July 17, 2020

Ms. Jessica Simpson
Manager, Compendial Operations
United States Pharmacopeia (USP)
Submitted via https://www.uspnf.com/pharmacopeial-forum

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

Dear Ms. Simpson:

The National Council for Prescription Drug Programs (NCPDP) is a not-for-profit, ANSI-Accredited Standards Developer (ASD) consisting of more than 1700 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.

For over 40 years, NCPDP has been committed to furthering the interoperable electronic exchange of information among a wide array of healthcare stakeholders. To assist in consistent and accurate identification of drugs and health-related products within NCPDP's stated mission, NCPDP's Work Group 2 Product Identification deals with product identification systems and any type of descriptive data, including naming, that serves to uniquely identify a product with the intent of establishing standards for product identification to avoid ambiguity in distinguishing one product from another.

The product information exchange procedures developed and maintained by NCPDP are used by all originator biologics and biosimilars licensed in the US to date, and it is anticipated they will also be used for all originator biologics, biosimilars, and interchangeable biologics in the future. As such, NCPDP is central to developing standards by which these products are distributed and recorded, including identification of products for the purpose of pharmacovigilance.

NCPDP appreciates this opportunity to provide additional comments on the revision to Section 2.20 Official Articles of the General Notices and Requirements. Please refer to NCPDP's original comments submitted to you on March 29, 2018, which continue to represent NCPDP's position opposing the addition of prefixes and/or suffixes to the nonproprietary ("core") (i.e., United States Adopted Names [USANs], International Nonproprietary Names [INNs]) names of biologics.

In response to the current revision proposal, NCPDP submits the following alternative wording for USP's consideration:

Revise Section 2.20 Official Articles to add the following language at the end of the second paragraph:

"For a biologic licensed under the Public Health Service Act, the *official title* shall be the title specified in the relevant monograph. Names used by the US Food and Drug Administration (FDA) may differ from the official USP-NF title by modifying the United States Adopted Name (USAN) (defined by FDA as the "core" name) with a prefix and/or suffix to create an FDA-designated "proper" name, but such modifications are informational only and not part of the official monograph title…"

The rationale for NCPDP's alternative wording follows.

NCPDP continues to disagree with the need for biologics prefixes and suffixes in Nonproprietary Names (NPNs): NCPDP continues to oppose ongoing efforts by the FDA that impose the inconsistent addition of prefixes and/or suffixes to the core names of certain biologics (including biosimilars), believing this practice is both unnecessary and unproven to substantively increase the accuracy of product-specific pharmacovigilance. Improved pharmacovigilance is FDA's unsubstantiated principal claim for the need to modify core names, and we continue to invite data as evidence to indicate the contrary. In fact, NCPDP's opposition has been further supported by the resultant confusion that already has occurred. Contrary to the FDA's assertions, electronic drug information and standards organizations as well as many associated industry sectors (e.g., prescribers, dispensers, prescription processors, drug knowledge bases) faced with implementing and interpreting this prefix/suffix NPN policy believe the altered naming policy will lead to even greater confusion in pharmacovigilance.

As a result, NCPDP also continues to strongly oppose USP's proposal to align its own naming conventions for biologics with those of FDA on this issue.

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 FDA biologics nonproprietary naming convention and USP's compendial naming approach. The USP proposal would accommodate the revised biologics naming convention proposed by the FDA, which would add a meaningless prefix and/or suffix to the nonproprietary name. 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, and allow USP monographs and reference standards to continue to apply. However, FDA's policy already has caused considerable confusion and adverse downstream stakeholder consequences and has not been established scientifically to improve pharmacovigilance. Such confusion can only be expected to increase as the use of suffixes and prefixes expands, especially as they continue to be inconsistently applied. Therefore, because NCPDP remains strongly opposed to FDA's naming convention for biologics, we must also oppose USP's proposed alignment with it.

Substantial opposition in public comments to USP on its proposal: NCPDP is surprised by USP's decision to move forward in aligning with FDA's biologics naming convention since all but two comments received by USP in response to the original September 2017 proposal for change in Section 2.20 opposed it and one of the commenters supporting it was FDA itself (https://www.usp.org/sites/default/files/usp/document/our-work/biologics/usp-stakeholder-

comments-biologics-nomenclature.pdf). We recognize that USP is not endorsing the use of prefixes and/or suffixes in nonproprietary naming of drugs and biologics. However, we remain concerned that the proposed revision to Section 2.20 may be interpreted incorrectly to implicitly support FDA's deviation from standard international naming practices for biologics.

In fact, it is notable that even the pharmaceutical industry's largest and most influential trade association—the Pharmaceutical Research and Manufacturers of America (PhRMA)—opposed USP's proposal stating that "the proposed change is unnecessary to achieve USP's intended goals and would cause confusion that could create a public health risk."

Absence of data to support the new biologics naming convention: Central to NCPDP's continued opposition to, and grave concern about, the addition of prefixes and/or suffixes to the USAN/INN is the complete absence of publicly accessible data supporting the contention that pharmacovigilance is enhanced by use of FDA's unique biologics naming convention. This 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 FDA's biologics naming policy as a superior means for enhancing pharmacovigilance. To the contrary, factual evidence from adverse drug event reports in both the US and Canada has shown that reporting is almost exclusively by brand name and has been largely successful in achieving accurate product-level attribution of spontaneously reported adverse effects for suspected biologics.

At its core, USP is a science-based standards development organization and therefore should have demanded FDA provide compelling evidence of superiority for its biologics naming convention from a pharmacovigilance perspective before accommodating the same naming convention in USP-NF. If FDA has compelling evidence from well-designed studies, FDA should be transparent and make the evidence and studies publicly accessible for review by experts in the field, including USP. Without such evidence, USP is simply acquiescing to FDA's unjustified opinion, and one that is not without risks that must also be considered.

In addition, NCPDP sees no essential need for FDA to continue pursuing introduction of prefixes and/or suffixes or any other unique naming forms for biologics since other, more effective means than nonproprietary names currently exist in the US for distinguishing biosimilar products (e.g., national drug codes [NDCs], track and trace regulations, the standardized numerical identifier [SNI], global trade item number [GTIN], other product identifiers, and brand names themselves).

FDA's biologics naming convention is very different from that proposed by the World Health Organization: NCPDP is further surprised with USP's decision to align with FDA's biologics naming policy since it runs counter to the rest of the world and the Pharmacopeia's emphasis on the need for global harmony in all nonproprietary naming, including biologics. As USP has noted, global alignment of the biologics naming convention would greatly assist in biosimilar acceptance that in turn would lead to an increase in patient access. While WHO did consider suffixes for those countries that lack brand names, their so-called biologics qualifier initiative was subsequently rejected. And it is notable that, even were it to have been pursued, it did not alter the nonproprietary name *per se*. Even FDA itself concurred with the established nonproprietary naming system, in their letter to WHO, September 1, 2006, entitled *U.S. FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible*

International Non-proprietary Name (INN) Policies for Biosimilars (attached as an appendix as it is no longer readily accessible at FDA.gov). A proliferation of biologics naming conventions will slow uptake, limit access, and result in worldwide confusion and confounded pharmacovigilance accuracy.

NCPDP's recommended alternative wording for section 2.20 revision: As a result of these concerns and to provide some needed clarification of naming differences that may exist between official USP monograph titles and FDA names for certain biologics, NCPDP proposes the following alternative wording for USP's consideration (also stated above in introductory comments):

> Revise Section 2.20 Official Articles to add the following language at the end of the second paragraph:
>
> "For a biologic licensed under the Public Health Service Act, the *official title* shall be the title specified in the relevant monograph. Names used by the US Food and Drug Administration (FDA) may differ from the official USP-NF title by modifying the United States Adopted Name (USAN) (defined by FDA as the "core" name) with a prefix and/or suffix to create an FDA-designated "proper" name, but such modifications are informational only and not part of the official monograph title…"

USP states in the *Pharmacopeial Forum (PF)* Briefing on this proposed change that, "it will not publish as official any new product-specific monographs for biologicals unless they have FDA and stakeholder support," and states further 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) transition biological products—products which transition on March 23, 2020 from an approved application under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) to a biologics license under section 351 of the PHS Act." (https://online.usppf.com/usppf/document/GUID-6E790F63-0496-4C20-AF21-E7C283E3343E_60101_en-US)

Finally, it is curious that despite FDA's position on biologics naming, a new insulin glargine product Semglee® that references Sanofi's Lantus® recently (June 11, 2020) was approved by FDA but does not include a suffix modifier. While the product was submitted under the generic 505(b)(2) New Drug Application pathway, it automatically is deemed a biologic under section 351(a) of the Public Health Service Act of the Biologics Price Competition and Innovation Act (BPCIA), based on a policy enacted March 23, 2020. This FDA action of not applying a suffix becomes all the more notable since the manufacturer already has announced its intent to pursue an interchangeability designation for this product. It also raises questions about FDA's intent on requiring suffixes and/or prefixes to the nonproprietary names for other yet-to-be-approved biologics that contain matching active moieties or reference those products that were rolled-over.

NCPDP's proposed wording change acknowledges the existence of naming aberrations imposed by FDA, while still maintaining international harmonization of biologics naming by USP and avoids placing USP's imprimatur on a naming approach that has not been shown to date to be scientifically based. It also addresses USP's goal of avoiding an interpretation of misbranding for FDA-imposed biologics names that include a prefix and/or suffix and thus do not agree with official USP titles.

In addition, USP's proposed alignment with FDA biologics naming convention will weaken pharmacovigilance. FDA biologics naming convention is already increasing the cost and complexity of the US healthcare system and will ultimately lessen confidence in and access to biosimilars. Given all these reasons, we do not support the revisions proposed by the USP and we urge the USP to reconsider its position and consider instead wording proposed by NCPDP.

Thank you for your consideration of our input.

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

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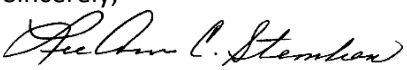
Sincerely,



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