

USP Roundtable on biologics nomenclature

Summary report



Overview

The United States Pharmacopeial Convention (USP) hosted a virtual Roundtable on Biologics Nomenclature on June 23, 2020. The goal of this Roundtable (RT) was to grant a diverse array of stakeholders an opportunity to provide feedback on a proposal to add the following language to *USP–NF General Notices (GNs) Section 2.20 Official Articles*: “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 prefix and/or suffix designated by the FDA unless otherwise specified in the applicable monograph.” The proposal was published in *Pharmacopeial Forum (PF)* 46(2) [Mar.–Apr. 2020] with an extended public comment deadline of July 31, 2020.

Participation in USP’s public feedback process helps ensure that the standards we develop have the intended effect of advancing quality. USP is committed to working closely with stakeholders as standards evolve to reflect public health needs and advances in science. The Council of Experts (CoE), the Expert Body responsible for the GNs, will consider the feedback from this RT and from the PF public comment process as it deliberates and votes on the proposal.

Introduction

Mr. Mario Sindaco noted that USP convenes RTs for standards that have a significant impact on stakeholder organizations. For this RT, speakers were invited to represent the perspectives of their constituencies. At the end of the meeting, attendees had the opportunity to reflect on and react to the stakeholder perspectives. USP also encouraged attendees to submit written comments through the *PF* process by July 31, 2020.

History of the biologics nomenclature proposal

Ms. Carrie Harney reviewed the history of this proposal. The proposal was originally published in September 2017 to maintain consistency with the January 2017 U.S. Food and Drug Administration (FDA) *Nonproprietary Naming of Biological Products* guidance. The revision to General Notices was intended to ensure consistency between USP and FDA in the naming of biological products licensed under the Public Health Service Act (PHS Act) and avoid potential issues and confusion for manufacturers and other stakeholders. After receiving numerous stakeholder



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comments, and in consultation with the CoE, USP decided to defer the revision and engage further with stakeholders.

In March 2019, FDA issued the *Nonproprietary Naming of Biological Products: Update* draft guidance. The draft guidance indicates that FDA no longer intends to apply an FDA-designated suffix to: (1) current and pending biological products licensed under section 351 of the PHS Act without FDA-designated suffixes; and (2) biological products which will transition from an approved application under section 505 of the of the Federal Food, Drug, and Cosmetic Act (FD&C Act) to a biologics license application under section 351 of the PHS Act (transition biological products). The draft guidance also indicates that FDA intends to continue to apply an FDA-designated suffix to all biological products at the time they are licensed under section 351(a) or 351(k) of the PHS Act. In March 2020, USP re-published its proposal in *PF* for another public comment period. The intent of the proposal was again to reduce confusion among manufacturers and other stakeholders with respect to FDA’s naming convention and USP’s official titles.

Dr. Jaap Venema, Chair of the CoE, explained that USP believes that this proposal would help reduce potential confusion between the FDA naming convention and the USP monograph naming approach, and address potential compliance issues for manufacturers, such as having a misbranded product. It is intended to clarify the application of USP standards to biological products. The additional language also provides flexibility, making it possible to apply compendial standards in situations where products share the same core name but have different prefixes and/or suffixes.

The revision is particularly important for transition biological products, a number of which have USP quality standards. The application of a suffix to the core name of future biosimilar products to transition products will mean that the nonproprietary name of those biosimilar products will not match the official title of the applicable USP monograph. This could cause confusion, and compliance issues for manufacturers, as the products would technically be misbranded. The proposed revision achieves the necessary match of the core name to the applicable USP monograph, independent of whether the product was approved before or after March 2020 and irrespective of whether the product is an originator biologic or a biosimilar.

Stakeholder perspectives on the USP biologics nomenclature proposal¹

Hillel Cohen, Ph.D., Executive Director, Scientific Affairs, Sandoz, Inc.

Dr. Cohen thanked USP for the opportunity to comment on the proposed revision.

- ▶ Sandoz opposes the proposed change because it is a misguided attempt to reconcile with the FDA biologics naming convention that is confusing and does not provide value. Instead, addition of suffixes and prefixes clearly suggest that the biological

product with the same active pharmaceutical ingredient (API) made by different companies may be clinically different when in fact they are not.

- ▶ Sandoz urges that USP reject the proposed change and instead maintain its existing naming standards whereby the active ingredient is defined solely by the United States Adopted Name (USAN) without prefixes or suffixes. This is the procedure adopted by the World Health Organization (WHO) and almost every other country worldwide. Modifying the USP naming standard for biological products will only misalign the U.S. with the rest of the world.
- ▶ It is noteworthy that FDA has recently rejected the use of suffixes and adopted the current USP naming standards for all insulins, somatropins, and other biological drugs that were regulated until March 2020 as 505(b)(1) drugs. The concept of adding suffixes or prefixes to biological drug names is based solely on a theoretical concern that pharmacovigilance of biological drugs will be challenging unless proprietary names are differentiated. This is not correct.
- ▶ To date, there is no published scientific data supporting this theoretical concern. Organizations that have strongly raised these so-called safety concerns in the past decade have been unable to point to any actual data to support their claims. In contrast, when reviewing pharmacovigilance data after biosimilars have been marketed for five years in the U.S. and after



¹ The comments in this section are taken almost verbatim from the virtual roundtable event.

10 years worldwide, and with over 700 million doses administered, there is no real-world evidence of any nature to support the theoretical concerns. When reviewing the actual safety report data presented in the FDA's adverse event database (FAERS) in the past 5 years, over 90% of all biological drug adverse events submitted to FDA are identified by the use of brand names, further accentuating that suffixes are not necessary to track adverse events.

- ▶ It is clear that additional work is required to modify many aspects of existing healthcare systems to accommodate prefixes and suffixes. There is no doubt that the additional work adds significant time and cost burden across the U.S. healthcare system.
- ▶ In summary, we strongly recommend that the proposed change be rejected. USP should not modify an already successful existing system in a manner that creates confusion while not adding value.

**Karin Bolte, Esq., Director, Health Policy,
American Pharmacists Association (APhA)**

Ms. Bolte thanked USP for the opportunity to express APhA's views on this issue. APhA represents pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care.

- ▶ APhA appreciates the intent of USP's proposed GNs revisions to clarify the continued application of USP public quality standards for biological products, including originator, biosimilar, interchangeable, and transition biological products such as insulin. APhA supports USP's role in setting a single standard for the quality, safety, and purity of medications. The quality benchmarks in the USP public standard allow for an independent determination that a product has been made according to quality expectations regardless of the manufacturer or manufacturing process. These standards are used by many entities to test for quality at any point along the supply chain. As such, USP's public quality standards foster trust in the quality of biologics for the practitioners who prescribe, dispense, and administer them, as well as trust from the patients who benefit from them.
- ▶ In previous comments to FDA and other federal agencies regarding biosimilar naming, APhA has consistently opposed the use of suffixes which create confusion in the marketplace and might compromise patient safety.
- ▶ APhA believes that USP should not adopt FDA's naming convention due to the following concerns:
 - FDA's application of a product-specific suffix approach to the naming of transition biologics and future biologics and biosimilars—but not to previously approved biologics—increases the risk of confusion and inaccurate product identification.



- The addition of a suffix to a biosimilar without a corresponding suffix in the name of the original biologic gives the false impression that the biosimilar is inferior to the originator product, which can hamper the acceptance of biosimilars by both providers and patients.
 - There is inadequate data and experience on whether suffixes enhance pharmacovigilance as FDA intends.
- ▶ APhA believes that USP should not adopt FDA's naming convention in *USP–NF*. APhA recognizes USP's role in developing and establishing names in the U.S. consistent with global standards for nonproprietary naming. APhA recommends that USP:
- Identify originator biologics and biosimilars in *USP–NF* by the same nonproprietary or core name as defined by FDA without the suffix.
 - 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).
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- Michael Ganio, Pharm.D., M.S., Senior Director, Pharmacy Practice, and Quality, American Society of Health-System Pharmacists (ASHP)**
- Mr. Ganio thanked USP for the opportunity to share ASHP's perspective on the GNs proposal. ASHP represents 55,000 members, including pharmacists, student pharmacists, and pharmacy technicians. ASHP has been on the forefront of efforts to improve medication use and enhance patient safety. A core activity in those efforts has been ASHP's publication of authoritative, federally recognized drug information that helps establish medically accepted uses of drugs.
- ▶ ASHP supports the following:
- The development, and implementation of policies that improve access to and affordability of biologic agents
 - Policies and regulations that improve the usability and safety of biosimilar adoption
 - A naming framework for biosimilars that mirrors small molecule drugs and generic counterparts, relying on a shared nonproprietary name without prefixes or suffixes
- ▶ ASHP is concerned about the following:
- The existing framework for nonproprietary naming is confusing and creates operational and safety challenges.
 - Non-pronounceable, non-meaningful suffixes or prefixes are not likely to be remembered or recalled by clinicians and will not accurately be associated with specific products.
 - These suffixes and prefixes will adversely impact adoption by clinics or patients who will perceive the difference in nomenclature to mean a difference in the product's clinical effectiveness or safety.
 - FDA's exemption of its nomenclature policy for certain biologics further complicates the operationalization and adoption of biologic products.
 - The maintenance of electronic health records (EHRs), printed labels, bar code scanning technologies, billing software, order sets, smart infusion pumps, and other forms of automation all require additional configuration for each individual biologic and biosimilar product. A respected drug information specialist estimates that the implementation of this nomenclature framework would take an estimated 40 hours of work across a health system.
 - While ASHP understands the importance of distinguishing products for the purposes of adverse event and outcome tracking, the subtlety of a non-meaningful suffix is likely to be missed in the context of an EHR, printed medication label, or smart infusion pump screen.
 - The Institute for Safe Medication Practices maintains a list of confused drug names for medications with similar spelling or pronunciation and recommends the use of tall-man lettering to emphasize differences and help clinicians distinguish between products. The use of a biologic name with a suffix or prefix to distinguish products poses a very real risk of improper medication selection due to the look-alike, sound-alike naming this framework establishes under the premise that these products are different.
- ▶ ASHP supports individual hospitals making decisions about biologic and biosimilar use in accordance with the formulary selection processes first used for small molecule drugs.

- Hospitals should have the ability to select products based on the most favorable pricing for patients and on the resources required for formulary adoption. These decisions should be made between clinicians and patients in the interest of medication safety and financial responsibility without the influence of policy makers or payors.
- ▶ Recognizing that USP standards extend beyond the borders of the U.S., where naming practices may vary, ASHP recommends that USP maintain biologic nomenclature similar to that of small molecule generics with the acknowledgement that FDA names with a prefix or suffix may be different from the official *USP-NF* title.
- ▶ ASHP recommends that the proposed GNs change not be adopted.
- Special naming practices for biologics and biosimilars can undermine healthcare provider and patient confidence in biosimilars, and perpetuate the notion that biosimilars are not comparable to originator biologics.
- ▶ FDA proposed its biological naming scheme in draft guidance in August 2015. When commenting to FDA, USP expressed concerns about the creation of a special naming scheme for biological products. USP noted that product names must be useful, simple, concise, and devoid of nonsensical information to allow them to be easily read and understood by practitioners, and to minimize the potential for medication errors. NACDS still agrees with this USP recommendation.
- ▶ NACDS agrees that standardization of USP and FDA biological naming practices is important. Rather than support FDA's new suffix-naming practices, we encouraged USP to leverage its patient safety expertise and continue to work with FDA to develop a more appropriate approach for biologic and biosimilar pharmacovigilance.

Kevin Nicholson, R.Ph., J.D., Vice President, Public Affairs, and Regulatory Affairs, National Association of Chain Drug Stores (NACDS)

Mr. Nicholson thanked USP for the opportunity to provide comments on the GNs proposal. NACDS represents traditional drug stores, supermarkets, and mass merchants with pharmacies.

- ▶ NACDS and its members have supported the development of a robust biosimilars market. They have also supported FDA's work to develop an efficient approval pathway for biosimilars to bring savings and access to America's patients.
- NACDS believes that naming policies for biosimilars and biologics have significant patient safety implications and are therefore of critical importance to the chain pharmacy community.
- NACDS supports naming policies for biosimilars and biologics that are consistent with the naming conventions for small molecule drugs. This naming approach is familiar to both healthcare providers and patients.
- NACDS will continue to oppose any naming scheme for biologics and biosimilars that deviates from traditional naming practices because this can lead to confusion on the appropriate use, safety, and efficacy of these medications, as well as therapeutic duplication that would be detrimental to patients.
- ▶ Regarding the transition insulin products, NACDS supports FDA's adoption of naming practices for these products that are consistent with small molecule drug naming practices.
- Biosimilar versions of insulin products should share the same nonproprietary name as their referenced products.
- Physicians and patients have come to understand that a shared nonproprietary name denotes that a generic product is at least comparable to the brand. A deviation from this naming convention may perpetuate the notion that biosimilars are not comparable to the originator biologic.
- While NACDS supports FDA's naming regime for insulin, they continue to have concerns about the FDA naming process for biosimilars, specifically the use of a suffix, and particularly a suffix that lacks meaning.
- ▶ NACDS supports USP's position on patient safety concerns pertaining to this naming scheme. We encourage USP to continue to work with FDA to find a solution, especially to address any pharmacovigilance concerns as noted by previous speakers.

Lisa Parks, R.Ph., Vice President, Scientific and Regulatory Affairs, Association for Accessible Medicines (AAM)

Ms. Parks spoke on behalf of Mr. Joseph Stewart who was unable to attend. AAM represents the manufacturers and distributors of finished generic pharmaceuticals, and biosimilars; manufacturers, and distributors of bulk active pharmaceutical chemicals; and suppliers of other goods and services to the generic and biosimilar industry. The Biosimilars Council, a division of AAM, works to ensure a positive regulatory, reimbursement, political, and policy environment for biosimilar products, and educates stakeholders and patients about the safety and effectiveness of biosimilars.

- ▶ AAM is fairly aligned with many of the previous RT speakers.
 - AAM encourages USP to minimize any unintended consequences that may negatively impact public health as it works to implement its proposal.
 - Diverse global naming schemes will create confusion and lead to unintended consequences and possible barriers to access for biologic and biosimilar products.
- ▶ Ms. Parks referred USP to more extensive written comments on this proposal submitted on May 31, 2020, through the PF process.

Open discussion

Ms. Claire Winiarek, VP, Public Policy, Pharmaceutical Care Management Association (PCMA) noted the following:

- ▶ PCMA is a national association representing America's pharmacy benefit managers which administer prescription drug plans and operate specialty pharmacies. PCMA members work closely with employers, health plans, and others to secure lower costs for prescription drugs and promote better individual health outcomes.
- ▶ PCMA shares the speakers' concerns about USP moving forward with the standard as proposed. They encouraged USP to revisit the standard.

Next steps

Mr. Sindaco thanked stakeholders for their input and noted the following next steps:

- ▶ USP will post a recording of the RT, slides, and a written summary of the meeting on USP.org.
- ▶ USP will also share this information with the CoE as they consider the naming proposal.
- ▶ Stakeholders may provide written comments through the online PF process by July 31, 2020. They may contact USP staff to request support with the commenting process

