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Re: Docket No. FDA-2013-D-1543: Draft Guidance for Industry on Nonproprietary Naming of Biological Products

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and Manufacturers of America (PhRMA) is pleased to provide comments on the Food and Drug Administration's (FDA's) draft guidance entitled "Nonproprietary Naming of Biological Products" (Draft Guidance).[1] PhRMA represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA companies are leading the way in the search for new cures, with members investing an estimated $51.2 billion in 2014 in the discovery and development of new medicines. Importantly, many of PhRMA's members are actively researching and developing new biosimilar products to bring to patients.

Summary

PhRMA supported the enactment of the Biologics Price Competition and Innovation Act (BPCIA) and has actively participated in FDA's ongoing efforts to implement the statute. PhRMA's consideration of these matters is guided by our support for:

- **Science-based implementation** of the BPCIA and regulatory decision-making;
- **Patient safety** through effective identification of biologics and robust pharmacovigilance;
- **Healthcare provider and patient choice** in prescribing;
- **Regulatory transparency** that enables stakeholders to understand the basis for FDA's decisions; and
- **Long-term stability of the biosimilar user fee program** through financial transparency, efficiency, and accountability.

PhRMA applauds FDA's issuance of the Draft Guidance and its proposal to adopt distinguishable nonproprietary names for biological products. As PhRMA has commented previously,

[1] 80 Fed. Reg. 52296 (Aug. 28, 2015).

patient safety should be the paramount concern when considering the naming of biological products, and distinguishable nonproprietary names are essential to ensure patient safety.[2] Distinguishable nonproprietary names will facilitate the attribution of adverse events to the correct biologic(s), which will in turn better enhance pharmacovigilance for all biological products. Further, distinguishable nonproprietary names will help ensure that physician decisions regarding treatment choices for individual patients are respected and will help prevent errors in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices for biological products.

Guided by these principles, **PhRMA supports the prospective assignment of distinguishable nonproprietary names—comprising a common "core name" (the United States Adopted Name (USAN) for the drug substance) and a suffix identifier connected by a hyphen—for all biological products.** PhRMA recommends that the suffix be unique to the license holder and generally shared across all of the license holder's newly approved products. As explained further below, in unique circumstances, we also recommend that FDA permit an individual license holder to use distinct but related suffixes for the license holder's related, non-interchangeable products to protect patient safety. PhRMA agrees with the agency that the use of distinguishable nonproprietary names as described will minimize inadvertent substitution, facilitate pharmacovigilance for multiple biological products containing related drug substances, and establish a consistent and recognizable mechanism for identifying biological products.

In order to enhance the memorability of suffixes and thus improve pharmacovigilance, PhRMA requests that FDA require license holders to propose suffixes that are, in general, derived from the name of the license holder. PhRMA believes that adopting meaningful suffixes that are generally derived from that name of the sponsor or application holder will enhance prescriber recognition, use, and memory of suffixes and thus, the utility of suffixes for their pharmacovigilance and safety objectives. We also believe that meaningful suffixes will minimize confusion and burdens associated with implementation of suffixes. Accordingly PhRMA respectfully disagrees with the proposal that such suffixes not be meaningful and submits that FDA should eliminate that restriction. Suffixes that are "devoid of meaning"[3] likely will prove difficult to remember and, as a result, are less likely to be used consistently throughout the healthcare delivery system. We recommend that FDA create a streamlined process for license holders to propose their suffixes to reduce burdens on both the agency and industry.

PhRMA also supports, in principle, the retrospective application of the described suffix convention to existing biologic nonproprietary names through an orderly process. We urge FDA to implement carefully any phase-in of the suffix convention to existing nonproprietary names in a manner that minimizes confusion and regulatory burdens on the agency, avoids disruption in the healthcare delivery system, and affords license holders sufficient flexibility to make labeling changes to meet the needs of patients as well as license holders' operational requirements.

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[2] *See*, *e.g.*, PhRMA, Comments to Generic Pharmaceutical Association Citizen Petition, Docket No. FDA-2013-P-1153 (Feb. 3, 2014).

[3] *See* Draft Guidance at Line 364.

We offer our specific comments on the Draft Guidance below.

I. Scope

A. Terminology

PhRMA recommends that the agency add, to Section III of the Draft Guidance, definitions of key terms of art used by the agency throughout the document. Specifically, the Draft Guidance refers to a "proper name" and "nonproprietary name," but does not define the latter or explain how these terms relate to the concepts of "established" names and "official" names.[4] These terms also are used in other contexts by FDA. For instance, in another draft guidance, FDA has indicated that it considers "established" and "proper" names to be synonymous for biological products.[5] Not all readers of the Draft Guidance, however, are necessarily familiar with this other draft guidance or versed in FDA's usage of the above terminology more broadly. PhRMA therefore recommends that FDA define each of these phrases in the guidance, as the agency has already done for the types of biological products licensed under the Public Health Service Act (PHSA).[6] These definitions will help clarify the contours of the agency's naming policy—and how it interplays with other governing provisions on naming—for all audiences without requiring the reader to cross-reference statutory provisions, FDA regulations, and other agency guidance documents. Further, we recommend that FDA add, to the Background section of the Draft Guidance, a discussion of the agency's statutory and regulatory

[4] The proposed rule entitled "Designation of Official Names and Proper Names for Certain Biological Products" also uses the term "official name." *See* 80 Fed. Reg. 52224 (Aug. 28, 2015) (Proposed Rule). This phrase is defined in FDA regulations. 21 C.F.R. § 299.3(c) ("The term official name means, with respect to a drug or ingredient thereof, the name designated in this part 299 under section 508 of the [Federal Food, Drug, and Cosmetic Act] as the official name.").

[5] *See* FDA, Draft Guidance for Industry – Product Name Placement, Size, and Prominence in Advertising and Promotional Labeling (Nov. 2013 Rev. 1), at n. 4 ("In this guidance, the term *established name* is used to refer to both the established name of a drug product and to the proper name of a biological product.") (emphasis in original).

[6] Draft Guidance at Lines 64-92. Although the Draft Guidance defines "biological product," it does not define "protein" or "chemically synthesized polypeptide" as used in that definition. *See* Draft Guidance at Lines 64-69 (noting that "*[b]iological product* means a . . . protein (except any chemically synthesized polypeptide)," among other things) (emphasis in original). Because FDA's regulations and guidance provide conflicting information about what peptides qualify as a "biological product," the scope of the "biological product" definition—and, by extension, the scope of the Draft Guidance—is unclear. On the one hand, a final guidance defines protein to "mean[] any alpha amino acid polymer with a specific defined sequence that is greater than 40 amino acids in size" and defines "chemically synthesized polypeptide" to refer to "any alpha amino acid polymer that (1) is made entirely by chemical synthesis; and (2) is less than 100 amino acids in size." FDA, Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (April 2015), at 14. On the other hand, 21 C.F.R. § 601.2(a)(2) and (c) state that therapeutic synthetic peptide products of 40 or fewer amino acids can be submitted for licensure under section 351 of the PHSA. PhRMA therefore recommends that the agency provide a consistent interpretation of the above terms through guidance and rulemaking, and we refer FDA to PhRMA's prior comments on defining "biological product." *See* PhRMA, Comments on Draft Guidance for Industry – Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009, Docket No. FDA-2011-D-0611 (Apr. 16, 2012).

framework for nonproprietary naming of biologics and its relationship to legal provisions on proper names, official names, and established names, to place the naming policy in its proper legal context.

B. Transition Provisions

The Draft Guidance notes that "FDA is continuing to consider the transition provisions" of the BPCIA that address biological product applications submitted or approved under the Federal Food, Drug, and Cosmetic Act (FDCA), including how these provisions affect the nonproprietary naming of transition biological products.[7]

For three reasons, PhRMA recommends that the agency treat transition biological products as falling within the scope of the Draft Guidance's nonproprietary naming policy. First, FDA's pharmacovigilance and safe use rationales for adopting this policy are equally applicable to transition biological products. There is no scientific reason to apply a different naming framework to transition biological products, and doing so would undermine the public health and patient safety goals FDA has articulated in the Draft Guidance and Proposed Rule. Second, transition biological products are "biological products" under the PHSA just like the other products to which FDA proposes to apply the nonproprietary naming policy of the Draft Guidance. Applying the Draft Guidance to transition biological products will ensure that nonproprietary name changes for these products can be implemented consistently with biological products licensed under section 351 of the PHSA. Third, this approach will ensure a smooth transition in 2020—when the statutory transition period ends and transition biological products will be deemed licensed under the PHSA[8]—and avoid unnecessary confusion by all stakeholders. In contrast, applying a different nonproprietary naming policy to transition biological products—only to subject them to the biological product naming framework once they are deemed licensed under section 351—not only would add to the complexity of the transition process but also could create greater confusion among healthcare professionals and patients.

In sum, excluding transition biological products from the Draft Guidance would create an unsustainable and unfounded distinction between the naming policies applicable to transition biological products and all other biologics. PhRMA therefore supports application of the Draft Guidance to transition biological products on a prospective and retrospective basis, with retrospective application carried out in an orderly manner as described further below.

II. Background: Evaluation of the Appropriate Naming Convention

A. Ensuring Safe Use for Biological Products

PhRMA strongly supports the Draft Guidance's emphasis on the safety of patients who are treated with any biological product. As explained in the Draft Guidance, "[b]iological products generally consist of large, complex molecules and raise unique safety concerns related to

[7] Draft Guidance at Lines 107-110.

[8] BPCIA § 7002(e)(4) ("[a]n approved application for a biological product under section 505 of the [FDCA] shall be deemed to be a license for the biological product under such section 351 on the date that is 10 years after the date of enactment of this Act.").

immunogenicity."[9] These key differences between biological products and small-molecule drugs strongly support a nonproprietary naming framework that differentiates among biological products.

As FDA recognizes in the Draft Guidance, permitting related biological products to share the same nonproprietary name could cause confusion among healthcare professionals, who "may incorrectly assume that FDA has determined biological products with the same proper name to be interchangeable."[10] This assumption would be erroneous whenever FDA has not determined that a biosimilar has been shown to meet the additional statutory standard of interchangeability. In these cases, FDA will not have determined whether the biosimilar "can be expected to produce the same clinical result as the reference product in any given patient" and that "the risk in terms of safety or diminished efficacy of alternating or switching between use of the [biosimilar] biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch."[11] Further, as FDA recognizes in the Proposed Rule accompanying the Draft Guidance, inadvertent switching between non-interchangeable biological products "may raise unique safety concerns related to immunogenicity."[12] Moreover, various biosimilars or interchangeable biologics of a single reference product likely will not be demonstrated to be biosimilar to or interchangeable with each other, and an application for the licensure of a "related biological product" need not include any data comparing it with any other biological product.[13] Assigning distinguishable nonproprietary names to biological products will help prevent the inadvertent or inappropriate substitution of biologics in circumstances like those described.

At the same time, the use of distinguishable nonproprietary names will protect patient and physician choice of a particular treatment for an individual patient. 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 physician's prescribed medication to the dispensing pharmacist in a reliable and efficient manner. Distinguishable nonproprietary names for all biological products offer an effective means for achieving these objectives.

B. Enhancing Biological Product Pharmacovigilance

PhRMA agrees with FDA that the use of distinguishable nonproprietary names for biologics will facilitate pharmacovigilance efforts by both the agency and individual license holders. The ability to accurately attribute adverse events to the involved product is undoubtedly critical to effective pharmacovigilance. In the absence of distinguishable nonproprietary names for 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. Other product identifiers, including National

[9] Draft Guidance at Lines 164-166.

[10] *Id.* at Lines 183-184 (emphasis omitted).

[11] PHSA § 351(k)(4).

[12] 80 Fed. Reg. 52224, 52226 (Aug. 28, 2015).

[13] *See* PHSA § 351(a).

Drug Codes (NDCs) and lot numbers, are insufficient to ensure robust pharmacovigilance due to their infrequent use in both active and passive pharmacovigilance systems. Similarly, as FDA states, proprietary names are not consistently used when ordering, prescribing, or dispensing products[14] or in adverse event reports,[15] and a sponsor seeking licensure of a biological product in the U.S. is not required to use a proprietary name for its 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; i.e., they 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.

In contrast, the use of distinguishable nonproprietary names will aid identification of the specific product associated with an adverse event—facilitating detection of product-specific signals and obviating the need for unwarranted class-wide remedial action—and also will enable the aggregation of adverse event data to detect class-wide safety issues. The adoption of meaningful suffixes will further promote these important objectives, as these suffixes will be easier for healthcare professionals and patients to remember and use correctly and consistently at the time of an adverse event. In contrast, random suffixes that are devoid of meaning are unlikely to be memorable and could cause confusion among products, resulting in the inaccurate reporting of adverse events.

PhRMA appreciates FDA's interest in soliciting feedback on how to "improve active pharmacovigilance systems for purposes of monitoring the safety of biological products."[16] We suggest that FDA host a public workshop during which the agency can discuss key implementation challenges with stakeholders.

C. Advancing Appropriate Practices and Perceptions Regarding Biological Products

PhRMA agrees that it is important to encourage routine use of designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices for biological products. We also concur that the suffix "will provide a consistent, readily available and recognizable mechanism for patients and healthcare professionals, including providers and pharmacists, to correctly identify these products."[17] PhRMA supports the inclusion of suffixes in nonproprietary names of all newly approved biological products, whether an originator, biosimilar, interchangeable, or related biological product.

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[14] Draft Guidance at Lines 189-191.

[15] *Id.* at Lines 220-221.

[16] *See* 80 Fed. Reg. at 52297.

[17] *Id.* at Lines 228-233.

Policies that promote clear, accurate, and scientifically sound communication about biological products will increase confidence in biosimilars, promote accurate perceptions about them, and facilitate their uptake. In this respect, the subject matter of the Draft Guidance overlaps considerably with that of FDA's planned draft guidance on biosimilar labeling. Indeed, it is difficult to fully evaluate the Draft Guidance in the absence of the labeling draft guidance. PhRMA believes that transparent biosimilar labeling that clearly identifies the product as a biosimilar and the studies that were conducted to demonstrate biosimilarity—together with the described nonproprietary naming framework—would advance appropriate practices and perceptions about biological products while also being in the best interests of prescribers and patients. Under the BPCIA, a product cannot be approved as biosimilar unless it has no clinically meaningful differences from the reference product for the approved indications.[18] Therefore, PhRMA does not believe that identifying a product as biosimilar will give rise to inaccurate perceptions about biosimilars or suggest they are somehow inferior to their reference products. Instead, PhRMA believes that regulatory transparency, including through adoption of the described nonproprietary naming policy, will advance the public health and best lead to a strong marketplace for biosimilars. The use of the same core nonproprietary name will indicate the similarity between a biosimilar and its reference product, while the inclusion of a unique suffix indicates that the products are not the same. This approach to naming satisfies both communication objectives.

We also believe that education has an important role to play to inform prescribers, patients, and pharmacists about how to identify biological products with which they are familiar. We understand from Dr. Janet Woodcock's testimony before the Senate Committee on Health, Education, Labor, and Pensions that FDA is "undertaking a multi-phase plan for communicating with stakeholders and educating them about biosimilars."[19] PhRMA applauds these efforts and recommends that these educational programs include content aimed at promoting understanding about the nonproprietary naming convention and encouraging routine use of designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices. We also recommend that FDA establish a dedicated page on the FDA website to provide information on the nonproprietary naming policy. Finally, we suggest that FDA offer webinars and continuing medical education courses on the nonproprietary naming policy and conduct outreach at major medical conferences on these issues.

D. Prospective and Retrospective Application of Naming Convention

PhRMA supports the prospective inclusion of distinguishable suffixes in the nonproprietary names of biological products. We also support retrospective application of this approach in principle; however, we urge FDA to carefully consider any phase-in of the suffix convention to minimize confusion and disruption in the healthcare delivery system, reduce the agency's administrative burdens, and ensure orderly implementation of the suffix convention. In particular, we recommend that FDA hold a public meeting to receive stakeholder input on these issues. We also recommend that FDA provide sufficient flexibility for license holders to update labeling and other materials to meet business needs, including by providing a process for license holders to reach

[18] PHSA § 351(i)(2).

[19] Testimony of Dr. Janet Woodcock on Biosimilars Implementation Before the Senate Committee on Health, Education, Labor, and Pensions (Sept. 17, 2015), at 11.

agreement with FDA on their plan for integration of a finally-adopted suffix into labeling, packaging, and promotional materials.

PhRMA recommends that FDA's retrospective implementation strategy appropriately reflect that healthcare professionals, pharmacists, and patients have years or even decades of experience with licensed biological products. The abrupt addition of a suffix to a familiar nonproprietary name of a biological product could cause significant confusion for all stakeholders. For instance, medical literature—which typically refers to biologics by their nonproprietary names—might not be updated to reflect the retrospective addition of suffixes to the nonproprietary names of licensed biologics.[20] The resulting discordance between the nonproprietary names used in medical literature and in product labeling could lead to misunderstandings about the applicability of the literature to individual products. Similarly, nonproprietary names are used throughout a wide variety of systems (e.g., electronic prescribing systems) over which FDA and license holders have little control. These other systems would need to be updated when existing names are changed, and these updates could come at different times, thereby increasing the potential for confusion for a wide array of stakeholders. Moreover, without robust education and orderly implementation of the suffix framework, healthcare professionals, pharmacists, and patients could develop the misimpression that the addition of a suffix to a familiar nonproprietary name means the product has changed. PhRMA therefore urges FDA to proceed deliberately with any retrospective implementation of the suffix convention—including with respect to the timing of its rollout and efforts to educate the public about the planned change and the fact that it does not signal the products have changed. In particular, PhRMA encourages the agency to introduce the retrospective application of the naming convention after stakeholders are more educated about the regulatory framework and nonproprietary naming convention in order to avoid unnecessary confusion.

PhRMA also recommends that, in developing its retrospective implementation strategy and priorities, FDA consider that retrospectively applying suffix naming convention to all previously-licensed and currently marketed biologics will also impose an enormous burden on agency resources. Individual condensed notice-and-comment rulemaking proceedings, review of compendial names,[21] and review of suffixes for potential to cause medication errors will be required. In light of these burdens, not to mention FDA's parallel obligations with respect to prospective application of the naming policy,

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[20] *See, e.g.*, The New England Journal of Medicine, *Author Center New Manuscripts*, http://www.nejm.org/page/author-center/manuscript-submission (last accessed Oct. 21, 2015) ("Generic names should be used.")

[21] As interpreted by at least one court, section 508 of the FDCA requires FDA to go through a compendial review before acting. The D.C. Circuit Court of Appeals found that section 508(b) "requires the Secretary to undertake an apparently comprehensive review of the names by which drugs are identified in official compendia—*i.e.*, in the USP" and noted that this review is "at least arguably a prerequisite to a [section 508] designation." *Novartis Pharms. Corp. v. Leavitt*, 435 F.3d 344, 351 (D.C. Cir. 2006); FDCA § 508(b) (providing that the Secretary, at "times as he may deem necessary," "shall cause a review to be made of the official names by which drugs are identified in the official [USP] . . . to determine whether revision of any of those names is necessary or desirable in the interest of usefulness and simplicity"; only "whenever he determines *after* such review that . . . any such official name is unduly complex or is not useful for any other reason," among other statutory bases, may the Secretary proceed under section 508(c) to designate an official name") (emphasis added). This review would add to FDA's notice-and-comment burden for retroactive implementation.

PhRMA urges the agency to establish a system of prioritization for its retrospective application process. We also suggest that FDA hold a public meeting to discuss the challenges raised by retrospective application and strategies and priorities for addressing them in a manner that causes minimal burden to the healthcare system.

Finally, PhRMA recommends that FDA work with individual license holders to reach agreement on plans for integrating suffixes (once finally adopted) into labeling, packaging, and promotional materials. We believe these agreements will help minimize confusion in the marketplace and limit unnecessary disruption. This approach also would provide appropriate flexibility to the agency and license holders, in that the integration plans could be tailored to the facts and circumstances involved and best ensure efficient integration of suffixes without interruption of supply or negative effects on pharmacovigilance or safe use. We also recommend that FDA commit to working with individual license holders that wish to implement a retrospective name change on an expedited basis.

III. Process for Adoption of a Suffix for the Proper Name of a Biological Product

As discussed above, PhRMA supports FDA's proposal to assign biological products distinguishable nonproprietary names comprising a suffix attached to a common "core name" using a hyphen. In order to enhance pharmacovigilance, we respectfully recommend that the agency reconsider its proposal to permit only unique suffixes that are "devoid of meaning."[22]

Sponsor-Application Holder Proposal of Suffixes. PhRMA recommends that FDA create a formal process through which each license holder or sponsor would propose a suffix or suffixes that would, in general, be derived from the sponsor's name. Under this process, each license holder or sponsor would be able to propose a suffix at any time, including before its submission of any new marketing applications for biological products. In other words, sponsors should be able to use this process separately from and in advance of the agency's review of a particular product that would be subject to this naming convention, so that the evaluation of the proposed suffix will not delay a product's licensure. We recommend that, once a license holder or sponsor proposes a particular suffix, FDA publish the proposal in the *Federal Register* or on an FDA web site for a limited comment period (i.e., 30 to 60 days). For example, a particular suffix could be perceived as too close to another company's name or to another product's name.

PhRMA recommends that each suffix be unique to the license holder and generally shared across all of the license holder's approved products. We suggest that, in unusual circumstances, FDA permit an individual license holder to use distinct but related suffixes for the license holder's related, non-interchangeable products when needed to protect patient safety. Specifically, unusual circumstances would exist where a license holder markets multiple, non-interchangeable products with the same active substance and sufficiently similar product characteristics that a prescription with nonproprietary name, dosage form, and strength would not differentiate the products. Assigning distinct suffixes to each of these products would help minimize the risk of inadvertent substitution and promote accurate pharmacovigilance.

[22] Draft Guidance at Line 364.

Rules for Objection to a Suffix. FDA should adopt rules to describe the grounds on which an objection to the suffix by a member of the public will be sustained and how the agency will assign priority to sponsors and license holders who seek the same or similar suffixes. This process would include clear deadlines for agency action on each proposed suffix after the close of the applicable public comment period. The agency would not need to review whether the suffix is in fact memorable or meaningful.[23] We recommend that the agency implement the described process expeditiously so that sponsors or license holders who wish to propose suffixes in the near term can do so.

FDA should refine the suffix selection criteria articulated in the Draft Guidance.[24] The Draft Guidance states that a suffix should be "unique," but we note that a suffix will not qualify as unique in a literal sense if a license holder uses the same one in the nonproprietary names of all of the biological products for which it holds the license. Because we generally support this approach, we recommend that the bullet on Line 362 of the Draft Guidance be amended to read, "Generally be unique to each license holder and derived from the license holder's name," which would be similar to the language used by the agency in its Federal Register notice announcing the availability of the Draft Guidance.[25] Similarly, we recommend that FDA make corresponding changes to the recommendation that the proposed suffix should not "[b]e too similar to *any other product's* suffix designation."[26]

PhRMA also requests that FDA delete the statement that a proposed suffix should not be "promotional."[27] "Promotional" is a vague term in this context, and this recommendation could be viewed as inconsistent with use of a suffix derived from a license holder's name.[28] We suggest that the agency instead clarify that suffixes should not make explicit or implicit safety, efficacy, or superiority claims. Further, when FDA evaluates whether a proposed suffix will cause a likelihood of confusion, the agency should keep in mind that the suffix will be used in conjunction with a core name, which will mitigate the degree of similarity between two nonproprietary names. Finally, we ask FDA to clarify that vowels may be used in suffixes, as vowels could make the suffixes easier to pronounce and remember.

PhRMA's proposed approach offers a number of advantages. First, and perhaps most significantly, the use of a memorable suffix will help minimize prescribing errors and promote robust pharmacovigilance. A suffix that is devoid of meaning would likely be difficult for prescribers to remember, especially as more products enter the market, and as a result, is not ideal for these purposes. If healthcare professionals struggle to recall the sequence of letters comprising a product's unique suffix, they will be more likely to record the wrong suffix in adverse event reports or might even choose to omit the suffix altogether. In such cases, the suffix will fail to serve its function of distinguishing the product from other related biologics and frustrate attribution and pharmacovigilance

[23] License holders and sponsors should be solely responsible for determining whether a suffix is meaningful.

[24] *See* Draft Guidance at Lines 358-380.

[25] *See* 80 Fed. Reg. at 52297 ("unique to each biological product versus *unique to each license holder* and shared by each biological product manufactured by that license holder") (emphasis added).

[26] Draft Guidance at Line 380 (emphasis added).

[27] *Id.* at Line 368.

[28] *Id.*

efforts. We therefore believe that license holders and sponsors should be permitted to adopt suffixes that are memorable.

As the Proposed Rule recognizes, one approach to developing a memorable suffix is to use a sequence of four letters derived from the license holder's name (e.g., "sndz" in the placeholder nonproprietary name "filgrastim-sndz").[29] This approach allows for a suffix that is meaningful to the prescriber and therefore, likely to be remembered, and it could be implemented to ensure distinct suffixes for all license holders. It is possible that this approach would occasionally introduce complexities, because product divestitures could cause the license holders for particular products to change. PhRMA also believes that FDA should permit but not require license holders to change their suffixes following a corporate transaction or other analogous development such as a product divestiture.

Second, allowing each license holder to adopt a single or limited number of related suffixes that can be used in the nonproprietary names of all of its biological products will drastically reduce administrative burdens for both FDA and license holders. Under the Draft Guidance, FDA would evaluate proposed suffixes on a product-by-product basis during review cycles and for purposes of retrospective application. The agency has proposed a suffix review that shares features with FDA's time-consuming and resource-intensive proprietary name review. Carrying out this process for every new biological product and every previously approved biological product will require devotion of substantial agency resources. This burden is even more undesirable in light of the separate proprietary name review that FDA must conduct whenever a sponsor proposes to use a proprietary name for its biological product. Undertaking a nonproprietary name review in addition to the agency's existing review obligations could double its workload with respect to the selection of a new product's names—not to mention the workload associated with retrospective reviews. In contrast, PhRMA's proposal would simplify the suffix review process: each license holder would need to go through the suffix adoption process only once for all biological products in its portfolio.[30] Rather than using a number of different suffixes, a single suffix (or, in unique cases, a limited number of suffixes) will also allow for a more orderly implementation process and streamline retrospective application of the naming convention.

IV. Framework for Designating the Proper Name of a Biological Product: Interchangeable Products Submitted Under Section 351(k) of the PHSA

PhRMA recommends that the nonproprietary name of each interchangeable biosimilar bear a suffix identifier that is distinct from the suffix used for the reference product and formulated as described above. Multiple interchangeable versions of a single reference product might be approved without being shown interchangeable to *one another*, and distinguishable suffixes for all interchangeable biosimilars will help prevent inadvertent substitution among these products. Further,

[29] 80 Fed. Reg. at 52229.

[30] PhRMA acknowledges that fact-specific scenarios may arise in which an approved suffix is not suitable for use in conjunction with a particular core name, e.g., due to medication error concerns. We expect that such scenarios will be rare, however, and impose a minimal, one-time burden on FDA and the license holder involved in the situation.

as FDA recognizes in the Draft Guidance, the use of a unique suffix helps identify a specific product, which in turn is critical for effective pharmacovigilance. The need to attribute adverse events to the correct biological product is equally pressing in the context of interchangeable biosimilars. Even extensive interchangeability studies might not detect rare, product-specific immunogenicity issues that develop in the postmarket setting. Designating unique suffixes for interchangeable biosimilars will help ensure appropriate attribution of these events. In the words of the Proposed Rule, "surveillance systems [must] be able to detect safety signals *throughout the lifecycle of a product*"[31]—not just until a biosimilar is deemed interchangeable with its reference product.

V. International Harmonization Issues

PhRMA supports globally harmonized suffixes to the extent feasible without delaying implementation of the suffix convention in the U.S. As the Federal Register notice states, the World Health Organization (WHO) is refining its biological qualifier (BQ) proposal.[32] According to WHO, "details [regarding the BQ policy] remain to be developed," and an ad hoc working group continues to hone a draft proposal for presentation.[33] WHO has stated that this version "could be close to final with possible adoption before the end of 2015, although it could take another year of deliberation."[34] PhRMA recommends that FDA continue to engage in discussions with WHO, as appropriate, but not delay the agency's implementation of a nonproprietary naming policy that provides for meaningful suffixes as discussed herein. In addition, given the evolving global regulatory landscape on the nonproprietary naming of biological products, PhRMA suggests that FDA hold a public meeting to further discuss these issues—including harmonization goals and the practical challenges associated with implementation—with stakeholders.

[31] *Id*. at 52226 (emphasis added).

[32] *Id*. at 52298.

[33] WHO, 60th Consultation on International Nonproprietary Names for Pharmaceutical Substances – Executive Summary (Aug. 2015), at 4.

[34] *Id.*

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PhRMA looks forward to continued collaboration with FDA on the nonproprietary naming of biological products and the agency's implementation of the BPCIA. We would welcome the opportunity to discuss these comments further.

Respectfully submitted,

/s/	/s/	/s/
Jeffrey K. Francer	David E. Korn	Jocelyn B. Ulrich
Vice President and	Vice President,	Senior Director
Senior Counsel	Intellectual Property & Law	Scientific & Regulatory Affairs