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May 7, 2019

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2013-D-1543: Nonproprietary Naming of Biological Products: Update; Draft Guidance for Industry; Availability

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to provide comments on the Food and Drug Administration's (FDA's or the Agency's) draft guidance entitled "Nonproprietary Naming of Biological Products: Update" (Draft Guidance).[1] PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member companies have invested more than $600 billion in the search for new treatments and cures, including an estimated $71.4 billion in 2017 alone.

PhRMA appreciates FDA's continued efforts to thoughtfully implement the Biologics Price Competition and Innovation Act of 2009 (BPCIA), including with respect to the nonproprietary naming of biological products. We support FDA's proposal in the Draft Guidance to designate a proper name comprising a core name and a distinguishing four-letter suffix (the naming convention) for interchangeable biological products.[2] This approach intends to put patient safety first by applying a four-letter suffix; it will enhance pharmacovigilance for all biological products which should enable targeted remedial action when necessary. It also will minimize burdens on stakeholders and FDA alike when a previously approved biosimilar is later deemed interchangeable.

PhRMA also supports exempting vaccines subject to the recordkeeping requirements of the National Childhood Vaccine Injury Act of 1986 from the naming convention.

We provide further thoughts on these issues below.

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[1] 84 Fe. Reg. 8534 (Mar. 8, 2019).

[2] FDA, Draft Guidance for Industry, Nonproprietary Naming of Biological Products: Update (Mar. 2019), at lines 70-72 [hereinafter Draft Guidance].

I. PhRMA Supports Distinguishing Suffixes for Interchangeable Biological Products

PhRMA agrees with FDA's proposal to apply the naming convention to interchangeable biological products.[3] PhRMA strongly supports the Draft Guidance's emphasis on the safety of patients who are treated with any biological product. As FDA notes in its final guidance for industry "Nonproprietary Naming of Biological Products" (Naming Guidance), biological products "raise unique safety concerns related to immunogenicity."[4] This key difference between biological products and small-molecule drugs strongly supports a nonproprietary naming framework that differentiates among biological products, including interchangeable biological products. Applying the naming convention to interchangeable biological products will facilitate pharmacovigilance and targeted remedial action, promote safe use, and minimize burdens.

A. *Distinguishable Suffixes Facilitate Pharmacovigilance and Targeted Remedial Action*

We agree with FDA about the pharmacovigilance benefits of including a distinguishing suffix in the nonproprietary name of an interchangeable biological product. As FDA explains in the Draft Guidance, distinguishable suffixes "will facilitate manufacturer-specific pharmacovigilance by providing a means of determining which biological product is dispensed to patients when other means to track this information are not readily accessible or available."[5]

The ability to accurately attribute adverse events to the involved product is undoubtedly critical to effective pharmacovigilance. Like other biosimilar products, interchangeable products need to be distinguishable from the reference product and from each other in the interests of safe use and accurate pharmacovigilance. As FDA previously explained, "surveillance systems [must] be able to detect safety signals *throughout the lifecycle of a product*"[6]—not just until a biosimilar is deemed interchangeable with its reference product. Multiple interchangeable versions of a single reference product likely will be approved without the availability of data demonstrating them to be interchangeable with one another. Individual interchangeable products could have greater differences in structure, container closure system, and other attributes from each other than from the reference product. Further, two interchangeable products generally will not have a data package that evaluates the impact of alternating or switching between the two products.[7] Consequently, not only might multiple

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[3] PhRMA has previously supported applying the naming convention to interchangeable biological products. *See, e.g.*, PhRMA, Comments on Draft Guidance for Industry: Considerations in Demonstrating Interchangeability With a Reference Product, Docket No. FDA-2017-D-0154 (May 19, 2017), at 13-14; PhRMA, Comments on Draft Guidance for Industry: Nonproprietary Naming of Biological Products, Docket No. FDA-2013-D-1543 (Oct. 29, 2015), at 11-12 [hereinafter PhRMA 2015 Draft Guidance Comments]; Comments to Generic Pharmaceutical Association Citizen Petition, Docket No. FDA-2013-P-1153 (Feb. 3, 2014), at 15.

[4] FDA, Guidance for Industry, Nonproprietary Naming of Biological Products (Jan. 2017), at 5 [hereinafter Naming Guidance].

[5] Draft Guidance at lines 196-99.

[6] 80 Fed. Reg. at 52,226 (emphasis added).

[7] *See* Draft Guidance for Industry: Considerations in Demonstrating Interchangeability With a Reference Product (Jan. 2017), at lines 586-588 ("[W]ith switching, multiple exposures to each product can prime

interchangeable products not meet the statutory standard of interchangeability with respect to one another, but switching among them may present the risk of additional or different immunogenicity issues than would result from switching between the reference product and a particular interchangeable product. Assigning a distinguishable suffix to each interchangeable biosimilar product would help identify the product associated with a given adverse event to help promote accurate monitoring of these issues in the postmarketing setting.

PhRMA thus agrees with FDA that distinguishable suffixes are "necessary to achieve adequate pharmacovigilance for [interchangeable biological] products."[8] In the absence of distinguishable nonproprietary names for interchangeable biological products, and depending on the types and accuracy of information provided in an adverse event report, license holders, physicians, and health authorities might not be able to identify the specific product within a class of products associated with a specific adverse event. We agree with FDA that other product identifiers, including National Drug Codes (NDCs) and lot numbers, are insufficient to ensure robust pharmacovigilance due to their infrequent use in both active and passive pharmacovigilance systems.[9] Similarly, as FDA has stated, proprietary names are not consistently used when ordering, prescribing, or dispensing products or in adverse event reports,[10] and a sponsor seeking licensure of a biological product in the U.S. is not required to use a proprietary name for its product. Distinguishable nonproprietary names thus play a crucial role in helping enable license holders, physicians, and health authorities to identify the specific product associated with a specific adverse event.

In contrast, if interchangeable biological products shared nonproprietary names with each other and their common reference product, confusion over the identity of the specific biological product(s) associated with an adverse event could impede or delay the effective analysis and correction of a potential safety or quality issue. Shared nonproprietary names could hinder detection of a signal associated with only one product or a subset of products. Moreover, shared nonproprietary names might cause the signal to be imputed erroneously to the entire product class. In the absence of an effective analysis of a potential safety issue and faced with the inability to identify whether the issue affects all products or just one product, FDA might determine it is necessary to recall the originator product and all biosimilar, interchangeable, and related biological products, which could result in shortages and supply issues for patients. Applying the naming convention to interchangeable biological products will help detection of product-specific signals and avoid unnecessary class-wide remedial action.

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the immune system to recognize subtle differences in structural features between products, and the overall immune response could be increased under these conditions.").

[8] Draft Guidance at line 196.

[9] *See* Naming Guidance at 5; 80 Fed. Reg. at 52227 ("Many therapeutic biological products are administered in settings, such as physician offices, clinics, or hospitals, where the administrative and billing data do not routinely include product identifiers such as brand name, manufacturer, NDC number, or lot number.") (citations omitted); *id.* ("[I]n many passive pharmacovigilance systems, proprietary names and NDC numbers are often not included in adverse event reports") (citations omitted).

[10] Naming Guidance, at 8.

B. *Distinguishable Suffixes Encourage Safe Use of Interchangeable Products*

PhRMA further believes that applying the naming convention to interchangeable biological products will promote safe use of these products.

If multiple interchangeable versions of a single reference product were assigned the same suffix without an FDA determination that they are interchangeable to each other, there might be inadvertent substitution among these products. In other words, as FDA has said, health care providers "may incorrectly assume that FDA has determined biological products with the same proper name to be interchangeable."[11] Distinguishing suffixes thus will help prevent inadvertent substitution among biological products not shown to be interchangeable with one another.[12]

Especially in the treatment of complex, debilitating, or life-threatening diseases, a physician must be able to communicate clearly with a patient about his or her treatment, and methods must be available to identify the product dispensed. Distinguishable nonproprietary names for all biological products, including interchangeable biological products, offer an additional means for supporting these objectives.

C. *Applying the Naming Convention to Interchangeable Biologics Products Will Minimize Burdens*

We concur with FDA that applying the naming convention to interchangeable biological products will reduce burdens and the potential for confusion. Under the alternative approach in which interchangeable biological products would share suffixes with the reference product, name changes would have been necessary for products initially licensed as biosimilar and later licensed as interchangeable biological products. Applying the naming convention to interchangeable biological products will obviate the need for these name changes.[13] This approach also will help avoid prescriber and patient confusion from these name changes. A consistent suffix throughout the lifecycle of a product will facilitate accurate identification of the biological product and thereby accomplish the naming convention's "core objectives" of pharmacovigilance and safe use.[14]

II. Certain Vaccines Should Be Exempt From the Naming Convention

PhRMA would support a decision by FDA to exempt vaccines subject to the recordkeeping requirements of the National Childhood Vaccine Injury Act of 1986 from the naming convention.[15] As the Agency notes, the requirements for administration of these vaccines and related documentation are unique: healthcare providers must record in detail the

[11] Naming Guidance at 6.

[12] *See also* PhRMA, Comments on Biosimilars Action Plan, Docket No. FDA-2018-N-2689 (Sept. 21, 2018), at 2 ("[T]o promote confidence in biosimilar and interchangeable products, the Purple Book should clarify that an interchangeability determination reflects FDA's judgment that an interchangeable biosimilar may be substituted for the reference product, not another biosimilar product").

[13] Draft Guidance at lines 199-203.

[14] *See id.* at lines 168-69.

[15] 42 U.S.C. 300aa–25.

specific vaccine—including manufacturer and lot number—that a patient receives.[16] Thus there are already robust mechanisms for ensuring effective pharmacovigilance and safe use of these products. Furthermore, the names of vaccines are often abbreviated in health care systems, making the introduction of a distinguishable suffix more challenging as a practical matter. Given special considerations for these vaccines, PhRMA believes that the naming convention should not apply to these products and that FDA should clarify whether the scope of any such exemption is limited to products subject to the recordkeeping requirements of the National Childhood Vaccine Injury Act of 1986.

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PhRMA appreciates FDA's consideration of these comments on the Draft Guidance. We are available to discuss these issues further if the Agency has any questions.

Respectfully submitted,

_____/s/_____	_____/s/_____	_____/s/_____
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[16] Draft Guidance at n.9 (discussing requirements in the National Childhood Vaccine Injury Act of 1986 (42 U.S.C. 300aa-25)).