



November 12, 2015

BY ELECTRONIC SUBMISSION

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

Re: Docket Nos. FDA-2013-D-1543 and FDA-2015-N-0648; Comments of Mylan, Inc. to FDA's Draft Guidance for Industry on the Nonproprietary Naming of Biological Products and Proposed Rule for the Designation of Official Names and Proper Names for Certain Biological Products

Dear Sir or Madam:

Mylan, Inc. ("Mylan") is pleased to provide its comments on the Food and Drug Administration's ("FDA" or "the Agency") draft guidance on the nonproprietary naming of biological products ("Draft Naming Guidance") (80 Fed. Reg. 52296 (Aug. 28, 2015)) and proposed rule for the designation of official names and proper names for certain biological products ("Proposed Naming Rule") (80 Fed. Reg. 52224 (Aug. 28, 2015)). Mylan previously provided detailed comments in support of the Citizen Petitions submitted by the Generic Pharmaceutical Association ("GPhA") and the Novartis Group of companies ("Novartis") requesting FDA to implement a policy requiring biosimilar and interchangeable drug products to use the same nonproprietary name as the reference product.<sup>1</sup> Because Mylan continues to support the position set forth in those comments, Mylan is incorporating its prior comments to the GPhA and Novartis petitions by reference herein.

Mylan is among the world's largest generic and specialty pharmaceutical companies and the largest global generics company headquartered in the United States. Today, one out of every 11 prescriptions dispensed in the United States, brand or generic, is a Mylan product. Over the course of its 50 year history, Mylan has demonstrated an unwavering commitment to enhancing patient access to high-quality, affordable generics, which are equally as safe and efficacious as their brand counterparts. As part of that commitment, Mylan is taking a leading role in the development of

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<sup>1</sup> See Docket Nos. FDA-2013-P-1153 (Sept. 17, 2013) and FDA-2013-P-1398 (Oct. 28, 2013). Mylan also submitted comments in opposition to the Citizen Petition submitted by the Janssen Pharmaceutical Companies of Johnson & Johnson ("J&J") on January 7, 2014, which requests FDA to require biosimilars to bear nonproprietary names that are distinguishable from the reference product. See Docket No. FDA-2014-P-0077 (Jan. 7, 2014).

biosimilars and interchangeable biologics for the U.S. marketplace and currently has five products in various stages of development. Mylan thus has a strong interest in ensuring that any regulatory policies regarding substitution, interchangeability or naming for biosimilars and interchangeable biological products are consistent with both patient safety and consumer access to affordable, high-quality medications.

Mylan strongly opposes the naming convention FDA seeks to implement in the Draft Naming Guidance and Proposed Naming Rule to require the use of distinguishable nonproprietary names for originator, related and biosimilar biological products by appending a meaningless, four-letter suffix to the otherwise applicable official name. FDA's proposal asks nonproprietary names to communicate content regarding interchangeability and product identification in a way that is counter to FDA practice in all other circumstances and counter to the role of nonproprietary names worldwide, which upends the public health benefits of the present international nonproprietary name ("INN") system. Further, this policy creates complex, difficult-to-remember nonproprietary names that are neither simple nor useful. As such, it is inconsistent with the standards set forth in Section 508 of the Federal Food, Drug, and Cosmetic Act ("FD&C Act"). 21 U.S.C. § 358. Worse, the proposed nonproprietary names will be misleading because distinct nonproprietary names generally communicate product differences and, in the case of biosimilars, will suggest that there are meaningful structural and clinical differences between biosimilars and their reference products contrary to the statutory requirement that biosimilars must be "highly similar" to the reference product, *with no clinically meaningful differences in terms of safety, purity, or potency*.

Although FDA argues that its proposed naming policy will help prevent inadvertent substitution and enhance pharmacovigilance, the policy is unnecessary to achieve these goals and, in fact, is highly likely to be counter-productive. The Agency has identified no data or experience suggesting that, in the absence of relying upon nonproprietary names as a vehicle for communicating interchangeability, inadvertent substitution is a real rather than theoretical risk for biological products. Moreover, prior experience with similar products (e.g., somatropin, pancrelipase) strongly suggests that distinguishable nonproprietary names are unnecessary to ensure safe use. In any event, FDA's publication of the Purple Book will clearly communicate the interchangeability status for all biological products to relevant health-care providers, including pharmacists responsible for substitution decisions, and other alternate mechanisms for preventing inadvertent substitution exist. By contrast, the use of meaningless suffixes is likely to cause confusion and misattribution between products that could facilitate inadvertent substitution and impede effective pharmacovigilance, especially when introduced into practices and systems that were not designed to accommodate such suffixes and may in fact be unable to do so.

Mylan also is concerned that FDA's proposal is inconsistent with the World Health Organization's ("WHO's") recent efforts to establish a Biosimilar Qualifier ("BQ") program that is separate from the nonproprietary name. The BQ program is intended to address the same concerns identified by FDA (e.g., inadvertent substitution, improved pharmacovigilance) without modifying the nonproprietary name or suggesting that there are significant differences between a biosimilar and its reference product. By directly modifying the nonproprietary name of biological products, FDA's proposed policy is inconsistent with the WHO approach and will cause confusion and potential safety issues internationally. Mylan believes FDA should ensure that any naming policies

it adopts are consistent with the WHO BQ program, whose principles preserve the benefits of the INN system.

Finally, Mylan is concerned that FDA’s proposed naming policy will hamper the legitimate substitution of interchangeable biological products or create significant administrative burdens for interchangeable biologics, contrary to the intent of the Biologics Price Competition and Innovation Act (“BPCIA”). If FDA requires interchangeable biological products to have distinguishable nonproprietary names, its policy will impede the legitimate substitution of interchangeable biological products by suggesting that the products have significant clinical differences necessitating different names to describe the active biological ingredient. If, on the other hand, FDA requires an interchangeable biologic to change its nonproprietary name to match the reference product’s when a biosimilar is later licensed as interchangeable (or requires both the interchangeable biosimilar and reference product to change their nonproprietary names to a new, unique nonproprietary name), FDA’s policy will create widespread confusion and significant administrative burdens for manufacturers of interchangeable biologics. One of the primary purposes of the BPCIA is to provide consumers with access to affordable biological products, including biological products that are interchangeable with a reference product without the intervention of a health care provider. Requiring biosimilars and interchangeable biological products to bear distinct nonproprietary names, or to submit to a confusing “name migration” system when subsequently licensed as interchangeable, would significantly undermine this important public health goal, contrary to the clearly expressed intent of Congress.

Accordingly, Mylan respectfully requests that FDA revise and reissue the Draft Naming Guidance by adopting a policy to require biosimilar and interchangeable biological products approved under Section 351(k) of the Public Health Service Act (“PHS Act”) to bear a nonproprietary name that is identical to the relevant reference product. The Agency also should withdraw the Proposed Naming Rule. Separately, the Agency should work toward improving the pharmacovigilance system as a whole and in a manner that does not inhibit the legitimate substitution of interchangeable biological products. The grounds for this request are set forth in more detail below.<sup>2</sup>

**I. Requiring Identical Nonproprietary Names Would Appropriately Reflect The FDA’s Scientific Determination That Biosimilars Are “Highly Similar” to Their Reference Products With No Clinically Meaningful Differences in Terms of Safety, Purity, or Potency, Consistent With Well-Established Past Precedent**

**A. The BPCIA’s “Highly Similar” Standard**

With the enactment of the BPCIA in 2010, Congress authorized the approval of biosimilar and interchangeable biological products subject to regulation under the PHS Act. Under the new law, FDA is authorized to approve a “biosimilar” if: (1) the biological product is “highly similar” to a single reference product notwithstanding minor differences in clinically inactive components; and

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<sup>2</sup> Mylan notes that there are numerous individual comments in the docket supporting FDA’s proposed naming policy for biologics that use the same language and phrasing, which strongly suggests they are orchestrated, corporate efforts rather than genuine “grassroots” participation and should be discounted accordingly.

(2) there are no clinically meaningful differences between the two products in terms of safety, purity and potency.<sup>3</sup> Biosimilarity must be demonstrated by means of robust analytical studies and non-clinical and clinical testing, including an assessment of immunogenicity (unless waived).<sup>4</sup> Consequently, although a biosimilar may not necessarily be interchangeable with a reference product, it nevertheless must be so similar to the reference product that the only differences are “minor” and without clinical relevance.

The BPCIA also authorized the approval of “interchangeable” biological products. Under the new law, a biological product will be considered “interchangeable” if it “may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.”<sup>5</sup> In other words, interchangeability reflects an FDA determination that two biological products can be substituted for one another at the pharmacy level without the knowledge or authorization of the prescribing physician, much like small molecule generic drugs. In order to be approved as “interchangeable,” a biological product not only must be biosimilar to a reference product but also must be “expected to produce the same clinical results as the reference product in any given patient.”<sup>6</sup> In addition, for biological products that are administered more than once, the risks associated with alternating or switching between products in terms of safety or diminished effectiveness must be no greater than the risk of using the reference product without such alternating or switching.<sup>7</sup> The scientific standard for interchangeability thus is demanding, comprehensive and rigorous.

Because of the heterogeneity and complexity of products produced in biological systems, the establishment of identicalness may not be possible. For this reason, Congress adopted a “highly similar” standard for the approval of biosimilars and interchangeable biological products, not the “sameness” standard applicable to generic drug products regulated under the FD&C Act. This, however, does not mean that a biosimilar meeting the “highly similar” standard has a *different* active ingredient than the reference product or that it should be identified by a different nonproprietary name. On the contrary, it simply reflects the fact that biosimilar products often are more complex than small-molecule drug products and may differ in minor ways that are not clinically meaningful.

Accordingly, FDA should ensure that all products meeting the stringent “highly similar” standard are identified with the same nonproprietary name as the reference product. This policy would appropriately reflect FDA’s scientific determination that biosimilars can incorporate only *slight variations* from the reference product and that *these minor differences have no clinical significance*. Using distinguishable nonproprietary names, on the other hand, could misleadingly suggest to physicians and pharmacists that there are significant and/or clinically relevant differences between a reference product and its biosimilar or interchangeable version when, in fact, there are none.

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<sup>3</sup> 42 U.S.C. § 262(i)(2).

<sup>4</sup> *Id.* § 262(k)(2)(A)(i)(I).

<sup>5</sup> *Id.* § 262(i)(3).

<sup>6</sup> *Id.* § 262(k)(4)(A).

<sup>7</sup> *Id.* § 262(k)(4)(B).

**B. FDA’s Long-Standing Practice Is to Apply the Same Nonproprietary Name to Complex, Biological Drug Products That Are Highly Similar to Each Other But Not Necessarily Chemically or Physically Identical**

Under the FD&C Act, which is generally applicable to biological products,<sup>8</sup> a drug or biologic will be deemed misbranded if its label does not bear its established nonproprietary name.<sup>9</sup> The statute defines an “established” nonproprietary name as either: (1) an applicable “official name” designated by FDA;<sup>10</sup> (2) the name identified in an applicable United States Pharmacopoeia (“USP”) monograph, if there is no “official name”; or (3) if neither of the above applies, the drug’s common or usual name.<sup>11</sup> Per its binding regulations, the Agency does not routinely designate official names for drug products, so the “established” nonproprietary name typically is the name identified in a USP monograph or, lacking a monograph, the common or usual name.<sup>12</sup>

USP monographs define standards for the identity, strength, quality and purity of both active ingredients and drug/biological products. In order to be identified by a compendial name, a biological product must meet the specifications for identity established in the relevant monograph. The USP establishes monographs not just for small-molecule drugs but also for biologics and biotechnology-derived products, including highly purified peptides such as insulin and complex biological mixtures such as enoxaparin. Moreover, USP has adopted a “flexible monograph” policy that can accommodate variations in active ingredients based upon different manufacturing processes. According to USP, the “flexible monograph” policy “allows different tests, procedures, and/or acceptance criteria, depending on characteristics that do not affect the primary safety and efficacy of a drug; e.g., different impurity tests to account for different impurities arising from different routes of production.”<sup>13</sup> *Consequently, two products may conform to the same USP monograph – and thus have the same “established” nonproprietary name – even though they are not chemically or physically identical to one another.*

Based upon the above-described statutory requirements, FDA’s past practice has been to apply the same nonproprietary name to complex, biological drug products that are “highly similar” to each other but not necessarily chemically or physically identical. Perhaps the best example of this – and the one most analogous to biosimilars and related biologics – is Omnitrope<sup>®</sup> (somatropin [rDNA origin] for injection). Omnitrope was approved in 2006 via a 505(b)(2) application, an approval pathway under the FD&C Act with striking similarities to the biosimilars approval pathway under the PHS Act.<sup>14</sup> The active ingredient in Omnitrope is somatropin, a single-chain, 191-amino-acid, recombinant protein hormone. Because of the complexity of somatropin, the sponsor could

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<sup>8</sup> *Id.* § 262(j).

<sup>9</sup> 21 U.S.C. § 352(e)(1)(A).

<sup>10</sup> FDA has authority to designate “official” names under section 508 of the FD&C Act, 21 U.S.C. § 358.

<sup>11</sup> *Id.* § 352(e)(3).

<sup>12</sup> 21 C.F.R. § 299.4(e).

<sup>13</sup> See Comments of USP on “Approval Pathway for Biosimilars and Interchangeable Biological Products; Request for Comments,” Docket No. FDA-2010-N-0477, at 8-9 (Dec. 21, 2010).

<sup>14</sup> A 505(b)(2) application, like a biosimilar application, relies upon a reference product for approval and may be supported by one or more clinical studies establishing safety and/or effectiveness (including immunogenicity). In addition, the 505(b)(2) process has been used to approve products based upon the same “highly similar” standard used for biosimilar applications.

not demonstrate that Omnitrope contains the “same” active ingredient as the reference product, Genotropin®. Instead, Omnitrope was approved based upon a showing that its somatropin active ingredient is “highly similar” to the somatropin in the reference product – the same standard that FDA now applies to biosimilars under the PHS Act.<sup>15</sup>

Even though Omnitrope was approved using the “highly similar” standard (rather than the “sameness” standard applicable to generic drug products), and even though it is not therapeutically equivalent to the reference product, Omnitrope nevertheless bears *the exact same non-proprietary name as the reference product, i.e., somatropin*. FDA explained this situation as follows:

Although they may differ in some respects, all products with the established name *somatropin* share relevant, identifying characteristics of their active ingredients. Accordingly, each of the seven rhGH product lines approved by FDA has the international nonproprietary name *somatropin*.<sup>16</sup>

In other words, the nonproprietary name *somatropin* is broad enough to include numerous variations of the complex protein hormone, including molecules that are “highly similar” to each other despite differing in some respects.

There are numerous other examples of complex peptide and protein products that share the same nonproprietary name even though they are not chemically or physically identical to one another. For example, all currently approved pancrelipase products use the same nonproprietary name (i.e., pancrelipase) even though, because of their complexity, FDA has questioned whether it is possible to demonstrate that the active ingredient in one product is the “same” as the active ingredient in another product from a different manufacturer.<sup>17</sup> Pancrelipase is a combination of porcine-derived pancreatic enzymes consisting of lipase, protease, and amylase. Because of uncertainty regarding its exact composition, every individual pancrelipase product is regarded by FDA as a New Chemical Entity (“NCE”)<sup>18</sup> – meaning it contains an active ingredient that has never been approved before in another application.<sup>19</sup> Moreover, no approved pancrelipase product is interchangeable with any other. Despite clear differences in the composition of the active ingredients (due, in part, to differences in source material and purification steps), all pancrelipase products

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<sup>15</sup> FDA Response to Omnitrope Petition, Docket No. FDA-2004-P-0339, at 14 (May 30, 2006) (“Omnitrope Petition Response”). Although Omnitrope currently is regulated as a drug under the FD&C Act, it is as complex as many biologics regulated under the PHS Act and, in fact, was approved using the same “highly similar” standard that now applies to biosimilars under the PHS Act.

<sup>16</sup> Omnitrope Petition Response, p. 15, n. 35.

<sup>17</sup> FDA Guidance for Industry, Exocrine Pancreatic Insufficiency Drug Products – Submitting NDAs, at 2 (Apr. 2006) (hereinafter “Exocrine Decision”) (“Because of the complexity of pancreatic extract products, it is unlikely that currently available physicochemical and biological analytical tools would be able to demonstrate that the active ingredients in pancreatic extract products from two different manufacturers are the same.”)

<sup>18</sup> See Approved Drug Products With Therapeutic Equivalence Evaluations, at ADA-227 (33<sup>rd</sup> ed. 2013) (showing NCE exclusivity for, *inter alia*, Creon, Pancreaze and Ultresa).

<sup>19</sup> 21 C.F.R. 314.108(a).

nevertheless share a common nonproprietary name.<sup>20</sup> In other words, for complex, biological products like pancrelipase (and hyaluronidase), FDA has applied the same nonproprietary name *even to multi-source products that cannot be fully characterized and are, in fact, regarded as NCEs*.

Finally, the example of Repronex<sup>®</sup> (menotropins for injection, USP) bears mentioning even though it involved FDA's approval of an Abbreviated New Drug Application ("ANDA"), which requires active ingredient "sameness." In that case, FDA approved a generic menotropins product whose active ingredient differed from the reference product in terms of glycosylation patterns. Menotropins is a complex hormone drug extracted from human post-menopausal urine that contains two active ingredients, follicle-stimulating hormone ("FSH") and luteinizing hormone ("LH"). Human FSH is a peptide hormone consisting of two polypeptide subunits with defined amino acid sequences that are glycosylated, i.e., carbohydrate side chains are attached to both of the main amino acid sequences.

In the Repronex case, FDA determined that even though the glycosylation patterns of the active ingredient in the proposed generic product differed from the reference drug, these differences "appear not to be clinically significant."<sup>21</sup> Accordingly, despite the differences in glycosylation patterns, FDA determined that the active ingredients were the same and approved the generic product with the same nonproprietary name as the RLD, i.e., menotropins. This example indicates that complex peptide and protein products with different glycosylation patterns nevertheless can be considered to have the "same" active ingredient – and can use the same nonproprietary name – provided the differences are not "clinically significant." As noted above, this is basically the same standard applied to biosimilars, which may be approved with structural differences from the reference drug, such as different glycosylation patterns, as long as those differences are minor and not "clinically meaningful."<sup>22</sup>

In numerous comments to the Draft Naming Guidance and Proposed Naming Rule, proponents of FDA's policy argue that distinguishable nonproprietary names are necessary for biosimilars and their reference products because, unlike generic drugs, biosimilars are not "exact copies" of their reference products.<sup>23</sup> These commenters, however, fail to recognize that even for small-molecule drugs, FDA does not require generic drugs to be "exact copies" of their reference products.<sup>24</sup> Moreover, as the above examples (and several others) indicate, FDA has established a long-standing practice of applying the same nonproprietary name to complex, biological drug products that are "highly similar" to each other but not necessarily chemically or physically identical. Significantly, the use of the same nonproprietary name in these circumstances has not caused any

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<sup>20</sup> Hyaluronidase products likewise share a common nonproprietary name even though they also cannot be fully characterized and thus are regarded as NCEs. Hyaluronidase products are protein enzyme products prepared from mammalian testicular tissue.

<sup>21</sup> FDA Response to Menotropins Petition, Docket No. 92P-0487 (Legacy Docket), at 13 (June 17, 1997) ("Menotropins Petition Response").

<sup>22</sup> See 42 U.S.C. § 262(i)(2).

<sup>23</sup> See, e.g., Amgen Comments to FDA Draft Guidance and Proposed Rule on biosimilar naming, Docket No. FDA-2013-D-1543, p. 2 (Oct. 27, 2015).

<sup>24</sup> For example, FDA considers different polymorphic forms of a drug substance, such as different crystalline forms or different solvates, to be the same active ingredient. FDA Guidance on ANDAs: Pharmaceutical Solid Polymorphism, pp. 5-6 (July 2007).

problems with respect to improper substitution or impaired pharmacovigilance. Accordingly, FDA should continue to follow this practice for the highly analogous situation regarding the naming of biosimilars. Otherwise, FDA could be treating similarly situated products in a dissimilar manner, and deviating from established precedent without adequate justification, contrary to bedrock principles of administrative law.<sup>25</sup>

## **II. The Proposed Policy Requiring Distinguishable Nonproprietary Names Is Not Necessary to Ensure Patient Safety and, Because It Is Potentially Confusing, May In Fact Be Counter-Productive**

In the Draft Naming Guidance and Proposed Naming Rule, FDA asserts that its proposed policy to require distinguishable nonproprietary names for biological products that have not been determined to be interchangeable is intended to ensure the safe use of biological products by helping to prevent inadvertent substitution and enhancing pharmacovigilance. *See e.g., Draft Naming Guidance* at 5-6. However, as described more fully below, the Agency has failed to explain why these risks are greater for biologics regulated under the PHS Act than for products, including complex products like enoxaparin and transitional biologics like insulin and somatropin, approved under the FD&C Act, which have never been subject to a distinguishable nonproprietary name requirement. Moreover, Mylan believes the Agency has failed to fully consider the implications of its proposed policy, including the risk that the use of meaningless suffixes is likely to cause widespread confusion and misattribution between products that could facilitate inadvertent substitution and impede effective pharmacovigilance. In other words, there is a good chance that the proposed naming policy will actually exacerbate the very problems it seeks to remedy.

### **A. The Proposed Policy Is Not Necessary to Prevent Inadvertent Substitution**

The Agency asserts that the proposed nonproprietary naming convention described in the Draft Naming Guidance and related Proposed Naming Rule is intended to help prevent inadvertent substitution for biological products. The Agency's concerns, however, are entirely theoretical and speculative. The Agency does not provide any solid evidence that there is an increased risk of inadvertent substitution with biological products, and the available evidence is to the contrary.

For example, as described in section I.B above, FDA has established a long-standing practice of applying the same nonproprietary name to complex, biological drug products that are "highly similar" to each other but not necessarily chemically or physically identical, including somatropin, pancrelipase, and hyaluronidase. Mylan is not aware of any evidence that the historical use of the same nonproprietary name in this context – and particularly for multi-source products that may or may not be interchangeable – has had any adverse impact on inadvertent product switching (or pharmacovigilance). On the contrary, during a public meeting last year sponsored by the Federal Trade Commission on biosimilars, a representative of Sandoz stated that Omnitrope has not been associated with any safety or pharmacovigilance problems as a result of using the same

<sup>25</sup> Federal agencies are required to treat similar situations in a consistent manner. "If an agency treats similarly situated parties differently, its action is arbitrary and capricious in violation of the APA." *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27-28 (D.D.C. 1997) (quoting *Allergan, Inc. v. Shalala*, 6 Food and Drug Rep. 389, 391, No. 94-1223 (D.D.C. Nov. 10, 1994) (Greene, J.)).

nonproprietary name as the reference product.<sup>26</sup> In a published article, the Sandoz representative (and other authors) concluded that “[t]his sharing of non-proprietary names has not resulted in any safety or traceability issues.”<sup>27</sup> If FDA is aware of documented safety concerns associated with the inadvertent substitution of non-interchangeable, multi-source biologics that share the same nonproprietary name, it should provide that evidence for public review. Mylan, however, is not aware of any such evidence and believes that the long history of safe use with products like somatropin, pancrelipase and hyaluronidase support the opposite conclusion. In this regard, it is telling that even commenters who support FDA’s proposed policy admit that it is based primarily on theoretical risks.<sup>28</sup>

FDA also seeks to justify the proposed naming policy by asserting that health care providers may assume that biologics with the same nonproprietary name are interchangeable based on their experience with small-molecule and generic versions of those drugs. This argument, however, is inconsistent with the reality of small-molecule drug use as well as with the Agency’s prior statements and actions. First, as the Agency well knows, the use of the same nonproprietary name does not imply that two drug products are bioequivalent or interchangeable and our healthcare system does not rely on nonproprietary names to communicate interchangeability information. On the contrary, there are numerous examples of products that share the same nonproprietary name but are not bioequivalent, therapeutically equivalent or interchangeable. These include, among other products, albuterol sulfate inhalers, sumatriptan autoinjectors, somatropin products, levothyroxine products, testosterone gels, pancrelipase products, and hyaluronidase products. For instance, Omnitrope<sup>®</sup> uses the same nonproprietary name as Genotropin<sup>®</sup>, its reference product, but is not therapeutically equivalent to or interchangeable with the reference product. Thus, contrary to the Agency’s assumption, health care providers have long-standing and extensive experience with drug products that share the same nonproprietary name but are not interchangeable.

Second, this situation does not create any confusion whatsoever because it is well established that interchangeability determinations are communicated not by a drug’s nonproprietary name but rather by its therapeutic equivalence code in FDA’s publication *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly referred to as the Orange Book. Indeed, if use of the same nonproprietary name implied that two drug products were bioequivalent, therapeutically equivalent or interchangeable, there would be no need for the Orange Book’s therapeutic equivalence evaluations. In the case of biological products, FDA’s Purple Book should serve the same function and effectively prevent the inadvertent substitution of non-interchangeable biological products that share the same nonproprietary name.

Even if there were legitimate concerns about inadvertent or improper substitution of biosimilars – a concern which is, at this point, wholly speculative – there are better, more targeted mechanisms to address this concern without requiring distinctive nonproprietary names. The best way, as noted above, is for the Agency to publish interchangeability determinations in, and educate

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<sup>26</sup> Testimony of Mark McCamish, Global Head of Biopharmaceutical Development, Sandoz, Inc., at FTC’s Follow-On Biologics Workshop, pp. 204-206 (Feb. 4, 2014), *available at* [http://www.ftc.gov/system/files/documents/public\\_events/171301/140204biologicstranscript.pdf](http://www.ftc.gov/system/files/documents/public_events/171301/140204biologicstranscript.pdf).

<sup>27</sup> *Biosimilar By Name and Biosimilar By Nature*, McCamish et al., The RPM Report (July/August 2013).

<sup>28</sup> Comment of Public Citizen, Docket No. FDA-2013-D-1543, p. 2 (Oct. 27, 2015).

health care providers to rely upon, the Purple Book in the same way they currently rely on the Orange Book. According to FDA, “The Purple Book will . . . enable a user to see whether a biological product licensed under section 351(k) of the PHS Act has been determined by FDA to be biosimilar to or interchangeable with a reference biological product (an already-licensed FDA biological product).” Because FDA’s Purple Book will become the *de facto* source of information on interchangeability, the contention that interchangeability is or should be communicated via the nonproprietary name is mistaken.

### **B. The Proposed Policy May Create Additional Confusion That Impairs Effective Pharmacovigilance**

FDA also asserts that the proposed nonproprietary naming convention described in the Draft Naming Guidance and Proposed Naming Rule is intended to improve pharmacovigilance for biological products. Mylan agrees that appropriate pharmacovigilance is fundamentally important for all biological products but is concerned that FDA’s proposal will cause significant confusion that actually impedes effective pharmacovigilance rather than improves it.

In its proposal, FDA recommends the use of four-letter suffixes that are meaningless. The problem with meaningless suffixes, however, is that they would not be particularly memorable to health care professionals and thus their usefulness in effectively identifying products would be diminished. For example, health care practitioners likely would find it difficult to distinguish between replicamab-cznm and replicamab-hixf or to remember which product or trade name is associated with a particular suffix. This diminished effectiveness could, in turn, lead to sub-optimal pharmacovigilance for biosimilars. Indeed, it could have the perverse effect of increasing misattributions of adverse events, as reporters might tend to simply drop or forget the meaningless suffix. In addition, accurate pharmacovigilance could be further confounded by introducing the possibility of increased discrepancies between the reported proprietary and nonproprietary names, particularly if the letters in a suffix are transposed or mixed up (e.g., cznm v. czmn). If the proprietary and non-proprietary names do not match up, it may be even more difficult to trace the suspect product. Even proponents of distinguishable names for biologics recognize that FDA’s proposal, far from improving pharmacovigilance, is likely to create additional, unnecessary confusion that actually impairs effective pharmacovigilance.<sup>29</sup>

In Mylan’s view, the safest, easiest, most effective and least confusing way to improve pharmacovigilance for biological products is to require a trade name that could be used as a unique identifier for prescribing and pharmacovigilance purposes, rather than require confusing suffixes in the nonproprietary names. This trade name-based system currently is being used successfully in Europe, which is one reason the European Union does not support the use of unique nonproprietary names for biosimilars. Although most biosimilar developers voluntarily are choosing to use trade names on their biosimilar products (e.g., Zarxio), FDA also has ample authority under applicable

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<sup>29</sup> See, e.g., Comment of the Janssen Pharmaceutical Companies of Johnson & Johnson, Docket Nos. FDA-2015-N-0648 and FDA-2013-D-1543, p. 5 (Oct. 27, 2015) (“Because providers and pharmacists are more likely to be unable to remember, or liable to misremember, meaningless suffixes, their use could be counterproductive to FDA’s pharmacovigilance and safe use goals.”).

statutes to require a proprietary name on reference products and biosimilars to ensure the safe use of a biological product in those rare cases where a trade name is not used voluntarily.

For example, in a similar situation, FDA refused to approve a 505(b)(2) application for a sumatriptan injectable product because its labeling failed to include a proprietary name. FDA was concerned about safety risks associated with inadvertent substitution of the product with other sumatriptan injectors and thus concluded that “a proprietary name is necessary to assure safe and effective use of your product, and prevent medication errors ....”<sup>30</sup> FDA could use the same authority to require proprietary names for biological products, including biosimilars. To the extent FDA believes it lacks clear statutory authority in the biosimilar context, it should request such authority from Congress rather than implement a deeply flawed and potentially counter-productive naming convention.

### **C. The Proposed Policy Misleadingly Suggests That There are Clinically Relevant Differences Between Biosimilars and Their Reference Products**

Finally, FDA asserts that its proposed naming convention would have the additional benefit of avoiding inaccurate perceptions of the safety and effectiveness of biological products based upon their approval pathway. Mylan agrees with FDA that its naming convention should not advance inaccurate perceptions about the safety and effectiveness of biosimilars and interchangeable biological products. All biological products approved under the PHS Act are considered to be safe and effective, regardless of the approval pathway.

Mylan is concerned, however, that FDA’s decision to require biosimilars and their reference products to have *distinguishable* nonproprietary names will, contrary to FDA’s intent, advance an inaccurate perception about the safety and effectiveness of biosimilars. In particular, requiring the use of distinguishable nonproprietary names suggests to physicians and pharmacists that there are significant and/or clinically relevant differences between a reference product and its biosimilar when, in fact, FDA has made a scientific and regulatory decision that there are none. While the use of a common core is helpful to communicate that the products are related, the addition of a distinguishable suffix affirmatively represents that the products are *different*, thereby suggesting to physicians and pharmacists that they may have clinically relevant differences. This representation is misleading, particularly if required for interchangeable products, and conflicts with the statutory and scientific standards established by the BPCIA.

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<sup>30</sup> See Complete Response Letter to King Pharmaceuticals for NDA 22-377 (May 15, 2009), available at [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2010/022377Orig1s000OtherActionLtrs.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/022377Orig1s000OtherActionLtrs.pdf).

### **III. The Proposed Policy Requiring Distinguishable Nonproprietary Names for a Biosimilar and Its Reference Product Would Conflict With the Relevant Statutory Provisions of the PHS Act and the FD&C Act**

A policy requiring biosimilar and interchangeable biological products to bear the *same* nonproprietary name as their reference products not only is consistent with the statutory “highly similar” standard and FDA’s past precedents (as discussed above), but also is fully consistent with (and in fact demanded by) the applicable statutory language and Congressional intent in enacting the BPCIA. By contrast, a proposed policy requiring *distinguishable* nonproprietary names would conflict with the relevant statutory provisions.

#### **A. The Language and Structure of the BPCIA Require Biosimilar and Interchangeable Biological Products to Bear the Same Nonproprietary Name As The Reference Product**

Judicial review of an agency’s interpretation of a statute it is responsible for implementing is generally reviewed pursuant to the familiar two-step framework set forth in *Chevron, U.S.A., Inc. v. Natural Resources Def. Council, Inc.*<sup>31</sup> Under step one, a court must determine “whether Congress has directly spoken to the precise question at issue.”<sup>32</sup> If a court determines, using traditional tools of statutory construction, that “the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress.”<sup>33</sup> The most powerful indicators of Congressional intent are the statutory language itself and the structure of the statute as a whole.<sup>34</sup>

In this case, although the BPCIA does not contain a standalone provision explicitly addressing the naming of biosimilars, the language and structure of the statute leave no doubt that Congress intended biosimilar and interchangeable products to be identified by the same nonproprietary name as the applicable reference product.

First, a “same name” requirement is more consistent with the BPCIA’s “highly similar” standard than the proposal to require distinguishable nonproprietary names. Under the BPCIA, FDA is authorized to approve a “biosimilar” if: (1) the biological product is “highly similar” to a single reference product notwithstanding minor differences in clinically inactive components; and (2) there are no clinically meaningful differences between the two products in terms of safety, purity and potency.<sup>35</sup> Requiring biosimilars and their reference products to use the same nonproprietary name would appropriately reflect FDA’s scientific determination that biosimilars can incorporate only *slight variations* from the reference product and that *these minor differences have no clinical significance*. Using distinguishable nonproprietary names, on the other hand, could misleadingly suggest to physicians and pharmacists that there are significant and/or clinically relevant differences

<sup>31</sup> 467 U.S. 837, 842-843 (1984), *reh’g denied*, 468 U.S. 1227 (1984).

<sup>32</sup> *Id.* at 842.

<sup>33</sup> *Id.* at 842-843; *see also Carciari v. Salazar*, 555 U.S. 379, 387 (2009) (explaining how, if the statutory language is “plain and unambiguous,” the court must “apply the statute according to its terms”).

<sup>34</sup> *See Amalgamated Transit Union v. Skinner*, 894 F.2d 1362, 1368 (D.C. Cir. 1990) (quoting *K Mart Corp. v. Cartier, Inc.*, 486 U.S. 281, 291 (1988)).

<sup>35</sup> 42 U.S.C. § 262(i)(2).

between a reference product and its biosimilar or interchangeable version when, in fact, there are none.

Second, the BPCIA requires biosimilar and interchangeable products to have the same “strength” as the reference product.<sup>36</sup> This “same strength” requirement makes sense only if biosimilar and interchangeable products bear the same nonproprietary name as the reference product, since strength always relates to a specific active ingredient, and there would be no rational basis for requiring a biosimilar to have the “same strength” as the reference product if the two products contain different active ingredients identified by different nonproprietary names. Indeed, in the context of drugs composed of complex, naturally-derived mixtures, FDA has stated that “[i]n order for the two products to have the same strength, their active ingredients would need to be: (a) identical, and (b) present in the same amount per dosage form.”<sup>37</sup> This principle also is illustrated by the botulinum toxin situation, in which FDA assigned distinguishable nonproprietary names to each product because “[t]he potency units [i.e., strengths] are specific to each botulinum toxin product, and the doses or units of biological activity cannot be compared or converted from one product to any other botulinum toxin product.”<sup>38</sup> In other words, FDA required different nonproprietary names because the strengths were not comparable, a situation that cannot occur with biosimilar and interchangeable products. The “same strength” requirement thus indicates that biosimilars should have the same nonproprietary name as the reference product.<sup>39</sup>

Third, the BPCIA includes a provision explaining how biosimilars will be treated for purposes of the pediatric assessment requirements under the FD&C Act (21 U.S.C. § 355c). According to that provision, a biosimilar that has not been determined to be interchangeable with a reference product “shall be considered to have a new active ingredient under [21 U.S.C. § 355c].”<sup>40</sup> Significantly, this clarification becomes necessary only if Congress intended biosimilars to share the same nonproprietary name as the applicable reference product. If FDA requires biosimilars to have distinct or distinguishable nonproprietary names, this provision would become superfluous, since a product with a new nonproprietary name, by definition, contains a new active ingredient. An interpretation of a statute that renders any provision inoperative and superfluous, however, contravenes well established rules of statutory construction and must be rejected.<sup>41</sup> Consequently,

<sup>36</sup> *Id.* § 262(k)(2)(A)(i)(IV).

<sup>37</sup> See Eric Coleman, Memo to File, Citizen Petition – Lovaza (Omega-3-Acid Ethyl Esters) Strength Listing (Docket No. FDA-2013-P-0148) (Jan. 24, 2014), available at [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2014/204977Orig1s000MedR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/204977Orig1s000MedR.pdf).

<sup>38</sup> FDA Alert: Information for Health Care Professionals on Botulinum Toxin Products (8/2009), available at <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm174949.htm>.

<sup>39</sup> The fact that the statute does not include a requirement for the “same active ingredient” does not undercut this point since, as explained above, Congress adopted a “highly similar” standard for biosimilars, not a “sameness” standard.

<sup>40</sup> 21 U.S.C. § 355c(m)(1). Pursuant to this provision, a biosimilar would need to comply with applicable pediatric testing requirements.

<sup>41</sup> See *Milner v. Dept. of Navy*, 131 S. Ct. 1259, 1268 (2011); *Edison Elec. Inst. v. EPA*, 996 F.2d 326, 335 (D.C. Cir. 1993) (applying “the elementary canon of construction that a statute should be interpreted so as not to render one part inoperative”) (citation omitted); *FTC v. Manager, Retail Credit Co.*, 515 F.2d 988, 994 (D.C. Cir. 1975) (“The presumption against interpreting a statute in a way which renders it ineffective is hornbook law.”); *Sprietsma v. Mercury Marine*, 537 U.S. 51, 63 (2002) (interpreting “law” narrowly, in part, because a broad interpretation could include regulations, thereby rendering the express reference to “regulations” superfluous); *Mackey v. Lanier Collection Agency*

the only way to give full effect to this provision – and thus comply with Congressional intent – is to adopt a policy requiring biosimilar and interchangeable biologics to have the same nonproprietary name as the reference product.<sup>42</sup>

Fourth, and perhaps most significantly, the fact that interchangeable biologics can be substituted for the reference product without the intervention of the prescribing physician<sup>43</sup> leaves little doubt that interchangeable products must have the same nonproprietary name as the reference product. Congress was certainly familiar with the rules and processes governing substitution and would have known that the type of automatic substitution contemplated in the BPCIA would not be possible, or would be severely impaired, if interchangeable products were required to have distinct nonproprietary names.<sup>44</sup> This is because, prior to enactment of the BPCIA, many state substitution laws permitted substitution only if two products shared the same nonproprietary name or contained the same active ingredient.<sup>45</sup> As the courts have noted, “Congress is presumed to preserve, not abrogate, the background understandings against which it legislates.”<sup>46</sup>

If interchangeable biologics must have the same nonproprietary name as the reference product to facilitate legitimate substitution, it follows that biosimilars likewise should be subject to the same naming convention. Indeed, it would be exceedingly odd – and highly confusing – to create a system in which biosimilars receive a distinguishable nonproprietary name upon initial approval and then, upon meeting the additional standards for interchangeability, transition to a new nonproprietary name that is the same as the reference product.<sup>47</sup> Yet, given FDA’s guidance that interchangeability likely will require a two-step process, this is exactly what would happen under the “distinguishable name” proposal.<sup>48</sup> However, it simply is not reasonable to assume that Congress would have created such an eccentric and confusing process for naming biologics approved via section 351(k), particularly without clear statutory language specifying this type of “name migration.” The lack of any such language is particularly telling given FDA’s past practices regarding the naming of complex drug products (discussed in section I.B above), about which Congress also can be assumed to have known. Accordingly, given the structure of the statute and the significant challenges and risks associated with this type of “name migration”, the only reasonable interpretation is that both biosimilars and interchangeable biologics must bear the same nonproprietary name as the reference product without any suffixes or qualifiers.

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*& Serv., Inc.*, 486 U.S. 825, 837 (1988) (rejecting interpretation of provision that made it redundant with another provision).

<sup>42</sup> We note that the companion provision regarding interchangeable products likewise is made operative under this interpretation because clarification is necessary in light of the biosimilar provision. *See* 21 U.S.C. § 355c(m)(2). Thus, this is the only interpretation that makes both subsections operative.

<sup>43</sup> 42 U.S.C. § 262(i)(3).

<sup>44</sup> “The concept of therapeutic equivalence . . . applies only to drug product containing the same active ingredients and does not encompass a comparison of different therapeutic agents used for the same condition.” *FDA Draft Guidance for Industry: Placing the Therapeutic Equivalence Code on Prescription Drug Labels and Labeling*, at 3 (Dec. 1998).

<sup>45</sup> *See, e.g.*, California Business and Professions Code § 4073(a); NY Pharmacy Law § 6816-a.

<sup>46</sup> *United States v. Wilson*, 290 F.3d 347, 356 (D.C. Cir. 2002).

<sup>47</sup> It also would render both provisions of 21 U.S.C. § 355c(m) superfluous.

<sup>48</sup> *Guidance for Industry on Biosimilars: Additional Questions and Answers Regarding Implementation of the BPCI Act of 2009*, at 7 (May 2015) (“At this time, it would be difficult as a scientific matter for a prospective biosimilar applicant to establish interchangeability in an original 351(k) application given the statutory standard for interchangeability and the sequential nature of that assessment.”).

Finally, the legislative history provides further support for this interpretation of the BPCIA. During its deliberations, Congress actually considered several provisions that would have required a biosimilar to have a *different* nonproprietary name than its reference product.<sup>49</sup> FDA likewise lobbied for a “different name” requirement.<sup>50</sup> In the end, however, Congress rejected these lobbying efforts and instead left the current rules and practices regarding naming in place. As discussed in section I above, those rules and practices have been to apply the same nonproprietary name to complex, biological drug products that are “highly similar” to each other but not necessarily chemically or physically identical.

In sum, although the BPCIA does not include any provision explicitly addressing the naming of biosimilar and interchangeable biologics, the language and structure of the statute evince a clear Congressional intent that biosimilars and interchangeable biologics should share the same nonproprietary name as the relevant reference product.

## **B. FDA’s Proposal Is Inconsistent With Section 508 of the FD&C Act**

In the Proposed Naming Rule, FDA relies, in part, on its statutory authority under section 508 of the FD&C Act to unilaterally designate distinguishable nonproprietary names for some biological products, including reference products and biosimilars.<sup>51</sup> Section 508 provides FDA with the authority to designate an “official name” for any drug (including biologics) if it determines that such action “is necessary or desirable in the interest of usefulness and simplicity.”<sup>52</sup> As noted above, the Agency does not routinely designate official names for drug products, so the “established” nonproprietary name typically is the name identified in a USP monograph or, lacking a monograph, the common or usual name.<sup>53</sup> FDA nevertheless indicates that it will begin utilizing section 508 much more actively to set agency policy requiring distinguishable names for biosimilars and other biological products. FDA’s proposal is inconsistent with section 508 for at least two reasons.

First, the addition of a meaningless, four-letter suffix to an otherwise applicable “core” nonproprietary name is contrary to the interests of both usefulness and simplicity. As discussed in Section II above, the proposed policy is not necessary to enhance patient safety and, because of the likelihood it will cause widespread confusion, there is a strong possibility that it will, in fact, have the perverse effect of *increasing* medication errors and *impairing* pharmacovigilance. Moreover, by causing the unnecessary proliferation of meaningless and confusing suffixes to distinguish products that are “highly similar” and have no clinically meaningful differences, the proposed naming policy can in no way be viewed as serving the interests of simplicity. On the contrary, it increases the complexity of biological naming exponentially, contrary to the intent of section 508.

<sup>49</sup> *E.g.*, H.R. 1956, 110<sup>th</sup> Cong. § 3(a) (2007); S. 1505, 110<sup>th</sup> Cong. § 3(a)(1) (2007).

<sup>50</sup> *See* Letter from Frank M. Torti, M.D., M.P.H., Principal Deputy Commissioner and Chief Scientist, to The Honorable Frank Pallone, p. 3 (Sept. 18, 2008).

<sup>51</sup> 80 Fed. Reg. 52224 (Aug. 28, 2015).

<sup>52</sup> 21 U.S.C. § 358(a).

<sup>53</sup> 21 C.F.R. § 299.4(e).

Second, there is no evidence that Congress intended FDA to take a more activist approach with respect to section 508 in the specific context of biologics and biosimilars. On the contrary, and as noted above, Congress considered several provisions that would have required a biosimilar to have a different nonproprietary name than its reference product but ultimately rejected those provisions.<sup>54</sup> Congress also was well aware of FDA’s existing policy – set forth in its binding regulations – that “[t]he Food and Drug Administration will not routinely designate official names under section 508 of the act.”<sup>55</sup> Because “Congress is presumed to preserve, not abrogate, the background understandings against which it legislates,”<sup>56</sup> it would be inconsistent with Congressional intent for FDA to begin to utilize section 508 in an activist manner, contrary to its existing regulations, to effectuate a naming policy that Congress considered but specifically rejected.

FDA has used section 508 in the past in a targeted manner to address emerging safety issues regarding the dosing of certain biological products (e.g., botulinum toxin products). Mylan believes this is the proper role of section 508, and the one intended by Congress. Consequently, consistent with FDA’s past practice, the baseline presumption should be that biosimilars and interchangeable biologics will be designated by the same nonproprietary name as the reference drug. If significant safety issues emerge after approval that could be mitigated by the adoption of distinguishable nonproprietary names, however, such as problems involving inconsistent or non-standard dosing across different products, section 508 could be utilized as a “safety valve” to effectuate such a name change. Mylan believes that the targeted use of section 508 in this manner is more consistent with Congressional intent (and FDA’s past practice) than re-making section 508 into a broad policy-making tool solely for biosimilar naming.

#### **IV. The Proposed Naming Policy for Biologics Would Impede Access to Lower Cost Biologics Contrary to the Intent of the BPCIA**

Mylan is concerned that FDA’s proposed naming policy for biologics will hamper competition and interfere with the authorized substitution of interchangeable biological products, contrary to the intent of the BPCIA. It is important to remember that optimal patient care encompasses not just *patient safety* once treatment has been received, but also requires *patient access* to safe and effective medicines as part of the treatment in the first place. As discussed previously, a major goal of the BPCIA and the establishment of the biosimilar pathway is increased patient access to important therapeutic medicines. The entrance of biosimilars on the market is expected to introduce price competition, helping to make the very high costs of current biologic treatments more affordable for patients.

Although the use of the same nonproprietary name does not imply anything about bioequivalence or interchangeability, the use of distinguishing nonproprietary names would severely hamper the legitimate substitution of two products found to be interchangeable. Indeed, a recent survey of pharmacists concluded that the use of distinguishable nonproprietary names “may influence pharmacists’ likelihood to substitute interchangeable biologics and prevent full adoption of biosimilars in the market, since *most pharmacists indicated feeling confident or very confident*

<sup>54</sup> E.g., H.R. 1956, 110<sup>th</sup> Cong. § 3(a) (2007); S. 1505, 110<sup>th</sup> Cong. § 3(a)(1) (2007).

<sup>55</sup> 21 C.F.R. § 299.4(e).

<sup>56</sup> *United States v. Wilson*, 290 F.3d 347, 356 (D.C. Cir. 2002).

*with biosimilar substitution only when the interchangeable biologic and the reference product shared a generic or nonproprietary name.*<sup>57</sup> For the same reason, different names also may impede adoption of biosimilars by payers and physicians, thus limiting access to patients and the potential cost savings to the U.S. healthcare system, as was intended by Congress.

It is particularly telling that the Federal Trade Commission (“FTC”), the expert federal Agency on competition issues, opposes FDA’s proposed naming policy on the grounds that it will impair competition. According to the FTC, “[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.”<sup>58</sup> These inaccurate perceptions of “differentiation” between biosimilars and their reference products, in turn, “could cause price differences to be a less salient feature in the competition between the products, which would diminish the incentives to price aggressively.” For these reasons, FTC requests FDA to address the safety issues it has identified through alternative means that raise fewer physician misperception concerns.

If, on the other hand, FDA requires an interchangeable biologic to change its nonproprietary name to match the reference product’s when a biosimilar is licensed as interchangeable (or requires both the interchangeable biosimilar and reference product to change their non-proprietary names to a new, unique non-proprietary name), FDA’s policy will create widespread confusion and significant administrative burdens for manufacturers of interchangeable biologics that will impede the development of interchangeable biological products. One of the primary purposes of the BPCIA is to provide consumers with access to affordable biological products, including biological products that are interchangeable with a reference product without the intervention of a health care provider. Requiring biologics, including biosimilars and interchangeable biological products, to engage in a confusing “name migration” process when transitioning from a biosimilar to an interchangeable product would significantly undermine this important public health goal, contrary to the clearly expressed intent of Congress.

Consequently, even if proposals to require distinguishable nonproprietary names are not intended primarily to interfere with legitimate substitution and product use, this nevertheless may be the foreseeable effect, particularly given the FTC’s warnings regarding competition. For this reason, the AMA has expressed concerns that “[a]ctions that solely enhance product identification during surveillance but act as barriers to clinical uptake are counterproductive.”<sup>59</sup> Mylan agrees. For the reasons set forth above, Mylan believes that an appropriate balance will not be achieved if distinguishable nonproprietary names are required for biosimilars and their reference products.

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<sup>57</sup> Assessment of Pharmacists’ Views on Biosimilar Naming Conventions. Fernandez-Lopez et al. J Manag Care Spec Pharm. 2015;21(3):188-95 (emphasis added).

<sup>58</sup> Comment of the Staff of the Federal Trade Commission, Docket No. FDA-2013-D-1543, p. 2 (Oct. 27, 2015).

<sup>59</sup> See Report of the AMA’s Council on Science and Public Health 4-A-14 (2014).

## V. FDA's Biologic Naming Policies Should Be Consistent With the WHO Approach

Mylan recommends that FDA consider adopting a naming convention that is consistent with the WHO's recent proposal for a BQ system. In July 2014, the WHO formally proposed a voluntary BQ system for all biological active substances, including biosimilars, for the primary purpose of improving pharmacovigilance. It is important to emphasize, however, that unlike FDA's proposal, there was a consensus that the BQ should not be part of the nonproprietary name itself but instead would be a parallel activity that would not impact the WHO's INN Programme. In its proposal, the WHO thus explained that "[t]he BQ code will not be part of the INN, whose selection by the usual procedure will remain unchanged." In comments to the WHO proposal, the United States Pharmacopeial Convention ("USP") stated that it "agrees that the BQ should not be part of the nonproprietary name itself in order to assure consistency with currently applied compendial approaches." While Mylan disagrees with some aspects of the WHO approach, it agrees that the creation of another qualifier to assist with pharmacovigilance should be separate and apart from the nonproprietary name to preserve the benefits of the INN system.

If FDA nevertheless decides to require distinguishable names for biosimilars and their reference products, Mylan would prefer the adoption of a meaningful suffix that designates the manufacturer of the biological product, similar to FDA's "placeholder" name for Zarxio, i.e., filgrastim-sndz. Although this would present its own set of issues, it would at least have the benefit of being more memorable, and thus less confusing, than a random collection of letters.

## VI. Conclusion

For the reasons set forth above, FDA should revise and reissue the Draft Naming Guidance by adopting a policy to require biosimilar and interchangeable biological products approved under Section 351(k) of the PHS Act to bear a nonproprietary name that is *identical* to the relevant reference product. The naming policy requested herein appropriately reflects the fact that biosimilar and interchangeable biological products have been demonstrated to be "highly similar" to a reference product, with no clinically meaningful differences in terms of safety, purity, and potency. Moreover, it is consistent with the relevant statutory language as well as FDA's longstanding practice of applying identical nonproprietary names to drug and biological products that have been shown to be highly similar to each other but not necessarily chemically or physically identical. In addition, the use of the same nonproprietary names for biosimilars and their reference products most effectively balances safety concerns with the interests of greater accessibility to affordable medications, a view supported by the FTC. For the same reasons, FDA should withdraw the Proposed Naming Rule.

Although Mylan agrees that robust pharmacovigilance is important for biosimilars and interchangeable biological products, this can be accomplished most effectively without requiring distinguishable nonproprietary names. Mylan believes the Agency should work separately toward improving the pharmacovigilance system as a whole and in a manner that does not inhibit the legitimate use of biosimilar products, including the substitution of interchangeable biological products.

Please do not hesitate to contact me directly if you have any questions regarding this submission.

Sincerely,

A handwritten signature in black ink, appearing to read 'C. M. Shepard', written in a cursive style.

Carmen M. Shepard  
Senior Vice President  
Global Policy and Regulatory Counsel