



February 27, 2015

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Margaret A. Hamburg, MD
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: *Nonproprietary Naming of Biologics, Biosimilars, and Interchangeable Biologics: Zarxio[®] (filgrastim)*

Dear Secretary Burwell and Dr. Hamburg:

The National Council for Prescription Drug Programs (NCPDP) is a not-for-profit ANSI-accredited Standards Development Organization (SDO) consisting of more than 1500 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. Our diverse membership develops solutions, including ANSI-accredited standards, and guidance for promoting information exchanges related to medications, supplies, and services within the healthcare system.

NCPDP has almost 40 years of commitment to furthering the electronic exchange of information about drug products within this broad range of healthcare stakeholders. Paramount to this commitment is the core principle that such information should be unambiguous and standards based. Essential to NCPDP activities is ensuring broad-based adoption of widely recognized and accepted standardized naming and coding practices for a wide array of data attributes about medications, including but not limited to nonproprietary naming conventions. Unambiguous, interoperable, meaningful data exchange is jeopardized anytime standard operating procedures (SOPs) are violated in these naming and coding practices. Unintended, potentially serious consequences result.

FDA recently deviated from standard practice by establishing the nonproprietary (generic) name of several biologic and biotechnology-derived products by introducing modifiers independent of the United States Adopted Name (USAN) Council and International Nonproprietary Name (INN) Programme. The introduction of these modifiers, as prefixes, has caused confusion, including within FDA itself (e.g., separate names for filgrastim and tbo-filgrastim but identical unique ingredient identifiers¹) and across agencies (e.g., FDA versus the National Cancer Institute and National Library of Medicine for preferred names) and has raised serious safety concerns. Another such deviation from standard practice (ado-trastuzumab emtansine) by FDA actually resulted in the issuance of an FDA warning

¹ tbo-filgrastim is described as a synonym for filgrastim here:
http://fdasis.nlm.nih.gov/srs/ProxyServlet?mergeData=true&objectHandle=DBMaint&APPLICATION_NAME=fdasrs&actionHandle=default&nextPage=jsp/srs/ResultScreen.jsp&TXTSUPERLISTID=PVI5M0M1GW&QV1=FILGRASTIM+%5BINN%5D

about potential medication errors, an Institute for Safe Medication Practices (ISMP) Medication Safety Alert,² and a National Alert Network (NAN) alert.³

NCPDP has commented to FDA on several occasions in writing, in a face-to-face meeting with FDA staff, and at a recent Oncology Drugs Advisory Committee (ODAC) meeting about serious concerns it has with any deviation from recognized naming standards such as the USAN and INNs for biosimilars.^{4 5 6} These concerns are consistent with those raised by the pharmacy sector at large (e.g., National Association of Boards of Pharmacy, American Society of Health-System Pharmacists, American Pharmacists Association, National Association of Chain Drug Stores, National Community Pharmacists Association) and medicine (e.g., American Medical Association).

On January 7, 2015, FDA's ODAC unanimously recommended for approval the first biologic (Sandoz's filgrastim, Zarxio[®]) submitted under an abbreviated licensure pathway for biological products shown to be "biosimilar" to or "interchangeable" with an FDA-licensed biological product (Amgen's filgrastim, Neupogen[®]; the "reference product").⁷ Of concern is the fact that FDA stated in its Briefing Document to the Committee that it still "is continuing to consider its approach to nonproprietary naming of biosimilar biological products," setting the stage for potentially approving a name for this product before issuing its proposed naming policy for public comment and before the Federal Trade Commission) issues its report.

The patient safety concerns that resulted from an earlier deviation from standards-based naming with adotrastuzumab emtansine demonstrate the risks of such deviation by FDA. Clearly, FDA should refrain from introducing another prefix-modified INN as it did with tbo-filgrastim because of the problems that such prefix forms already have been shown to create.

NCPDP concerns about deviation from standard naming practices (e.g., USAN, INN) for biosimilars also apply to FDA consideration of modifying suffixes. For example, NCPDP shares the concerns that the American Society of Health-System Pharmacists (ASHP) raised with WHO concerning its proposed biological qualifiers.⁸ Because WHO has delayed any decision about this proposal pending further deliberation,⁹ FDA should refrain from introducing such modification or other suffixes until a final decision is made. Even then, FDA should rely principally on advice it receives from various US stakeholders and standards organizations such as NCPDP since existing mechanisms (e.g., national drug codes [NDCs], track and trace regulations, the standardized numerical identifier [SNI], global trade item number [GTIN], and other product identifiers) obviate the need for such naming modifiers in this country.

Because it is likely that FDA will need to decide on a nonproprietary name for Zarxio[®] in the upcoming weeks before issuing its biosimilar naming policy for public comment, NCPDP strongly recommends that the Agency take the only reasonable path of applying the same USAN and INN that already has been applied to this product for

² ISMP Acute Care Medication Safety Alert! Safety brief: Confusion between two HER2-targeted monoclonal antibodies. Vol 18, Issue 5. 2013 Mar 7. (<https://www.ismp.org/newsletters/acutecare/issue.aspx?id=42>)

³ National Alert Network (NAN) alert. Confusion regarding the generic name of the HER2-targeted drug Kadcylla (ado-trastuzumab emtansine). 2013 Apr 17. (<http://www.ashp.org/DocLibrary/Policy/PatientSafety/NAN-Alert-April-2013.pdf>)

⁴ Please see prior correspondence to FDA from NCPDP on 6 Jun 2010, 20 Aug 2012, 31 Jul 2013, and 6 Jun 2014; in person meeting materials 1 May 2014; and ODAC testimony 7 Jan 2015.

⁵ Haseley D. Drug compendia officials warn FDA that nontraditional biosimilar names pose safety issues. *IWP News*. 18 Jun 2014.

⁶ Cabibbo J, Bruce M. NCPDP provides guidance to FDA panel at historic FDA meeting on biosimilars. *PR News*. 7 Jan 2015. (<http://www.prweb.com/releases/2015/01/prweb12430674.htm>)

⁷ FDA Briefing Document, Oncologic Drugs Advisory Committee Meeting, January 7, 2015; available at: <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/UCM428780.pdf> (accessed 20Feb15)

⁸ ASHP letter to comments to the World Health Organization (WHO) on the proposed biological qualifier to International Nonproprietary Names (INNs) for similar biotherapeutic products (biosimilars). 29 Sep 2014

⁹ Balocco RM, Group Lead, INN International Nonproprietary Names (INN) Programme (personal communication). 2015 Jan 21.

many years in other countries, i.e., “filgrastim” without modification. This approach also would be consistent with FDA’s only existing public position on biosimilar naming as stated in its 2006 comments to WHO:¹⁰

“INNs should be based, as now, on considerations of molecular characteristics and pharmacological class. No specific process should be introduced for naming biosimilars. INNs for these products should be assigned according to the standard process for naming biologicals. **There should be no change in policy and no distinctive INN designation introduced to indicate a biosimilar product...**it should be explained that INN policy relates solely to nomenclature and that no distinctive INN designation is introduced to indicate a biosimilar product.”

NCPDP would like to help avoid the problems created by breaks with established naming conventions in the future. We anticipate similar challenges with filgrastim, tbo-filgrastim, and any other situation where the ingredient is given a different name, whether a prefix or a suffix, let alone where multiple different names become the norm as may be anticipated with more than one biosimilar to the same reference product in the future. Any difference in a nonproprietary name, were the US nonproprietary name on these products to differ from their USAN and INN, however big or small, is a difference that will impact how data are pooled, sorted, and transferred in the US (and potentially combined with data from elsewhere where the same products anticipated to be approved in the US already have the same INN as their reference product).

NCPDP has been actively engaged on the issue of biosimilars for many years. Because of the unique role NCPDP plays in electronic data and messaging standards involving drug products, it is critical that FDA fully engage the advice of our organization and its members on any proposals for biosimilar naming practices in the US, especially if any deviation from USAN and INN is considered.

NCPDP has consistently cautioned FDA against seemingly simple changes to current nonproprietary naming conventions, and the dangers to patient safety that will result. There is a critical need for a full understanding of the ramifications of any change for the practice of pharmacy and medicine as it applies across the US today, along with planning and testing for any proposed changes. The considerable resources required to accommodate such deviations from existing systems also must be assessed.

NCPDP has years of experience in observing how small, seemingly inconsequential, changes in product descriptions and data formatting or structure can have significant consequences within healthcare. NCPDP and our members are available to work with you through a consensus-building process in collaboration with other industry organizations to develop solutions to improve safety, privacy, and healthcare outcomes for patients and healthcare consumers, while reducing costs in the system. We have almost 40 years of commitment to furthering the electronic exchange of information about medications among healthcare stakeholders. In the absence of compelling evidence to the contrary, NCPDP continues to strongly support the use of existing USAN and INN naming standards for biosimilars.

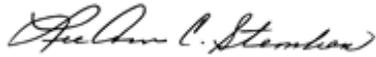
NCPDP remains very willing to work with FDA to evaluate other options or solutions. We caution against implementing any untested and unestablished naming proposals simply for expediency sake (e.g., for Zarxio[®]) before publishing for and duly considering public comment about FDA’s proposed biosimilar naming policies. In the interim, existing USAN and INN policies should be followed without deviation. NCPDP is interested in working with the FDA to find alternative ways to address concerns about existing practices and the safest ways to implement any new requirements to maximize their effectiveness and ensure a safe transition.

NCPDP looks forward to working with the FDA to establish practical but standardized ways to ensure the safety and proper product identification of medications.

¹⁰ World Health Organization (WHO) informal consultation on International Nonproprietary Names (INN) policy for biosimilar products. 2006 Sep; available at: http://www.who.int/medicines/services/inn/BiosimilarsINN_Report.pdf (accessed 2015 Feb 25)

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Respectfully,



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