

March 30, 2018

Jessica Simpson
Manager, Compendial Operations
United States Pharmacopeia

Re: Revision to Section 2.20 Official Articles of the General Notices and Requirements

Dear Ms. Simpson,

The Academy of Managed Care Pharmacy (AMCP) thanks the United States Pharmacopeia (USP) for the opportunity to submit comments in response to Revision to Section 2.20 of the Official Articles of the General Notices and Requirements related to monographic naming for Food and Drug Administration (FDA) approved biologics, including biosimilars. In the notice, USP indicates that the monograph shall include the “title specified in the relevant monograph plus any suffix designed by FDA unless otherwise specified in the applicable monograph.”¹ AMCP understands the need for monographs for biologic products to reflect the name associated with the product, including any suffixes, but remains opposed to the addition of a suffix to the nonproprietary name of biosimilars and biologics. AMCP recommends that USP, as a scientific standards development organization, work with stakeholders to obtain from FDA compelling scientific evidence for the new naming convention, including the rationale for its use in pharmacovigilance in lieu of the existing national drug code (NDC) system.

AMCP is the nation’s leading professional association dedicated to increasing patient access to affordable medicines, improving health outcomes and ensuring the wise use of health care dollars. Through evidence- and value-based strategies and practices, the Academy’s 8,000 pharmacists, physicians, nurses and other practitioners manage medication therapies for the 270 million Americans served by health plans, pharmacy benefit management firms, emerging care models and government.

In a March 8, 2018 presentation before a Policy Conference of America’s Health Insurance Plans, FDA Commissioner Scott Gottlieb supported the need for a robust biosimilars marketplace in the United States. AMCP also supports the need for a robust biosimilars marketplace that includes the need for clear and harmonious guidance and regulations that promotes adoption by patients, providers and payers. AMCP opposes regulatory barriers to marketplace adoption of biosimilars, including the use of random four-letter suffixes attached to the international nonproprietary name (INN).² In FDA’s final guidance on biologics naming, the Agency acknowledges the possibility of inequity with biologic naming conventions if random suffixes are

¹ USP-NF General Notices and Requirements: Notice of Intent to Revise Section 2.20 of the General Notices. Posted September 29, 2107; Updated October 5, 2017.

² AMCP Comments to FDA: Nonproprietary Naming of Biological Products (Docket – FDA-2013-D-1543) Designation of Official Names and Proper Names for Certain Biological Products (Docket – FDA-2015- N-0648). Submitted October 2015. <https://bit.ly/2GDMmk>. Accessed March 30, 2018.

applied only for biosimilar approvals under the 351(k) pathways of the Public Health Services Act and not for reference products approved under the 351(a) pathway. FDA indicates that such a difference in naming conventions “could be misinterpreted as indicating that the biosimilar products differ from their reference products in a clinically meaningful way or are inferior to their reference products for their approved conditions of use.”³ This logic follows AMCP’s perspective that the adoption of random four-letter suffixes could imply that biosimilar products differ in a clinically meaningful way or are inferior to the reference biologic and therefore, does not promote a robust biosimilar marketplace.

AMCP also notes that the naming convention for biologics currently recognized by FDA is different from the World Health Organization’s proposed biologics qualifier that rejects the use of a suffix as a component of the official INN convention.⁴ USP indicates in its proposal the need for global harmonization in biologics naming and therefore, should use its responsibility as a standard setting organization to urge FDA to adopt naming conventions that comport with global standards to promote biosimilar acceptance across the world and thus increase the potential for acceptance as alternatives to reference biologics.

AMCP would like to work with USP and other stakeholders to urge FDA to provide the scientific and clinical evidence to support that the randomized four-letter suffix would, in fact, promote safer use of biologics and biosimilar products. If FDA cannot produce this evidence, then the currently recognized naming convention must be overturned.

AMCP appreciates your consideration of the concerns outlined above and looks forward to continuing work on adoption of biosimilars with USP. If you have any questions regarding AMCP’s comments or would like further information, please contact me at 703-683-8416 or scantrell@amcp.org.

Sincerely,

Susan A. Cantrell, RPh, CAE
Chief Executive Officer

³Guidance for Industry: Nonproprietary Naming of Biologic Products. FDA; January 2017. <https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf>. Accessed March 30, 2018.

⁴ Biological Qualifier, An INN Proposal. INN Working Doc. 14.342, Rev. Final October 2015.



March 31, 2018

[Submitted electronically to Jessica Simpson at jcs@usp.org]

Re: Revisions of the *General Notices and Requirements Section of the USP and National Formulary*

Dear Ms. Simpson:

The American Pharmacists Association (APhA) is pleased to respond to the U.S. Pharmacopeial Convention (USP) notice regarding revisions of the *General Notices and Requirements Section of the USP and National Formulary* (USP-NF) impacting nonproprietary naming of biological products. Founded in 1852 as the American Pharmaceutical Association, APhA represents 64,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and the uniformed services.

Pharmacists and other practitioners rely on the monographs in the United States Pharmacopeia-National Formulary (USP-NF) to set a single standard for quality, safety, and purity of medications, but also as the source for the nonproprietary name of medications. APhA understands the desire for USP to align its compendial naming approach with FDA's naming convention due to FDA's release of its regulatory activity which may lead to misbranded products.¹

As FDA continues approving innovative medications², APhA recommends greater communication between USP and FDA regarding new terms and naming approaches. APhA does not support FDA's independent creation of new naming conventions that are inconsistent with the USP-NF. APhA recommends USP work with FDA and other stakeholders to implement mechanisms to enhance pharmacovigilance and to monitor for unintended consequences of naming policies, such as the use of suffixes.

Thank you for the opportunity to provide comments regarding USP's revisions of the *General Notices and Requirements Section of the USP-NF*. APhA supports USP's role in setting a single standard for the quality, safety, and purity of medications and recognizes USP's role as the primary entity to develop and establish names in the United States consistent with global

¹ Food and Drug Administration, (January 2017). *Nonproprietary Naming of Biological Products*, available at: <https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf>, last accessed, March 27, 2018.

² See Food and Drug Administration, (November 2017), *FDA approves pill with sensor that digitally tracks if patients have ingested their medication*, available at: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm584933.htm>, last accessed: March 27, 2018.

standard for nonproprietary naming. If you have any questions or require additional information, please contact Jenna Ventresca, Director, Health Policy, at jventresca@aphanet.org, or by phone at (202) 558-2727.

Sincerely,

A handwritten signature in black ink that reads "Thomas E. Menighan". The signature is written in a cursive, flowing style.

Thomas E. Menighan, BSPHarm, MBA, ScD (Hon), FAPhA
Executive Vice President and CEO

cc: Stacie Maass, BSPHarm, JD, Senior Vice President, Pharmacy Practice and Government
Affairs



March 31, 2018

[Submitted electronically to JCS@usp.org]

Jessica Simpson
Manager, Compendial Operations
United States Pharmacopeia (USP)
12601 Twinbrook Parkway
Rockville, MD 20852

Re: Revision to Section 2.20 Official Articles of the General Notices and Requirements

Dear Ms. Simpson,

ASHP is pleased to submit comments on the United States Pharmacopeia's (USP) general notice regarding biosimilar and biologics nomenclature. ASHP represents pharmacists who serve as patient care providers in acute and ambulatory settings. The organization's 45,000 members include pharmacists, student pharmacists, and pharmacy technicians. For more than 75 years, ASHP has been at the forefront of efforts to improve medication use and enhance patient safety.

ASHP has consistently expressed serious administrative and safety concerns regarding the FDA's naming framework for biologics and biosimilars, which we believe deviates unnecessarily from the framework for small-molecule and generic drugs. In response to USP's notice, which is consistent with the FDA's previous guidances, we would like to again reiterate the significant adverse consequences of adopting the FDA's naming framework (consisting of a core name + a random four-letter suffix, which can be substituted for a drug's United States Adopted Name (USAN)). Specifically, we are concerned that the naming framework may potentially delay biosimilar uptake, impede pharmacovigilance, and result in significant financial costs for healthcare stakeholders. Thus, based on the factors discussed below, we urge the USP to reconsider its position.

- **Biosimilar Uptake:** We remain concerned that assigning different suffixes to biosimilars and their reference biologics may impede biosimilar uptake. As USP is aware, assigning a unique name to a drug traditionally indicates that the drug has meaningful differences from other drug products. Despite the fact that biosimilars and their reference drugs share a core name, the different suffix for each product may be sufficient to confuse prescribers and deter prescribing of a biosimilar product. Further, the fact that suffixes are unique to biologics may suggest to clinicians that there is an additional inherent risk to biosimilars, which could impede uptake.

USP's proposal is also at odds with the World Health Organization's proposed biologics naming convention (currently on hold). This inconsistency seems to run counter to USP's emphasis on the criticality of a harmonized global approach to biosimilars naming. A harmonized framework for biosimilars and biologics could assist in biosimilar acceptance, but multiple naming systems will almost certainly create confusion, hinder pharmacovigilance, and negatively impact patient access and uptake.

- **Pharmacovigilance:** ASHP questions the assertion that the use of suffixes will assist with pharmacovigilance. We are troubled that this justification for the imposition of suffixes has been accepted absent substantive evidence confirming their efficacy relative to other pharmacovigilance methods. In particular, it seems counterintuitive to introduce a new naming framework for pharmacovigilance purposes at a time when the United States is in the midst of implementing the Drug Supply Chain and Security Act (DSCSA). The DSCSA establishes a national system for tracing drugs through the entire supply chain at the unit level. The DSCSA will provide the same opportunities for pharmacovigilance without requiring an entirely new nomenclature framework for a single drug class. Thus, we urge USP to reconsider adopting the FDA's naming convention in USP-NF until the FDA can offer compelling scientific evidence that the pharmacovigilance merits of the suffixes outweighs their substantial costs and risks.
- **Financial Cost:** As finalized, FDA's naming framework imposes a unique nomenclature structure on one class of drugs and requires renaming of existing biologic drugs, including drugs that have been marketed for years under a different nonproprietary name. In practice, this change will require every segment of healthcare, including but not limited to hospitals, payers, and providers, to engage in thousands of hours of information technology redesign and reprogramming.

FDA's rationale for imposing suffixes fails to account for the comprehensive electronic programming that undergirds the prescribing and dispensing of drugs in the United States, which is due in large part to federal efforts to promote healthcare information technology and critical interoperability. In this environment, all drugs are categorized by ingredient (generally using the USAN/INN), and the resulting categories are employed in computer coding on which drug ordering, clinical review, and claims administration are dependent. Although individual drug names and national drug codes (NDCs) are not routed through these systems, classes of products with the same ingredient, route of administration, dosage form, and strength serve as the primary inputs in algorithms that determine a broad scope of multiple, long-established workflows. Any change to a product name requires associated programming based on that name to change as well.

Attaching suffixes to biologic and biosimilar names will result in considerable costs for healthcare stakeholders, including clinics, health centers, and hospitals. According to ASHP member Dr. Erin Fox, who serves as the Director for the University of Utah Health Care's Drug Information Service, "a reasonable estimate [of burden] is about 40 hours per product, which would include impacts on [medication lists in electronic medical records], labels, scanning, billing, changing order sets, changing smart pumps, pharmacy automation, automated dispensing cabinets, etc." Further, there are additional burdens associated with cycling through existing stock. Dr. Fox noted that "it will be nearly impossible to use up all of the 'old' product without the new suffix and then switch out to the new product with the suffix. The pharmacy will have to bear the cost of the unusable 'old' product because the system can't handle a mixed inventory for the same item." She also suggested that if contracts need to be revised and reviewed to accommodate the Guidance's new naming framework, these contractual changes could push the burden estimate up to 50 to 70 hours per product. All of this work would need to be accomplished using existing resources, thereby diverting human and financial capital that could otherwise be applied to clinical priorities. Conservatively, the dollar value of this work is thousands of dollars per each product. With thousands of biologics currently on the market, extrapolating these costs

ASHP Comments re: USP Biosimilars Naming

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across our healthcare system produces implementation cost estimates of, at absolute minimum, hundreds of millions of dollars.

Given the concerns outlined above, ASHP urges USP to reconsider its position on biosimilar naming. We encourage USP to use ASHP as a resource as it continues its vital work. Please contact me at jschulte@ashp.org or (301)-664-8698 if you have any questions or wish to discuss our comments further.

Sincerely,

A handwritten signature in black ink that reads "Jillanne M. Schulte". The signature is written in a cursive, slightly slanted style.

Jillanne Schulte Wall, J.D.

Director, Federal Regulatory Affairs

Ms. Jessica Simpson
Manager, Compendial Operations, USP
JCS@usp.org

October 27, 2017

Re: Notice of Intent to Revise dated September 29, 2017

Dear Ms. Simpson,

Amgen, Inc. would like to thank USP for the opportunity to comment on its Notice of Intent to Revise that it posted on September 29, 2017 and updated on October 5, 2017 (“the Notice”).¹ Amgen is one of the world’s leading biotechnology companies, and is deeply rooted in science and innovation to transform new ideas and discoveries into medicines for patients with serious illnesses. As a manufacturer of over a dozen U.S. Food and Drug Administration (FDA)-licensed biologic products, including two biosimilars, Amgen has intimate understanding of and experience with the distinctive characteristics of biologics, the challenges of biologic development, and the critical need for effective pharmacovigilance.

In the Notice, USP announced its intent to make modifications to the USP-National Formulary. Specifically, USP has proposed revising Section 2.20 (Official Articles of the General Notices and Requirements) by adding a provision stating that, for a biologic 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.” The Notice explains that this revision is “intended to ensure consistency between USP and FDA in the naming of biological products...” and that it is “important that FDA’s naming convention is implemented in a consistent, coordinated way that resolves any discrepancy between names and avoids potential issues for manufacturers.”²

To the extent that USP’s proposal is intended to clarify publicly that biologics with proper names that include suffixes are not misbranded even though the title of a USP product monograph is identified by a core name with no suffix, we do not believe such clarification is necessary. We believe that legally, even without the change proposed in the Notice, biologics with suffixes would not be considered misbranded.³

¹ See <http://www.uspnf.com/notices/general-notices-requirements>.

² The Notice refers to FDA’s new naming scheme for biologics that is set forth in FDA’s “Guidance for Industry: Nonproprietary Naming of Biological Products” (Jan. 2017), available at <https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf>.

³ See, e.g., Letter from Janet Woodcock, M.D., CDER, and Peter Marks, M.D., Ph.D., CBER, responding to Docket No.s FDA-2013-P-1153, FDA-2013-P-1398, FDA-2014-P-0077 (Jan. 19, 2017), at 10 (“Novartis argues that under section 502(e)(1)(A)(i) and (e)(3)(8) of the [Federal Food, Drug, & Cosmetic Act], if there is a USP monograph for a biological product, a ‘biosimilar will be deemed misbranded unless its label bears the official title recognized in USP-NF’ unless FDA supersedes the existing compendial name using notice-and-comment rulemaking under section 508 of the [Federal Food, Drug, & Cosmetic Act] (Novartis Petition at 5). Under the approach described above, however, the established name of a biosimilar is the proper name designated in the license. Accordingly, the product would not be misbranded under section 502(e). We note further that the approach urged by Novartis - that the Agency defer to nonproprietary names established by USP, a nongovernmental body, without exercising its independent judgment - would be untenable for biological products. Such an approach would be inconsistent with FDA’s independent role in designating the proper name during licensure of a biological product. In exercising this authority, FDA intends to use its scientific judgment to assign proper names that help ensure safe use and adequate pharmacovigilance of these products.”) (internal citation omitted).

Further, we believe that rather than diminishing risk of misbranding allegations, USP's proposal may increase risk of adulteration allegations. To any extent that USP intends for a biologic with an FDA-assigned suffix to be subject to the standards and specifications of a product monograph that is identified solely by core name,⁴ Amgen has significant scientific and legal concerns.

As a scientific matter, we believe that attempts to use product monographs to define the identity, purity, and potency of biologics are inappropriate. Product monographs are appropriate for use with traditional, chemical drugs, which have relatively simple and uniform molecular structures that can be fully described using analytical methods. Biologics, in contrast, are structurally much more complex and consist of a mixture of many slightly different molecules that may or may not have the same properties. Unlike chemical medicines, biologics cannot be described or characterized as a single pure substance. In addition, structural features of all biologics can vary with time and changes to the manufacturing processes and analytical processes, and are regularly assessed by FDA to ensure product quality, safety, and efficacy. It is all but impossible for different manufacturers to create two identical biologic medicines. Further, in the rapidly developing area of biotechnology, product monographs have the potential to inhibit innovation by forcing the use of outdated analytical methods and standards. Given the variation of characteristics among biologic medicines, and even between an originator medicine and a related biosimilar, specifications in a biologic product monograph identified by core name often may be too narrow or too broad for a specific manufacturer's licensed biologic that shares the core name.

As a legal matter, we believe that product monographs with titles that lack suffixes do not apply to products with proper names that include FDA-assigned suffixes.⁵ We therefore do not believe, as the Notice states, that suffixes create "potential compliance issues" or that the Notice's proposal is needed to ensure "that a biological product that is given an FDA-designated suffix is not out of compliance with an applicable USP monograph." Rather, we believe USP's proposal creates compliance risk by subjecting biologics with suffixes to monographs that otherwise would not apply to those products.

Separately, Amgen supports USP's intention, as stated in meetings and at public conferences during the past year, that it will not prioritize further development of product-specific monographs for biologics and instead will focus on expanding the development of non-product-specific performance standards and standards for raw materials relevant and useful to manufacturers of biologics. We understand that these new performance standards would support analytical testing of biologics and be voluntary. We believe USP's announced approach will be valuable to biologic manufacturers, researchers, and developers, and look forward to learning more about, and engaging with USP on, these efforts. Also, by not developing additional product monographs for biologics, USP will facilitate FDA's naming scheme by recognizing that no two biologics are identical and will minimize confusion around whether an FDA-approved biologic might be deemed adulterated simply due to failure to comply with compendial specifications. This approach could further be supported by USP through the recall of the product-specific monographs for epoetin alfa and filgrastim.

⁴ The Notice states, for example, that the proposed 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. At the same time, the additional language provides flexibility, making it possible to apply different compendial approaches in situations where products share the same core name but have different suffixes."

⁵ See, e.g., Letter from Janet Woodcock, M.D., CDER, and Peter Marks, M.D., Ph.D., CBER, responding to Docket No.s FDA-2013-P-1153, FDA-2013-P-1398, FDA-2014-P-0077 (Jan. 19, 2017), at 9-10 ("[I]n certain cases, USP has published monographs for biological products. ... A biological product is 'an article recognized' in an official compendium only if its proper name matches the official title of a monograph, and it otherwise meets the identity and definition set forth in the monograph. Thus, at the time FDA is licensing a biological product, under FDA's interpretation of section 502(e) [of the Federal Food, Drug, & Cosmetic Act], such a monograph would apply to the newly licensed biological product only if FDA designates a proper name in the license for the biological product that matches the official title of the relevant USP monograph, and the biological product otherwise meets the identity and definition set forth in that monograph. Thus, if FDA assigns a proper name to the biological product that differs from the monograph's official title— for example, because the proper name features a suffix and the official title does not— the product would not be 'an article recognized' in a USP monograph within the meaning of section 502(e)(3)(B).") (internal citation omitted).

We appreciate USP's stated objective of facilitating implementation of FDA's naming scheme; we share that interest.⁶ In furtherance of that interest, we respectfully request that USP clarify that the Notice is not intended as a means to subject biologic products with suffixes to the specifications of a product monograph identified by core name. We also request that USP reaffirm its commitment to performance-based approaches by ceasing to release or develop any new biologic product monographs. We value USP's continued partnership with industry and remain open to working with USP on scientifically and legally acceptable ways of recognizing FDA's naming scheme for biologics.

Respectfully Submitted,

A handwritten signature in black ink, appearing to read "S. Galson". The signature is fluid and cursive, with a large initial "S" and a long, sweeping underline.

Steven Galson, M.D., M.P.H.
Senior Vice President, Global Regulatory Affairs and Safety
Amgen, Inc.

⁶ Amgen supports the approach to biologic naming adopted by FDA. We believe that FDA's assignment of distinguishable suffixes as part of the proper names of all biologics will enhance pharmacovigilance and facilitate the safe use of biologics, including by helping minimize the risk of medication errors and the inadvertent substitution of biologics that FDA has not determined to be interchangeable.



Your Generics & Biosimilars Industry



March 30, 2018

The United States Pharmacopeial Convention
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Comments from The Association for Accessible Medicines (AAM) and the Biosimilars Council (The Council) on behalf of our member companies, regarding the proposed revision to the General Notices and Requirements section of the United States Pharmacopeia—National Formulary concerning biosimilar naming.

AAM represents the manufacturers and distributors of finished generic pharmaceutical products, manufacturers and distributors of bulk active pharmaceutical chemicals, and suppliers of other goods and services to the generic pharmaceutical industry. Our members manufacture more than 90% of all generic pharmaceuticals dispensed in the U.S., and their products are used in more than three billion prescriptions every year. Generics represent greater than 89% of all prescriptions dispensed in the U.S., but only 26% of expenditures on prescription drugs. AAM is the sole association representing America's generic pharmaceutical sector.

The Council works to ensure a positive regulatory, reimbursement, political and policy environment for biosimilar products so that the U.S. can have a robust biosimilar market and realize the Biologic Price Competition Innovation Act's (BPCIA) promise of delivering cost-savings to U.S. patients and the U.S. healthcare system, generally. We also work to educate the public and patients about the safety and effectiveness of biosimilars. Areas of focus include education, access, the nascent regulatory environment, reimbursement and legal affairs. Member organizations include any companies or stakeholder organizations working to develop biosimilar products with the intent to compete in the U.S. market.

AAM and the Council support the licensure of high quality biosimilar products that meet the U.S. statutory and regulatory standard of high similarity with no clinically meaningful differences from the Reference Product (RP).

The USP is proposing to revise the process by which the name of biological medicines would be named in product monographs and is seeking input from impacted stakeholders on this proposal. Representing many companies that are working to develop and market biologics and biosimilars in the U.S., the Council is pleased to provide input on the USP proposal.

The USP proposal largely aligns with the new biologics naming convention as described in the FDA Guidance for Industry: Nonproprietary Naming of Biological Products (January 2017). In this new biologic naming convention, a meaningless four-letter suffix is to be appended to the INN by use of a hyphen. The guidance states that this would apply to all biologics, including those already approved. Furthermore, biosimilars and their respective RPs would share the same INN but would have different meaningless suffixes.



Your Generics & Biosimilars Industry



In this global regulatory marketplace, when it comes to naming of biosimilars that have met the U.S. statutory standard of high similarity with no clinically meaningful differences from RP, AAM and the Council agrees with USP and FDA that both biosimilars and their RPs should share the same INN.

However, we do not believe a suffix to the INN - as proposed in FDA guidance document - is necessary and; as the FTC has concluded, the meaningless suffix(s) may interfere with the development of a robust biosimilars market. Moreover, alternative means for addressing FDA's stated pharmacovigilance goals currently exist that would not result in such interference. We remain concerned about FDA's approach as mentioned in our February 13, 2017 comments to Docket FDA-2013-D-1543: Nonproprietary Naming of Biological Products, and provide the following key points.

First, it is not clear that the Agency's preferred approach to naming will effectively address FDA's stated goal of improving pharmacovigilance. Instead, it may create confusion for health care professionals and patients, and the confusion would be expected to increase as additional biosimilars enter the market and are prescribed, dispensed, and processed through the various systems. We have requested that the Agency evaluate, through data driven research, the impact of its naming convention, both in terms of effectiveness at improving pharmacovigilance and in terms of generating unintended confusion and risks to patients. Additionally, we requested that this evaluation/research should be completed and shared with the public at the earliest time that data will be available. If the results demonstrate that use of meaningless suffixes has not increased medication error rates in safety reporting, we respectfully requested that the Agency reconsider the new biologics naming convention.

Second, it is unclear, to date, if FDA plans to apply its naming proposal to biological products currently on the market, as none have received a meaningless suffix. For those reference products approved without a suffix, we request that FDA initiate a notice-and-comment rulemaking within the next 6-months to include those products.

Third, we are concerned about the lack of clarity surrounding the nonproprietary naming convention that will apply to interchangeable biological products. This is particularly important since the current approach of requiring different meaningless suffixes could mislead doctors and pharmacists to conclude that a product that FDA has deemed to be interchangeable is not.

While we disagree with FDA's approach on biosimilars naming, and to date have not received a response to our 2017 comments, we appreciate USP's efforts to minimize confusion that may result. Additionally, we encourage USP to minimize any unintended consequences that may negatively impact the public health as it works to implement its proposal. Diverse global naming schemes would create confusion and lead to unintended consequences and barriers to access for biologic and biosimilar products.



Your Generics & Biosimilars Industry



In conclusion, a major goal of the BPCIA is to create competition in the marketplace for biologics, thereby expanding access to, and increasing the affordability of, these critical medicines. As its title suggests, the BPCIA also is intended to stimulate innovation and investment in the next generation of originator biologics. As such, it is mutually beneficial if this happens alongside the availability of biosimilars. The biosimilars market in the U.S. is beginning to take shape, but we remain concerned that the policy decisions that FDA has made regarding the naming of these critical therapies will affect patient access, market competition, and standards to the detriment of U.S. patients and the U.S. healthcare system generally.

Sincerely,

A handwritten signature in black ink, appearing to read 'D.R. Gaugh', is written over a light blue horizontal line.

David R. Gaugh, R.Ph.
Senior Vice President for Sciences and Regulatory Affairs



Your Generics & Biosimilars Industry



Current AAM Membership List

Regular Members

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Argentum Pharmaceuticals
Aurobindo Pharma USA
Baxter Healthcare Corporation
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Your Generics & Biosimilars Industry



Current Biosimilar Council Membership List

Regular Members

Amneal Biosciences
Apobiologix
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Lupin Pharmaceuticals, Inc.
Momenta Pharmaceuticals Inc.
Mylan N.V.
Sandoz Inc.
Teva Pharmaceuticals USA
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Associate Members

AmerisourceBergen
Axinn, Veltrop & Harkrider LLP
Biorasi

March 29, 2018

Jessica Simpson
Manager, Compendial Operations
United States Pharmacopeia (USP)
JCS@usp.org

Re: Revision to Section 2.20 Official Articles of the General Notices and Requirements

Dear Ms. Simpson:

The National Association of Chain Drug Stores (NACDS) appreciates the opportunity to comment to the United States Pharmacopeia (USP) on the revision to Section 2.20 Official Articles of the General Notices and Requirements section of the United States Pharmacopeia—National Formulary to align USP’s compendial naming approach with FDA’s biologics naming convention. We thank USP for considering our views on this matter.

NACDS represents traditional drug stores, supermarkets and mass merchants with pharmacies. Chains operate over 40,000 pharmacies, and NACDS' nearly 100 chain member companies include regional chains, with a minimum of four stores, and national companies. Chains employ nearly 3 million individuals, including 152,000 pharmacists. They fill over 3 billion prescriptions yearly, and help patients use medicines correctly and safely, while offering innovative services that improve patient health and healthcare affordability. NACDS members also include more than 900 supplier partners and over 70 international members representing 20 countries. Please visit www.NACDS.org.

Naming policies for biological and biosimilar drugs have significant patient safety implications and are therefore of critical importance to the chain pharmacy community. NACDS supports naming policies for biosimilar drugs and biologics that are consistent with the naming conventions for brand and generic small molecule drugs. This naming approach is familiar to healthcare providers and patients alike.

We have concerns with any naming scheme for biological and biosimilar products that deviates from traditional naming practices, as this can lead to general confusion relative to the appropriate use, safety, and efficacy of these medications, as well as therapeutic duplication that would be detrimental to patients’ health. Moreover, special naming practices for biological and biosimilar products can undermine healthcare provider and patient confidence in biosimilars and perpetuate the notion that biosimilars are not comparable to the innovator biologic.

NACDS Comments to USP re: Revision to Section 2.20 Official Articles of the General Notices and Requirements
March 29, 2018

When commenting to the Food and Drug Administration (FDA) in response to the Agency's proposed biological product naming scheme outlined in the Draft Guidance on Nonproprietary Naming of Biological Products (August 2015), USP expressed concerns with the creation of special naming scheme for biological products, noting that product "[n]ames must be useful, simple, concise, and devoid of nonsensical information to allow them to be easily read and understood by practitioners and minimize the potential for medication errors." NACDS strongly agrees with this USP recommendation.

We understand USP's intentions for revising Section 2.20 of the General Notices, and we agree that standardization between USP's and FDA's biological product naming practices is important. However, we encourage USP not to yield to FDA's new naming scheme for biological and biosimilar products. Notably, FDA's rationale for the new naming approach is to facilitate pharmacovigilance for biological and biosimilar products. Given the confusion the new naming scheme creates, this is not the appropriate way for FDA to address its pharmacovigilance concerns. We therefore encourage USP to leverage its patient safety expertise and work with FDA to develop a more appropriate approach for biological and biosimilar product pharmacovigilance rather than support FDA's new naming practices for biological and biosimilar products.

NACDS thanks USP for the opportunity to communicate our perspectives related to biological product nomenclature. Given the potential patient safety implications of FDA's naming policy, we appreciate USP considering our comments on this important policy matter. Please do not hesitate to contact me at 703-837-4200 or mcope@nacds.org if we can provide any further assistance or clarification to USP on this matter.

Sincerely,

A handwritten signature in cursive script that reads "Michelle Cope".

Michelle Cope
Director, Federal and State Public Policy



March 29, 2018

Jessica Simpson
Manager, Compendial Operations
United States Pharmacopeia (USP)
JCS@usp.org

Re: Revision to Section 2.20 Official Articles of the General Notices and Requirements

Dear Ms. Simpson:

NCPDP is a not-for-profit ANSI-Accredited Standards Development Organization (SDO) consisting of more than 1,400 members who represent drug manufacturers, chain and independent pharmacies, drug wholesalers, insurers, mail order prescription drug companies, pharmaceutical claims processors, pharmacy benefit managers, physician services organizations, prescription drug providers, software vendors, telecommunication vendors, service organizations, government agencies, professional societies, and other parties interested in electronic standardization within the pharmacy services sector of the healthcare industry. NCPDP provides a forum wherein our diverse membership can develop solutions, including ANSI-accredited standards, and guidance for promoting information exchanges related to medications, supplies, and services within the healthcare system.

NCPDP appreciates this opportunity to provide the following comments to the revision to Section 2.20 Official Articles of the General Notices and Requirements.

NCPDP continues to disagree with need for a biologics suffix: USP is proposing to revise the General Notices and Requirements (GN) section of the United States Pharmacopeia—National Formulary (USP-NF) to ensure alignment between the Food and Drug Administration’s (FDA) biologics naming convention and USP’s compendial naming approach. The USP proposal will adopt the revised biologics naming convention proposed by the FDA, which would add a meaningless four-letter suffix to the nonproprietary name¹. NCPDP understands USP’s rationale for proposing to align its naming practices with those of FDA in order to reduce confusion among pharmacists, other healthcare providers, manufacturers, and other stakeholders. However, NCPDP remains strongly opposed to FDA’s new naming convention for biologics and USP’s proposed alignment.

NCPDP and its members have previously articulated a position and continue to firmly believe the new naming convention is unnecessary and will, contrary to the FDA’s assertions, lead to even greater confusion in pharmacovigilance. Furthermore, implementation of the new naming convention in the US will create time and administrative barriers. As was expressed previously in our comments to FDA Dockets FDA–2013–D–1543 and FDA–2015–N–0648, the cost is estimated to run into the billions of dollars.

¹ Guidance for Industry. Nonproprietary Naming of Biological Products (Jan 2017)

Absence of data to support the new biologics naming convention: We are very concerned that there is a complete absence of publically accessible data supporting the contention that pharmacovigilance will be enhanced by use of the new biologics naming convention. The new convention is based entirely on hypothetical concerns and conjectures about how the proposed system will be used. We are not aware of any well-designed quantitative or qualitative studies supporting the new biologics naming policy as a superior means for enhancing pharmacovigilance.

It is self-evident from a simple look at the suffixes approved to date (refer to Table 1 on the last page) that they are very difficult to remember or accurately associate with the applicable branded commercial product. It will become more difficult to recall the suffixes as more are introduced into the market. And yet being able to more accurately distinguish biologics based on these meaningless suffixes is the underlying premise used to justify FDA's new naming convention. Without substantial evidence confirming the superiority of the proposed suffixes as a means to greatly enhance the accuracy of pharmacovigilance relative to existing means, how can the substantial downstream burden and unknown potential negative consequences of adopting FDA's new naming convention be supported by USP?

At its core, USP is a science-based standards development organization and therefore should demand FDA provide compelling evidence of superiority for its new naming convention from a pharmacovigilance perspective before adopting the same naming convention in USP-NF. To not do so would be a dereliction of USP's science-based core mission. If FDA has compelling evidence from well-designed studies, it should be transparent and made publically accessible for review by experts in the field, including USP. Without such evidence, USP is simply acquiescing to FDA's unjustified opinion, one that is not without risk.

Need to support a robust biosimilar marketplace: Dr. Scott Gottlieb, Commissioner of the FDA, strongly supported a biosimilar market that encourages adoption of these drugs. In a speech given on March 7, 2018 to the America's Health Insurance Plans National Health Policy Conference he stated:

"Physician and patient confidence in the quality and safety of biosimilar products is critical to their market acceptance. And at FDA, we want to address any misconceptions or concerns that may be out there."²

As delineated by the Federal Trade Commission (FTC) in its October 27, 2015 comments to FDA, the FTC recommended FDA reconsider its proposed new naming convention of meaningless suffixes for biologics and instead consider alternative methods for improved pharmacovigilance that are less likely to hinder competition from biosimilars.³

² <https://www.fda.gov/NewsEvents/Speeches/ucm599833.htm> (accessed March 12, 2018)

³ Federal Trade Commission. Comment of the staff of the Federal Trade Commission. Submitted to the Food and Drug Administration in response to a request for comments on its guidance for industry on the "nonproprietary naming of biological products; draft guidance for industry; availability. [Docket No. FDA-2013-D-1543] https://www.ftc.gov/system/files/documents/advocacy_documents/ftc-staff-comment-submitted-food-drug-administration-response-fdas-request-comments-its-guidance/151028fdabiosimilar.pdf (accessed 2018 Mar 20).

There is an inequity in the current biologics naming convention that disadvantages biosimilars: The first biosimilar was approved three years ago, but there are still no reference products to which suffixes have been issued. There is no question this has been sending an unambiguous message to healthcare providers about the quality of a biosimilar with respect to the reference product. The FDA acknowledges this as a possibility in the Final Guidance on biologics naming:

“Applying this naming convention only for products licensed under section 351(k) of the PHS Act—but not for the reference product licensed under 351(a) of the PHS Act—could adversely affect health care provider and patient perceptions of these new products. Specifically, such an approach could be misinterpreted as indicating that biosimilar products differ from their reference products in a clinically meaningful way or are inferior to their reference products for their approved conditions of use.”

The FTC expressed similar concerns that assigning different suffixes to biosimilar drug substance names and their reference biologics could result in prescribers incorrectly believing biosimilar drug substances differ in clinically meaningful ways from the reference product, especially since differences in drug substance names have traditionally connoted meaningful differences in drug substance. Such misinterpretation could deter clinicians from prescribing biosimilars, thus impeding the development of biosimilar markets and competition.³

Impact of the new biologics naming convention: The overall impact of implementing a new biologics naming convention should not be underestimated. We believe this new naming convention has raised barriers to uptake in the US:

1. In a period of limited healthcare funding, a wide variety of stakeholders in the US healthcare system will need to expend time and money on modifications to electronic systems, including distribution, dispensing, and pharmacovigilance.
2. The disparate treatment of biosimilars relative to reference products, and the very fact the biologics naming convention emphasizes differences has contributed to lower confidence in biosimilars. This may be a factor in the relatively slow uptake of biosimilars in the US, although there are certainly other contributing factors.

US biologics naming convention is very different from that proposed by the World Health Organization: The USP proposal emphasizes the need for global harmony in biologics naming. While the World Health Organization (WHO) biologics qualifier is currently on hold, a close look at the WHO proposal reveals that it is very different than the new US biologics naming convention (refer to Table 2 on the last page). As the USP has noted, global alignment of the biologics naming convention will greatly assist in biosimilar acceptance that in turn will lead to an increase in patient access. Conversely, a proliferation of biologics naming conventions will slow uptake, limit access, and result in worldwide confusion and confounded pharmacovigilance accuracy.

Drug Supply Chain Security Act: It is also important to note the US is aggressively moving forward to implement the Drug Supply Chain Security Act (DSCSA). This will establish a national system for tracing pharmaceutical products through the entire supply chain. Implementation of the DSCSA will achieve all of the stated goals for increased pharmacovigilance of biologics, but

will do so more efficiently and with no increase in effort or cost over what is already being expended to comply with this Act.

The proposed changes are not appearing to be based on sound science and evidence, will weaken pharmacovigilance, will increase the cost and complexity of the US healthcare system, and will ultimately lessen confidence in and access to biosimilars. Given all of these reasons, we do not support the revisions proposed by the USP and we urge the USP to reconsider its position.

Thank you for your consideration of our input.

For direct inquiries or questions related to this letter, please contact:

Terry Fortin
Standards Specialist, Standards Development
NCPDP
E: tfortin@ncdpd.org

Sincerely,



Lee Ann Stember
President & CEO
NCPDP
9240 East Raintree Drive
Scottsdale, AZ 85260
(480) 477-1000, ext 108
(602) 321-6363 cell
lstember@ncdpd.org

cc: NCPDP Board of Trustees

Table 1. Naming of biological drugs to which suffixes have been appended.

| Sequence of Approval | Brand Name (non-proprietary name) | Biosimilar ? |
|----------------------|--|--------------|
| 1 | Zarxio [®] (filgrastim-sndz) * | Yes |
| 2 | Inflectra [®] (infliximab-dyyb) | Yes |
| 3 | Erelzi [®] (etanercept-szsz) | Yes |
| 4 | Amjevita [®] (adalimumab-atto) | Yes |
| 5 | Renflexis [®] (infliximab-abda) | Yes |
| 6 | Cyltezo [™] (adalimumab-abdm) | Yes |
| 7 | Mvasi [™] (bevacizumab-awwb) | Yes |
| 8 | Ogivri [™] (trastuzumab-dkst) | Yes |
| 9 | Ixifi [™] (Infliximab-qbtx) | Yes |
| 10 | Hemlibra (emicizumab-kxwh) | No |
| 11 | Mepsevii (vestronidase alfa-vjbjk) | No |
| 12 | Luxturna (voretigene neparvovec-rzyl) | No |

* Zarxio was the first biosimilar to be named, and was issued a meaningful suffix

Table 2. Comparison of new US and WHO biologic naming systems.

| | BQ proposal * | US suffix ** |
|---|---------------|--------------|
| 4 letter non-meaningful suffix | Yes | Yes |
| Numbers (checksum) | Yes | No |
| Linked to core with a hyphen | No | Yes |
| Multiple formats acceptable | Yes | No |
| Vowels permitted | No | Yes |
| Mandatory | No | Yes |
| Applies to vaccines and blood products | No | Yes |
| Can be suggested by manufacturer/sponsor | No | Yes |
| Assessment of suffix as if it were a proprietary name | No | Yes |
| Applied retroactively | Optional | Yes |
| Qualifies active ingredient | Yes | No |
| Qualifies final medicinal product | No | Yes |

* Biological Qualifier, An INN Proposal, INN Working Doc. 14.342, Rev. Final October 2015

** FDA guidance, Nonproprietary naming of biological products, January 2017

November 3, 2017

Ms. Jessica Simpson
Manager, Compendial Operations
The United States Pharmacopoeial Convention
12601 Twinbrook Parkway
Rockville, MD 20852-1790
JCS@usp.org

**Re: Comments on Notice of Intent to Revise Section 2.20 of the
Official Articles of the General Notices and Requirements**

Dear Ms. Simpson:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to submit these initial comments on the United States Pharmacopoeial Convention's (USP's) Notice of Intent to Revise Section 2.20 of the Official Articles of the General Notices and Requirements (Notice of Intent to Revise).¹ PhRMA may provide additional comments if and when USP issues a call for public comment upon publication of the Notice of Intent to Revise in the *USP Pharmacopeial Forum*.

PhRMA represents the country's leading innovative biopharmaceutical research and biotechnology companies, which are devoted to discovering and developing medicines that enable 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 \$65.5 billion in 2016 in the discovery and development of new medicines.

In the Notice of Intent to Revise, USP proposes to amend the second paragraph of Section 2.20 of the Official Articles of the General Notices and Requirements by adding the text underlined below:

The title specified in a monograph is the *official title* for such article. Other names considered to be synonyms of the official titles may not be used as substitutes for official titles. 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.²

¹ USP, *Notice of Intent to Revise* (posted Sept. 29, 2017; updated Oct. 5, 2017) (Proposed Revision), <http://www.uspnf.com/notices/general-notices-requirements> (last visited Nov. 1, 2017).

² *Id.*

USP explains that the proposed revision is intended to accomplish the following goals:

1. “[E]nsure consistency between USP and FDA in the naming of biological products,”
2. “[H]elp 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,” and
3. “[M]aking it possible to apply different compendial approaches in situations where products share the same core name but have different suffixes.”³

PhRMA urges USP to retain Section 2.20 in its present form because the proposed revision is unnecessary to achieve USP’s intended goals and would cause confusion that could create a public health risk. First, the proposed change is not needed to ensure consistency between USP and FDA in the naming of biological products, particularly in light of FDA’s approach to identifying the “established name” of such products. Second, the proposed revision could cause confusion as to which biological products comply with a monograph.

I. The Proposed Revision Is Not Necessary to Ensure Consistency Between USP and FDA in the Naming of Biological Products.

The proposed revision is not needed to ensure consistency between USP and FDA in the naming of biological products because FDA already has taken steps to harmonize the agency’s approach with USP procedures. Specifically, FDA has adopted an approach to identifying the “established name” of a biological product that takes into account any applicable “official title” and the agency’s use of distinguishing suffixes in the nonproprietary names of biological products.⁴

In a recent citizen petition response, FDA explained how the agency believes its approach to the nonproprietary naming of biological products accords with applicable statutory and regulatory provisions.⁵ Under one such provision—section 502(e) of the Federal Food, Drug, and Cosmetic Act (FDCA)—a drug is deemed to be misbranded unless its label bears,

³ *Id.*

⁴ Under FDA’s naming convention, “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.” See FDA, Guidance for Industry, *Nonproprietary Naming of Biological Products*, at 1 (Jan. 2017) (emphases omitted).

⁵ See FDA, Letter from Janet Woodcock, M.D., and Peter Marks, M.D., Ph.D., FDA, to Chester Davis, Jr., Generic Pharm. Ass’n, et al., re: Docket Nos. FDA-2013-P-1153, FDA-2013-P-1398, and FDA-2014-P-0077 (Jan. 19, 2017) (Citizen Petition Response), at 8-10.

among other things, the “established name . . . of the drug, if there is such a name.”⁶
“Established name” is defined as:

- (A) the applicable official name designated pursuant to [FDCA] section 508, or
- (B) if there is no such name and such drug . . . is an article recognized in an official compendium, then the official title thereof in such compendium, or
- (C) if neither clause (A) nor clause (B) of this subparagraph applies, then the common or usual name, if any, of such drug⁷

FDA explained that the “official title” specified in a USP monograph would constitute the established name of a biological product, under clause (B) quoted above, only if, at the time of approval, “FDA designates a proper name in the license for the biological product that matches the official title of the relevant USP monograph, and the biological product otherwise meets the identity and definition set forth in that monograph.”⁸

If, instead, “FDA assigns a proper name to the biological product that differs from the monograph’s official title—for example, because the proper name features a suffix and the official title does not—the product would not be ‘an article recognized’ in a USP monograph within the meaning of section 502(e)(3)(B),” so the official title would not supply the established name.⁹ Rather, the product’s “common or usual” name would serve as the established name.¹⁰ The common or usual name would be the proper name assigned by FDA in the product’s license and would include the core name plus a distinguishing suffix under FDA’s naming convention.¹¹ Because the FDA-assigned proper name would be the product’s established name, the use of that proper name on the product’s label would comply with section 502(e)(1) of the FDCA, so the product would not be deemed misbranded.

In this way, FDA already has achieved consistency between the USP and FDA as to the nonproprietary naming of biological products. In particular, FDA has explained that the FDA-assigned proper name will be the established name if a biological product is approved with an FDA-designated suffix that is not included in the official title. Because FDA has reconciled its new naming convention with USP procedures, there is no need for USP to revise Section 2.20.

II. The Proposed Revision Could Cause Confusion as to Whether a Biological Product Complies with a USP Monograph.

⁶ FDCA § 502(e)(1)(A)(i).

⁷ *Id.* § 502(e)(3).

⁸ See Citizen Petition Response, at 9-10.

⁹ *Id.* at 10.

¹⁰ *Id.*

¹¹ *Id.*

Also, the proposed revision could lead to confusion as to whether a biological product complies with a USP monograph. A biological product might not meet the specifications of a monograph that was developed using a different product with the same core name due to, for example, differences between a reference product and biosimilar product. A biosimilar product may be approved notwithstanding “minor differences” from the reference product “in clinically inactive components” and differences that are not “clinically meaningful . . . in terms of the safety, purity, and potency of the product.”¹² But the proposed revision would create the impression that all products sharing the same core name comply with that monograph, by extending the official title of a monograph to cover all products sharing the same core name “unless otherwise specified in the applicable monograph.”¹³ In practice, the monograph might not be amended to expressly exclude a biosimilar or other biological product before its approval, and it is unclear whether any existing monographs need to be revised to state that they do not cover specific biological products that currently are licensed. Accordingly, there is a significant risk that the proposed revision would suggest that a product that was not the basis for the development of the monograph complies with a USP monograph when it does not, if the monograph has not yet been revised to reflect that fact. PhRMA recommends that USP not adopt the proposed revision to prevent this risk of confusion.

III. Conclusion

PhRMA appreciates USP’s consideration of these comments. We would welcome the opportunity to discuss any of these points further.

Sincerely,

_____/s/
David Korn
Vice President, Intellectual Property and Law

_____/s/
Lucy Vereshchagina
Vice President, Science & Regulatory Advocacy

¹² Public Health Service Act § 351(i)(2).

¹³ Proposed Revision.



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 biosimilars¹ 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).



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

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.



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).

March 31, 2018

[Submitted electronically to JCS@usp.org]

Jessica Simpson
Manager, Compendial Operations
United States Pharmacopeia (USP)
12601 Twinbrook Parkway
Rockville, MD 20852

Re: Revision to Section 2.20 Official Articles of the General Notices and Requirements

Dear Ms. Simpson:

Vizient, Inc., appreciates the opportunity to provide input to the United States Pharmacopeia's (USP) intended revision to Section 2.20 Official Articles of the General Notices and Requirements regarding biosimilar nomenclature.

Background

Vizient, Inc., is the largest member-driven health care performance improvement company in the country. At Vizient, our purpose is to ensure our members deliver exceptional, cost-effective care. Vizient is member-driven and member-minded, working tirelessly to amplify every organization's impact by optimizing every interaction along the continuum of care.

Vizient provides innovative data-driven solutions, expertise and collaborative opportunities that lead to improved patient outcomes and lower costs. Vizient serves a diverse membership and customer base including academic medical centers, pediatric facilities, community hospitals, integrated health delivery networks and non-acute health care providers. Vizient is headquartered in Irving, TX with locations in Chicago, Washington, D.C., and other cities across the country.

Recommendations

Vizient previously expressed serious administrative and safety concerns regarding the Food and Drug Administration's (FDA) naming framework for biologics and biosimilars in our [comments](#) to the agency on its draft guidance on "*Nonproprietary Naming of Biological Products*." We continue to believe that the application of a differentiating, "devoid of meaning", suffix to biosimilars and originator reference products is an unnecessary and potentially dangerous approach – which serves only to increase the complexity of managing medication information throughout the transitions of care process.

While well intentioned, we do not believe that the FDA's approach advances the goals of improved product differentiation and enhancement of patient safety, but actually reinforces the perception that biosimilars are in fact not highly similar to their reference counterparts. **As such, Vizient urges the USP to refrain from adopting the same approach for its compendial naming, to recognize the availability of other identifiers to support appropriate pharmacovigilance, and to reinforce the scientifically established comparability of originator biologics and biosimilars.**

Previous reports have documented evidence of medication errors caused by a healthcare practitioner's failure to identify, recognize, or correctly interpret the prefix or suffix of the drug's name¹ and expert panels have identified recommendations to mitigate the risk of these issues, specifically as it relates to suffixes²:

- The suffix should be easily understood whether communicated verbally or in writing.
- The suffix meaning should be evaluated as appropriate.
- The suffix should not contribute to medication errors (e.g., sound-alike and look-alike errors) and may warrant careful evaluation with the intended audiences, including healthcare practitioners and consumers, during the drug name development phase.
- The suffix should be clear, distinctive and not easily confused with medical abbreviations, acronyms, dosing intervals, etc.

Vizient strongly believes that FDA's chosen strategy of a devoid of meaning suffix attached to the core name of each biosimilar (and eventually each originator) does not comply with the above recommendations – and actually increases the risk of medication errors. In addition, the European Medicines Agency has endorsed biosimilars since 2006, which have been used safely and effectively despite that they share the same non-proprietary name as their respective originator reference products³. Furthermore, the ongoing implementation of the Drug Supply Chain and Security Act (DSCSA) – including product serialization – provides a more effective mechanism to ensure pharmacovigilance for all pharmaceuticals⁴.

Due to these concerns, we respectfully request that USP not adopt a similar approach for its compendial naming convention. Rather, all originator biologics and their biosimilar counterparts should be identified in USP compendia according to the same nonproprietary or core name (as defined by FDA) without inclusion of the devoid of meaning suffix. This approach acknowledges the inherent risk of medication errors caused by the inclusion of a suffix, and more importantly reinforces the definition of a biosimilar as a biological product that is “highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product⁵.” **Given the influence of USP in shaping the understanding of pharmacists and pharmaceutical scientists, we believe this approach is critical to improving and expanding the foundational understanding of biosimilars as thoroughly vetted, highly comparable versions of previously licensed biologics⁶.**

Vizient believes that biosimilars represent one of the most important avenues for cost mitigation within the pharmaceutical supply chain in the near future. Therefore, we strongly support strategies that allow for the creation of a robust and diverse market of biosimilars and encourage the removal of barriers that might inappropriately curtail the adoption of these products. We believe our recommended approach balances patient safety concerns and further reinforces the fact that biosimilars should be managed as agents that have similar safety, efficacy, and potency as the originator biologics to which they are compared.

¹ MEDMARX Data Report. A Report on the Relationship of Drug Names and Medication Errors in Response to the Institute of Medicine's Call for Action: Findings 2003-2006 and Trends 2002-2006. (Published January 2008).

² National Coordinating Council for Medication Error Reporting and Prevention. Promoting the Safe Use of Suffixes in Prescription Drug Names. www.nccmerp.org/promoting-safe-use-suffixes-prescription-drug-names. Accessed March 2018.

³ McCamish M, Woollett G. The State of the Art in the Development of Biosimilars. Clin Pharmacol Ther. 2012; 91:405-17.

⁴ Drug Supply Chain Security Act of 2013. Title II of Pub. L. 113-54 amending the FDC Act, (21 U.S.C. 351 et seq.).

⁵ Biosimilar and Interchangeable Products.

www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580419.htm#biosimilar. Accessed March 2018.

⁶ Lucio, S. Recognition is nice, but accuracy is most important when it comes to biosimilars.

www.centerforbiosimilars.com/contributor/steven-lucio/recognition-is-nice-but-accuracy-is-most-important-when-it-comes-to-biosimilars. Accessed March 2018.

Conclusion

Vizient appreciates the USP and its emphasis on receiving comments on proposed standards from stakeholders. This provides a significant opportunity for Vizient to inform the USP on how these proposals will impact our members.

Vizient membership includes a wide variety of hospitals ranging from independent, community-based hospitals to large, integrated health care systems that serve acute and non-acute care needs. Additionally, many are specialized, including academic medical centers and pediatric facilities. Individually, our members are integral partners in their local communities, and many are ranked among the nation's top health care providers.

In closing, on behalf of Vizient, Inc., I would like to thank USP for providing us this opportunity to comment on the new and revised compendial standards. Please feel free to contact me at (202) 354-2600 or Steven Lucio, PharmD, BCPS, Associate Vice President, Pharmacy Services (steven.lucio@vizientinc.com), if you have any questions or if Vizient can provide any assistance as you consider these issues.

Respectfully submitted,



Shoshana Krilow
Vice President of Public Policy and Government Relations
Vizient, Inc.

March 28, 2018

Jessica Simpson
Manager, Compendial Operations
United States Pharmacopeia (USP)
JCS@usp.org

[Re: Revision to](#) Section 2.20 Official Articles of the General Notices and Requirements

Dear. Ms. Simpson,

I am writing as a concerned pharmacist about the implementation of a biologics suffix. As Senior Director of Drug Information and Support Services at University of Utah Health, I am currently responsible for all of the medication use policy at the University, although I am not writing on behalf of my organization. I understand that USP intends to align the General Notices and Requirements (GN) section of the United States Pharmacopeia – National Formulary with FDA’s naming convention. I have strong concerns about this naming convention and am opposed to both FDA’s changes as well as USP’s proposed alignment.

The nonsense suffix is not based in science and significantly deviates from international naming conventions such as INN and USAN. As a member of the American Society of Health-System Pharmacists, I fully support [policy 1535](#) “To advocate that originator biological products, related biological products, and biosimilar products share the same global nonproprietary name as defined by the United States Adopted Name Council, the World Health Organization Programme on International Nonproprietary Names, and United States Pharmacopeial Convention.”

Key concerns include:

- **Time** for pharmacies to make changes to pharmacy systems (EHR, labels, scanning, billing, order sets, smart pumps, pharmacy automation, automated dispensing cabinets) to accommodate changes.
- **Cost** to organizations in switching products. Modern EHR systems mandate that organizations use a single NDC at any given time. It will be impossible for organizations to use up all remaining stock while purchasing new stock.
- **Shortages** during the switch. A name change will likely involve a change to the NDC. Changes to NDCs frequently disrupt the supply chain as wholesalers do not always have products loaded correctly, and manufacturers may not honor previous contracts.
- **Higher prices.** Nonsense suffixes disproportionately impact biosimilars because no innovator products have been issued a suffix. This promotes the misconception that there are significant clinical differences between biosimilars and innovator products when there are not differences. The Federal Trade Commission warned about potential lack of competition in their [comments on FDA’s guidance for industry](#). “A misperception that the drug substance in a

biosimilar differs in clinically meaningful ways from that in the reference biologic could deter physicians from prescribing biosimilars, thus impeding the development of biosimilar markets and competition.”

- **Inefficiency.** Health systems and manufacturers are already expending significant time and money to fully implement the he Drug Supply Chain Security Act (DSCSA) which allows for a trace of pharmaceuticals from the supplier to the end user throughout the entire supply chain. (Of note, even with DSCSA, transparency to which company actually manufactured the product is not required). The DSCSA will meet all of the goals for increased pharmacovigilance of biologics. It is inefficient to also implement unnecessary nonsense suffixes.

Thank you for the opportunity to comment. I strongly urge USP to reconsider aligning naming conventions with FDA. The recommended changes are not evidence based and are out of line with the global market.

Best Regards,

A handwritten signature in black ink, appearing to read 'ERIN R. FOX', with a stylized flourish at the end.

Erin R. Fox, PharmD, BCPS, FASHP

April 27, 2018

Peter Marks, M.D., Director, Center for Biologics Evaluation and Research
Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Marks and Dr. Woodcock:

USP appreciates FDA's comments on USP's proposed revision to the USP General Notices and Requirements¹ relating to nomenclature of biological products. In USP's comments² to FDA's Nonproprietary Naming of Biological Products, Final Guidance for Industry, USP made the commitment that once FDA finalized its naming convention, USP would work to ensure that official titles assigned by USP were aligned with FDA's approach, as envisioned by the Federal Food, Drug, and Cosmetic Act (FDCA) and reflective of our longstanding partnership with FDA. USP fully embraces the opportunity to dialogue with FDA and other stakeholders to explore potential resolutions that will achieve this objective and advance our common goals of promoting access to and protecting the quality of biological products.

In addition, USP remains committed to ongoing collaboration with the Agency to support successful implementation of the Biologics Price Competition and Innovation Act (BPCIA). As you know, BPCIA seeks to increase patient access to critical drugs through the creation of an abbreviated regulatory pathway for licensing biosimilar biological products. Numerous diverse stakeholders are working together to ensure that this goal is achieved. These efforts have generated robust dialogue on legal, regulatory, and scientific issues, engendering various perspectives that continue to evolve. USP appreciates FDA's readiness to engage on these issues as we believe working together is essential for determining appropriate paths forward — paths that recognize, reconcile, and unify the approaches required to ensure the success of BPCIA.

Public standards play a critical role in ensuring the quality of all drugs, including biologics, and facilitating access to them. Recognizing that there are unique aspects to biologics, USP has convened discussions with FDA, industry, and other stakeholders and evolved our approach to ensure that USP standards ultimately assist manufacturers and regulators in advancing the objectives of BPCIA. These interactions have highlighted the need for standards that are broadly applicable across product families and classes. USP's focus on this type of standard will help industry resolve quality-related challenges commonly shared among products within a

¹ USP, Notice of Intent to Revise, General Notices and Requirements (September 29, 2017; updated October 05, 2017) (available at <http://www.uspnf.com/notices/general-notices-requirements>).

² USP comments to FDA: (1) February 13, 2017, regarding "Nonproprietary Naming of Biological Products, Final Guidance for Industry," Docket No. FDA-2013-D-1543; (2) October 26, 2015, regarding "Nonproprietary Naming of Biological Products, Draft Guidance for Industry," Docket No. FDA-2013-D-1541; (3) November 12, 2015, regarding Proposed Rule "Designation of Official Names and Proper Names for Certain Biological Products," Docket No. FDA-2015-N-0648.



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biological class or family. As we have previously stated, USP is committed to deploying our resources to address this need and will not publish as official any new product-specific monographs for biologics unless they have FDA and stakeholder support. At the same time, USP is implementing a process to facilitate early and sustained engagement with FDA and stakeholders on biologics to help ensure that standards will be relevant and useful.

The General Notices proposal is intended to avoid concerns about a product being deemed misbranded when a suffix is added to its name, with a particular focus on facilitating a flexible approach to USP's naming process for biologics. The proposal is aimed in particular at those products that are transitioning from the FDCA to the Public Health Service Act under the BPCIA, and as a result, are expected to be assigned suffixes by FDA.³ Many of these products - including widely used medicines such as insulins - have USP monographs, which for decades have ensured consistency and quality for patients as these medicines evolved. As these products transition, this General Notices approach would ensure that these products do not lose the long-standing protection that has been afforded by their USP standards by aligning FDA-assigned names and suffixes with USP's official monograph titles.

USP acknowledges FDA's concerns expressed in its comments regarding the proposed approach and also notes the diversity of views expressed by other stakeholders in their comments on the General Notices proposal.⁴ USP appreciates FDA's willingness, as stated in its comments, to have further interaction with USP on these issues. Therefore, in the spirit of working collaboratively with FDA and other stakeholders, USP will not move the General Notices proposal forward until USP has further engagement to better understand the implications of the General Notices proposal.

Please do not hesitate to contact Elizabeth Miller, Vice President U.S. Public Policy & Regulatory Affairs at ehm@usp.org or (240) 221-2064 for any additional information or questions, and we look forward to further discussion.

Sincerely,



Ronald T. Piervincenzi, Ph.D.
Chief Executive Officer

³ A transitional biological product is a biological product approved under section 505 of the Federal Food, Drug, and Cosmetic Act that will be "deemed to be a license" under section 351 of the Public Health Service Act (PHS Act) on March 23, 2020. Guidance for Industry: "Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009," March 2016 (available at

<https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm490264.pdf>).

⁴ USP has made all comments submitted on its General Notices proposal available on its website at <https://www.usp.org/usp-stakeholder-comments-biologics-nomenclature.pdf>.