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Practice Groups:

Biosimilars and Follow-On Biologics

Pharma and BioPharma Litigation

Food, Drugs, Medical Devices and Cosmetics (FDA)

The Next Move in the Name Game: FDA Provides Long-Awaited Draft Guidance on Biosimilar Labeling

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On March 31, 2016, the U.S. Food and Drug Administration (FDA) released its long-awaited Draft Guidance on labeling for biosimilar products (the "Draft Guidance") and is currently soliciting comments on its proposals. The FDA's Draft Guidance explains when to use the brand name (reference product name), when to use the biosimilar product name, and when to use a "core name" or "proper name." It also recommends that specific statements on biosimilarity be included in different portions of the labeling.

We have previously reported on issues concerning biosimilar labeling. The Name Game: Institutional Investors Submit Citizen Petition Regarding Biosimilar Labeling; The Name Game Continues: AbbVie Files Supplemental Citizen Petition Raising Additional Concerns Regarding Biosimilar Labeling.

The Draft Guidance's General Principles for Biosimilar Product Labeling

The Draft Guidance pertains only to biosimilars, and distinguishes between "biosimilarity" and "interchangeability." (Draft Guidance at 2, 12.) In general, it recommends that biosimilar labeling should rely primarily on the reference product's labeling with additional relevant data and information incorporated where appropriate, i.e., when necessary to inform safe and effective use of the biosimilar. (*Id*.)

Notable Specific Recommendations

The Draft Guidance provides the following specific labeling recommendations:

- When to use the biosimilar product name:
  - Labeling Sections with information specific to the biosimilar product: INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, DOSAGE FORMS AND STRENGTHS, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING.
  - Directive statements and recommendations for preventing monitoring, managing, or mitigating risks: BOXED WARNING, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and DRUG INTERACTIONS. (*Id*. at 6.)
- When to use the reference product name:
  - When clinical studies or data derived from studies with the reference product are included in the biosimilar product labeling: ADVERSE REACTIONS (Clinical Trials Experience) and CLINICAL STUDIES. (*Id*.)

- When to use the core name:
  - Instances where the brand label includes a serious adverse reaction or other risk not observed with the biosimilar: use the core name followed by the word "products," i.e., *replicamab products*. (*Id*. at 6–7.)
- A biosimilarity statement directly below the initial U.S. approval date. The Draft Guidance provides a fictitious example biosimilar product NEXSYMEO of a fictitious example reference product JUNEXANT, which would read: "NEXSYMEO (replicamab-cznm) is biosimilar* to JUNEXANT (replicamab-hjxf). The asterisk would appear as a footnote that reads:

  > *Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. (*Id*. at 8–9.)

Interestingly, the Draft Guidance continued to differentiate between biosimilars and reference products by use of a four-letter suffix added to the end of the active ingredient — e.g., "replicamab-cznm" and "replicamab-hjxf." (*See id*.) The name "replicamab-cznm" is a "proper name," which combines the "core name," "replicamab," with the four-letter suffix "cznm," the suffix being lowercase, unique, and devoid of meaning per previous draft guidance. (*See* Draft Guidance, Nonproprietary Names of Biological Products, p. 1 (FDA, August 2015); Biological Qualifier: An INN Proposal, Draft, July 2014, p. 4.)

- Immunogenicity information:
  - A specific immunogenicity statement should be included in a subsection of the ADVERSE REACTIONS section of the biosimilar labeling, providing an explicit warning that "comparison of the incidence of antibodies to [reference product's proper name] in the studies described below with the incidence of antibodies in other studies or to other products may be misleading." (*Id*. at 9–10.)
- Clinical study information:
  - The biosimilar label should include the reference product's clinical data but should not imply that the biosimilar is approved for a reference product indication or use that has not been approved for the biosimilar. (*Id*.)
  - FDA recommends that biosimilarity study information and data should not be included in the labeling of the proposed biosimilar product. (*Id*. at 3–4.)

The Draft Guidance does not recommend including data from biosimilarity studies because such data are "not likely to be relevant" to a health care practitioner and may be confusing because they can differ in, *e.g.*, patient population and study endpoints from the clinical studies regarding safety and efficacy of the reference product. (*Id*. at 2–3.) "As a general matter, it is FDA's view that biosimilar product labeling should not include a description of these data, given that a clinical study supporting the licensure of the biosimilar product generally would not be designed to independently demonstrate the safety and efficacy of the product, but rather to support a demonstration that there are no clinically meaningful differences between the proposed biosimilar product and the reference product for the approved indications." (*Id*.)

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Looking Forward

The Draft Guidance will remain open for comments until June 3, 2016. K&L Gates will continue to monitor further developments.

Link to Draft Guidance:
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM493439.pdf

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