Docket No. FDA-2025-N-2787
Title: *Advancing the Development of Interchangeable Products: Identifying Future Needs* (Public Workshop, September 19, 2025)
Submitted to: U.S. Food and Drug Administration, Center for Drug Evaluation and Research (CDER)

Date: October 19, 2025

To Whom it May Concern,

Thank you for the opportunity to provide comments on the September 19, 2025 Public Workshop entitled "*Advancing the Development of Interchangeable Products: Identifying Future Needs.*" Founded in 2010, the Alliance for Safe Biologic Medicines (ASBM) is a diverse group of stakeholders including physicians, pharmacists, patients, researchers, and manufacturers of biologic and biosimilar medicines, working together to advance patient-centered health policy in the U.S. and worldwide. It is ASBM's position that patients should have affordable access to innovative medicines, and that biosimilars are an important tool to expand that access by creating cost savings through market competition.

ASBM supports a competitive biosimilars market built on science that sustains physician and patient confidence. However, recent FDA signaling—including CDER Director George Tidmarsh's keynote remarks at the September 19 workshop and subsequent agency statements—suggest a troubling shift toward "genericizing" biosimilars: modeling their development, approval, and substitution on the small-molecule generic framework.[1] [2]

ASBM strongly opposes this direction. Biosimilars are not generics, and leading regulators including FDA and EMA have consistently affirmed this indisputable scientific fact.[3] [4] Europe's own policies confirm the distinction: European physicians, like their U.S. counterparts, may choose to prescribe a biosimilar in place of its reference product. However, "automatic" substitution (that is, substitution by a third party such as a pharmacist without physician involvement- a practice widely accepted with generics) remains rare - and is frequently banned in advanced European countries.[5] [6] Thus, the U.S. treating biosimilars as generics for substitution purposes would diverge it from—not harmonize—with Europe. Further, data show this approach would be rejected by majorities of physicians on both continents.[5] [6]

FDA's own workshop materials further acknowledge that analytical similarity aka "what's in the vial" is only part of the biosimilar experience.[1] Safe substitution requires consideration of device and user-interface differences, delivery mechanisms, and individual patient variability—including comorbidities, prior treatment failures, and immunogenicity risks—that cannot be captured by analytics alone.[1]

Finally, ASBM emphasizes that the largest barrier to biosimilar access is PBM formulary design and rebate contracting, not FDA's scientific standard. Lowering approval requirements or declaring all biosimilars interchangeable by fiat would not improve access; it would only erode confidence among physicians and patients, destabilize treatment, and jeopardize the integrity of the U.S. biosimilars framework.[5] [7] FDA should reaffirm—not dilute—its rigorous, data-driven, case-by-case approach to interchangeability, preserve the role of clinical evidence, and ensure that patients and clinicians have a seat at the table in future policymaking discussions.[1]

Biosimilars aren't generics; it is inappropriate for FDA to "genericize" them.

At the workshop, FDA leadership described an intent to "streamline" biosimilar assessment and model it on the generic framework—arguing that an "analytical revolution" brings biosimilars "very, very close to generic drugs." In his keynote address, CDER director Dr. George Tidmarsh announced "the genericization of biosimilars." A subsequent *Pink Sheet* report reiterates this, quoting Dr. Tidmarsh pledging to "update our regulatory standards" so that, going forward, FDA will take a "streamlined" approach "modeled on the generic drug framework."[2] These statements greatly concern the patient and clinician advocacy communities because they inappropriately disregard the consequential differences between biologics and small molecules. Calling a tiger a cat doesn't make it a good house pet. Such a cavalier attitude toward patient safety and treatment stability risks undermining hard-won physician and patient confidence.

For the record, FDA and other regulators including the EMA have long and consistently explained that biosimilars are not generics. FDA's own materials explicitly state "Biosimilars are not generics—and important differences exist between them," and its educational pages distinguish the two pathways.[3] EMA's core biosimilar resources likewise state: "A biosimilar is not regarded as a generic of a biological medicine."[4] For this reason, state Pharmacy Practice Acts needed to be updated over a period spanning roughly 2013-2021 to create a substitution system that recognizes this critical distinction.

These new laws empowered U.S. pharmacists to do something their European counterparts remain largely unable to do: offer lower-cost biosimilars to patients. This unique arrangement rests on the foundation of the FDA's evidence-based clinical trials that provide assurances to prescribers, patients, and pharmacists that substitutions will not disrupt treatment through reduced safety or efficacy. They were passed with the support of the physician and patient communities, but that support was contingent on substitution being limited only to FDA-interchangeable biosimilars (those backed by additional switching data) and assurances that only biosimilars meeting current FDA evaluation criteria would ever be substituted by third parties; i.e; insurers, pharmacy benefit managers. Treating biosimilars as generics for substitution purposes would betray these promises to patients and clinicians.

Generic-Style Substitution of Biosimilars Would Diverge—Not Harmonize—with Europe

It is a common misconception that in Europe, "all biosimilars are considered interchangeable" and that the U.S. needs to "catch up" by abandoning its two-tier system for biosimilar approvals. In 2022–2023, EMA and HMA issued scientific statements confirming that biosimilars approved in the EU can be used "interchangeably" with their reference products. However, this refers specifically to a physician's ability to select a biosimilar *when prescribing* (as U.S. physicians may do). These same documents emphasize that pharmacy-level automatic substitution remains a national decision and is outside EMA's authority- individual member countries regulate this and the majority of EU and EEA countries still restrict or prohibit automatic substitution of biologics at the pharmacy.[8] [9] In fact, automatic substitution by third parties is rare and frequently banned in advanced European countries.[6]

While the EMA's 2025 *Reflection Paper on a Tailored Clinical Approach for Biosimilar Development* explores streamlining development through greater reliance on analytical and functional comparability, it does not eliminate the expectation of confirmatory clinical evidence, nor does it propose changes to substitution policy.[10] In contrast, the FDA's emerging "genericization" approach not only minimizes the role of clinical studies, it effectively usurps state law on the topic and imposes third party substitution despite states having thoughtfully restricted when, how, and by whom substitution can occur.

Given U.S. state laws permitting automatic substitution of generics and interchangeables, declaring biosimilars generics—or de facto generics by designating all as interchangeable by default—would result in a generic-style automatic substitution system once interchangeability is broadly applied to biosimilars as a class.[1] [11]

Such a policy would be anathema to physicians on both sides of the Atlantic. Majorities of both European (76%) and U.S. physicians (59%) oppose substitution of biosimilars by anyone other than the prescribing physician, according to ASBM physician surveys[5] Moreover, 88% of U.S. physicians support FDA's current case-by-case evaluation of interchangeables, while only 11% support treating all biosimilars as interchangeable.[5]

In short: Europe is refining biosimilar science; FDA appears poised to undermine it. Where the EMA seeks efficiency within the established framework, the FDA's proposed shift risks converting a science-based biosimilar system into a generic-style mass-substitution model—a step that would undermine both physician confidence and patient safety.

"What's in the vial" neglects much of the real-world biosimilar experience

FDA's workshop slides repeatedly contrasted "what's inside the vial" with the additional, real-world considerations that affect safe pharmacy-level substitution. The workshop explicitly noted that while the same "inside-the-vial" data support both biosimilar and interchangeable approvals, additional substitution-related considerations may require more data—including differences in the user interface for combination products and accessory products such as pumps and diluents used with certain insulins.[1]

Likewise, FDA's human-factors session emphasized that user-interface and device differences can necessitate comparative human-factors analyses and, where appropriate, additional human-factors study data. FDA also pointed sponsors to forthcoming guidance on container-closure systems and device constituent parts, underscoring that device- and use-environment issues sit outside the reach of analytics alone.[1]

Finally, analytics cannot account for individual patient variability and medical history—for example, comorbidities, concomitant therapies, prior treatment failures, and patient-specific immunogenicity risks—which shape real-world safety and effectiveness. This is precisely why the statute's interchangeability standard speaks to producing the same clinical result "in any given patient," and why FDA's deck discusses immunogenicity considerations beyond laboratory characterization.[1]

Comparative clinical evidence (including switching studies) is data- and data drives uptake

FDA has been moving to reduce routine reliance on comparative clinical efficacy studies and switching studies for interchangeability, citing improved analytics and pooled switching data.[12] Yet clinical studies have been shown to significantly bolster physician confidence in biosimilars. In ASBM's 2024 national physician survey, 88% of U.S. physicians say switching studies increase their confidence in interchangeability, 87% prefer switching only when the biosimilar has been rigorously evaluated for switch impact, and only 11% favor treating all biosimilars as interchangeable by default (i.e. "genericizing" them by treating them as if they were generics—such as declaring them all interchangeable thus permitting automatic pharmacy substitution).[5]

FDA's workshop deck itself frames the policy shift: "Switching studies are not generally expected" now, based on the view that modern analytical tools are more sensitive than clinical studies—yet that same deck acknowledges those outside-the-vial issues that analytics can't fully address. Moving from analytics + targeted clinical confirmation to analytics-only may improve application efficiency, but it risks reducing provider confidence, especially where substitution introduces device or use-environment variables.[1]

FDA's mission requires balancing speed, affordability, and safety/quality—not trading quality for speed and price

The classic "iron triangle" of product development—frequently articulated as "good, fast, cheap: pick any two"—is a widely recognized model of trade-offs. In regulatory science, the analogue is FDA's duty to protect and advance public health: ensuring products are safe and effective while helping to speed innovations and improve affordability. When policy proposals prioritize faster, easier approvals explicitly to drive short-term cost savings, the implied trade-off tilts toward "fast and cheap," risking erosion of the "good" (quality and confidence). The *Pink Sheet* coverage of Dr. Tidmarsh's keynote statement explicitly ties the push to streamline interchangeability to an "analytical revolution," to modeling biosimilars on generics, and to policy goals tied to affordability.[2] ASBM cautions that regulatory framing matters: simply declaring biosimilars to be generics and eliminating the role of comparative efficacy studies (CES) will be heard by prescribers and patients as "lowering standards," undercutting years of stakeholder education that biosimilars are highly similar but not identical—and must be evaluated and substituted with appropriate safeguards.[3]

The market shows biosimilars thrive without lowering standards; the access bottleneck is formulary design

The U.S. now has more than 70 biosimilars approved; FDA's own deck tallied ~73 as of the workshop, while FDA's biosimilar product list shows 76 as of October 16, 2025.[1] [13] The agency and leading journals have also documented a trend toward interchangeability without dedicated switching studies in many cases—under existing authority—so there is no "insurmountable hurdle" requiring a wholesale lowering of standards.[12] Indeed, 9 of the first 13 interchangeable biosimilars were approved without such studies, as were 12 of the 27 interchangeables approved as of October 2025.[5] [14]

Humira (adalimumab) is a concrete case study in the success of biosimilars. By 2024–2025, PBMs moved to delist *Humira* from major national formularies, often steering to PBM-affiliated private-label adalimumab biosimilars; market list prices spanned a wide range (≈14% to 95% of the *Humira* list price).[15] In parallel, at least one interchangeable adalimumab (Boehringer's *Cyltezo*) was offered via GoodRx at ~92% discount, and other manufacturers (e.g., Coherus) publicly offered very deep list discounts.[15] This tremendous success is the result of natural market competition, not the result of lowering FDA's scientific standard.

What actually hinders biosimilar access is not FDA approval standards, but rather formulary and rebate incentives. The FTC's 2024–2025 interim reports detail how PBM contracting and exclusion practices can steer away from lower-cost options, including generics and biosimilars, and highlight the outsize influence PBMs exert over what gets covered and at what cost.[7]

Lowering FDA approval standards will not change PBMs' economic calculus; it will only diminish physician and patient confidence.

The interchangeable designation already enables generic-style automatic substitution—yet PBM designs still block access

Under U.S. law, only FDA-designated interchangeables may be automatically substituted at the pharmacy, subject to state law.[11] FDA's workshop reiterated this, and state substitution laws are generally consistent in recognizing interchangeables, though implementation details such as notification and consent vary slightly by state.[1] Notwithstanding this ability, interchangeable products have not consistently received the preferred formulary position; PBMs have excluded them while favoring high-rebate products or their own private-label biosimilars. Pretending all biosimilars are generics and may be safely automatically substituted like generics would not eliminate these formulary incentives. It would only undermine physician and patient confidence in biosimilar approval standards, and risk potentially jeopardizing treatment stability for millions of American patients by enabling mass-third party substitution of biosimilars that do not meet current data-driven approval standards for interchangeables.

Process concerns: the Sept. 19 workshop's "landscape of stakeholder perspectives" deliberately excluded critical stakeholders: patients and clinicians.

While FDA's agenda described a session on "The Landscape of Stakeholder Perspectives," in practice, the panel represented only the narrow perspectives of pharmaceutical manufacturers and trade associations (AAM, Biosimilars Forum, PhRMA). Absent were clinicians, pharmacists, and patient advocates—the end users of these medicines- all of whose confidence in biosimilars is central to their acceptance and resulting savings. They were not included as presenters.[1]

In a letter to Sarah Ikenberry, Senior Communications Advisor in the Office of Communications, within the Center for Drug Evaluation and Research (CDER) dated Sept. 4, 2025, ASBM co-founder and Executive Director of the Global Colon Cancer Association Andrew Spiegel, requested to speak at this meeting to share the concerns of patients and physicians about proposed changes to interchangeable biosimilar approval standards and the effects these changes would have on patients—but his request was denied. From his letter:

> While the perspectives of manufacturers are well represented at the workshop through three trade associations, and FDA staff will present valuable scientific insights, there is a notable absence of the voices of patients and clinicians at this hearing. But patients depend on the FDA's rigorous standards to ensure treatment stability is not jeopardized when switched to an interchangeable biosimilar. The clinicians we trust, too, are

underrepresented—they are the ones who prescribe these medicines and can attest to the variability of individual patient response which gives physicians confidence in the FDA's current data-driven approach to approving interchangeable biosimilars. For example, ASBM's recent survey of 270 U.S. physicians revealed that 88% favor the FDA's current case-by-case evaluation of interchangeables, while only 11% support a blanket approach that would treat all biosimilars as interchangeable—a policy now being advanced in Congress and by certain manufacturer trade groups.[5]

The exclusion of patient and clinician participation at a meeting explicitly devoted to stakeholder perspectives is worrisome. It risks marginalizing these indispensable stakeholders—relegating them from their traditional role as partners in policymaking to mere subjects of it, and undermining their confidence that the FDA has their best interests in mind. This dynamic is often summarized by the adage that *"those without a seat at the table often find themselves on the menu."*

For a topic so tightly tied to prescriber confidence and patient experience, it is critical that future FDA workshops on biosimilars should include these voices live among the presenters.

Conclusion

FDA's workshop and recent public statements signal a pivot toward "genericizing" biosimilars. That pivot is both unnecessary (the U.S. already has 76 biosimilars, strong competition, and deep discounts) and counterproductive- it risks eroding physician and patient confidence precisely when substitution decisions are becoming more complex as new, more complex therapeutic proteins become available and devices, accessories, and combination therapies affect real-world use beyond what simple analytics can model.

ASBM respectfully urges FDA to regulate in a manner consistent with the long-recognized scientific fact that biosimilars are not generics.

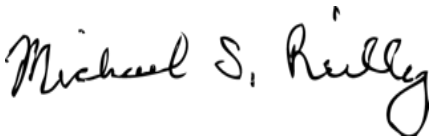
This fact has been clearly acknowledged by both FDA and EMA and guided the tailoring of a regulatory framework that supports a shortened approval pathway consistent with the science. We support maintaining FDA's flexible, case-by-case interchangeable biosimilar approval framework, which permits use of analytical and clinical data—including switching studies when appropriate—to ensure strong physician and patient confidence in substitution decisions. Comparative clinical studies should remain available tools that strengthen prescriber trust, not be abandoned in pursuit of regulatory speed.

ASBM further recommends that FDA finalize relevant guidance to address the role of the many "outside-the-vial" factors such as user interface, delivery mechanisms, patient-use environments, and individual patient variability, in efficacy and safety.

Importantly, ASBM emphasizes that the true barrier to biosimilar uptake lies in PBM formulary design and rebate practices, not in FDA's scientific standards; lowering those standards will not improve access and will only undermine confidence in biosimilars and risk jeopardizing treatment stability for millions of American patients. Finally, ASBM calls on FDA to ensure inclusive and balanced stakeholder participation at future workshops by including clinicians and patient advocates alongside industry representatives.

Thank you for the opportunity to comment on this important policy matter.

Sincerely,



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Endnotes

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