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Client Alert

FDA Issues Biosimilar Guidance for Label Carve-Outs and Supplements

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On February 6, 2020, the U.S. Food and Drug Administration ("FDA") issued a draft guidance ("Guidance") that addresses the licensure of a biosimilar or biosimilar interchangeable product for fewer than all of the conditions of use for which the reference product has been licensed. The Guidance addresses an issue of paramount importance to the biosimilar industry. As noted in the Guidance, there are a variety of circumstances that may lead a biosimilar applicant to pursue licensure for fewer than all of the reference product's licensed conditions of use, including the existence of orphan-drug and/or pediatric exclusivity or the existence of patents protecting one or more conditions of use.

The draft Guidance addresses four issues in detail: 1) the general requirements for seeking licensure of a biosimilar or interchangeable biosimilar product for fewer than all of the reference product's licensed conditions of use, 2) proposed labeling for such abbreviated BLAs ("aBLAs"), 3) submission of a supplement to an aBLA to seek licensure for a condition of use previously licensed for the reference product (e.g., where the biosimilar was originally licensed for fewer than all possible indications or where the reference product was recently licensed for a new condition of use after licensure of the biosimilar), and 4) timing of submission of an aBLA or supplement to a licensed aBLA with the goal to obtain licensure for a condition of use as soon as possible after expiration of any relevant exclusivity period or patents. A link to the draft Guidance is here.

Biosimilars vs. Interchangeable Biosimilars

Section 351(k) of the Public Health Services Act (42 U.S.C. §262(k)), which was added by the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), sets forth the requirements for the licensure of a biosimilar or interchangeable biosimilar. A biosimilar or interchangeable biosimilar may be licensed only for a condition or conditions of use that have been previously licensed for the reference product. Moreover, a biosimilar applicant generally may obtain licensure for a biosimilar or interchangeable product for *fewer* than all of the conditions of use for which the reference product is licensed. However, where a biosimilar applicant seeks licensure as an *interchangeable biosimilar*, "FDA recommends [the applicant] seek licensure for *all* of the reference product's licensed conditions of use when possible." (Guidance at 3). Indeed, FDA has stated that it expects that aBLA applicants seeking to demonstrate interchangeability will submit data and information showing that the proposed interchangeable product can be expected to produce the "*same clinical result as the reference product in all of the reference product's licensed conditions of use*." (*See* Guidance for Industry: *Considerations in Demonstrating Interchangeability With a Reference Product* (May 2019)).

Orphan-Drug Exclusivity

Where a reference product is licensed for one or more indications that are protected by orphan-drug exclusivity, FDA is not able to license a biosimilar or interchangeable product for the protected indications. However, FDA may be able to license the biosimilar or interchangeable for one or more indications of the reference product that are not protected by orphan-drug exclusivity. After the expiration of the orphan-drug exclusivity, the biosimilar applicant can submit a supplement in accordance with 21 CFR §601.12 seeking licensure for a previously protected indication.

Labeling Considerations

As part of the original aBLA, the biosimilar applicant is expected to submit draft labeling that includes the conditions of use for which the applicant is seeking licensure. In general, the draft labeling for the proposed biosimilar or interchangeable biosimilar should incorporate the relevant data and information from the reference product label relevant to the proposed condition(s) of use, *with appropriate modifications*. The Guidance recommends that the biosimilar applicant "carefully scrutinize the content of all sections of the labeling to ensure that relevant information is included." (Guidance at 5-6). The labeling must include the essential scientific information needed for the safe and effective use of the biosimilar product. In a previous guidance, FDA noted that "in certain circumstances it may be necessary to include information in the biosimilar product labeling relating to an indication(s) for which the biosimilar product is not licensed, in order to help ensure safe use." (*See* Guidance for Industry: *Labeling for Biological Products* (July 2018)). In addition, "although biosimilar labeling need not be identical to reference product labeling, deviations should be carefully considered to ensure that the condition or conditions of use prescribed, recommended, or suggested in the draft labeling for the proposed biosimilar product have been previously approved for the reference product." (Guidance at 6).

Timing of aBLA or Supplement Submissions

The Guidance provides the following recommendations for a biosimilar applicant who seeks to obtain licensure as soon as possible after expiration of any relevant exclusivity or expiration of a patent. In accordance with the Biosimilar User Fee Act goals, FDA expects to review and act on original aBLAs within 10 months of the 60-day filing date. Also, the current Guidance states that "[t]o the extent practicable, FDA intends that a supplement to a licensed 351(k) BLA seeking licensure of the biosimilar or interchangeable product for an additional condition of use that has been previously licensed for the reference product will be reviewed and acted upon in a *6-month timeframe*." The FDA cannot license a biosimilar or interchangeable product for an indication protected by orphan-drug or pediatric exclusivity until the expiration of that exclusivity. The BPCIA, however, does not limit FDA's ability to license an aBLA or a supplement to an aBLA where a biosimilar seeks licensure for a condition of use that may be subject to one or more patents. In case the biosimilar applicant may seek to time the submission with the goal of obtaining licensure after the expiration of a patent, the applicant can request in its submission that FDA not take action before a specified date. Such request must be in boldface type above the body of the cover letter. (Guidance at 8). The specified date, however, must be on or before the applicable BsUFA goal date.

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