PARAGON HEALTH INSTITUTE POLICY BRIEF

December 22, 2025

Platinum-Standard Science

FDA's New Streamlined Framework for Biosimilars and Interchangeability

By Chris Medrano

On October 29, 2025, the FDA announced a series of new policies to streamline biosimilar development—that is, lower-cost versions of biologic medications. Rather than requiring costly and often unnecessary studies, the FDA will rely on new technologies that have proven to be as effective, if not more so, at determining biosimilars' safety and efficacy compared to their originator biologics.[1] At a press conference announcing the changes, Health and Human Services Secretary Robert F. Kennedy Jr., FDA Commissioner Marty Makary, and Centers for Medicare and Medicaid Services (CMS) Administrator Mehmet Oz noted that they expect these actions will accelerate development and expand patient access to lower-cost biosimilars.[2]

The Trump administration's focus on promoting biosimilar competition as a means of reducing costs is encouraging. A recent report reveals that 106 biologics are set to lose their patents in the next decade without any biosimilar competitors in development.[3]

Current FDA regulations indirectly impact prices by increasing product development timelines and development costs for new biosimilars. This slows competition that would otherwise put downward pressure on biologic prices. According to Commissioner Makary, while the FDA approved 76 biosimilars over 10 years, a more streamlined approach would have likely resulted in "two hundred, three hundred" approvals.[4] He also noted that streamlining would reduce the cost of bringing a biosimilar to market by as much as $100 million, thus saving money for manufacturers and encouraging competition.[5]

KEY TAKEAWAYS

In November 2025, the Food and Drug Administration (FDA) announced a policy to eliminate routine switching and comparative efficacy studies for biosimilar approval, relying instead on advanced analytical technologies that better detect safety and structural differences. This will reduce development costs by up to $100 million and accelerate the speed at which biosimilars come to market.

After more than a decade of real-world evidence and a 2023 FDA meta-analysis showing no increased risks when patients switch, maintaining a separate interchangeability designation has become outdated and does not improve patient protection.

The two-tier system of "approved" versus "interchangeable" biosimilars creates confusion, allows brand manufacturers to cast doubt on safety, and slows uptake, indirectly keeping biologic prices high despite expiring patents.

Lawmakers should recognize all FDA-approved biosimilars as interchangeable, remove unnecessary clinical trials, and enable pharmacy-level substitution under state law. Further streamlining would thus expand access and increase competition, benefitting patients and the health system overall.

As technology has advanced and evidence has accumulated, biosimilars have proven to work the same as the originators without negative immune reactions when patients switch between the products. Therefore, streamlining the approval and interchangeability designations into one process would reduce the regulatory cost of developing new biosimilars without affecting health and safety.

These new policies are only a first step, and lawmakers should also address payment barriers to biosimilar uptake through market-based solutions. But the FDA's effort to streamline development would also help lower the price of existing biosimilars, because the current distinction between approved and interchangeable biosimilars discourages pharmacy-level substitution.

Background on Biologics

Biologics are medications made from living organisms. Examples include insulin to treat Type 1 diabetes and adalimumab to treat rheumatoid arthritis. The Public Health Service Act defines *biological product* as

> a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.[6]

The definitions of *drugs* and *biologics* overlap. Some biologics were even initially approved as drugs.[7] Today, the word *drug* is commonly used to refer to both. The main difference is that drugs are chemically synthesized, while biologics derive from living organisms, which are more complex and harder to characterize.[8]

Given their complexity and higher development cost, biologics are also some of the most expensive drugs on the market. In 2018, despite making up only 0.4 percent of prescriptions, biologic drugs accounted for 46 percent of prescription drug costs.[9] In 2025, the FDA notes that biologics comprise 5 percent of prescriptions and 51 percent of drug costs.[10]

Biosimilars and Interchangeability

Biologics also differ from drugs in how the law treats their follow-on competitors. Follow-on copies of drugs are known as generics, and by definition they must be chemically identical to the original drugs. But biologic molecules are highly complex and harder to characterize. So, Congress created a different approval pathway in the Biologics Price Competition and Innovation Act (BPCIA) that allows a biosimilar to be approved if it is similar enough that there is no meaningful clinical difference between it and its reference product. The statute used the term *biosimilar* because, unlike generic drugs, biosimilar products are not exact replicas of their reference products. (We explore later what this means for safety.)

In 2015, the FDA approved its first biosimilar, filgrastim (Neupogen).[11] Since then, the biosimilars market has expanded significantly. As of November 2025, the FDA has approved 78 biosimilars.[12]

Under BPCIA's framework, the FDA can approve biosimilars only if there are no clinically meaningful differences in terms of safety and effectiveness between them and their respective reference biologics.[13] To make that determination, the FDA has historically required[14] biosimilar manufacturers to submit:

- structural and functional analyses,
- animal data, and
- clinical studies.

In recent years, the FDA has placed greater emphasis on the first of these—analytic assessment—which involves detailed lab-based comparisons of the biosimilar's molecular structure and biological function. With the passage of the FDA Modernization Act 2.0 in 2022,[15] Congress authorized the agency to reduce or eliminate the requirement for animal studies, further signaling a shift toward modern analytical methods, such as cell-based assays and computer models.[16]

The analytic assessment is less burdensome than clinical studies because it requires fewer resources. Clinical studies, on the other hand, are resource intensive for many reasons. To conduct a clinical study, the sponsor must recruit patients and comply with extensive regulations to ensure that patients are treated ethically and that researchers accurately record data. A 2021 study found that the median cost of comparative efficacy trials was $21 million.[17] In total, producing one biosimilar costs between $100 million and $250 million.[18] Therefore, no longer requiring these studies will reduce costs for manufacturers, which will spur more competition.

Conventional wisdom is that clinical trials are the "gold standard" of medical research, because they show how real patients react to the medication. However, modern technology has advanced to the point that analytic assessments can offer a *platinum-standard* level of precision—and often better identify potential issues with biosimilars (more on this later)—while also being less burdensome to conduct.

Interchangeability: Definition, Rationale, and FDA Requirements

The BPCIA also created an additional designation for biosimilars called *interchangeability*.[19] A biosimilar can receive an interchangeable designation if the FDA determines that there is no risk of switching between it and its biologic reference product.

Representative Anna Eshoo (D-CA), whose legislation served as the basis for the BPCIA and included the interchangeability standard, contrasted her bill to other proposals that "would allow the FDA to permit pharmacists and insurers to substitute a biosimilar for a physician's prescription for an innovator biologic product even when they cannot be demonstrated to be identical in their composition or effectiveness."[20]

As a result of that language, the statute authorizes the FDA to deem a biosimilar interchangeable only if, in addition to having no clinically meaningful difference in safety and effectiveness,

- it can be expected to produce the same clinical result as the reference product, and
- the risk of switching between the biosimilar and its reference biologic is "not greater than the risk of using the reference product without such alteration or switching."[21]

To meet that standard, the FDA has historically required a biosimilar manufacturer to submit the results of a type of clinical study known as a switching study. In a switching study, a patient goes back and forth between a reference biologic and its biosimilar. Generally, the FDA no longer requires such studies because they no longer

provide value compared to analytical assessments.[22] No evidence exists that any biosimilar has "failed" a switching study, while previous studies have failed to identify any risk.[23] As of September 2024, the FDA reported it had deemed five out of nine biosimilars interchangeable without additional switching studies.[24]

How Interchangeability Relates to State Laws

The FDA's interchangeability designation does not bind doctors, because the agency is prohibited from regulating the practice of medicine. However, many states allow a pharmacist to substitute a biosimilar only if the FDA has deemed it interchangeable.[25] According to one 2023 review, 46 states and Washington, DC, allow pharmacists to switch patients to biosimilars only if the FDA has deemed them interchangeable.[26] The remaining four states (Washington, Indiana, Alabama, and South Carolina) are even more restrictive and require physician permission before pharmacies can switch to biosimilars.[27] Regardless of prior physician approval for switching, 48 states require pharmacists to at least communicate to the prescribing physicians when they switch.

By contrast, once generic drugs are approved, most states generally allow pharmacists to substitute generic drugs for their brand-name versions without physicians' prior approval. According to one 2020 survey of state laws, 31 states and Washington, DC, permit pharmacists to substitute generic drugs, while 19 states *require* pharmacists to substitute generics (unless the doctor and patient specify otherwise).[28] The vast majority of states (all but seven and Washington, DC) do not require patient consent prior to generic substitution.

Changing Landscape Regarding Interchangeability

The FDA has evolved its position on biosimilarity and interchangeability as it has gained more experience with these products. More than a decade of empirical data has not revealed increased risks to patients from switching.

Current analytical technologies outperform comparative clinical and switching studies in detecting and managing any patient-relevant risks associated with manufacturing or molecular variations.

International Experience

Europe's experience with biosimilars has strongly influenced the global regulatory landscape. Since approving its first biosimilar in 2006, the European Medicines Agency (EMA) has accumulated nearly two decades of real-world data showing no increased risk from switching between biologics and biosimilars.

Initially, most European countries prohibited automatic substitution, and regulators in the United Kingdom (UK) even discouraged biosimilar prescribing.[29] That stance changed as public health systems recognized the potential for major cost savings. When AbbVie's Humira patent expired in 2018, the UK's National Health Service (NHS) prioritized biosimilar adoption.[30] Then-NHS Chief Executive Simon Stevens announced that the savings would be "the biggest … in NHS history from a single drug negotiation," adding that it would free up resources to pay for "11,700 more community nurses or 19,800 more breast cancer treatments for patients."[31]

As biosimilar use expanded, evidence continued to show that switching was safe and clinically equivalent. A 2019 EMA report reviewing more

than 10 years of data found that "harmful immunogenicity is unlikely after manufacturing changes or switching."[32] In 2022, the EMA went further, declaring all biosimilars interchangeable and stating that additional switch studies are unnecessary once biosimilarity is established. (It updated the statement in 2023.[33])

While the EMA distinguishes between interchangeability (prescriber-level switching) and substitution (pharmacy-level switching), both frameworks share the same underlying rationale: mitigating the risk that a patient's immune system might negatively react when switched from a biologic to its biosimilar. As no risks have emerged, some European nations have since adopted automatic substitution policies.[34]

In April 2025, the EMA suggested that structural, functional, and pharmacokinetic comparability data may be sufficient to demonstrate biosimilarity.[35] This guidance proposes reducing or eliminating the need for comparative clinical studies.

Changing Views in the United States

In recent years, the United States has rapidly shifted toward eliminating the regulatory distinction between biosimilars and interchangeable biosimilars.

In 2023, the American Society of Clinical Oncology urged the FDA to abolish the interchangeability category altogether, citing a decade of consistent safety data.[36] Lawmakers from both parties followed suit: Senators Mike Lee (R-UT) and Ben Ray Luján (D-NM) introduced legislation[37] to automatically deem all FDA-approved biosimilars interchangeable,[38] while then-Senate HELP Committee Chair Bernie Sanders (I-VT) advanced a similar proposal in committee.[39]

That same year, the FDA signaled its own shift. New draft guidance recommended removing interchangeability language from biosimilar labeling.[40] Shortly afterward, an FDA meta-analysis reviewing 31 studies found no meaningful differences in safety, efficacy, or discontinuation rates between patients who switched and those who did not.[41]

Momentum toward reform continued in 2024. The Biden administration's fiscal year 2025 budget proposed allowing biosimilar substitution without a formal FDA interchangeability determination.[42] The FDA also proposed formally eliminating the statutory distinction between approval standards for biosimilars and interchangeable biosimilars. New draft guidance in June 2024 allowed analytical and clinical evidence to demonstrate interchangeability.[43] However, the Biden administration did not address the requirement for comparative efficacy trials in the initial biosimilar approval.

By 2025, the FDA began signaling it would no longer routinely require comparative efficacy trials. Senator Rand Paul (R-KY) introduced legislation to reduce such studies, earning support from FDA Commissioner Makary during a Senate hearing. In August 2025, biosimilar developer Dr. Sarfaraz Niazi reported that the FDA waived a clinical efficacy study for his Stelara (ustekinumab) biosimilar—the first time the agency accepted an application without it.[44] Representatives August Pfluger (R-TX) and Greg Landsman (D-OH) introduced House legislation streamlining interchangeability.[45]

Finally, at its October 29, 2025, announcement, the FDA released new draft guidance stating it would no longer automatically require comparative efficacy studies for biosimilars and that it would finalize guidance streamlining

interchangeability.[46] This marked the agency's most explicit move yet toward a unified, data-driven biosimilar approval pathway.

Four Arguments in Favor of Streamlining the Biosimilar Approval Process

Distinguishing between biosimilars deemed interchangeable and biosimilars that have only been approved stunts the latter group's uptake by sending inaccurate information to stakeholders. The distinction between approved biosimilars and interchangeable biosimilars is now outdated.

1. Technology has advanced to the point that the FDA can analyze both biosimilarity and the risk of switching through the initial approval process, so requiring clinical studies and having an entirely separate interchangeability designation does not add any new information.

According to conventional wisdom, clinical trials are necessary because they show how patients react to the medication in a clinical setting. That may seem like a more reliable predictor than an analytic assessment, where researchers examine the biosimilar in a lab setting. However, modern technology has advanced to the point that analytic assessment is better at identifying potential issues with biosimilars, even though it is less burdensome to conduct. For example, in the past decade, analytical technologies have become increasingly able to detect smaller "differences between originators and biosimilars," with a corresponding "tenfold increase in sensitivity" for identifying protein variants.[47]

To show just how accurate these tools have become, the FDA compared the analytic assessment's track record to that of clinical studies. As of September 2024, the FDA noted that analytic assessments identified issues with six biosimilar applications (out of 80 total) that resulted in their non-approval.[48] By contrast, clinical studies identified only one of those same six issues and did not identify any unique issues.

While the FDA formally updated its guidance in June 2024 to no longer require switching studies,[49] agency leaders noted that they had already abandoned the practice and had deemed nine biosimilars as interchangeable (out of 13 total as of September 2024) without the need for switching studies.[50]

So what remains of the interchangeability designation without switching studies? It is not entirely clear. However, the FDA's guidance and its separate legislative recommendation seem to indicate that the answer may well be nothing.

Rather than outline what kind of new information might be useful, the FDA's guidance recommends that an approved biosimilar seeking the interchangeability designation should include an "explanation" of why the data from the original approval "is enough" as well as any other information the sponsor "considers relevant." Similarly, a biosimilar that has not yet been approved can "submit an amendment" with the same information.

Given that the initial approval may be sufficient to establish interchangeability, the FDA has sensibly recommended that Congress get rid of the distinction between approved and interchangeable biosimilars.[51]

2. There is no evidence of switching risk, so there is no longer a need for a separate interchangeability standard.

The FDA's meta-analysis published in October 2023 examined the results of 31 unique studies involving 5,252 participants who underwent at least one switch and 5,770 individuals who did not experience a switch.[52] The authors concluded that "there were no differences in the risk of death, serious adverse events, or treatment discontinuations between the switch and no-switch arms."

The meta-analysis focused on safety concerns rather than efficacy because, as the authors explain, "the primary efficacy determination of a proposed biosimilar occurs earlier in a clinical study prior to the switching period." However, the authors also noted that in other published reviews, studies that collected and analyzed pharmacokinetic data (how the body absorbs/metabolizes the drug) related to efficacy found that "there were no associated differences in efficacy or safety related to changes in [pharmacokinetics] for patients in the No Switch and Switch arms."[53]

Even before the FDA's meta-analysis, other studies that examined data from Europe as well as from the United States similarly did not identify risks from switching.[54] The FDA's meta-analysis adds another layer of confidence that biosimilar switching is safe.

3. Amending current law would increase confidence in biosimilars by sending accurate signals about safety and efficacy.

Biosimilars are relatively new. Initially, doctors were hesitant to prescribe them due to their complexity and concerns about their comparative effectiveness. As more data has come out and doctors have become more informed, they have become more willing to prescribe biosimilars or encourage switching.[55] But concerns persist. In 2024, the FDA's Center for Drug Evaluation and Research observed that uncertainty about biosimilars arises, not only from limited experience, but also from "a general lack of understanding of what they are and how the FDA reviews and approves them."[56]

Because the statute's framework divides biosimilars into those that are "interchangeable" and others that are not, it naturally raises questions about the need for additional evidence. Branded manufacturers have even shaped their communications around these regulatory categories, engaging in a "whisper campaign" implying that interchangeable biosimilars offer a higher degree of assurance.[57] At the October 29, 2025, press conference, Secretary Kennedy spoke on how branded manufacturers initially argued that biosimilars are "too delicate" or "too mystical," thus undermining their biosimilar competitors.[58]

Federal agencies have cautioned that such marketing creates confusion. In response, the FDA and Federal Trade Commission announced in 2020 that they would address manufacturers' "false or misleading statements and promotional communications."[59] At a workshop a month later, they provided examples of some disparaging claims against biosimilars:[60]

- "[A]lthough the biosimilar is highly similar to its reference product, a patient may react differently to the biosimilar than to the reference product."
- "[O]nly interchangeable products provide the same degree of safety and efficacy as the reference product."

- "[T]he biosimilar has different effects than the reference product."

By acknowledging that all biosimilars are interchangeable, the FDA would reinforce the importance of accurate information in manufacturer marketing as well as encourage physicians and patients to explore biosimilars as treatment options.

4. Getting rid of the biosimilar-interchangeable distinction would allow greater substitution at the pharmacy.

While the FDA should not base its clinical determinations on pharmaceutical prices, greater streamlining would indirectly reduce prices by increasing substitution. Getting rid of the distinction between approved and interchangeable biosimilars would accurately signal to states that switching is safe. This is important for prescribers generally, but it is especially important for pharmacies. Today, state laws allow pharmacists to automatically switch out a prescribed biologic for a biosimilar only if the biosimilar is deemed interchangeable and less expensive for the patient.

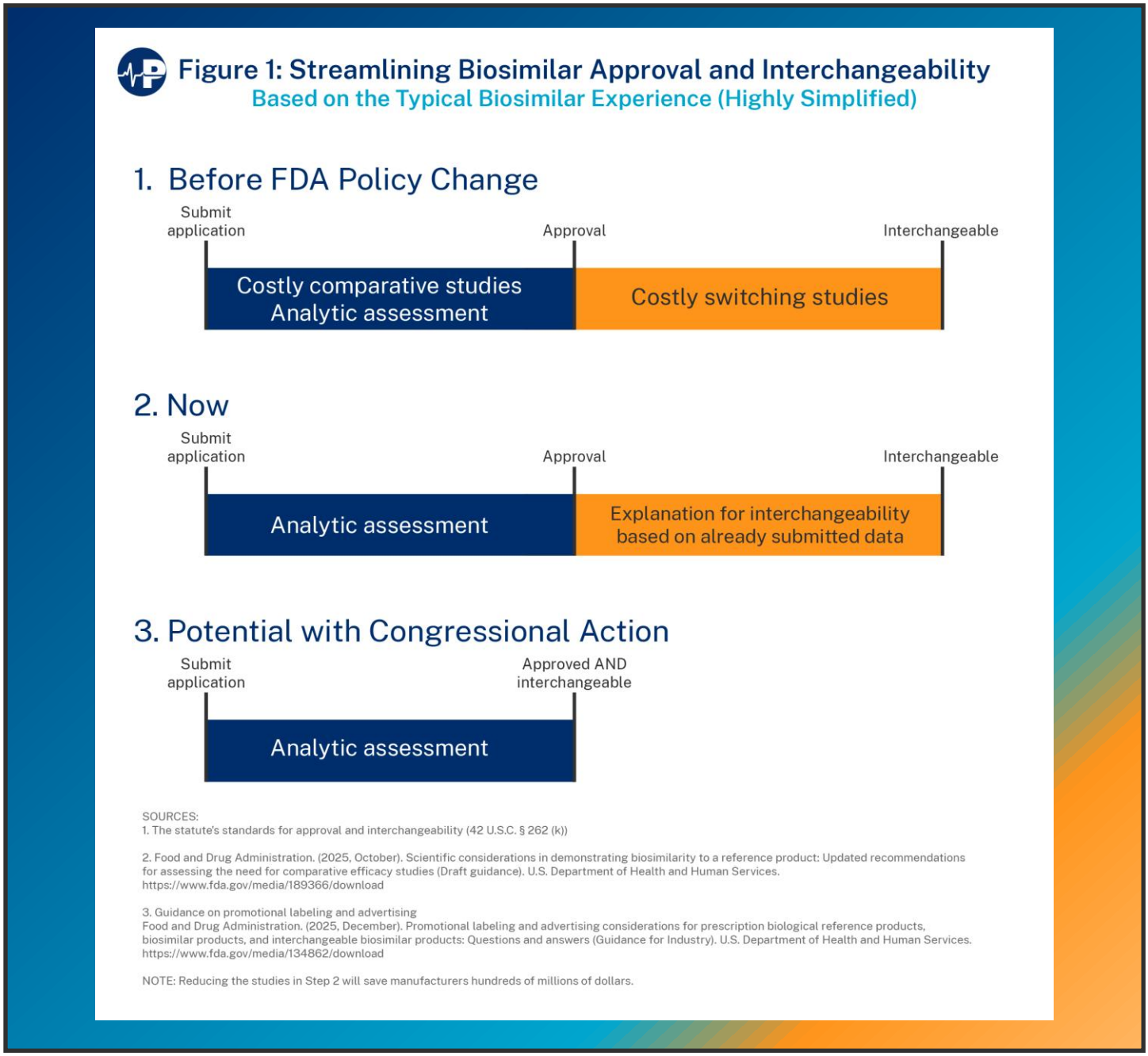
Because states have chosen to rely on federal standards, streamlining biosimilar approval and interchangeability could decrease costs for payers and patients because of greater competition. A recent study found that individuals seeking to fill prescriptions for insulin glargine were 7.03 percentage points more likely to fill their prescriptions with the interchangeable biosimilar if they were in states with "less stringent" biosimilar substitution laws.[61] Given that biosimilars cost 15–35 percent less than their respective reference biologics, the potential cost-savings from greater substitution could be significant.[62]

Not all biosimilars are dispensed directly to patients at the pharmacy. Many biosimilars that are classified by insurers as a "medical benefit" (as opposed to a "prescription" or "pharmacy" benefit) are accessible only under provider supervision. One recent industry report from the Association for Accessible Medicines noted that of the 17 biologics that face biosimilar competition, only four are "prescription benefit" biologics that would be impacted by pharmacy substitution.[63]

Nonetheless, eliminating the regulatory distinction between interchangeable and other biosimilar products could set the stage for future savings as biologic exclusivities expire and more prescription benefit biosimilars come to market. Currently, a significant number of biologics available at the pharmacy do not face any biosimilar competition. Biosimilars comprise only 2–3 percent of the total biologics market.[64] Biologics tend to dominate the specialty drug market.[65] Given that approximately 63.8 percent of specialty drugs are prescription or pharmacy benefit,[66] there is a significant potential market for biosimilars that will be impacted by state substitution laws.

Recommendations

- Congress should amend the statute to reflect that biosimilars, once approved, are automatically interchangeable with the branded versions. Because the United States has been using the interchangeable designation for the past 15 years, keeping the word *interchangeable* would prevent any confusion or perception of downgrade if existing interchangeable biosimilars were to lose that status. Moreover, because states follow the FDA's



interchangeability designation for purposes of pharmacy-level substitution, keeping the word *interchangeable* would allow for minimal disruption to state laws.

- The FDA should continue to find more applications to replace burdensome studies with more reliable technological assessments. And Congress should amend any statute that stands in its way. The FDA has already started using analytics to reduce animal testing for new drugs[67] and is poised to reduce them even further.

Similarly, as Kev Coleman has written, the FDA should leverage AI capabilities to reduce the manual labor involved in postmarket surveillance while still adequately monitoring for adverse events.[68] This may require updating Section 522 guidance[69] to specify the condition(s) under which the FDA would require postmarket surveillance for drugs and devices as well as for biologics.

Figure 1 illustrates how these changes would affect the biosimilar approval process.

Conclusion

Good regulatory governance means ensuring that regulations evolve with new information. When frameworks are left unchanged, they can outlive their usefulness and inadvertently create barriers rather than safeguards. The interchangeability standard for biosimilars is a prime example. At the time it was created, the FDA lacked the analytic tools to confidently evaluate switching. Today, however, modern analytic tools allow the FDA to evaluate biosimilars with a level of precision that makes the older "interchangeability" distinction unnecessary.

By retiring an outdated standard and streamlining biosimilar approval while reducing reliance on clinical studies, the FDA is showing how regulatory structures should work by adapting when the evidence changes. This shift not only aligns policy with scientific evidence but also builds trust, encourages competition, and opens the door to meaningful savings in one of the most expensive areas of medicine. Congress can further build on those changes through to the statute's language.

While formulary challenges and prescribing habits[70] have been the largest barriers to biosimilar uptake, eliminating the outdated distinction between biosimilars and interchangeable biosimilars is a common-sense step toward a more competitive market for some of the costliest treatments in health care.

About the Author

Chris Medrano is the Legal Research Analyst at the Paragon Health Institute. His work focuses on administrative rule making and policy analysis. Previously, he served as a Legislative Assistant to Senator Mike Lee (R-UT), where he managed the Health, Education, Labor, and Pensions (HELP) portfolio, including legislative reforms for the FDA and CMS.

---

[1] FDA, "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Updated Recommendations for Assessing the Need for Comparative Efficacy Studies," October 2025, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/scientific-considerations-demonstrating-biosimilarity-reference-product-updated-recommendations.

[2] Department of Health and Human Services (HHS), "Biosimilars Reform," press conference, October 29, 2025, https://www.youtube.com/watch?v=uqqMfugt-U8.

[3] IQVIA, "Assessing the Biosimilar Void in the U.S.: Achieving Sustainable Levels of Biosimilar Competition," February 3, 2025, https://www.iqvia.com/Insights/The-IQVIA-Institute/Reports-and-Publications/Reports/Assessing-the-Biosimilar-Void-in-the-US.

[4] HHS, "Biosimilars Reform."

[5] Dr. Marty Makary (@DrMakaryFDA), "A quick FDA Direct conversation today! Biologic drugs are incredible, but they're expensive – and they account for 51% of all drug spending. How can we bring cheaper alternatives to market?," X, November 5, 2025, https://x.com/DrMakaryFDA/status/1986087412074717650.

[6] Public Health Service Act, § 351(i)(1), 46 U.S.C. § 262, https://uscode.house.gov/view.xhtml?req=(title:42%20section:262%20edition:prelim).

[7] FDA, "List of Approved NDAs for Biological Products That Were Deemed to Be BLAs on March 23, 2020," https://www.fda.gov/media/119229/download.

[8] FDA, "What Are 'Biologics' Questions and Answers," https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/what-are-biologics-questions-and-answers.
[9] Avik Roy and Gregg Girvan, "The Growing Power of Biotech Monopolies Threatens Affordable Care," Foundation for Research on Equal Opportunity, September 15, 2020, https://freopp.org/whitepapers/the-growing-power-of-biotech-monopolies-threatens-affordable-care/.
[10] Dr. Marty Makary (@DrMakaryFDA), "A quick FDA Direct conversation today!"
[11] Lisa A. Raedler, "Zarxio (Filgrastim-sndz): First Biosimilar Approved in the United States," *American Health and Drug Benefits*, March 2016, https://pmc.ncbi.nlm.nih.gov/articles/PMC5013845/.
[12] FDA, "Biosimilar Product Information," https://www.fda.gov/drugs/biosimilars/biosimilar-product-information.
[13] Public Health Service Act, § 351(i)(2).
[14] FDA, "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product," April 2015, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/scientific-considerations-demonstrating-biosimilarity-reference-product.
[15] FDA Modernization Act 2.0, S.5002, 117th Cong. (2022), https://www.congress.gov/bill/117th-congress/senate-bill/5002.
[16] This is a significant shift. As of 2019, all biosimilars had conducted animal studies. See Parag Pipalava et al., "An Update on the Animal Studies Conducted for Biosimilar Approvals—Regulatory Requirement vs Actual Scenario," *Regulatory Toxicology and Pharmacology* 107 (2019): 104415, https://pubmed.ncbi.nlm.nih.gov/31254556/.
[17] Tony Hagen, "Study: Biosimilar vs Originator Spending on Comparative Efficacy Trials," Center for Biosimilars, March 4, 2021, https://www.centerforbiosimilars.com/view/study-spending-on-biosimilar-comparative-trials-is-greater-than-for-originators.
[18] Erwin A. Blackstone and P. Fuhr Joseph, "The Economics of Biosimilars," *American Health and Drug Benefits*, September/October 2013, https://pmc.ncbi.nlm.nih.gov/articles/PMC4031732/.
[19] Public Health Service Act, § 351(k).
[20] 155 Cong. Rec. E687 (daily ed. Mar. 17, 2009), https://www.congress.gov/111/crec/2009/03/17/CREC-2009-03-17-pt1-PgE687-3.pdf.
[21] 42 U.S.C. § 262 (k)(2)(B).
[22] Patrizia Cavazzoni and Sarah Yim, "The Science of Biosimilars—Updating Interchangeability," *JAMA* 332, no. 15 (2024):1235–1236, https://jamanetwork.com/journals/jama/article-abstract/2823807.
[23] Sarfaraz K. Niazi, "Scientific Justification and Policy Recommendations to the US Food and Drug Administration for Waiving Comparative Efficacy Studies," *Pharmaceuticals* 18, no. 6 (2025): 779, https://doi.org/10.3390/ph18060779.
[24] Niazi, "Scientific Justification and Policy Recommendations."
[25] Cardinal Health, "State Laws for Biosimilar Interchangeability," https://www.cardinalhealth.com/en/product-solutions/pharmaceutical-products/biosimilars/state-regulations-for-biosimilar.html.
[26] Sophia Humphreys, "Understanding Interchangeable Biosimilars at the Federal and State Levels," *American Journal of Managed Care* 29, no. 7 (August 2023): SP545–SP548, https://www.ajmc.com/view/understanding-interchangeable-biosimilars-at-the-federal-and-state-levels.
[27] Humphreys, "Understanding Interchangeable Biosimilars."
[28] Chana A. Sacks et al., "Assessment of Variation in State Regulation of Generic Drug and Interchangeable Biologic Substitutions," *JAMA Internal Medicine* 181, no. 1 (August 31, 2020), https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769770.
[29] "All of the five major European markets (France, Germany, Italy, Spain, and the UK) have banned automatic biosimilar substitution. Physicians in the UK are encouraged to prescribe brand-name biologics." *Pharmaceutical Technology*, "Market Outlook for Biosimilars," September 1, 2009, https://www.pharmtech.com/view/market-outlook-biosimilars.
[30] Alexandra Heal, "NHS Replaces Highest-Spend Drug with £300m Cheaper Alternative," *The Guardian*, November 25, 2018, https://www.theguardian.com/society/2018/nov/26/nhs-replaces-highest-spend-drug-with-300m-cheaper-alternative.
[31] Heal, "NHS Replaces Highest-Spend Drug."
[32] EMA and European Commission, *Biosimilars in the EU: Information Guide for Healthcare Professionals*, 2019, https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf.
[33] EMA, "Statement on the Scientific Rationale Supporting Interchangeability of Biosimilar Medicines in the EU," April 21, 2023, https://www.ema.europa.eu/en/documents/public-statement/statement-scientific-rationale-supporting-interchangeability-biosimilar-medicines-eu_en.pdf.
[34] S. Gokul et al., "The Biosimilar Revolution: Assessing the European Union's Approach to Biosimilarity, Interchangeability, Patient Access, and Its Market Analysis," *Cureus* 16, no. 8 (August 29, 2024): e68103. https://doi.org/10.7759/cureus.68103.
[35] EMA, "Streamlining Development and Assessment of Biosimilar Medicines," April 1, 2025, https://www.ema.europa.eu/en/news/streamlining-development-assessment-biosimilar-medicines.
[36] Gladys Rodriguez et al., "ASCO Policy Statement on Biosimilar and Interchangeable Products in Oncology," *JCO Oncology Practice* 19, no. 7 (April 7, 2023), https://ascopubs.org/doi/pdf/10.1200/OP.22.00783.
[37] Biosimilar Red Tape Elimination Act, S. 1954, 119th Cong.
[38] The author of this brief worked on this legislation as a legislative staffer.
[39] See page 281 of the bill at https://www.sanders.senate.gov/wp-content/uploads/TAM23D25_07.19.2023.pdf.
[40] FDA, "Labeling for Biosimilar Products," Regulations.gov, https://www.regulations.gov/docket/FDA-2016-D-0643.
[41] Thomas M. Herndon et al., "Safety Outcomes When Switching Between Biosimilars and Reference Biologics: A Systematic Review and Meta-Analysis," *PLoS ONE* 18, no. 10 (October 3, 2023), https://doi.org/10.1371/journal.pone.0292231.
[42] Office of Management and Budget, *Budget of the U.S. Government: Fiscal Year 2025*, p. 143, https://www.whitehouse.gov/wp-content/uploads/2024/03/budget_fy2025.pdf.

[43] FDA, "Considerations in Demonstrating Interchangeability with a Reference Product: Update," June 2024, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-demonstrating-interchangeability-reference-product-update.
[44] PR Newswire, "Professor Sarfaraz K. Niazi Secures First-Ever FDA Acceptance to Waive Clinical Efficacy Studies for Monoclonal Antibody Biosimilars," September 1, 2025, https://finance.yahoo.com/news/professor-sarfaraz-k-niazi-secures-142300145.html.
[45] Biosimilar Red Tape Elimination Act, H.R. 5526, 119th Cong.
[46] HHS, "FDA Moves to Accelerate Biosimilar Development and Lower Drug Costs," October 29, 2025, https://www.hhs.gov/press-room/fda-accelerates-biosimilar-development-and-lowers-drug-costs.html.
[47] Erik Doevendans et al., "The Devolution of Biosimilars Regulations," *Nature Biotechnology* 43 (2025): 19–22, https://doi.org/10.1038/s41587-024-02497-5.
[48] Cavazzoni and Yim, "The Science of Biosimilars."
[49] FDA, "Considerations in Demonstrating Interchangeability."
[50] Cavazzoni and Yim, "The Science of Biosimilars."
[51] FDA, "FY25 Legislative Proposals," p. 2, https://www.fda.gov/media/176924/download?attachment.
[52] Herndon et al., "Safety Outcomes When Switching Between Biosimilars and Reference Biologics."
[53] Herndon et al., "Safety Outcomes When Switching Between Biosimilars and Reference Biologics."
[54] Liese Barbier et al., "The Efficacy, Safety, and Immunogenicity of Switching Between Reference Biopharmaceuticals and Biosimilars: A Systematic Review," *Clinical Pharmacology and Therapeutics* 108, no. 4 (October 2020): 734–755, https://doi.org/10.1002/cpt.1836.
[55] IQVIA, "Unlocking Biosimilar Potential: Learning from Physicians Across Therapy Areas," April 4, 2023, https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/unlocking-biosimilar-potential.
[56] Sarah Ikenberry, "Education Efforts to Help Increase Biosimilar Understanding and Acceptance," FDA, February 14, 2024, https://www.fda.gov/drugs/our-perspective/education-efforts-help-increase-biosimilar-understanding-and-acceptance.
[57] Derrick Gingery, "Biosimilar Firms Fight Against 'Whisper Campaign' On Interchangeability," *Citeline*, October 22, 2017, https://insights.citeline.com/PS121810/Biosimilar-Firms-Fight-Against-Whisper-Campaign-On-Interchangeability/.
[58] HHS, "Biosimilars Reform."
[59] "Joint Statement of the Food and Drug Administration and the Federal Trade Commission Regarding a Collaboration to Advance Competition in the Biologic Marketplace," February, 2020, https://www.fda.gov/media/134864/download.
[60] Ibid.
[61] Youngmin Kwon et al., "State Substitution Laws and Uptake of an Interchangeable Insulin Biosimilar," *JAMA Health Forum* 6, no. 4 (2025): e250406, https://jamanetwork.com/journals/jama-health-forum/fullarticle/2831940.
[62] Kimberly Feng et al., "Patient Out-of-Pocket Costs for Biologic Drugs After Biosimilar Competition," *JAMA Health Forum* 5, no. 3 (2024): e235429, https://jamanetwork.com/journals/jama-health-forum/fullarticle/2816952.
[63] Those four are Sanofi's Lantus, Janssen's Stelara, Abvie's Humira, and Amgen's Enbrel. Association for Accessible Medicines, "The U.S. Generic and Biosimilar Medicines Savings Report," September 2024, https://accessiblemeds.org/sites/default/files/2024-09/AAM-2024-Generic-Biosimilar-Medicines-Savings-Report.pdf.
[64] Biosimilars and the Era of Interchangeability," editorial, *The Lancet Rheumatology*, September 2023, https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(23)00213-8/fulltext.
[65] Peter Wehrwein, "In the Specialty Drug Spend, Biologics Rule," *Managed Healthcare Executive*, July 29, 2024, https://www.managedhealthcareexecutive.com/view/in-the-specialty-drug-spend-biologics-rule.
[66] Wehrwein, "In the Specialty Drug Spend, Biologics Rule."
[67] FDA, "Roadmap to Reducing Animal Testing in Preclinical Safety Studies," https://www.fda.gov/files/newsroom/published/roadmap_to_reducing_animal_testing_in_preclinical_safety_studies.pdf.
[68] Kev Coleman and Michael J. Pencina, "Targeted Postmarket Surveillance: The Way Toward Responsible AI Innovation in Health Care," Paragon Health Institute, September 24, 2025, https://paragoninstitute.org/private-health/targeted-postmarket-surveillance-the-way-toward-responsible-ai-innovation-in-health-care/.
[69] FDA, "522 Postmarket Surveillance Studies Program," http://fda.gov/medical-devices/postmarket-requirements-devices/522-postmarket-surveillance-studies-program.
[70] Chad Rieger et al., "Barriers and Enablers Affecting the Uptake of Biosimilar Medicines Viewed Through the Lens of Actor Network Theory: A Systematic Review," *BioDrugs* 38 (2024): 541–555, https://link.springer.com/article/10.1007/s40259-024-00659-0.