Comment of the Staff of the Federal Trade Commission[1]

Submitted to the Food and Drug Administration
Department of Health and Human Services

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"Nonproprietary Naming of Biological Products; Draft Guidance for Industry; Availability"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][2]

80 Fed. Reg. 52296 (Aug. 28, 2015)

Submitted on October 27, 2015

I. INTRODUCTION AND SUMMARY

The staff of the Federal Trade Commission's Office of Policy Planning, Bureau of Economics, and Bureau of Competition ("FTC staff") appreciates the opportunity to respond to the Food and Drug Administration's ("FDA") Request for Comments on its "Nonproprietary Naming of Biological Products: Guidance for Industry."[3] As the FDA has noted, the "nonproprietary name" of a pharmaceutical identifies its active ingredient, also known as its drug substance.[4] Nonproprietary names appear on each drug's FDA-approved label and in the databases used both by physicians when prescribing, and by pharmacists when fulfilling orders for, recording, and dispensing, each pharmaceutical.

---

[1] This comment represents the views of the Federal Trade Commission's Office of Policy Planning, Bureau of Economics, and Bureau of Competition. This comment does not necessarily reflect the views of the Commission or any individual Commissioner. However, the Commission has voted to authorize the staff to submit this comment.

[2] Notice of Nonproprietary Naming of Biological Products: Draft Guidance for Industry; Availability, 80 Fed. Reg. 52296 (Aug. 28, 2015), https://federalregister.gov/a/2015-21383 [hereinafter Notice of FDA Draft Naming Guidance]. *See also* FOOD & DRUG ADMIN., DEP'T HEALTH & HUM. SERVS., NONPROPRIETARY NAMING OF BIOLOGICAL PRODUCTS: GUIDANCE FOR INDUSTRY (2015) [hereinafter DRAFT NAMING GUIDANCE], www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/-guidances/ucm459987.pdf; Designation of Official Names and Proper Names for Certain Biological Products, 80 Fed. Reg. 52224 (proposed Aug. 28, 2015), http://www.gpo.gov/fdsys/pkg/FR-2015-08-28/pdf/2015-21382.pdf [hereinafter Proposed Rulemaking].

[3] *See* Notice of FDA Draft Naming Guidance, *supra* note 2; DRAFT NAMING GUIDANCE, *supra* note 2.

[4] DRAFT NAMING GUIDANCE, *supra* note 2. The FDA generally uses the term "drug substance" to refer to the active ingredient in any FDA-approved medicine, and this comment uses the same terminology.

The FDA's Draft Naming Guidance would require that each biological product licensed under the Public Health Service Act bear a nonproprietary name that includes a unique FDA-designated suffix, in order to improve pharmacovigilance and to help minimize inadvertent substitution of biological products that FDA has not determined to be interchangeable.[5] FTC staff appreciates FDA's concern that in order to promote and ensure patient health and safety, every drug product, including biologics, should be chosen, prescribed, and recorded with accuracy. Accurate record keeping is essential for pharmacovigilance.

The question is how best to achieve this outcome. FTC staff is concerned that FDA's proposal—to assign different suffixes to the drug substance names of biosimilars and their reference biologics—could result in physicians incorrectly believing that biosimilars' drug substances differ in clinically meaningful ways from their reference biologics' drug substances, especially since differences in drug substance names have traditionally connoted meaningful differences in drug substances.[6] 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.

Biosimilar competition is important because biologics are among the most promising medicines for the treatment of a variety of medical conditions for which patients have no other

[5] "The proposed suffix should

alternative.[7] However, biologic prices are relatively high, with biologics 22 times more expensive, on average, than traditional medications.[8] The annual cost for some biologic drugs is $200,000, or more.[9] Moreover, prices for biologics are rising rapidly, increasing about 10 to 15 percent each year, with the average price of biologics doubling from 2006 to 2012.[10] At the

For the reasons set forth below, FTC staff respectfully suggests that the FDA reconsider its proposed system for nonproprietary names of biologic products in favor of other means to accomplish its purposes that are less likely to hinder competition from biosimilars. The alternatives discussed herein could enable the FDA to achieve its goal of improved pharmacovigilance and address its concern about the possible inadvertent substitution of biosimilars for biologics, without unintended adverse consequences for biosimilar competition.

II. INTEREST AND EXPERIENCE OF THE FTC

FTC staff offers this comment because it has a longstanding interest in fostering competition and promoting competitive outcomes. It has more than 40 years of experience in evaluating competition in healthcare markets. The FTC has worked to preserve generic drug price competition through enforcement and policy actions,[14] thereby gaining extensive expertise in the market dynamics that contribute to robust competition among pharmaceuticals. The FTC also has studied competitive issues affecting biologics.[15] Before Congress passed the Biologics Price Competition and Innovation Act ("BPCIA") in 2009,[16] the FTC held a 2008 workshop, and the following year issued its report, "*Emerging Health Care Issues: Follow-on Biologic Drug Competition*" ("FOB Report"). The FOB Report examined market factors likely to limit biologic competition, including: (1) lack of automatic substitution for biosimilar products; (2) potential chilling effects if products do not share the same nonproprietary names; and (3) concerns about

[14] The FTC has brought enforcement actions against anticompetitive strategies and transactions, issued reports, and advocated against anticompetitive policies in pharmaceutical markets. *See, e.g.*, Fed. Trade Comm'n, *Competition in the Health Care Marketplace*, https://www.ftc.gov/tips-advice/competition-guidance/industry-guidance/health-care

market acceptance of biosimilar drugs.[17]

The FTC predicted that, due to these and other factors, follow on biologic ("FOB") entry would be less frequent than generic drug entry, with discounts between 10 and 30 percent of the pioneer product's price, instead of the typically greater discounts on generic drugs.[18] Nevertheless, the FOB Report pointed out that even a 10 to 30 percent discount represents significant savings, given biologics' higher prices.[19] In 2014, the FTC held a second workshop addressing biosimilar competition in the United States. Many participants at that workshop agreed that biosimilars may have difficulty achieving the same successes as small-molecule generics for a variety of reasons, including the current absence of mechanisms for automatic substitution between a biosimilar and its reference biologic.[20]

[17] FTC FOB REPORT, *supra* note 15, Exec. Summ. at 3-5, *see id*. at 16 ("FOB market penetration also is likely to be hampered by lingering or institutionalized uncertainty about interchangeability and safety differences between pioneer and FOB products. This uncertainty may be heightened if the FOB product does not share the same name as the pioneer biologic product."). *See also* Fed. Trade Comm'n Public Workshop Notice, 78 Fed. Reg. 68840-02, 68843 (Nov. 15, 2013), https://www.federalregister.gov/articles/2013/11/15/2013-27406/public-workshop-follow-on-biologics-impact-of-recent-legislative-and-regulatory-naming-proposals-on [hereinafter FOB Workshop Notice]; Public Comment from Hospira to the FTC 5 (Feb. 28, 2014) (#0019), https://www.ftc.gov/system/files/documents/public_comments/2014/02/00019-88670.pdf [hereinafter Hospira Comment] ("Based on Hospira's experience in Europe since 2007, none of the FTC's predictions from 2009 need to be revised at this time.").

[18] FTC FOB REPORT, *supra* note 15, at v, 26, 53.

[19] *Id.* at v ("Although not as steep a discount as small-molecule generic drugs, a 10 to 30 percent discount on a $48,000 drug product represents substantial consumer savings.").

[20] FOB Workshop Notice, *supra* note 17, at 68841. *See also* Workshop Tr., *supra* note 7, at 34 (Dr. Kesselheim, Harvard Medical School) (noting state automatic substitution laws were "key" to small-molecule generic penetration, and biosimilars will struggle due to the absence of automatic substitution); *id.* at 104 (Dr. Miller, Express Scripts) (predicting the financial harm from slow uptake of biosimilars in future spending on biologic medicines at around "a quarter of a trillion dollars"); *id.* at 69-75 (Dr. Gal, Sanford Bernstein) (recommending against additional barriers to biosimilar uptake in the U.S.); Public Comment from Am's Health Ins. Plans to the FTC 5, 7-9 (Feb. 28, 2014), https://www.ftc.gov/system/files/documents/public_comments/2014/02/00017-88667.pdf

III. ANALYSIS

A. The FDA Draft Naming Guidance May Hinder Biosimilar Competition.

1. Increased Perceived Product Differentiation Dampens Price Competition.

Standard economic logic suggests that physicians' misperceptions of product differences between biosimilars and their reference biologics would likely reduce biosimilar competition. A common property of economic models of differentiated products is that price competition is more intense when the products are seen as close substitutes for one another. Conversely, price competition is less intense when goods are more differentiated, or are perceived as such by the economic actors selecting among them.[21] Consumers can compare and substitute similar goods more readily than differentiated goods. This encourages sellers of similar goods to compete intensely on price, since that becomes a salient decision factor for consumers.[22] For example, generic drugs tend to compete based primarily on price.

By contrast, differentiated goods are less easily substituted, and firms are less likely to compete aggressively on price. Therefore, reference biologics may compete less vigorously with biosimilars if physicians are reluctant to prescribe biosimilars due to concerns that they differ from their reference biologics in clinically meaningful ways. Physician perceptions of differentiation could cause price differences to be a less salient feature in the competition between the products, which would diminish the incentives to price aggressively.

[21] *See* DENNIS W. CARLTON & JEFFREY M. PERLOFF, MODERN INDUSTRIAL ORGANIZATION 225 (4th ed. 1994) ("The greater the perceived difference between two firms' products, the more each firm can charge.").

[22] *See id.*

2. Physicians May Mistakenly Believe that Different Suffixes Indicate Clinically Meaningful Differences Between a Biologic and its Biosimilar.

Physicians' familiarity with biosimilars may be relatively limited because the first U.S. biosimilar only launched in September 2015.[23] Limited survey data from 2013 indicated that U.S. physicians have "a low level of understanding" about various aspects of biosimilars, including "the difference between biosimilars and reference biologics" and "the current regulatory pathway for biosimilars," although "[f]amiliarity is increased among practitioners who regularly use biologics products in their practice."[24] A more recent survey from August 2015 indicated that even specialists who deal more frequently with biologics desired additional educational information about biosimilars' safety and efficacy.[25]

Consequently, the American Medical Association ("AMA") has recommended further research: "Any change in current nomenclature rules or standards should be informed by a better, and more complete, understanding of how such changes, including requiring a unique identifier for biologic INNs [International Nonproprietary Names], would influence prescriber attitudes and patient access, and affect postmarketing surveillance."[26] As the AMA noted, actions that solely enhance product identification during surveillance activities but act as barriers to clinical uptake are counterproductive.[27]

---

[23] Press Release, Novartis, Sandoz Launches ZarixoTM (filgrastim-sndz), The First Biosimilar in the United States (Sep. 3, 2015), https://www.novartis.com/news/media-releases/sandoz-launches-zarxiotm-filgrastim-sndz-first-biosimilar-united-states.

[24] Public Comment from Am. Med. Ass'n to the FTC 3 (Feb. 28, 2014), https://www.ftc.gov/system/files/documents/public_comments/2014/02/00023-88679.pdf [hereinafter AMA Comment]; *see* N. AM. CTR. FOR CONTINUING MED. EDUC., CME SURVEY ON BIOSIMILARS 4 (May 24, 2013), http://www.naccme.com/2013-biosimilars-cme-survey-results-full-report.

[25] *See, e.g.*, Kevin McCaffrey, *Most Docs Are in the Dark About Biosimilars: Survey*, MED. Mnaoars," st7.2999 191.7601 Tm.0078

Historically, all originator biologics that met the same identification tests and other aspects of identity set forth in an official USP monograph received the same nonproprietary name.[29] Just as biologics with the same nonproprietary name share a drug substance that is "essentially the same," biosimilars share a drug substance that is "essentially the same" as that of their reference biologics. [30] By contrast, any differences in nonproprietary names generally signal pharmacological and chemical relationship differences between the products. Although the FDA's proposal will use the same USAN as the core name for each biosimilar and its reference biologic, based on historical practice, the addition of unique differentiating suffixes may lead physicians to believe mistakenly that the products necessarily have clinically meaningful differences.[31]

3. *An Example from Europe May Suggest that Biosimilars with Distinct Nonproprietary Names Are Less Commercially Successful than Those with the Same Nonproprietary Names.*

An example from Europe suggests that biosimilars with distinct nonproprietary names are less commercially successful than biosimilars with the same nonproprietary name as the reference biologic. While the significance of this

4. *FDA's Proposal May Create Unnecessary Costs and Inefficiencies Due to Inconsistencies with Other Naming Systems.*

FDA's proposal also is not consistent with a proposal for biologic naming currently under consideration by the World Health Organization ("WHO").[38] Although biosimilars in most other countries with biosimilar regulations, including members of the European Union,[39] share the same INN as their reference biologics,[40] a few countries have adopted non-proprietary names for biosimilars different from that of their reference biologics in particular cases.[41] To facilitate global harmonization,[42] the WHO is developing a system to assign "Biological Qualifiers" ("BQs") to similar biotherapeutic products.[43] A BQ would be a four-letter, alphabetic code assigned at random to a biological active substance manufactured by one manufacturer.[44] That is, unlike FDA's proposed suffix, which would be part of the nonproprietary name, the BQ would be separate from the nonproprietary name in pharmacy databases.[45] Because FDA's proposal is inconsistent with the WHO BQ proposal, it risks undermining international harmonization efforts.

---

[38] The WHO administers the International Nonproprietary Naming ("INN") system, which corresponds to the USAN system in the U.S. *See International Nonproprietary Names*, WORLD HEALTH ORG., http://www.who.int/medicines/services/inn/en/ (last visited Oct. 20, 2015). The USAN of virtually all small-molecule and biologic drugs currently is identical to the INN for those drugs. *Guidance on INN*, WORLD HEALTH ORG., http://www.who.int/medicines/services/inn/innquidance/en (last visited Oct. 20, 2015) ("United States Accepted Names (USAN) are nowadays, with rare exceptions, identical to the INN.").

[39] The European Union began approving biosimilars in 2006, and presently nineteen biosimilars are marketed in various European countries. *See EPAR: Biosimilars*, *supra* note 33. *See generally Biosimilar Medicines*, EUROPEAN MEDICINES AGENCY, http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/document_listing/document_listing_000318.jsp&mid=WC0b01ac0580281bf0 (last visited Oct. 20, 2015).

[40] *See Naming of Biosimilars*, GENERIC PHARM. ASS'N, http://www.gphaonline.org/gpha-media/gpha-resources/1naming-biosimilars (last visited Oct. 20, 2015) ("The INNs assigned to biosimilars and already used in Europe, Japan, and other highly regulated markets match that of their reference.").

[41] Workshop Tr., *supra* note 7, at 206 (Dr. McCamish, Sandoz).

[42] WHO's goal is that a single global "BQ" will avoid separate national qualifier systems. *See* Programme on Int'l Nonproprietary Names, World Health Org., *Biological Qualifier, An INN Proposal* (INN Working Doc. 14.342, Rev'd Draft, June 2015), http://www.who.int/medicines/services/inn/bq_innproposal201506.pdf.pdf.

[43] *Id*.

[44] *Id.* at 2. The WHO Secretariat would first approve a manufacturer's application for a BQ and then assign the BQ. *Id.* at 3.

B. FDA Should Consider Alternative Means to Prevent Inadvertent Substitution and Track Adverse Events That Raise Fewer Physician Misperception Concerns.

FDA's Draft Naming Guidance explains that the FDA-designated suffix is necessary to "clearly identify biological products to improve pharmacovigilance [,]" and "to help minimize *inadvertent* substitution [, which] may lead to *unintended* alternating or switching of biological products that have not been determined by FDA to be interchangeable."[46] During the FTC's 2014 workshop and in public comments, market participants suggested that alternatives exist that would not raise the same concerns with physician misperception.

First, reliance on trade names may improve pharmacovigilance and prevent inadvertent substitution. Trade names identify the manufacturer of a product—as FDA's proposed suffix would—but, unlike that suffix, do not run the same risk of conveying an inaccurate implication that a biosimilar's drug substance differs in a clinically meaningful way from that of its reference biologic. Most adverse event reports already contain trade names. For example, a study by Pfizer of the adverse event reports it received for a biologic with multiple branded products showed that "in about 99 percent of the cases, there was identification of the trade name."[47] Pfizer concluded "distinct trade names or brand names do allow for more accurate reporting to the appropriate manufacturer, irrespective of the INN in a setting in which all similar products have a distinct invented trade name."[48] Similarly, the European Union's adverse event reporting system also

---

[46] DRAFT NAMING GUIDANCE, *supra* note 2, at 1 (emphasis added).

[47] Workshop Tr., *supra* note 7, at 240 (Dr. Hartman, Pfizer); *see also id*. at 294-95 (Dr. Ramachandra, Hospira) ("Pfizer's data . . . they are seeing 99 percent in the biologics field are identifiable by brand name and that is exactly what we are seeing.").

[48] *Id*. at 241 (Dr. Hartman, Pfizer). Pharmacies using NDCs achieve even greater pharmacovigilance results. For example, Dr. Miller reported that Express Scripts dispensed about 160,000 prescriptions for Avorstatin in a one-week period, from almost 52,000 pharmacies and 15 different manufacturers," and "[w]e could tell you the exact product in the hands of every patient because of the use of the NDC codes that are required for pharmacy reimbursement." *Id.* at 109 (Dr. Miller, Express Scripts). *See also supra* note 23 (noting that Sandoz launched its biosimilar product under the trade name Zarxio.).

relies on the trade name plus a batch number, and the EU reportedly has had success with that system.[49]

Second, the *Purple Book* can prevent inadvertent substitution by pharmacists. The FDA-published *Purple Book* is comparable to the FDA-published *Orange Book*, but lists biological products. Pharmacists "only substitute a generic for a prescribed brand in accordance with FDA's determinations as set forth in the Orange Book and with prescriber consent to substitution, [so] there is no associated patient safety risk with the brand and generic product having the same nonproprietary name."[50] As one 2014 FTC workshop commenter noted, "[t]his model has worked well for small molecule prescription drugs. Accordingly, we believe there is no sound public safety reason to deviate from the established naming conventions for biologics and biosimilar products."[51] Using the *Purple Book* in the same manner as the *Orange Book* is used today, *together* with physician/prescriber consent to substitution, provides an existing mechanism to prevent inadvertent substitution.[52]

---

[49] Niels S. Vermeer et al., *Traceability of Biopharmaceuticals in Spontaneous Reporting Systems: A Cross-Sectional Study in the FDA Adverse Event Reporting System (FAERS) and EudraVigilance Databases*, 36 DRUG SAFETY 617-625 (2013); Workshop Tr., *supra* note 7, at 290 (Dr. Ramachandra, Hospira) (at public workshop, an EMA representative stated that "they are quite proud of the pharmacovigilance reporting of biosimilars and biologics . . . in Europe.").

[50] APhA Comment, *supra* note 27, at 2-3.

[51] *Id*.

[52] Moreover, CVS has noted that, because many state statutes require that medicines have the same nonproprietary names in order to permit automatic substitution by the pharmacist, a different nonproprietary name for an *interchangeable* biosimilar could prevent a pharmacist from substituting the interchangeable for its reference biologic:

> If resolution of the non-proprietary naming issue requires biosimilars to have a different non-proprietary name (such as a distinct prefix/suffix to the non-proprietary name of the reference) states will likely not allow the substitution of a brand product with a biosimilar—even when it explicitly cites it as its reference product, and even when the FDA has designated a biosimilar as interchangeable with its reference. *The different proprietary name will be used to prevent substitution by suggesting that the active ingredient in the two medicines is different.*

CVS Comment, *supra* note 27 at 3 (emphasis added).

IV. CONCLUSION

FTC staff is concerned that FDA's proposal for distinct suffixes on biologics' nonproprietary names could reduce biosimilar competition. It is unclear to what extent physician misperception resulting from FDA's proposal might threaten the full potential benefits that healthcare consumers could recognize from biosimilar competition. However, given the availability of alternative approaches that also appear likely to achieve the FDA's objectives for this naming convention without introducing the potential harm to competition discussed herein, FTC staff respectfully suggests that the FDA reconsider its approach as set forth in the Draft Naming Guidance.