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FDA-FTC Biosimilar Push Clarifies Antitrust Stance

By **Kellie Combs and Deborah Cho** (February 19, 2020)

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On Feb. 3, the U.S. Food and Drug Administration and the Federal Trade Commission announced a collaboration to promote biosimilar competition. The two agencies issued a joint statement outlining goals for the collaboration, which includes sponsoring a public workshop to hear from industry and other stakeholders.

The FDA also issued a draft guidance as part of this effort, titled "Promotional Labeling and Advertising Considerations for Prescription Biological Reference and Biosimilar Products: Questions and Answers," to provide firms guidance on developing FDA-regulated promotional materials, both for prescription reference and biosimilar biologic products.

Coordination with the FTC and guidance on promotional materials for biologic products are part of the FDA's broader biosimilars action plan, first announced by former Commissioner Scott Gottlieb in July 2018, which aims to increase access to medicine and reduce health care costs. Below, we describe key aspects of the FDA/FTC collaboration and draft guidance.

FDA/FTC Collaboration

The joint statement issued by the FDA and FTC describes how the agencies will work together to "promote competitive markets for biologic products and to take appropriate steps to address false or misleading statements and promotional communications by biologic manufacturers."

While the agencies acknowledge that biologics are critical to the treatment of many serious illnesses, the joint statement claims that biologics are the fastest growing and one of the most expensive segments of prescription medicine spending. A competitive marketplace is essential, the statement asserts, because it would lead to price reductions, increased consumer access and choice, and innovation. In furtherance of these broad objectives, the agencies jointly outline the following four goals:

1. The FDA and FTC will coordinate to promote greater competition in biologic markets, including by sponsoring a public workshop to discuss competition for biologics and by developing materials to educate consumers and health care providers about biosimilars.

The FDA/FTC Workshop on a Competitive Marketplace for Biosimilars is scheduled for March 9, and will focus on "FDA and FTC's collaborative efforts to support appropriate adoption of biosimilars, discourage false or misleading communications about biosimilars, and deter anticompetitive behaviors in the biologic product marketplace."[1] The event is open to the public, and the agencies encourage stakeholders to present at the meeting and to submit written comments to the docket, which is open through April 9.

2. The FDA and FTC will work together to deter behavior that impedes access to samples needed for the development of biologics, including biosimilars. For example, the agencies will collaborate to identify and deter practices that they view as preventing access to reference product samples needed for biosimilar or interchangeable product development.

Although not mentioned in the joint statement, this initiative follows the December 2019 passage of the Creating and Restoring Equal Access to Equivalent Samples Act, which among other things permits the developer of a generic drug or biosimilar product to file a civil action against an innovator manufacturer that declines to provide sufficient quantities of product samples for use in generic or biosimilar product development.

3. The FDA and FTC intend to take regulatory or enforcement action against false or misleading communications about biologics, including biosimilars.

4. The FTC will review patent settlement agreements involving biologics, including biosimilars, for antitrust violations.

Draft Guidance on Promotional Labeling and Advertising Considerations for Prescription Biological Reference and Biosimilar Products — Q&A

The FDA's draft guidance comes after calls from industry and other stakeholders for clarity in this area. It addresses several important issues related to the promotion of reference and biosimilar biologic products, while also underscoring that the general framework for prescription drug promotional requirements, such as the requirement that advertising and labeling must be truthful and nonmisleading, forms the basis for the agency's biologic product-specific recommendations.

Key Considerations for Biologic Reference and Biosimilar Products

The draft guidance, which follows a Q&A format, includes the following recommendations, among others:

- Promotional materials should accurately identify the products described in the materials (e.g., the reference product, the biosimilar product, or a non-U.S.-licensed comparator product).

- When considering what information or data about a reference product should be included in promotional materials for a biosimilar, firms should refer to the biosimilar product's labeling, as the labeling includes reference product information and data that the FDA believes is relevant to the biosimilar and that supported FDA's finding of safety and effectiveness.

- The FDA states, for example, that where a biosimilar is licensed for fewer conditions of use than the reference product, the biosimilar's labeling generally contains the data and information from the reference product's labeling that is relevant to the licensed conditions of use of the biosimilar product.

- Information and data from studies conducted to support a demonstration of biosimilarity to the reference product do not commonly appear in the biosimilar product's labeling, but firms may consider providing information

about such studies in their promotional materials. The FDA encourages firms that do so to apply the principles outlined in the 2018 guidance “Medical Product Communications That Are Consistent With the FDA-Required Labeling — Questions and Answers."

- As an example, the FDA states that it would not object to a presentation describing outcomes observed in a comparative clinical study of the biosimilar and a non-U.S.-licensed comparator product, so long as the presentation is consistent with the CFL guidance (e.g., it clearly and prominently provides contextual information about the study design and methodology, the role the study played in the biosimilarity evaluation, relevant data from the biosimilar product’s labeling, and any material limitations of the data) and accurately describes the comparator as non-U.S.-licensed.

- The draft guidance includes a number of recommendations regarding promotional materials that compare reference products and biosimilars and states that firms should carefully evaluate comparative presentations to ensure that they are not false or misleading. In particular, firms should avoid any presentations that create the impression that there are clinically meaningful differences between the reference product and biosimilar, or that the products are not highly similar.

- Presenting data on response rates in patients treated with the reference product as compared to response rates in patients treated with the biosimilar product may be appropriate if the header states that the biosimilar product is just as effective as the reference product.

- In contrast, the same data presentation with a different header (e.g., that the biosimilar product has greater efficacy than or is superior to the reference product because of nonclinically meaningful differences in response rate) would create a misleading impression.

- The draft guidance also posits that accurate statements, when provided in a comparative context, could contribute to a misleading presentation; for example, a statement that a biosimilar is licensed for fewer conditions of use than the reference product, or that approval for a particular indication was based on extrapolation, could contribute to the net impression that the biosimilar product is less safe or effective than the reference product.

- Firms should avoid suggesting that a biosimilar product is interchangeable with its reference product if it has not been licensed as interchangeable; similarly, because a biosimilar is not required to be identical to the reference product, firms should not represent that a reference product is safer or more effective than a biosimilar that has not been licensed as interchangeable.

- The draft guidance does not cover considerations relevant to promotional materials that discuss interchangeable biosimilars, which may not be viewed as pressing given that the agency has yet to license a biosimilar as interchangeable. That said, in its request for public comment on the draft guidance, the FDA asked stakeholders to weigh in not only on the issues discussed in the draft guidance, but also on the unique considerations that may apply in the context of interchangeable biosimilars and on other considerations that would help promotional materials convey truthful and non-misleading information about interchangeable products.

While the draft guidance provides a few examples of promotional materials that would or would not be appropriate, it ultimately emphasizes that the determination of whether a presentation is truthful and nonmisleading will be fact-specific and take into account factors such as how the information is presented, the type and quality of the data relied on to support the presentation, and contextual and disclosure considerations.

Implications for Industry

This much-anticipated draft guidance describes the FDA's views on many of the questions that have arisen as more biosimilar products have come to market. Although the development of promotional materials for reference and biosimilar products presents unique challenges, the draft guidance makes clear that the agency's existing promotional framework for prescription drugs — including the CFL guidance — generally applies to the promotion of these products.

An understanding of the CFL guidance is particularly important, as the clinical and other studies conducted to support biosimilar approval do not typically appear in biosimilar product labeling but may nevertheless be consistent with label and otherwise appropriate for promotion.

The CFL guidance describes a three-factor test for determining whether a promotional communication is consistent with label, which involves an analysis of whether the communication is covered by the labeled conditions of use, alters the risk-benefit profile of the product, and enables safe and effective use of the product.

The CFL guidance also recommends that communications be substantiated by information that is scientifically appropriate and statistically sound. The FDA states that information based on speculation or belief, as well as information based on a poorly designed or conducted study or analysis, would not meet the substantiation standard but otherwise does not elaborate on what types of data would or would not be sufficient.

In general, it may be reasonable to assume that studies submitted to the FDA and sufficient to support a biosimilarity determination would meet the substantiation standard, but it is critical that the promotional communication accurately characterize and appropriately contextualize the study and its results (e.g., by disclosing material limitations of the study, including relevant information from the FDA-required labeling).

The draft guidance also underscores the distinction between presenting data and making promotional claims, a distinction that is especially important when presenting data comparing reference products and biosimilar products. As described above, the draft guidance recommends that firms avoid any presentations that create the impression that there are clinically meaningful differences between the reference product and biosimilar, or that the products are not highly similar.

That recommendation does not mean that firms should avoid presenting comparative data or drawing other distinctions between biosimilar and reference products, but it highlights that firms should be mindful of headers, conclusory statements, disclaimers and other contextualizing information that accompanies the presentation of data and impacts the way the data are interpreted.

On the whole, the determination of whether a particular communication is appropriate for promotion is fact-specific, and while the draft guidance provides general recommendations, firms should carefully evaluate promotional claims and supporting data, ideally with the input of qualified medical or scientific, legal and regulatory personnel.

Conclusion

In recent years, the FDA has taken several steps aimed toward increasing patient access to medicine and lowering drug prices for consumers, including promoting competition in the biologic product market. The agency has expressed its concerns about, inter alia, false or misleading comparisons of reference products and biosimilars that may undermine public confidence in and uptake of biosimilars.

The collaboration with the FTC and the joint public workshop signals the FDA's commitment to addressing what the agencies consider to be anti-competitive behavior in the biologic market, and the draft guidance describes the FDA's thinking on common but previously unanswered questions, such as whether and when promotional materials for biosimilars may present data not included in their FDA-approved labeling.

Stakeholders have the opportunity to participate in this important dialogue by attending the public workshop on March 9, or by submitting comments on the draft guidance by April 6.

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[1] 1 85 Fed. Reg. 6203 (Feb. 4, 2020).