Nonproprietary Naming of Biological Products: Update

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) Sandra Benton, 301-796-1042, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2019
Labeling

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Nonproprietary Naming of Biological Products: Update Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This draft guidance describes FDA's current thinking on *nonproprietary names*[2] of biological products licensed under section 351 of the Public Health Service Act (PHS Act) that do not include an FDA-designated suffix. Specifically, the nonproprietary names of these products need not be revised in order to accomplish the objectives of the naming convention described in the *Guidance for Industry: Nonproprietary Naming of Biological Products* (Naming Guidance).[3] Similarly, FDA does not intend to apply the naming convention described in the Naming Guidance to biological products that are the subject of an approved application under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) as of March 23, 2020, when such an application is deemed to be a biologics license application (BLA) under section 351 of the PHS Act on March 23, 2020 (*transition biological products*).[4]

In addition, this draft guidance describes FDA's current thinking on the appropriate suffix format for the *proper name* of an interchangeable biological product licensed under section 351(k) of the PHS Act. For each *interchangeable product*, FDA intends to designate 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.[5]

FDA is also reconsidering whether vaccines should be within the scope of the naming convention.

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[1] This guidance has been prepared by the Office of New Drugs and the Office of Surveillance and Epidemiology in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research at the Food and Drug Administration.

[2] Terms italicized on first use (other than the names of guidance documents) are found in the Glossary.

[3] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[4] See section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) (sections 7001 through 7003 of the Patient Protection and Affordable Care Act (Public Law 111-148)).

[5] The nonproprietary name designated by FDA in the license for a biological product licensed under the PHS Act is its proper name (section 351(a)(1)(B)(i) of the PHS Act (42 U.S.C. 262(a)(1)(B)(i)); 21 CFR 600.3(k)).

FDA believes this approach to implementing the naming convention is appropriate to: (1) facilitate pharmacovigilance for *originator biological products, related biological products, biosimilar products*, and interchangeable products when other means to track a specific dispensed product are not readily accessible or available; (2) facilitate accurate identification of these biological products by health care practitioners and patients; and (3) help minimize inadvertent substitution of biological products. Application of the naming convention to interchangeable products as described in this guidance should also further encourage routine use of designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices.

This draft guidance document is not intended to be finalized. FDA is issuing this draft guidance document to seek public comment on these issues through the accompanying docket. Based on the comments received in the docket, we intend to revise the Naming Guidance and to amend sections, such as sections IV.D and V.B, in that document regarding the subjects addressed in this guidance and issue a revised, final version of the Naming Guidance.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. SCOPE

This draft guidance describes FDA's current thinking on nonproprietary names of biological products licensed under section 351 of the PHS Act that do not include an FDA-designated suffix. Specifically, the nonproprietary names of these products need not be revised in order to accomplish the objectives of the naming convention described in the Naming Guidance. For similar reasons, FDA does not intend to apply the naming convention described in the Naming Guidance to transition biological products.

In addition, this draft guidance describes FDA's current thinking on the appropriate suffix format for the proper name of an interchangeable product licensed under section 351(k) of the PHS Act. For interchangeable products, FDA intends to designate 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.

FDA is also reconsidering whether vaccines should be within the scope of the naming convention.

For the purposes of this document, unless otherwise specified, references to biological products include biological products licensed under the PHS Act, such as therapeutic protein products, vaccines, allergenic products, and blood derivatives, and do not include certain biological products that also meet the definition of a device in section 201(h) of the FD&C Act (21 U.S.C. 321(h)), such as in vitro reagents (e.g., antibody to hepatitis B surface antigen, blood grouping

reagents, hepatitis C virus encoded antigen), blood donor screening tests (e.g., HIV and hepatitis C), and those reagents used in determining donor/recipient compatibility in transfusion medicine. Also, for the purposes of this document, unless otherwise specified, references to biological products do not include products for which a proper name is provided in the regulations (e.g., 21 CFR part 640) or to certain categories of biological products for which there are well-established, robust identification and tracking systems to ensure safe dispensing practices and optimal pharmacovigilance (e.g., ISBT 128 for cord blood products and blood components).

III. BACKGROUND

A. The Biologics Price Competition and Innovation Act of 2009

The Biologics Price Competition and Innovation Act of 2009 (BPCI Act), enacted in 2010, established an abbreviated licensure pathway for products demonstrated to be biosimilar to or interchangeable with an FDA-licensed *reference product*. FDA anticipates that licensure of new biosimilar and interchangeable products — in addition to licensure of new products in "stand-alone" BLAs — will contribute to a growing number of biological products entering the marketplace in the coming years.

Section 351(k) of the PHS Act (42 U.S.C. 262(k)), added by the BPCI Act, sets forth the requirements for an application for a proposed biosimilar product and an application or a supplement for a proposed interchangeable product. Section 351(i) defines biosimilarity to mean "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product" (see section 351(i)(2) of the PHS Act). To meet the additional standard of interchangeability, an applicant must provide sufficient information to demonstrate biosimilarity and also to demonstrate that the biological product can be expected to produce the same clinical result as the reference product in any given patient and, if the biological product is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch (see section 351(k)(4) of the PHS Act). Interchangeable products may be substituted for the reference product without the intervention of the prescribing health care provider (see section 351(i)(3) of the PHS Act).

B. Evaluation of the Appropriate Naming Convention

The proper name of a biological product reflects certain scientific characteristics of the product, such as chemical structure and pharmacological properties. This name is different from a *proprietary name*, which generally is trademarked and registered for private use. For biological products licensed under the PHS Act, FDA designates the proper name in the license for use upon each package of the biological product (see section 351(a)(1)(B)(i) of the PHS Act and 21 CFR 600.3(k)). Among other things, the proper name of a biological product helps health

care providers identify the product's drug substance and distinguish biological products from one another.

As part of FDA's implementation of the BPCI Act, the Agency requested public comment on its development of a framework for safe use and optimal pharmacovigilance for biosimilar products and interchangeable products that is informed by current experience and industry best practices, including the role of a product's proper name.

FDA has evaluated comments received on approaches to naming biological products, including biosimilar products and interchangeable products.[6] In light of the issues considered for biosimilar products and interchangeable products, FDA also evaluated its approach to designating proper names for biological products licensed under section 351(a) of the PHS Act.

In implementing the BPCI Act, FDA has carefully considered the appropriate naming convention to maximize the success of biosimilar products and interchangeable products and to help ensure the safety of patients receiving biological products licensed under the PHS Act.

The Naming Guidance currently states that application of the naming convention to originator biological products, related biological products, and biosimilar products will facilitate pharmacovigilance when other means to track a specific dispensed product are not readily accessible or available. The Naming Guidance explains that distinguishable nonproprietary names will facilitate accurate identification of these biological products by health care practitioners and patients, and that distinguishing suffixes should help minimize inadvertent substitution of any such products that have not been determined to be interchangeable. In addition, the Naming Guidance explains that application of the naming convention to biological products licensed under 351(a) or 351(k) of the PHS Act should encourage routine use of FDA-designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices, and should avoid inaccurate perceptions of biological products based on their licensure pathway. The Naming Guidance also states that a proper name that includes a distinguishing suffix is warranted for all licensed products.

IV. REVISED APPLICATION OF THE NAMING CONVENTION

A. Biological Products Licensed Without a Suffix and Transition Biological Products

[6] See, for example, notices published in the *Federal Register*: "Approval Pathway for Biosimilar and Interchangeable Biological Products; Public Hearing; Request for Comments" (75 FR 61497, October 5, 2010); "Draft Guidances Relating to the Development of Biosimilar Products; Public Hearing; Request for Comments" (77 FR 12853, March 2, 2012); "Nonproprietary Naming of Biological Products; Draft Guidance for Industry; Availability" (80 FR 52296, August 28, 2015); "Nonproprietary Naming of Biological Products; Guidance for Industry; Availability" (82 FR 4345, January 13, 2017); and other public dockets established by FDA.

FDA no longer intends to modify the proper names of biological products that were licensed under the PHS Act without an FDA-designated suffix in their proper names.[7] FDA also does not intend to apply the naming convention to the proper names of transition biological products.[8]

FDA has determined that the core objectives of the naming convention — pharmacovigilance and safe use — can be accomplished by applying the naming convention to biological products at the time they are licensed under section 351 of the PHS Act, and without applying it to licensed biological products that do not contain a suffix in their proper names. This approach is intended to minimize the potential burden for sponsors and the healthcare systems, and to avoid potential confusion for healthcare providers and patients, given that the nonproprietary names of drugs seldom change postapproval. Under this approach to applying the naming convention, most biological products that share the same core name will have nonproprietary names that are distinct from each other. Furthermore, applying the naming convention to all biological products at the time they are licensed under 351(a) or 351(k) is expected to mitigate the risk of inaccurate perceptions of the relative safety and effectiveness of biological products based on licensure pathway.

B. Vaccines

Vaccines are currently within the scope of the naming convention described in the Naming Guidance. However, FDA is reconsidering that approach and is evaluating whether the currently available identification systems associated with the administration of vaccines[9] are sufficiently robust to ensure safe dispensing practices and optimal pharmacovigilance without requiring distinguishable proper names.

V. SUFFIX FORMAT FOR INTERCHANGEABLE PRODUCTS SUBMITTED UNDER SECTION 351(k) OF THE PHS ACT

FDA considered two approaches to the format of the suffix for interchangeable products: A unique suffix that distinguishes an interchangeable product from other products sharing the same core name, or a suffix shared with the reference product.[10] FDA believes a distinguishing suffix is necessary to achieve adequate pharmacovigilance for these products. A unique suffix will facilitate manufacturer-specific pharmacovigilance by providing a means of determining which

[7] FDA has licensed, under section 351 of the PHS Act, several biological products with proper names that include a four-letter suffix.

[8] See the guidance for industry *Interpretation of the "Deemed To Be a License" Provision of the Biologics Price Competition and Innovation Act of 2009* (December 2018). For the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[9] For example, the National Childhood Vaccine Injury Act of 1986 requires each healthcare provider (HCP) who administers a vaccine included in the "Vaccine Injury Table" to any person to "record … in such person's permanent medical record … (1) the date of administration of the vaccine, (2) the vaccine manufacturer and lot number of the vaccine, (3) the name and address and, if appropriate, the title of the [HCP] administering the vaccine, and (4) any other identifying information on the vaccine required pursuant to regulations promulgated by the Secretary" (42 U.S.C. 300aa–25).

[10] See "Nonproprietary Naming of Biological Products; Draft Guidance for Industry; Availability" (80 FR 52296, August 28, 2015).

biological product is dispensed to patients when other means to track this information are not readily accessible or available. Use of a distinguishing suffix will also avoid the need for changes to the nonproprietary name of a biological product that is first licensed as a biosimilar product and later determined to be an interchangeable product. Such changes could be burdensome on sponsors, FDA, and the health care system, and could confuse health care practitioners or patients.

Application of the naming convention to interchangeable products should further encourage routine use of designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices, and should help mitigate the risk of and avoid inaccurate perceptions of the safety and effectiveness of biosimilar biological products that do not have an interchangeability determination.

An applicant for a proposed interchangeable product submitted under section 351(k) of the PHS Act should propose a suffix composed of four lowercase letters for use as the distinguishing identifier included in the proper name designated by FDA at the time of licensure. Such submissions can be made during the investigational new drug application (IND) phase[11] or at the time of BLA submission. An applicant should submit up to 10 proposed suffixes, as described in the Naming Guidance, in the order of the applicant's preference. We recommend including any supporting analyses of the proposed suffixes for FDA's consideration based on the factors described in the Naming Guidance.

An applicant seeking a determination of interchangeability in a supplement to an approved 351(k) application will keep the nonproprietary name of its product including the FDA-designated suffix without submitting further proposed suffix requests to FDA for review. At the time of supplement submission, the applicant would reflect the proper name, including the previously designated suffix, throughout the proposed labeling for the interchangeable product.

[11] A request for FDA review of a proposed suffix submitted during the investigational new drug application (IND) phase should be submitted no earlier than at the request for a biosimilar biological product development (BPD) type 4 meeting for biological products to be submitted under section 351(k) of the PHS Act.

GLOSSARY

Biosimilar Product means a biological product submitted in a 351(k) application that has been shown to be highly similar to the reference product notwithstanding minor differences in clinically inactive components, and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product (see section 351(i)(2) of the PHS Act).

Core Name means the component shared among an originator biological product and any related biological product, biosimilar product, or interchangeable product as part of the proper names of those products. Two examples of a *core name* are filgrastim and epoetin alfa.

Interchangeable Product means a biological product that has been shown to meet the standards described in section 351(k)(4) of the PHS Act and may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product (see section 351(i)(3) of the PHS Act).

Nonproprietary Name means a name unprotected by trademark rights that is in the public domain. It may be used by the public at large, both lay and professional.

Originator Biological Product means a biological product submitted in a BLA under section 351(a) of the PHS Act (i.e., a stand-alone BLA) that is not a related biological product.

Proper Name means the nonproprietary name designated by FDA in the license for a biological product licensed under the PHS Act (21 CFR 600.3(k)).

Proprietary Name means the trademark or brand name.

Reference Product means the single biological product licensed under section 351(a) of the PHS Act against which a biological product is evaluated in a 351(k) application (section 351(i)(4) of the PHS Act).

Related Biological Product means a biological product submitted in a BLA under section 351(a) of the PHS Act (i.e., a stand-alone BLA) for which there is a previously licensed biological product submitted in a different section 351(a) BLA that contains a drug substance for which certain nomenclature conventions (e.g., United States Adopted Names (USAN) Guiding Principles[12]) would be expected to provide for use of the same drug substance name.[13]

[12] The United States Pharmacopeial Convention, 2016, Guiding Principles for Coining United States Adopted Names for Drugs (*2016 USP Dictionary of USAN and International Drug Names at* http://www.uspusan.com/usan/pub/index1.html).

[13] FDA's description of a biological product as a *related biological product* in this guidance is separate from any determination FDA may make about whether a related biological product is eligible for a period of exclusivity under section 351(k)(7) of the PHS Act.

Transition Biological Product means a biological product that is the subject of an approved application under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) as of March 23, 2020, that will be deemed to be a biologics license application (BLA) under section 351 of the PHS Act on March 23, 2020 (see section 7002(e)(4) of the BPCI Act).