U.S. FOOD & DRUG ADMINISTRATION

March 28, 2018

Ronald T. Piervincenzi, PhD
Chief Executive Officer
The United States Pharmacopeial Convention
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Dear Dr. Piervincenzi:

Thank you for the opportunity to comment on USP's proposed revisions to the USP General Notices and Requirements Section 2.20, relating to USP drug product monographs for biological products. We appreciate USP's outreach to FDA regarding the proposed revisions, including USP's October 2017 presentation to FDA. However, as we describe in detail below, FDA remains concerned that efforts to develop biological product monographs could impede or delay licensure of biosimilars[1] and other biological products.

We understand that USP's proposed revisions are intended to harmonize its approach to biological product monographs with the policy described in FDA's guidance for industry, *Nonproprietary Naming of Biological Products* ("Naming Guidance"). As the Naming Guidance explains, FDA's policy was developed to clearly identify biological products with the goal of facilitating pharmacovigilance and safe use. According to the Naming Guidance, the nonproprietary name designated for each originator biological product, related biological product, and biosimilar product will be a proper name that is a combination of the core name and a distinguishing suffix that is devoid of meaning and composed of four lowercase letters. The suffix format described in this guidance is applicable to originator, related, and biosimilar biological products previously licensed and newly licensed under section 351(a) or 351(k) of the Public Health Service Act (PHS Act). The Naming Guidance explains that, among other things, FDA is continuing to consider the appropriate suffix format for interchangeable products and the approach to implementing the naming convention for previously approved biological products that are deemed to be licensed under section 351 of the PHS Act on March 23, 2020.[2]

[1] Under the abbreviated licensure pathway created by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act), FDA will license a proposed biosimilar product that is shown to be "highly similar" to a previously licensed "reference product," notwithstanding minor differences in clinically inactive components, and that also meets other statutory requirements. An interchangeable product must be demonstrated to be biosimilar to the previously licensed reference product and meet additional criteria described in the BPCI Act.

[2] On March 23, 2020, an approved application for a biological product under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) shall be deemed to be a license under section 351 of the PHS Act (section 7002 (e)(4) of the BPCI Act).

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On September 29, 2017, USP issued a Notice of Intent to Revise, which proposed revising Section 2.20, "Official Articles of the General Notices and Requirements" to include the following text:

> "For a biologic product licensed under the Public Health Service Act, the official title shall be the title specified in the relevant monograph plus any suffix designated by FDA unless otherwise specified in the applicable monograph."[3]

USP stated that these revisions are "intended to ensure consistency between USP and FDA in the naming of biological products licensed under the PHS Act...."[4] On January 2, 2018, USP proposed the same revisions to the General Notices provisions through its Pharmacopeial Forum (PF) Process and provided a 90-day comment period.[5]

FDA has already communicated to USP the Agency's detailed concerns regarding biological product monographs.[6] In a 2014 letter to USP, FDA cited significant concern that monographs for biological products may impede or delay innovative technology and present an additional, unnecessary burden on regulated industry. As an alternative, FDA encouraged USP to develop optional standards that are "consistent with the flexible approach FDA uses to properly account for the complex nature of biological products."[7]

USP's proposed revisions to the General Notices and Requirements do not appear to FDA to provide the flexibility needed to support innovation in product development, despite USP's statement that the proposed revisions "provide[] flexibility, making it possible to apply different compendial approaches in situations where products share the same core name but have different suffixes."[8] In fact, if these revisions are implemented, FDA believes they could magnify the concerns the Agency has described previously.

As in 2014, FDA's ongoing concerns about biological product monographs are focused on the possibility that a sponsor of a proposed biosimilar or interchangeable product could be deterred from seeking licensure under the abbreviated pathway Congress created in the BPCI Act, which does not require the biosimilar applicant "to demonstrate that its product contains the 'same' drug substance as the reference product, evaluated using the same tests and assays."[9] USP's approach could complicate licensure of a

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[3] USP, Pharmacopeial Forum Posting PF 44(1), § 2.20 (Jan. 2, 2018). PF 44(1) also proposed additional revisions, which are not the subject of this letter.

[4] USP, Notice of Intent to Revise, General Notices and Requirements (Sept. 29, 2017; updated Oct. 5, 2017) ("2017 USP Notice of Intent to Revise"), available at http://www.uspnf.com/notices/general-notices-requirements. USP stated that the "revision will help address any potential compliance issues by ensuring that a biologic product that is given an FDA-designated suffix is not out of compliance with an applicable USP monograph." *Id.* FDA does not agree that a USP monograph (e.g. a monograph for which the official title lacks a suffix) applies to a biological product whose name contains an FDA-designated suffix.

[5] USP, Pharmacopeial Forum Posting PF 44(1), § 2.20 (Jan. 2, 2018).

[6] Letter from Karen Midthun and Janet Woodcock to Ronald T. Piervincenzi (March 13, 2014) ("2014 FDA letter to USP").

[7] 2014 FDA letter to USP, at 3.

[8] 2017 USP Notice of Intent to Revise.

[9] 2014 FDA letter to USP, at 2.

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biosimilar that meets the approval requirements under section 351(k) of the Public Health Service Act, but that does not match the standards in the USP monograph associated with the reference product.

Although USP's proposed revisions appear intended to provide some leeway to decide, for example, that a pre-existing monograph associated with a reference product does not apply to a biosimilar,[10] this does not address our concerns that USP's proposal could delay or impede licensure of a biosimilar that meets the licensure requirements under section 351(k) of the PHS Act, and could create substantial uncertainty for biosimilar applicants. We are particularly concerned that such a process will not be adequate to prevent delays in the licensure of biosimilars.

FDA is committed to supporting a robust marketplace of biological products that provide innovative, accessible therapeutic options to patients. The timely licensure of biosimilar and interchangeable products is essential to achieving greater price competition in this marketplace, which can help bring down the costs of biological products. Thus, any delay in licensure of biosimilar or interchangeable products could cause these potential savings to consumers and the healthcare system to be lost. Because USP's proposed revisions would aggravate existing concerns that a monograph could impede or delay the licensure of biosimilars and other biological products, FDA strongly encourages USP to withdraw its proposal. FDA welcomes future interaction with USP on these issues, with a goal of ensuring that biological product monographs do not create an unnecessary barrier to the availability of biosimilars and other biological products to patients. For example, we see opportunities for optional methodological standards that could encourage innovation and product development.

Sincerely,

Peter Marks, MD
Director, Center for Biologics Evaluation and Research

Janet Woodcock, MD
Director, Center for Drugs Evaluation and Research

[10] The proposed revisions conclude with the following phrase: "...unless otherwise specified in the applicable monograph." USP, Pharmacopeial Forum Posting PF 44(1), § 2.20 (Jan. 2, 2018).

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