FDA's Biosimilarity Guidance Holds Uncertain Implications

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On Jan. 20, the public comment period for the U.S. Food and Drug Administration's draft guidance on demonstrating biosimilarity closed.[1] This document, issued Oct. 29, 2025, proposes "major updates to simplify biosimilarity studies and reduce unnecessary clinical testing," while also making it "easier for biosimilars to be developed as interchangeable with brand-name biologics."[2]

Despite the draft guidance's aim to increase access to high-cost biologic therapies, its effects remain far from certain. In particular, the implications for the agency's stated objectives, as well as for broader trends in biosimilar development, patent litigation and marketplace uptake, are unclear.

In this article, we review historical and persisting barriers to biosimilar competition, particularly in light of some of the public comments on the draft guidance lodged with the agency during its notice and comment period. We then discuss how the draft guidance, while intended to remove certain barriers to biosimilar access, could affect these dynamics in unexpected ways.

Context in Brief: FDA's Motivation for Revising Regulatory Guidance on Biosimilars

The Biosimilars Price Competition and Innovation Act was implemented in 2010 to provide the FDA with a framework for approving biosimilar products to "promote competition, reduce healthcare costs, and increase access to biologic therapies."[3]

In the years following the passage of the BPCIA, the U.S. biosimilar industry advanced through several key milestones, including approval of the first biosimilar in 2015 and FDA guidance for interchangeability in 2019.[4,5]

However, more than 15 years after the BPCIA's enactment, industry observers warn of a looming biosimilar void — a dearth of biosimilar products in development to challenge hundreds of biologics losing exclusivity over the coming decade.[6]

A report from the IQVIA Institute last year notes that "[o]f the 118 biologic patent expiries over the next decade, [only] 10% currently have biosimilars in development."[7]

While these patent expirations represent a $232 billion opportunity for biosimilar manufacturers, the report notes that numerous challenges continue to limit biosimilar development, such as burdensome regulatory requirements, high investment costs and confusion over interchangeability.[8]

Noting the hurdles outlined in the report, the trade association America's Health Insurance Plans opined in a public comment that without policy changes, "many of the next generation of biosimilar therapies may never reach the market and be available to patients."[9]

Upon the release of the draft guidance, FDA Commissioner Marty Makary noted, "We need to cut the red tape for biosimilars." The new guidance was intended to achieve this goal by removing years from the typical biosimilar development process.[10]

Specifically, it would allow biosimilar developers to rely on less burdensome comparative analytic assessments, instead of the comparative efficacy studies and switching studies that are currently required for approval — these studies can take one to three years and an average of $24 million to complete.[11]

In its public comment in support of the draft guidance, a representative for the Campaign for Sustainable Rx Pricing noted that the comparative efficacy study requirement "reflect[s] regulatory caution from the early years of the biosimilars program," which "more than a decade of experience with biosimilars in the U.S. has shown ... to often be redundant."[12]

Importantly, this modification would make it easier for biosimilars to obtain the interchangeability designation, a clinical determination of sufficient similarity to the reference — also known as the originator or innovator — biologic that allows pharmacists to substitute biosimilars without physician approval.[13]

This was a consideration that Kaiser Permanente called attention to. In its public comment, a representative from the company pointed out that the current interchangeability designation "imposes avoidable costs, contributes to confusion

among clinicians and patients, and reinforces the inaccurate perception that biosimilars without the designation are of lower quality."

According to Kaiser, moving to "a pharmacy substitution model similar to that used for generic small molecule drugs would still allow prescribers to indicate 'dispense as written' when the reference biologic is necessary while making biosimilar uptake much simpler."[14]

Looking Back: Barriers to Biosimilar Development and Uptake in the U.S.

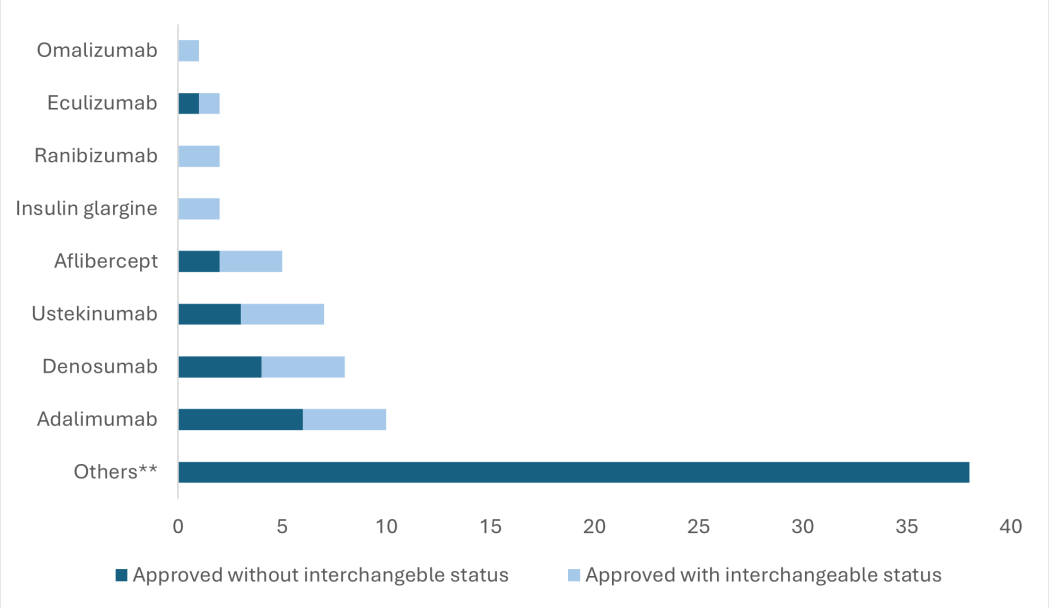
While the FDA hopes its draft guidance will incentivize more biosimilar development and competition, several key factors have likely limited biosimilar manufacturers' appetite for prioritizing this category of medicines in recent years. In the face of the obstacles described below, it remains uncertain whether the draft guidance, if implemented, would substantially increase biosimilar adoption.

Interchangeability

Unlike small-molecule generics, which are more readily substituted for reference products, biosimilars are derived from living organisms, and hence are far more structurally complex and tend not to be identical to the original biologic.[15]

As a result, less than a third of biosimilar products approved by the FDA as of May 2025 carried an interchangeable designation, limiting pharmacists' autonomy in substituting these products at the counter.[16]

Figure 1: Number of FDA-Approved Biosimilars by Molecule and Interchangeability as of May 22, 2025



The category labeled as "Others" includes bevacizumab, epoetin alfa, etanercept, filgrastim, infliximab, insulin aspart, natalizumab, pegfilgrastim, rituximab, tocilizumab and trastuzumab.[17]

Many biologics are administered directly by a healthcare provider rather than distributed through a pharmacy, minimizing the impact of pharmacy substitution. Industry research suggests that, while healthcare providers prefer biosimilars with an interchangeability designation, the process to achieve it is costly and time-consuming for manufacturers.[18]

However, even interchangeability does not appear to satisfy certain practitioners' concerns, limiting their willingness to switch to biosimilars. A survey of U.S. specialists published in 2019 found that 84% of biologic-prescribing physicians did not want stable patients undergoing a nonmedical switch to a biosimilar, with majorities of surveyed physicians citing negative impacts on treatment efficacy, safety and physician office management.[19]

Echoing this point, the American College of Rheumatology, in its public comment, insisted that insurers should not mandate switching from a reference biologic to a biosimilar, and that "the final decision to switch a stable patient … must rest with the treating physician and the patient, not a third-party payer."[20]

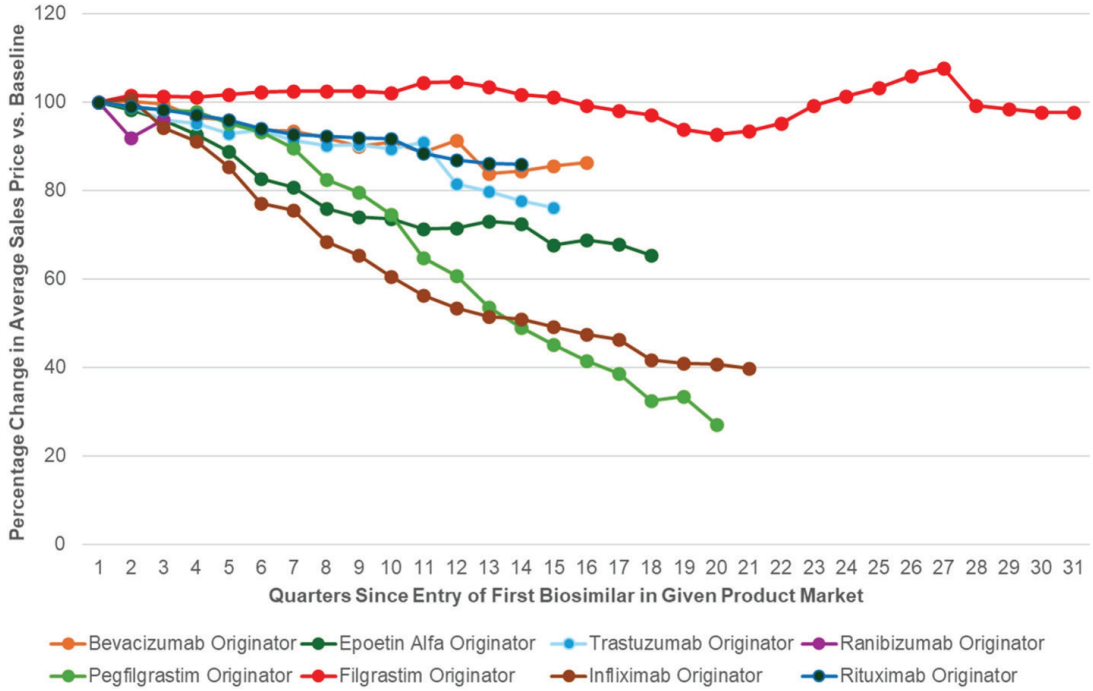
Pricing and Contracting

Small-molecule generics typically launch with steep discounts to reference products, and their impact on molecule pricing has been studied exhaustively.[21] Coupled with the more automated nature of generic substitution, generic manufacturers may leverage certain historical examples and marketplace drivers to set prices around product launch.[22]

In contrast, the average sales price of biosimilars relative to reference products has varied significantly in the years following launch: Some biosimilars dropped by as much as 80% of the prelaunch brand average sales price, while others have increased to a premium of more than 20% above the prelaunch brand average sales price.

Similarly, as shown in Figure 2, the trajectories of brand reference biologic prices, which can be influenced by contracting responses adopted by brand manufacturers, have also seen substantial variation following biosimilar launches.[23]

Figure 2: Change in Reference (Originator) Biologic Pricing Following Initial Biosimilar Entry



Uptake of biosimilar products has also been shown to vary substantially across therapeutic areas and products. A 2024 report from biosimilar manufacturer Samsung Bioepis found that, while biosimilars with oncology and ophthalmology indications reached an average market share of 75% three years after launch, biosimilars targeting immunology, blood disorders and metabolic disease reached an average market share of only 23% after three years.[24]

This variation in pricing and market share means that prospective biosimilar manufacturers may be partially disincentivized by relatively unpredictable returns on the substantial investments required to bring a biosimilar to the marketplace.

Biologic Patent Litigation

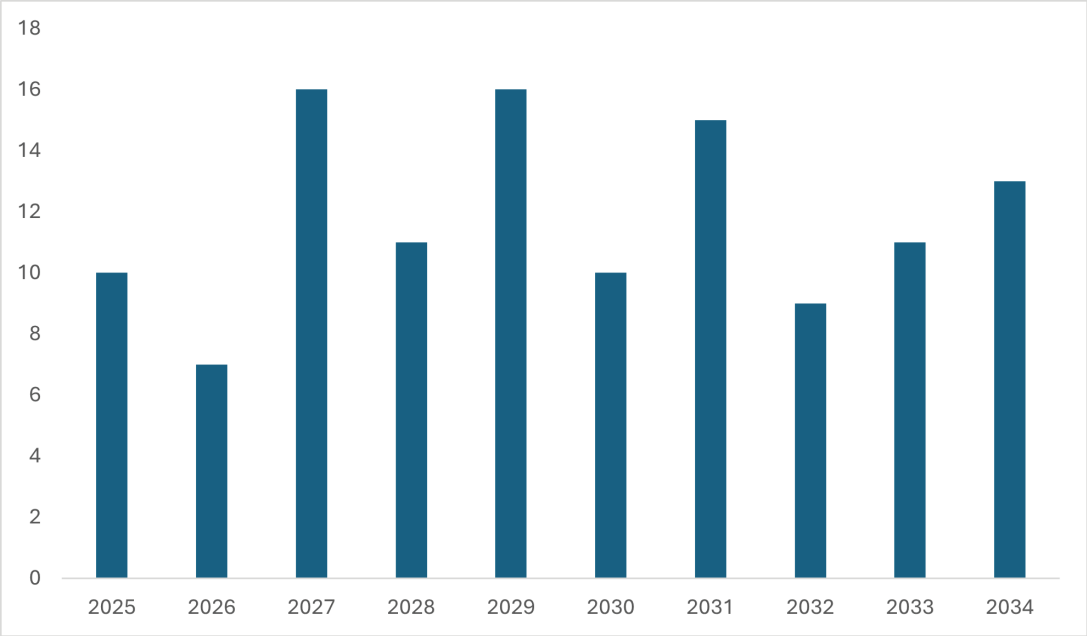
Patent protection for brand biologic products poses an additional hurdle for biosimilar manufacturers. The BPCIA allows biosimilars to file applications with the FDA as early as four years after the brand biologic is approved but has a statutory restriction preventing approval of the biosimilar until 12 years after brand approval.[25]

The uncertain outcome of such litigation also creates substantial uncertainty regarding the timing at which a biosimilar may launch. For example, a Value in Health study of 30 biosimilars launched between 2010 and 2021 found that those that lost patent litigation entered the market a median of 9.9 years later after FDA approval than those that won litigation.[26]

Moving Forward: More Biosimilar Approvals, More Marketplace Uncertainty

With 118 biologics expected to lose patent protection between 2025 and 2034 at an estimated $232 billion market opportunity, it is possible that the new FDA guidance may incentivize biosimilar manufacturers to take more aggressive approaches to market entry.[27]

Figure 3: Number of Biologics Set for Patent Expiration by Year in U.S., 2025-2034



But if such an uptick in biosimilar market entry attempts were to occur, it would almost certainly come with a new set of marketplace uncertainties for both biosimilar and innovator biologic manufacturers.

Interchangeability and Provider Adoption

While interchangeability designations may become more pervasive, in certain cases, some barriers to uptake may originate with prescribing physicians and thus remain unaffected by the new guidance.

This is particularly likely in instances where automatic pharmacy substitution does not apply, such as provider-administered therapies or physician prescriptions that specify that the brand drug be dispensed.

While an interchangeability rating may provide some physicians with greater certainty in use of the biosimilar, others may become more hesitant due to reduced requirements for clinical evidence.

It remains far from clear whether relaxing regulatory requirements for interchangeability will satisfy evidence needs for clinical stakeholders, who in some instances may serve as gatekeepers for biosimilar dispensing.[28]

Pricing and Competition

If reduced regulatory requirements encourage more biosimilar manufacturers to enter biologic marketplaces, the influx of competition could increase downward pressure on biosimilar prices and margins, further complicating the economic incentives to develop and launch these products.

The push for greater competition among generic drugs, e.g., due to increasing numbers of generic competitors in a reference-molecule marketplace, as a way of increasing downward pressure on generic prices is well documented.[29]

Similar trends have been observed in biosimilar marketplaces.[30] Further, more biosimilars introduced to compete with a reference biologic could result in less perceived differentiation between products. In such scenarios, lower prices may affect long-run entry decisions and change brand biologic pricing and contracting decisions with uncertain impacts on biosimilar uptake.

Additional Legal Challenges

If the draft guidance achieves the intended effects of reducing regulatory burdens, shortening biosimilar development times and increasing the likelihood of product approval, the numbers of biologic patent challenges and at-risk biosimilar launches, i.e., biosimilar launches prior to the resolution of patent litigation, may rise. The resulting increase in patent litigation may have unintended consequences for biosimilar and originator biologic manufacturers alike, such as:

- Increased litigation costs for innovator biologic manufacturers in response to more patent challenges, which may lead to shifts in economic incentives for innovator biologic product development and investment;
- Greater incentives for at-risk biosimilar launches to reap the benefits of early marketplace entry before additional biosimilar competitors follow suit;
- Deepening uncertainty for innovator manufacturers' ability to capture end-of-patent-life profits, with potential unintended consequences for recouping product investments and subsidizing organizational research and development initiatives; and
- Reallocation or reprioritization of innovator manufacturer investments in new biologic product development, acquisition and operations, with the potential to dim the allure of one of the brightest modalities in therapeutic innovation over the past few decades.

Conclusion

As the FDA and industry stakeholders await the agency's final decision on the draft guidance, it is important to note that reducing clinical development requirements alone may not overcome the barriers that have historically constrained biosimilar competition.

As this article shows, provider hesitation toward interchangeability, uncertainty in pricing and contracting, and the complexity of biologic patent litigation have limited biosimilar uptake even after FDA approval.

If the guidance accelerates approvals without addressing these downstream dynamics, biosimilar manufacturers may face the same, or even newly introduced, entry-stage pricing, uptake and litigation uncertainties.

Indeed, the draft guidance may also introduce additional marketplace and legal uncertainties for biosimilar and branded drug manufacturers alike by reshaping competitive incentives and entry dynamics.

Whether the guidance ultimately expands patient access will, therefore, likely depend less on regulatory simplification than on how these market and legal forces evolve.

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