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 name[1]. 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]

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[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.

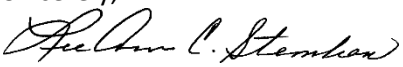
The proposed changes are not appearing to be based on sound science and evidence, will weaken pharmacovigilance, will increase the cost and complexity of the US healthcare system, and will ultimately lessen confidence in and access to biosimilars. Given all of these reasons, we do not support the revisions 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@ncpdp.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@ncpdp.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-szzs)	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-vjbk)	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