



Your Generics & Biosimilars Industry



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Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Comments of the Association for Accessible Medicines and the Biosimilars Council on behalf of our member companies regarding Docket No. FDA-2013-D-1543: Nonproprietary Naming of Biological Products: Update; Draft Guidance for Industry; Availability.

The Association for Accessible Medicines (“AAM”), and its Biosimilars Council (“Council”) (collectively referred to in these comments as AAM), submit these comments to FDA’s updated guidance on Nonproprietary Naming of Biological Products.

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 Council, a division of AAM, works to ensure a positive regulatory, reimbursement, political and policy environment for biosimilar products, and educate stakeholders and patients about the safety and effectiveness of biosimilars. Member organizations include companies and stakeholder organizations working to develop biosimilar products with the intent to participate in the U.S. market.

AAM appreciates and supports FDA’s continued efforts to foster biosimilar competition in the interest of building a sustainable marketplace for these innovative medicines for America’s patients. President Trump, Secretary Azar and former FDA Commissioner Gottlieb have all championed biosimilars as critical to the Administration’s efforts to lower drug prices and reduce out of pocket costs for America’s patients. Indeed, competition from FDA-approved biosimilars for costly medicines that treat many forms of cancer, rheumatoid arthritis, psoriasis, Crohn’s and colitis and other conditions, stands to save the U.S. healthcare system an estimated \$54 billion over ten years.¹ Biosimilars are already coming to market at an average 47% discount off the reference (brand name) biologic list price and 18% discount off of their Average Sales Price (ASP) in Medicare Part B.²

A robust biosimilars market is vital to spur future innovation while ensuring health care costs benefit from competitive alternatives. Yet, the few launched biosimilar medicines in the U.S.

¹ Mulcahy, Andrew W., Jakub P. Hlavka, and Spencer R. Case, Biosimilar Cost Savings in the United States: Initial Experience and Future Potential. Santa Monica, CA: RAND Corporation, 2017.

<https://www.rand.org/pubs/perspectives/PE264.html>.

² Analysis of IQVIA WAC Data for February 2019.; CMS Pricing Files April 2019.

have been slow to gain market share, to the detriment and disappointment of America's patients and payors alike. This is largely due to tactics used by some originator biologic companies that abuse their dominant market position to create barriers to biosimilars competition and utilization, ranging from building patent thickets, to refusing biosimilar developers access to samples of reference biologics, to sowing seeds of doubt regarding the safety and efficacy of FDA-approved biosimilars through misleading communication to prescribers and patients.³

Misguided policymaking such as the updated FDA biologic naming convention also plays a significant role in delaying and derailing the development of biosimilars. FDA proposes to require meaningless 4-letter suffixes to the non-proprietary names of biosimilar products and is no longer requiring the addition of retroactive suffixes to previously approved reference biologics. This guidance serves only to confuse patients, prescribers, pharmacists, and other healthcare professionals, while simultaneously undermining confidence in the safety and efficacy of all biologics.

Particularly troubling is FDA's proposal to add suffixes to interchangeable biologics that the Agency has deemed safe and effective to automatically substitute at the pharmacy counter. This will absolutely create a barrier to biosimilars, especially when the majority of the reference products to date will NOT have a suffix, due to the reversal of the retroactive position the Agency has taken with this draft guidance. Moreover, the Agency's proposal allows for the continued spread of misinformation about the safety and efficacy of biosimilars by implying that they require an identification standard different from already approved reference products.

The FDA's draft updated guidance represents a serious policy misstep that puts the benefits of biosimilars at risk for America's patients. **It is misaligned with the Agency's own Biosimilars Action Plan, and the Administration's commitment to lowering drug prices for America's patients.**

Therefore, AAM urges the FDA to reverse course on its current proposal for the naming of biological products, and rescind the policy, thereby removing the 'core name construct' (nonproprietary name + a suffix) and eliminating suffixes from ALL biologic products. Failure to do so puts the potential of the U.S. biologic and biosimilars market at risk.

FDA's Naming Policy Serves No Safety Purpose and Creates an Artificial Barrier to the Uptake of Biosimilars in the United States

There is a growing global consensus that the naming of brand biologics and their competitive biosimilar alternatives should not differ. Worldwide, biosimilars are identified by their brand name and International Non-Proprietary Name (INN) and share the same INN as the brand referenced biologic product. Most recently, both Health Canada and Australia decided to adopt a biologic naming policy that identifies all biologic medicines, including biosimilars, by their unique brand name and non-proprietary name, without the addition of a product-specific suffix. As stated above, the suffix requirement is misaligned with the Agency's own Biosimilars Action Plan, and the Administration's commitment to lowering drug prices for America's patients.

The Agency's assertion that the requirement is necessary to ensure adequate pharmacovigilance in case of an adverse event with these products is unfounded and the Agency has no data that a

³ Citizen Petition from Pfizer Inc. Available: <https://www.regulations.gov/document?D=FDA-2018-P-3281-0001>.

suffix increases pharmacovigilance. Existing naming conventions in use for the thousands of FDA-approved medicines are sufficient to address safety concerns, as evidenced by the fact that FDA will not retroactively apply the suffix requirement to marketed biologics. According to FDA's own Adverse Event Reporting System, 99% of biosimilars adverse events were reported using the product's brand name, directly contradicting FDA's stated purpose for the suffix.⁴ This point was also affirmed by Dr. Janet Woodcock⁵, Director of the FDA Center for Drug Evaluation and Research (CDER), and is likely due to the fact that a random 4-letter suffix is difficult to remember for patients and providers, and the brand name is most memorable.

Numerous stakeholders, including the Federal Trade Commission,⁶ pharmacists, health plans, manufacturers, and consumer groups, agree that imposition of a suffix confers no safety benefit.⁷ Meanwhile, the European Union, which has approved the greatest number of biosimilar medicines worldwide and has acquired more than 700 million patient days of safe and efficacious biosimilar use,⁸ has not identified any difference in the "nature, severity or frequency of adverse effects between biosimilars and their reference medicine"⁹ during the last 10 years. Further, the results of a European Medicines Agency pharmacovigilance study showed that 96.7% overall product identification was achieved across 10 classes of biologic products, including biosimilar medicines, sharing the same INN.¹⁰

FDA officials have also cited the ability to identify specific lots of biologic products as a rationale for the purpose of the suffix. All biologic medicines experience an inherent variability lot-to-lot, as the result of being manufactured in a living system. While we agree that traceability of biologic medicines from lot-to-lot is a key aspect of pharmacovigilance for these products, a random 4-letter suffix would not address this issue. Once a suffix is assigned to the product, it does not change from lot-to-lot. Therefore, the addition of the suffix does not address FDA's concern – the ability to identify the specific lot number to the product being reported.

Additionally, the majority of reference products to date do not and will not have a suffix, due to the reversal of the retroactive position the Agency has taken with this draft guidance. It is unclear how the Agency will be able to address its own concerns regarding the identity of the lot of a reference product if it does not have a suffix assigned. The suffix sets-up a dual system for the Agency and all stakeholders to create, evaluate and maintain. In fact, FDA regulations already require lot and/or batch number on the label of every pharmaceutical product.¹¹ Additionally, a National Drug Code (NDC) which is a unique set of digits that identifies the manufacturer,

⁴ Pink Sheet. "Biosimilar Suffixes Appear Superfluous In Adverse Event Reporting." Available: <http://bit.ly/2ZfVn92>.

⁵ Pink Sheet. "Woodcock: Concerns About US FDA's Biosimilars Suffix Policy Detached From Reality." Available: <http://bit.ly/2ZfGQtR>.

⁶ Statement of the Federal Trade Commission to the Department of Health and Human Services Regarding the HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs. Available: <http://bit.ly/2GhDgqo>.

⁷ <https://www.biosimilarscouncil.org/wp-content/uploads/2019/05/FINAL-Naming-Guidance-Group-Letter-5.7.19.pdf>; <https://www.theamericanconsumer.org/wp-content/uploads/2019/05/Letter-to-Commissioner-Sharpless.pdf>.

⁸ Presentation by Adrian van den Hoven. "Biosimilar medicines clinical use: an experience based-EU perspective." Available: <http://bit.ly/2Ph6aey>.

⁹ [European Medicines Agency – European Commission: Biosimilars in the EU – Information guide for healthcare professionals, 2017. Available: http://bit.ly/2ZggS9r](http://bit.ly/2ZggS9r).

¹⁰ [A Clinician's Guide to Biosimilars in Oncology: Understanding the Science of Extrapolation and Interchangeability. Dr. Elena Wolff-Holz. Available: http://bit.ly/2UY4DiI](http://bit.ly/2UY4DiI).

¹¹ 21 CFR §§ 211.130

product, strength, dosage form and package size is required to be assigned to all approved and marketed pharmaceutical products sold in the U.S.¹²

Based on this evidence, we believe the FDA biological product naming convention requesting the inclusion of a random 4-letter suffix is arbitrary and capricious and should be abandoned altogether.

The Updated Naming Policy Undermines the “Gold-Standard” of FDA Approval

As FDA noted in the January 2017 final guidance Nonproprietary Naming of Biological Products, “Applying this [suffix] 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.”¹³

As the Agency has highlighted, applying suffixes only for biosimilars and not their reference products conveys the message that the drug substance in a biosimilar differs in clinically meaningful ways from that in the reference product. This is false and would consequently deter physicians from prescribing biosimilars and patients from being comfortable with biosimilars, thus impeding competition.¹⁴ Biosimilars are approved on the basis that they have “no clinically meaningful differences” from their respective reference product.¹⁵

In contrast, while there are differences between biosimilars and generics, generics do have the same non-proprietary name as their reference products, which eases the transition from brand to generic for patients and providers alike. Ensuring that physicians and patients are comfortable with these products is integral. Comfort with the non-proprietary name of the product is a key step to adoption.

FDA-approved products have other names and unique identifiers for distinct recognition including a brand name, company name, a lot number and an NDC number that readily distinguish it from other products. The Federal Trade Commission (FTC) has also weighed in several times publicly to the FDA that they believe the suffix naming convention would, and is currently, harming competition.¹⁶

To that end, the Center for Medicare and Medicaid Services (CMS) identifies biosimilars by their brand name in its “short description” of Healthcare Common Procedure Coding System (HCPCS) codes to limit confusion during reporting that might arise from the suffix during reimbursement report submission.¹⁷

¹² 21 CFR §§ 207.33

¹³ Nonproprietary Naming of Biological Products: Final Guidance for Industry. January 2017. Available: <https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf>.

¹⁴ Nonproprietary Naming of Biological Products: Final Guidance for Industry. January 2017. Available: <https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf>.

¹⁵ 42 U.S. Code § 262.

¹⁶ Statement of the Federal Trade Commission to the Department of Health and Human Services Regarding the HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs. Available: <http://bit.ly/2GhDgqo>.

¹⁷ Centers for Medicare and Medicaid Services (CMS), ASP Pricing Files. April 2019.

Sandoz has recently released reporting data on its experience with Zarxio, the biosimilar with the most time on the market. Out of 65 safety reports registered with Sandoz since 2015, 62 were identified with the brand name.¹⁸ None of the 65 reports were entered with the 4-letter suffix. It is exceptionally telling that in the 3 years Zarxio has been on the market, none of the adverse events were reported using the product's suffix as an identifier. Brand name was almost always used.

The difference in naming conventions also plays directly into the hands of those brand manufacturers seeking to protect their biologics monopolies by creating doubt around biosimilars. As Pfizer has highlighted in its Citizen Petition, numerous brand companies have embarked on “misinformation campaigns” that sow seeds of doubt about biosimilars by insinuating that biosimilars are in some way not as safe and efficacious as their reference products. Biosimilars face any number of obstacles to competing on a level playing field, including exclusionary contracting, the “rebate trap,” and overcoming misinformation,¹⁹ and the naming convention is yet another unnecessary hurdle.

FDA's Approach Creates Two Distinct Categories for Biologic Medicines

FDA's updated draft guidance proposes to add a random 4-letter suffix to newly approved biologic products and all biosimilars. The updated proposal is counter to the FDA's prior policy of adding suffixes retroactively to previously approved biologics, including those that may serve as reference products. This change results in creating two distinct naming standards for the same class of products.

FDA states that the Agency “has carefully considered the appropriate naming convention to maximize the success of biosimilar products and interchangeable products and to help ensure the safety of patients receiving biological products licensed under the PHS Act.” However, the Agency is in fact creating a safety issue by not treating currently approved reference products the same as their respective biosimilars. Although no safety concerns have been observed in highly regulated pharmaceutical markets that do not use the suffix naming convention for biologics, at present, any safety report provided to the FDA without a suffix is automatically assumed to be associated with the reference product and not a biosimilar.

In addition, incorrect safety reports are more likely to occur with a random non-memorable suffix than if reporting was simply required by brand name, NDC, or any number of identifiers that are unique to each product. Incorrect attribution of a biosimilar safety report (submitted with the core non-proprietary name without the suffix) to its reference product may hamper the ability to detect a safety signal with the biosimilar, which is the underlying premise of the suffix.

Additionally, FDA's proposed policy for transitional products first approved under the Food, Drug & Cosmetic Act (FD&C) that will be regulated under the Public Health Services Act (PHSA) starting in March 2020 directly contradicts FDA's own logic in purporting the requirement supports pharmacovigilance. For example, there are several analog insulins, including 505(b)(2) “follow-on” products, that share the same INN including 3 insulin glargine products and 2 insulin lispro products. FDA's new policy would not add a suffix to the names of

¹⁸ Product Profile: Filgrastim-sndz (Zarxio). Biosimilars Review & Report. Available: <http://bit.ly/2logCQI>.

¹⁹ Remarks from FDA Commissioner Scott Gottlieb, M.D., as prepared for delivery at the Brookings Institution on the release of the FDA's Biosimilars Action Plan.

these products and would seemingly run counter to the reasoning for adding a suffix to other biological products for the purposes of pharmacovigilance. This is particularly contradictory because these products will not be deemed “interchangeable” under the PHSA and none are currently AB-rated for automatic substitution under the FD&C. This will cause confusion amongst patients, prescribers, pharmacists, payers, and pharmacy benefit managers, especially as future biosimilars are approved for the transitional products that share a non-proprietary name. This is counter to the FDA’s stated goal of creating “a framework for safe use and optimal pharmacovigilance for biosimilar products and interchangeable products that is informed by current experience and industry best practices.”²⁰

FDA’s updated position on implementation of the naming convention creates new pharmacovigilance issues contrary to its intended objective. It also creates inconsistency across categories of biological products where recently approved biosimilars have suffixes, and their reference product and products “deemed to be license” that share a common core non-proprietary name will not. This is likely to further confuse healthcare professionals and challenge both the adoption of biosimilar and interchangeable products as well as the use of the suffix itself.

The Proposed Policy for Interchangeable Biologics Naming Puts Patient Uptake and Automatic Substitution in Jeopardy

The updated draft guidance proposes to add a suffix to the non-proprietary name for interchangeable biologics. If a product is approved and marketed prior to applying and receiving the interchangeability designation, that product will retain the original suffix assigned at the time of the original approval even after gaining the interchangeable designation. This may create confusion about when a product can be substituted. For instance, a product may be on the market and not automatically substitutable at the pharmacy counter, and then later gain the interchangeable designation allowing for automatic substitution. These types of scenarios could introduce unnecessary barriers and will require re-education of healthcare professionals for specific products.

Further, pharmacy substitution laws vary state to state, and in some instances, a product with a different non-proprietary name than its reference product cannot be automatically substituted by law or may be perceived by pharmacists to be unsuitable for substitution given the ambiguity of such laws. Elimination of the suffix concept would obviate all of these concerns related to interchangeability.

Conclusion

Unfortunately, the fraught development of the U.S. biosimilars marketplace has some experts discouraged enough to suggest abandoning efforts to create a competitive biosimilar market here²¹, in favor of price controls for branded biologics. But we strongly agree with former FDA Commissioner Scott Gottlieb that it is “far too early to throw in the towel on biosimilars.” While FDA has done much to foster the development of biosimilars, consistent with its Biosimilars Action Plan, we believe that addressing AAM’s and the Council’s serious concerns with the naming guidance will help ensure that America’s patients will benefit from the type of competition that has successfully delivered huge costs savings from generic drugs and allow

²⁰ FDA Nonproprietary Naming of Biological Products: Update. April 2019.

²¹Preston Atteberry Peter B. Bach Jennifer A. Ohn Mark Trusheim. “Biologics Are Natural Monopolies (Part 1): Why Biosimilars Do Not Create Effective Competition.” Available: <http://bit.ly/2Gj7kCb>.

them to enjoy the same gains in affordability and access to biosimilars that Europeans have enjoyed for over a decade, namely less costly versions of critically needed treatments for serious and life-threatening conditions.

Based on the evidence provided in these comments, AAM requests the FDA to reverse course on its current proposal for the naming of biological products, and we propose complete rescission of the policy. Failure to do so puts the potential of the U.S. biosimilars market at risk of failing to fulfill their promise of access to affordable biosimilar products to America's patients and the relief they have provided globally. We look forward to continuing to work with the Agency to facilitate the development of a robust biosimilars market in the U.S.

Sincerely,

A handwritten signature in blue ink, appearing to read "C. M. S.", with a stylized flourish at the end.

Christine Simmon
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Executive Director, Biosimilars Council

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