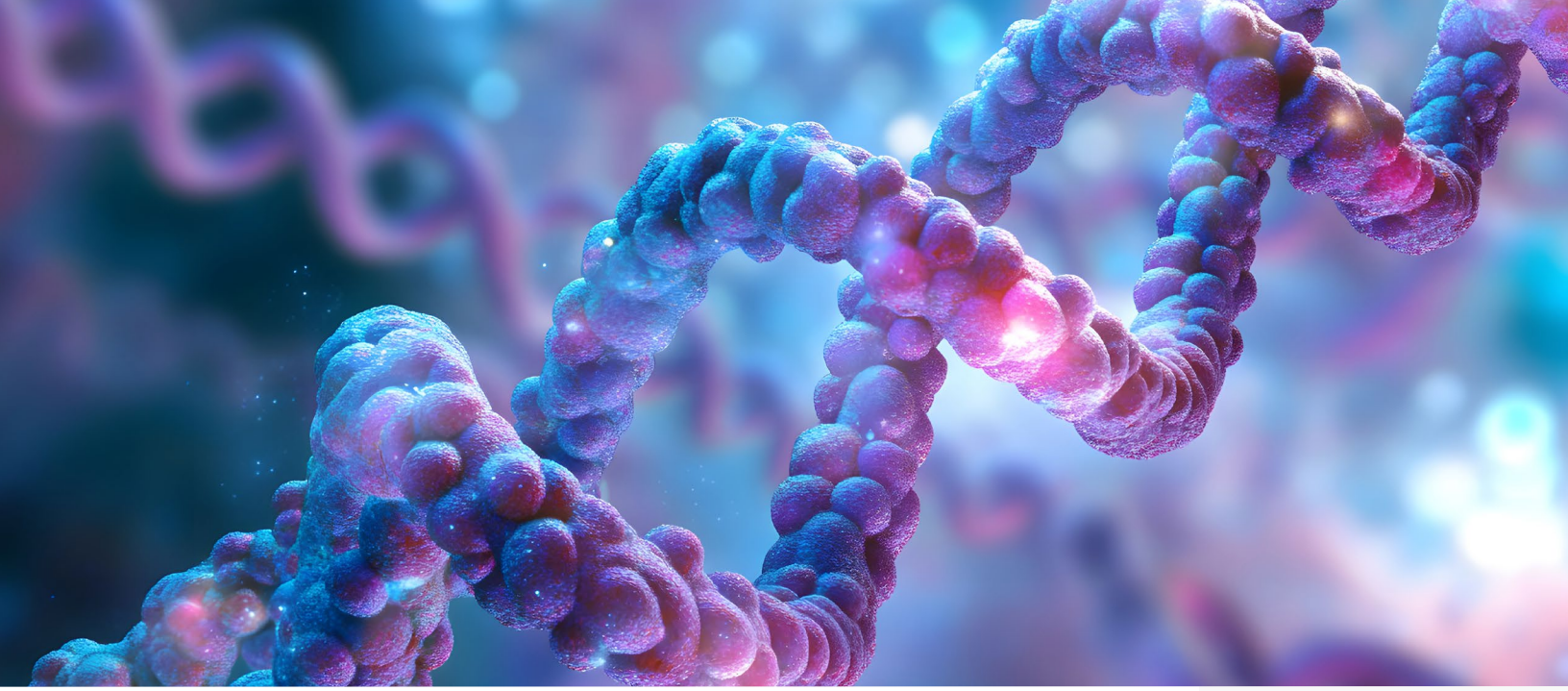
Workshop on the Future Needs in the Development of Interchangeable Biosimilar Products

The public workshop on the development of interchangeable biosimilar products was held both virtually and in-person at the FDA White Oak Campus on September 19, 2025. Following opening remarks by the Director of the Office of Therapeutics Biologics and Biosimilars (OTBB), and a keynote address by the Director of the Center for Drug Evaluation and Research (CDER), industry representatives from The Association for Accessible Medicines (AAM), Biosimilars Forum, and Pharmaceutical Research and Manufacturers of America (PhRMA) provided their perspectives on the future needs for successful development and adoption of interchangeable biosimilar products.

FDA speakers from CDER presented on the following scientific topics:

- Analytical Considerations Around Interchangeability of a Biological Product
- User Interface and Human Factors Considerations to Support Biosimilarity and Interchangeability
- Other Considerations Around Interchangeability of Biological Products: Facilitating Development of Interchangeable Biosimilars

Industry representatives and FDA speakers participated in a panel discussion on current challenges in the development of interchangeable biosimilar products and future opportunities, and answered questions submitted by in-person and virtual attendees.



Themes of the Workshop's Discussions

Communication and Guidance Should Remain Iterative as the Science and Policy Around Interchangeability Evolves

Throughout the workshop, industry stakeholders identified a gap between evolving scientific understanding and regulatory communication as a challenge for interchangeable biosimilar development. For example, although FDA published draft guidance that switching studies would not generally be expected for interchangeability, similar guidance was not available regarding other aspects of interchangeable biosimilar product development, e.g., delivery device and user interface differences. Another topic of concern was the confusion that may stem from lack of clarity among relevant stakeholders regarding the actual differences, if any, between products determined to be interchangeable and other biosimilar products. Furthermore, some industry speakers indicated that the "interchangeable" designation is not a scientific or safety term, but rather, an artificial legislative definition, suggesting that the terminology itself may be contributing to confusion among stakeholders.

During the panel discussion, industry acknowledged FDA's evolving and updated scientific understanding of interchangeability. At the same time, industry expressed the need for these developments to be communicated in a timely manner to other stakeholders. Additionally, for areas where guidance is not available e.g., for interchangeable biosimilar combination products or newer therapeutic products, sponsors may not have sufficient clarity about regulatory expectations to make product development and investment decisions. More timely dissemination of information about evolving regulatory expectations for interchangeable biosimilar products would help address these practical challenges for the biosimilar industry.

FDA acknowledged the challenges, but also noted that development decisions often depend on the context and characteristics of a specific product and cannot always be addressed through broad, generalized guidance. Industry representatives noted that early communication and regulatory feedback from the Agency is critical for informing decisions before a sponsor commits to the development of a product.

Industry would like FDA to provide greater clarity around the underlying principles driving how case-by-case determinations are made, particularly with respect to differences between the delivery devices for a proposed interchangeable biosimilar product and its reference product and what information FDA may expect to justify those differences. In particular, stakeholders noted that more detailed communication earlier in development would help with industry's decision-making.

To address these challenges, industry called for more comprehensive and practical guidance that addresses specific development scenarios and provides clearer expectations for sponsor activities. Areas identified for additional clarity included comparative analysis expectations, delivery device considerations, and other product-specific development scenarios where sponsors would benefit from more detailed, example-based recommendations.

User Interface and Human Factors Analyses Remain as Opportunities to Facilitate Interchangeable Development

Beyond traditional analytical and clinical considerations, participants of the workshop also identified device-related human factors (HF) as a development challenge for interchangeable biosimilar products. During the speaker presentations and the panel discussion, participants acknowledged that user interface and HF considerations are a significant challenge in current interchangeable biosimilar product development processes, with a major focus on the practical challenges of device differences and Agency expectations for evaluating them.

FDA presenters outlined the complexity of evaluating biosimilar (including interchangeable biosimilar) combination products from an HF perspective. The presentation detailed specific evaluation requirements: Use-Related Risk Analysis (URRA) of all product use steps; assessment of potential user errors; evaluation of clinical consequences from mistakes; and side-by-side analysis of physical characteristics, tasks, and labeling between biosimilar and reference products. FDA speakers demonstrated these considerations through a concrete product walkthrough that illustrated how differences between devices should be evaluated for user impact. In one example, speakers noted that minor differences, such as colors or graduation lines, might be expected to have insignificant user implications in certain contexts, while major variations requiring different use instructions should be evaluated for potential impact, safety, and effectiveness. In another example, differences in button press duration for drug administration would be an "other than minor" product difference, but if users of the reference product are instructed to hold the button press for longer than the proposed interchangeable biosimilar product, this may not require additional data to justify, since previous reference product users holding the interchangeable product button down for longer would not be expected to negatively impact dose delivery.

In the panel discussion, industry representatives proposed the use of validation studies with experienced users to better understand real-world device performance, rather than comparative use HF studies. FDA representatives acknowledged that evaluation of differences in delivery devices for proposed interchangeable biosimilar products can pose significant challenges and that more publicly available data and information on the topic would be helpful. However, as noted during the discussions on the BsUFA III Regulatory Science Research Pilot Program public meeting, there is limited research being conducted in this field, and FDA did not receive any proposals that sought to address this research priority in the Pilot Program. The Agency continues to seek other viable ways to address these information gaps.

Approaches to Interchangeability Should Follow the Science

Perhaps the most significant advances underlying evolution in approaches to biosimilar and interchangeable biosimilar product development involve the growing breadth, predictability, and reliability of advanced analytical methodologies. Participants of the workshop discussed the shift in scientific understanding regarding the relative sensitivity and value of analytical versus clinical data in biosimilar (including interchangeable biosimilar) product evaluation and highlighted the most common scenario where analytical data is more sensitive than clinical data. This perspective reflected the significant advances in analytical capabilities since the BPCI Act was enacted in 2010, and also since the first biosimilar product was approved by the Agency in 2015. The evolution of analytical capabilities was further detailed during the discussion of other considerations around interchangeability.

During the panel discussion, FDA suggested that the Agency's growing confidence in analytical methods to detect meaningful product differences supports the view that clinical data may not always be necessary to demonstrate biosimilarity and interchangeability. There has been increasing recognition that comparative clinical studies do not offer the same caliber of sensitivity for detecting differences in the quality attributes between the proposed interchangeable biosimilar and the reference product (physicochemical, structural, and functional testing) as compared to modern analytical technologies. Furthermore, the increasing experience has come with better understanding of the clinical implications, if any, of differences observed during analytical comparisons. FDA noted that during application review, product differences are more likely to be revealed through the analytical data rather than the clinical data, highlighting the sensitivity of current analytical approaches. Industry representatives echoed this sentiment and indicated that analytical approaches represent scientific advancement, and that by deploying them for biosimilar and interchangeable biosimilar product development, standards for safety and efficacy will not be compromised.

FDA and industry both shared the perspective that scientific advancements justify a greater reliance on advanced analytical methods, and that this evolution should be accompanied by a clear understanding that streamlined approaches still require scientific rigor to enable their compliance with regulatory expectations.

Docket Comments

In response to the Federal Register Notice for the workshop,[8] FDA received several public comments[9,10,11,12,13] that each described their positions, concerns, and suggestions for the future of interchangeable biosimilar development. This section provides a high-level summary of the most relevant recurring topics discussed in the public comments and the varying viewpoints expressed by stakeholders.

Streamlined Regulatory Pathway

The comments submitted to FDA on the topic of whether interchangeability should continue to be a separate designation varied widely. Some expressed support for the elimination of separate biosimilar and interchangeable biosimilar designations because all biosimilar products, including interchangeable biosimilar products, are required to meet the same high standard of biosimilarity to obtain FDA approval and both are as safe and effective as the reference product. However, others highlighted that biosimilars are not the same as generics and expressed concerns about patient safety and physician confidence. One docket comment was in favor of a flexible approach in which designations are made on a case-by-case basis after consideration of several factors, such as product complexity, mechanism of action, patient populations, and chronic versus acute treatment.

Evidence Requirements and Scientific Standards

The docket comments addressed evidence requirements and scientific standards, specifically on the topic of switching studies and analytical assessments. Current FDA draft guidance notes that FDA's scientific approach to when a switching study or studies may be needed to support a demonstration of interchangeability has evolved. Specifically, in the draft guidance, FDA explains other ways that sponsors may demonstrate that the switching standard set forth in section 351(k)(4)(B) of the PHS

Act has been met.[14] This evolution is based on accumulated evidence from the experience with approved biosimilar products to date that has shown the safety risk is insignificant following single or multiple switches between a reference product and a biosimilar product. Some commenters supported the use of comparative analytical assessments, given their high degree of specificity and sensitivity, as primary evidence over the need for switching studies, while others advocated for a case-by-case determination of when switching studies should be considered. Those in favor of a case-by-case approach cited examples that might include the value that additional data could provide for complex or less well-understood products, and clearer guidance and standards from the FDA for when switching studies are needed. However, another commenter expressed strong support for maintaining clinical evidence and switching studies, highlighting some limitations of analytical assessments, such as device differences or potential immunogenicity risks. Furthermore, this commenter noted that the availability of clinical study data can increase physician confidence in interchangeability.

Pharmacy-Level Substitution

One of the primary concerns about pharmacy-level substitution of interchangeable biosimilars with a reference product, where allowable under state law, is the potential for user error when patients are unexpectedly faced with differences in delivery device design. Though comparative use HF studies (CUHF) have been proposed as an approach to better understand the potential for user errors associated with a device change, these studies can be costly and challenging to conduct. One docket comment was in favor of allowing some flexibility in device designs to foster sustainable biosimilar competition and leverage emerging technologies and platforms for novel delivery methods. Other commenters emphasized the need for clear substitution procedures and information on product-specific accessories, such as autoinjectors, pumps, or diluents, to help prevent confusion and ensure safe use. Along these lines, another docket comment noted that the FDA guidance that is currently being drafted on presentations, container closure systems, and device constituent parts will hopefully provide needed information for industry during the product development process. One comment encouraged global harmonization and alignment with EMA, Health Canada, and WHO practices, as well as FDA's participation in the ICH guidance development process.

Future Directions

Discussions at the workshop highlighted the need for continued science-based evolution of regulatory approaches to sustain future biosimilar and interchangeable biosimilar product development and that supports increased efficiency. Ultimately, FDA's objective and public health mission is to increase access to high quality, safe, and effective biologic therapies for patients.

In the last five years, there has been significant progress made in developing and approving interchangeable biosimilar products (Figure 1). At the time of BsUFA III negotiations in 2021, there were 29 approved biosimilars, none of which were designated interchangeable, and there was more uncertainty regarding scientific gaps that could be hindering the development and licensure of interchangeable biosimilar products. Since that time, we have focused on science-based approaches intended to streamline development to support interchangeable biosimilar product development with great success. This includes issuing draft guidances for industry "Considerations in Demonstrating Interchangeability With a Reference Product: Update" in June 2024[15] and Biosimilar and Interchangeable Biosimilar Products: Considerations for Container Closure Systems and Device Constituent Parts in July 2026.[16] Previously, FDA generally recommended switching studies as part of the data package needed to demonstrate interchangeability and the draft guidance update describes other approaches to meet the standard for interchangeability without the need for switching studies. Therefore, under these alternative approaches, the data needed to support a determination of interchangeability would typically be less burdensome for biosimilar applicants to generate. FDA plans to issue additional guidance on relevant topics related to interchangeability in the future, as needed. For example, FDA will strive to publish a revised version of the guidance "Considerations in Demonstrating Interchangeability With a Reference Product" that takes into account, among other things, recent scientific advances and changes in regulatory approach, by the end of FY 28.

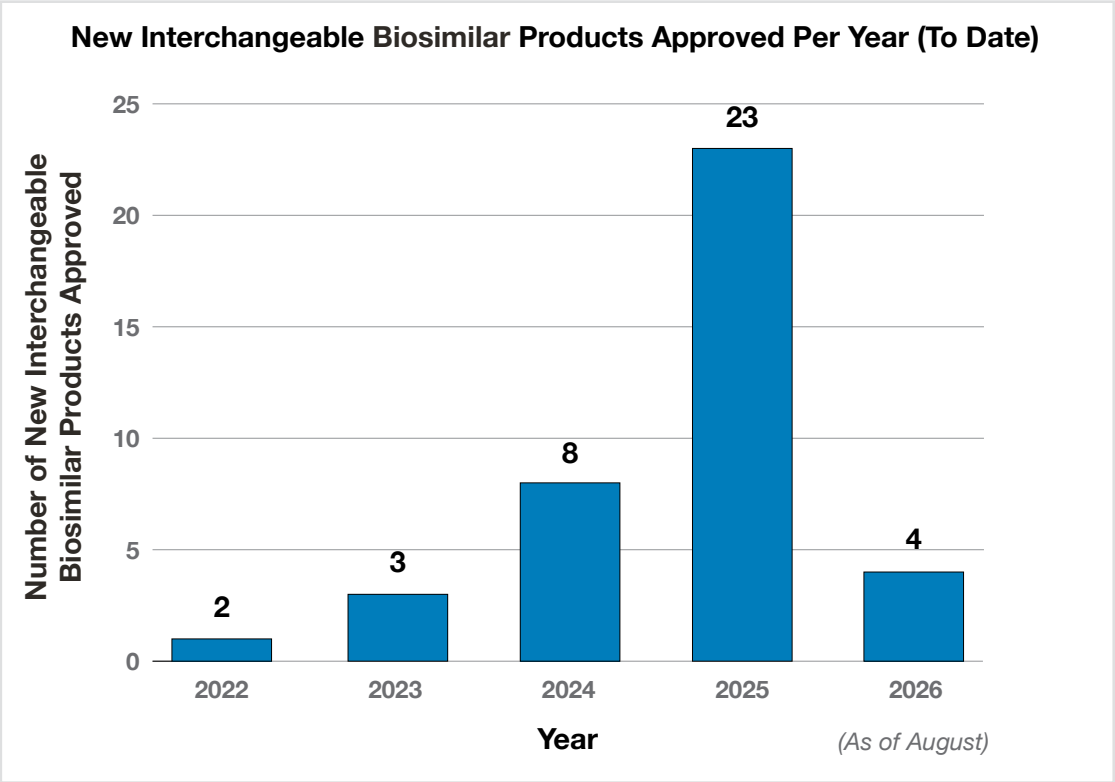


Figure 1. Interchangeable Biosimilar Products Approved by FDA per Year (To Date)

As the biosimilar landscape matures, FDA must remain responsive to emerging scientific evidence that informs interchangeability designations, while maintaining transparent, ongoing dialogue with stakeholders to clarify regulatory expectations and reduce uncertainty in the development pathway. FDA must also remain forward-looking and anticipate the scientific and regulatory changes that may accompany novel biologic technologies, as well as the information needed to address the questions that will arise about interchangeability.

Underpinning these commitments is a fundamental principle: approaches to interchangeability must follow science. This means allowing regulatory policy to adapt as our understanding of biosimilar immunogenicity, switching studies, and experience with interchangeability in practice deepens. Additionally, FDA will continue to develop training and education resources for providers, prescribers, and patients to promote enhanced understanding of the safety and efficacy of biosimilar products, including interchangeable biosimilar products. By maintaining this science-driven foundation while simultaneously addressing practical barriers to development and adoption, FDA will foster an environment that supports innovation, increases regulatory efficiency, reduces development costs and timelines, and ultimately expands patient access to high-quality, safe, and effective biological products.

Acknowledgements

CDER extends thanks to all speakers, panelists, public docket commenters, workshop attendees, and FDA staff that supported and organized the workshop for their participation in this event.

Public Meeting Resources

The public workshop recordings and slide decks are available at https://www.fda.gov/industry/fda-public-workshop-future-needs-development-interchangeable-products-09192025#event-materials.

References

1 See https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars for more information on biosimilars and interchangeable biosimilars.

2 See FDA's Biosimilar Action Plan at https://www.fda.gov/media/114574/download for more information on FDA's efforts to encourage innovation and competition among biological products and support the development of biosimilar products.

3 See https://www.fda.gov/drugs/biosimilars/review-and-approval for more information on the review and approval of biosimilars and interchangeable biosimilars.

4 Section 351(i)(2) of the Public Health Service (PHS) Act.

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

6 Biosimilar Biological Product Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027 https://www.fda.gov/media/152279/download

7 FDA Public Workshop: Future Needs for the Development of Interchangeable Products https://www.fda.gov/industry/fda-public-workshop-future-needs-development-interchangeable-products-09192025

8 Advancing the Development of Interchangeable Products: Identifying Future Needs; Public Workshop https://www.federalregister.gov/documents/2025/08/15/2025-15572/advancing-the-development-of-interchangeable-products-identifying-future-needs-public-workshop

9 Comment from Mitchell Berger https://downloads.regulations.gov/FDA-2025-N-2787-0002/attachment_1.pdf

10 Comment from Alliance for Safe Biologic Medicines https://downloads.regulations.gov/FDA-2025-N-2787-0006/attachment_1.pdf

11 Comment from Association for Accessible Medicines https://downloads.regulations.gov/FDA-2025-N-2787-0003/attachment_1.pdf

12 Comment from Prime Therapeutics LLC https://downloads.regulations.gov/FDA-2025-N-2787-0005/attachment_1.pdf

13 Comment from Pharmaceutical Research and Manufacturers of America (PhRMA) https://downloads.regulations.gov/FDA-2025-N-2787-0004/attachment_1.pdf

14 Considerations in Demonstrating Interchangeability with a Reference Product: Update. https://www.fda.gov/media/179456/download

15 Considerations in Demonstrating Interchangeability with a Reference Product: Update. https://www.fda.gov/media/179456/download

16 Biosimilar and Interchangeable Biosimilar Products: Considerations for Container Closure Systems and Device Constituent Parts https://www.fda.gov/media/193917/download

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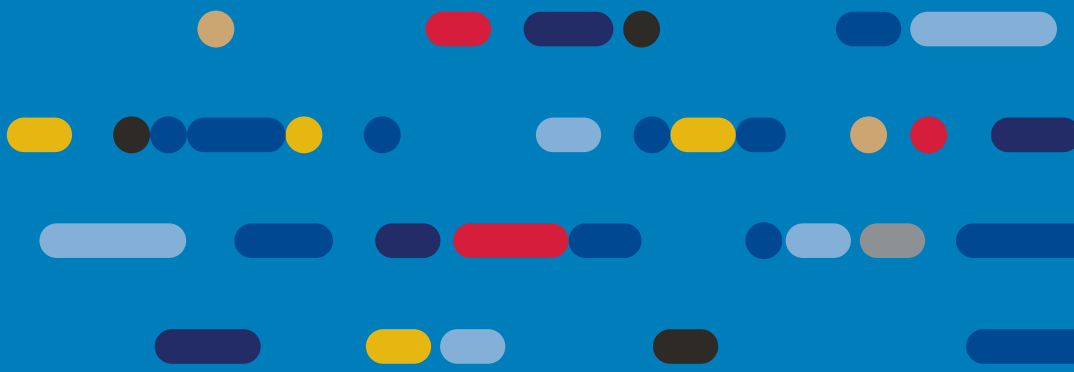

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