May 11, 2026

Docket No. FDA-2011-D-0611
Submitted to: U.S. Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

To Whom It May Concern,

Thank you for the opportunity to comment on the Food and Drug Administration's (FDA) Draft Guidance, *New and Revised Draft Q&As on Biosimilar Development and the BPCI Act (Revision 4) Guidance for Industry*. 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 efforts to modernize biosimilar development; unfortunately, this latest guidance follows a troubling trend that appears to shift the FDA toward the deliberate and inappropriate genericization of biosimilars, which would upend long-established scientific distinctions and move toward a system of mass substitution. We have specific concerns with *Q.I.8* and the use of comparative clinical data with a non-U.S.-licensed product to support demonstrations that proposed products are biosimilar to the reference product.

Comparative Clinical Data from Non-U.S.-Licensed Products Undermines Existing Standards

The FDA has established strict standards around biosimilar development in the United States, grounded in a rigorous scientific approach. Biologics are complex products whose clinical performance cannot be fully characterized through indirect comparisons alone. Direct comparative evidence for the U.S.-licensed reference product plays an essential role in the existing FDA framework, and weakening that foundation risks diminishing trust among physicians and ultimately patients. This draft guidance threatens to erode the confidence physicians and patients have in the FDA's gold-standard science that has put the United States at the forefront of global biopharmaceutical development.

Allowing comparative clinical data from a non-U.S.-licensed product would introduce unacceptable levels of uncertainty into the review process, and reduced reliance on direct comparison with a U.S.-licensed reference product creates risks that may only become apparent in real-world clinical use. As with prior policy proposals that sought to reduce evidentiary requirements for biosimilars, this change raises concerns that the FDA is moving away from its long-established patient-centered and evidence-based standards.

Impact On Physician and Patient Confidence in Biosimilars

The FDA's proposed approach to biosimilar approval stands in stark contrast to the rigor traditionally expected of innovator medicines, which must independently demonstrate safety and effectiveness through substantial evidence, generally grounded in well-controlled clinical investigations. For example, in Q.I.8.a, lines 164–168, the draft permits "analytical differences identified in product quality attributes between the non-U.S.-licensed comparator product used in the clinical study and the U.S.-licensed reference product included in the applicant's comparative analytical assessment," so long as the sponsor provides "an adequate scientific rationale" for those differences. This language could be read to suggest that if a biosimilar manufacturer offers a plausible explanation for detected quality differences, that rationale may be accepted without requirement to demonstrate its basis in fact. This raises an alarming possibility, as physicians and patients expect confidence in the quality of FDA-approved medicines, not merely adequate or plausible explanations - particularly when those medicines are complex biologics used by patients with serious and chronic conditions.

Maintaining physician and patient confidence in third-party biosimilar substitutions is critical, as biologic treatment is highly individualized and often involves patients with chronic, complex conditions. In ASBM's national physician surveys[1], 89% of prescribers expressed high confidence in the safety and effectiveness of biosimilars[2], and 88% of U.S. physicians supported maintaining the FDA's case-by-case approach to interchangeability, but only 11% favored treating all biosimilars as interchangeable by default.[3] This suggests that the FDA's rigorous, evidence-based framework has been effective at building confidence in biosimilars among physicians, but that confidence could be undermined if biosimilars are treated more like generics without proper, individual evaluation.

Reliance on foreign comparator products, manufactured under different conditions and outside of the FDA's gold-standard regulatory oversight, will result in a review process that does not account for real-world variability in patient populations or immune responses. These considerations are particularly important for patients with multiple comorbidities or heightened immunogenic risk. Direct comparative evidence for the U.S.-licensed reference product plays an essential role in the existing FDA framework and weakening that foundation risks diminishing trust among physicians and ultimately patients.

Conclusion

ASBM supports the FDA's goal of increasing patient access to biosimilars but achieving it cannot come at the cost of lowering scientific standards. Expanding reliance on non-U.S.-licensed comparator products risks lowering or appearing to lower these standards, threatening to undermine physician and patient confidence in biosimilars generally and in the FDA's guidance as a whole.

Thank you for the opportunity to comment on this important guidance.

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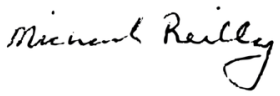
[1] http://www.safebiologics.org/surveys

[2] https://safebiologics.org/wp-content/uploads/2023/08/ASBM-2021-US-Biologics-Prescribers-Survey-Specialty-Data.pdf

[3] https://safebiologics.org/wp-content/uploads/2024/09/ASBM-US-Physician-Survey-IC-Biosims.pdf

Sincerely,



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