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FDA Issues Guidance to Industry in Effort to Accelerate Development and Reduce Costs of Biosimilar Drugs

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By Theodore Thompson

The U.S. Food and Drug Administration's (FDA) new draft guidance may reduce the cost and time to market for some applicants with biosimilar Biologic License Applications (BLAs). This draft guidance pivots from requiring comparative efficacy studies (CES) to demonstrate interchangeability to reference products, but the FDA may still require some applicants to collect substantial amounts of data, including expensive clinical study data.

BACKGROUND

The FDA presented a draft guidance directed to submitters of BLAs on October 29, 2025. The FDA explained that "biologic medications make up only 5% of prescriptions in the U.S. but account for 51% of total drug spending as of 2024." The administration recognizes the ability of biosimilar products to help reduce costs to patients and it explained that one purpose of the guidance is "to simplify biosimilarity studies and reduce unnecessary clinical testing." *See* FDA News Release.

Reducing the costs of development may facilitate market entry of interchangeable biosimilars, thereby increasing competition amongst biological product manufacturers and potentially reducing patient expense.

With this draft guidance, the FDA signaled that costly CES may not be necessary in many cases. The FDA stated in its October 29, 2025 news release that "[d]espite requiring 1-3 years and costing $24 million on average, comparative efficacy studies generally have low sensitivity compared to many other analytical assessments." Instead of using CES data, applicants may substitute relatively less expensive Comparative

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Analytical Assessments (CAA) in their biosimilar BLA submission.

Definition of Biological Products

In this context, biological product "means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings," 42 U.S.C. § 262(i)(1). These products take many forms and they are very important in treating a variety of conditions. This importance will likely continue growing as new biologics are produced and marketed.

Definition of Biosimilars

Biosimilar means a biological product that is highly similar to the reference product. *See* 42 U.S.C. § 262(i)(2). Demonstrating biosimilarity to reference products is necessary to obtain approval for a biosimilar BLA, but it is not sufficient for demonstrating interchangeability for the reference product. These reference products are already legally marketed.

Differences Between Biosimilarity and Interchangeability

According to 42 U.S.C. § 262(k), biosimilars may be legally marketed after the FDA determines that the product is either (a) biosimilar, or (b) interchangeable with the reference product. It may sound complicated, but biosimilars are sort of like generic equivalents of biological drugs that have two distinct categories: (bio)similar and interchangeable.

Biosimilar products are deemed to be highly similar to the reference product despite some minor differences. *See, e.g.*, 42 U.S.C. § 262(i)(2). Interchangeable products are so similar to the reference products that they "may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product," 42 U.S.C. § 262(i)(3). This substitutability represents a significant difference between the marketing of a biosimilar and an interchangeable product. The ability of pharmacists to substitute an interchangeable drug in place of a reference product without obtaining a new prescription from the prescribing caretaker may make interchangeable products more valuable than those that are determined to be merely biosimilar.

Switching Studies May Help Demonstrate Interchangeability

BLA applicants that request a determination of interchangeability must submit relevant data to the FDA. Applicants could use "switching studies" for this purpose. Switching studies are a type of CES involving human subjects that demonstrate "the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of

using the reference product without such alternation or switch," 42 U.S.C. § 262(k)(4)(B). Such studies support the conclusion that interchangeable biosimilar products may be substituted for reference products without detrimental effects to patients or reduced efficacy.

GUIDANCE SUGGESTS APPLICANTS RECONSIDER COMPARATIVE EFFICACY STUDIES

The FDA's draft guidance speaks directly to submitters of biosimilar BLAs. It states:

"Generally, if the CAA supports a demonstration that the proposed biosimilar is highly similar to its reference product, notwithstanding minor differences in clinically inactive components, an appropriately designed human pharmacokinetic similarity study and an assessment of immunogenicity may be sufficient to evaluate whether there are clinically meaningful differences between the proposed biosimilar and the reference product in terms of safety, purity, and potency." *See* Draft Guidance at 4.

More specifically, FDA states that a streamlined approach (e.g., use of a CAA instead of a CES) may be appropriate where:

"The reference product and proposed biosimilar product are manufactured from clonal cell lines, are highly purified, and can be well-characterized analytically; the relationship between quality attributes and clinical efficacy is generally understood for the reference product, and these attributes can be evaluated by assays included in the CAA; and a human pharmacokinetic similarity study is feasible and clinically relevant." *See* Draft Guidance at 4.

CONCLUSION

In sum, substation of a CAA for a CES may not work for all applicants. However, in instances where it is appropriate, it could save BLA applicants considerable amounts of money, and perhaps more importantly, time. Applicants must still acquire and submit substantial amounts of data to obtain a biosimilar BLA, but this draft guidance should be welcomed by industry and the patients they serve.

For more information on the FDA's draft guidance regarding biosimilar Biologic License Applications, please contact Theodore Thompson or the Stinson LLP contact with whom you regularly work.

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