5 Takeaways From FDA's Biosimilars Promotion Guidance

By **Abeba Habtemariam, Mahnu Davar and Kasia Foster** (May 9, 2024)

Abeba Habtemariam

Mahnu Davar

Kasia Foster

On April 24, the U.S. Food and Drug Administration released a revised draft guidance regarding promotional labeling and advertising considerations for prescription biological reference products, biosimilar products and interchangeable biosimilar products.

The revised draft guidance provides updated information about developing FDA-regulated promotional labeling and advertisements for biologics, outlining considerations for promotional communications for prescription reference products licensed under Section 351(a) of the Public Health Service Act and prescription biosimilar products, including interchangeable biosimilar products, licensed under Section 351(k) of the PHSA.

The revised draft guidance replaces an earlier draft guidance issued on Feb. 4, 2020. The revised draft guidance now includes additional recommendations, an example of an interchangeable biosimilar product and clarifying editorial changes.

The draft biosimilar promotion guidance also serves as a final step to accomplish the FDA's goals from its 2018 biosimilars action plan.

Five key takeaways about promotional communications for biologics from the draft biosimilar promotion guidance include the following.

1. Claims or studies referenced in promotional communications for biologics should be connected to the product for which that specific information applies.

The draft biosimilar promotion guidance includes recommendations for identifying products to help prevent presentations that are inaccurate because they attribute data or information to the wrong product.

Each time a promotional communication addresses a reference product or biosimilar product, or collectively addresses some combination of biosimilar products and reference products, the FDA recommends correctly and specifically identifying the product.

For example, the draft biosimilar promotion guidance states that "if a biosimilar product's FDA-approved labeling uses the core name of the reference product followed by the word 'products' to convey that a risk applies to both the biosimilar product and the reference product, it would also be appropriate for similar presentations about this risk in promotional communications for the biosimilar product to use this nomenclature."

2. Promotional communications should not imply that reference products are superior to biosimilar or interchangeable products.

The draft biosimilar promotion guidance emphasizes that biosimilars and interchangeable biosimilars are as safe and effective as their reference product and includes many

recommendations to ensure that promotional communications that present comparisons between reference products, biosimilars and interchangeables are not false or misleading.

For example, the guidance states that promotional communications that suggest a biosimilar product is less safe or less effective than a reference product because the licensure pathway for the biosimilar product differs from that for the reference product would be misleading.

The draft biosimilar promotion guidance also recommends that promotional communications for reference products avoid representing or suggesting that a biosimilar is less safe or effective than the reference product because the biosimilar has not been licensed as interchangeable.

Additionally, promotional communications for reference products should not imply that the reference product is superior to a biosimilar or interchangeable product by noting that the reference product is approved for more indications.

However, noting that biologics generally cannot be copied exactly, the draft biosimilar promotion guidance also states that promotional communications suggesting that a finding of biosimilarity means that the reference and biosimilar product are identical to one another generally would not be accurate.

The FDA has previously expressed concerns over promotion for biologics that implies that a reference product is superior to a biosimilar, showing a willingness to send enforcement letters over false or misleading statements that could undermine confidence in FDA-licensed biosimilar products.

For example, in 2021, the FDA sent an untitled letter to Amgen Inc. for misbranding of its biological product, Neulasta injection, for subcutaneous use.

Amgen had released a promotional communication citing an observational study, and made claims and presentations that the FDA said create a misleading impression about the benefit of Neulasta by stating that there is a statistically significant higher risk of febrile neutropenia when pegfilgrastim is administered through a prefilled syringe compared to an Onpro on-body injector.

The FDA found that the claims were not supported due to limitations of the study and expressed concerns that the claims could cause healthcare providers to conclude that pegfilgrastim delivered through the Onpro on-body injector is more effective than pegfilgrastim delivered through a prefilled syringe, or that it is more effective than FDA-licensed biosimilar pegfilgrastim products, which are only delivered through a prefilled syringe.

3. Promotional communications should not imply that interchangeable biosimilars are clinically distinct from other biosimilars.

The draft biosimilar promotion guidance includes a new example to emphasize that promotional communications should not imply that interchangeable biosimilars are superior to noninterchangeable biosimilars for the same reference product because of their difference in licensure.

The example uses a fictional reference product, Clarexant, a fictional product, Hilezeo, which is licensed as biosimilar to and interchangeable with Clarexant, and a fictional

product, Ompiram, which is licensed as biosimilar to, but not licensed as interchangeable with, Clarexant.

Under the example, if "[p]romotional communications for HILEZEO state that, unlike patients using OMPIRAM, patients using HILEZEO can be assured of HILEZEO's safety and effectiveness because HILEZEO is licensed as interchangeable with CLAREXANT while OMPIRAM is not," this presentation would be misleading because it suggests that a product licensed as interchangeable is superior in safety and effectiveness to a biosimilar product that has not been licensed as interchangeable with the reference product.

4. Promotional communications for biosimilars that present information from the studies conducted to support licensure of the reference product that is reflected in both the reference product and biosimilar product's labeling should refer to the biosimilar product's labeling.

When using information from the studies conducted to support licensure of the reference product that is reflected in both the reference product and biosimilar product's labeling, the FDA recommends that biosimilar promotional communications refer to the biosimilar product's labeling if it incorporates relevant data and information from the reference product's labeling.

For example, a biosimilar product's labeling usually contains data and information from the clinical studies section of the reference product's FDA-approved labeling for the conditions of use for which the biosimilar product is licensed, so the FDA recommends referring to the biosimilar product's labeling.

5. Promotional communications can sometimes include data or information about a biosimilar product that is not specifically included in the product's labeling.

The FDA addresses whether it is appropriate for promotional communications to include data or information that is not included in the biosimilar product's FDA-approved labeling, e.g., studies that supported the demonstration of biosimilarity between the biosimilar product and the reference product, which are generally not included in the FDA-approved labeling for the biosimilar product.

The FDA recommends that any promotional communications that include data or information that is not included in the FDA-approved labeling, but is consistent with the FDA-approved labeling for that product, follow the principles outlined in the guidance for industry titled "Medical Product Communications That Are Consistent With the FDA-Required Labeling: Questions and Answers."

Conclusion

This draft biosimilar promotion guidance follows other recent efforts to clarify expectations for biosimilar and interchangeable labeling and promotion, including the FDA's 2023 draft guidance regarding labeling for biosimilar and interchangeable biosimilar products.

The 2023 labeling guidance removed labeling distinctions between biosimilar and interchangeable products by no longer recommending use of the term "interchangeable" and providing that all products, whether biosimilar or interchangeable, should be referred to as "biosimilar" on the product label.

We expect that the FDA will continue to field questions and focus on biosimilar and

interchangeable promotion, as there has been an increasing number of biosimilar and interchangeable approvals.

Abeba Habtemariam and Mahnu Davar are partners, and Kasia Foster is an associate, at Arnold & Porter Kaye Scholer LLP.