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COMMENTS SUBMITTED ON BEHALF OF THE FOOD, DRUG AND COSMETIC LAW SECTION AND THE HEALTH LAW SECTION COMMITTEE ON MEDICAL RESEARCH AND BIOTECHNOLOGY on U.S. Food and Drug Administration (FDA) Guidance Entitled "Nonproprietary Naming of Biological Products: Guidance for Industry" Docket No. FDA-2013-D-1543-0001

Food, Drug and Cosmetic #3
Health Law #2

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As members of the New York State Bar Association Food, Drug and Cosmetic Law Section and the Health Law Section Committee on Medical Research and Biotechnology, we are pleased to offer these comments on the U.S. Food and Drug Administration (FDA) Guidance entitled "Nonproprietary Naming of Biological Products: Guidance for Industry" ("Guidance") issued on August 28, 2015.

As an overarching matter, we wholeheartedly agree that there should be some differentiating naming scheme to "avoid inaccurate perceptions of the safety and effectiveness of biological products based on their licensure pathway."[1] Our comments below focus on how that naming scheme can create that differentiation, yet provide informative guidance to health care providers, pharmacists, and patients alike. By assigning meaning to the proposed naming scheme, we believe that suffixes that identify a reference listed biologic ("RLB") or the respective similarity of a biosimilar product (a "biosimilar" or "biosimilars") to the RLB under the Public Health Service Act ("PHS Act")[2] will make it easier to encourage "routine use of designated suffixes in ordering, prescribing, dispensing, and recordkeeping practices" of biosimilars.[3] We also believe there are sound public health and pharmacovigilance reasons to include manufacturer information in the suffix, as the FDA had proposed in its "placeholder name" for the first approved biosimilar. In sum, we make the following recommendations:

[1] Guidance at 1-2.

[2] 42 U.S.C. § 262.

[3] Guidance at 1.

- All biological products should have the same core name (as defined in the Guidance).[4]
- Following the core name and hyphen, all biological products should have a multi-letter suffix following the proper name that designates the therapeutic similarity of a biological product, *i.e.*, if the biological product is a RLB (pursuant to 351(a) of the PSH Act), a highly similar biosimilar product (pursuant to 351(k)(2) but not 351(k)(4) of the PHS Act), or an interchangeable biosimilar product (pursuant to 351(k)(2) and 351(k)(4) of the PHS Act). For example, the suffixes could be a two-letter code: "RB" (RLB), "HB" (highly similar biosimilar), or "IB" (interchangeable biosimilar), respectively, similar to the two-letter coding in FDA's related publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book").
- To the extent there are multiple RLBs with the same core name, each RLB should be provided a distinguishing number coinciding with the sequence when they were approved. So the first RLB using that core name would receive the suffix RB1, and the second RLB with that same core name would receive the suffix RB2, and so on. Similarly, biosimilar versions would receive a distinguishing number to link it with the appropriate RLB, similar to how drugs are linked in. So a highly similar version of RB1 would get the code HB1, and an interchangeable version of RB2 would get the code IB2, and so on, much like multiple reference listed drugs (RLDs) in the Orange Book with different therapeutic equivalence codes.
- Following the core name-hyphen-therapeutic code would be another hyphen and then either 1) the full first name of the manufacture or 2) a readily-identifiable letter code that consistently applies to the same manufacturer, *e.g.* "sndz" for Sandoz.

By adhering to a naming system that denotes the potential interchangeability of the biosimilar, the prescriber or dispenser is on notice of the level of substitutability of the biosimilar while triggering the need to refer to the *Purple Book: Lists of Licensed Biological Products With Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations* (the "Purple Book") as appropriate to ensure safe and effective use. Since many biologics are administered in a health care setting, accuracy and efficiency are often competing demands. Biosimilar names that flag differentiating characteristics between the products will appropriately limit the amount of investigative time spent by health care providers while simultaneously making these same providers cognizant of the need to evaluate the information provided in the Purple Book.

The Guidance states that there are four main considerations for the proposed suffix naming convention:

1. Ensuring Safe Use for Biological Products;
2. Enhancing Biological Product Pharmacovigilance;
3. Advancing Appropriate Practices and Perceptions Regarding Biological Products; and,

[4] FDA defines a "proper name" as the nonproprietary name designated by the FDA in the license for a biological product under the PHS Act. Guidance at 2. FDA has proposed that a proper name for any biological product will consist of a core name adopted by the United States Adopted Names Council, which normally is the name of the drug substance in the RLB followed by a hyphen and a "designated suffix" comprised of four lowercase letters to aid in distinguishing products. The designated suffix letters do not connote any meaning. FDA stated that in concept the designated suffix letters would not be: a) promotional, b) include abbreviations commonly used in clinical practice to mean something, c) contain or suggest any drug substance or core name, d) look similar to a currently-marketed product or could cause confusion / medication errors, or e) be similar to another product's suffix designation. *Id*. at 10.

4. Prospective and Retrospective Application of Naming Convention.

We believe that our suggested naming convention aligns with these considerations, which we address in turn.

A. Ensuring Safe Use for Biological Products

Not all biosimilars are created equal. As the Guidance correctly points out, biosimilar products may be licensed for a subset of the RLB indications. Moreover, the route of administration may vary in comparison to the RLB. Because of these differences and the impact these differences may have on the patient, it is critical that prescribers and dispensers select the appropriate biosimilar. Based on our review of the current available literature, it appears that experience in the small molecule space may lead to the misperception that all biosimilars are equal when labeled with the same proper name when, indeed, they are not.[5] Therefore, concern stemming from the potential inappropriate use of biosimilars is tangible and well founded. Applying an informative naming convention may curtail these errors, particularly as the number of biosimilars available to the public increases.

Using a suffix with the core name[6] calls attention to the fact that biosimilars are different than their small molecule counterparts; however, failing to assign meaning to these suffixes may ultimately lead to identification / medication errors or inefficient dispensing. Although there are few biosimilars to date, the number is likely to increase over time, making memorization and categorization of suffixes that are devoid of meaning a difficult, if not futile, exercise. By assigning a meaningful suffix that is correlated to the therapeutic similarity of a biological product, prescribers can quickly select a RLB or make a determination that an interchangeable or highly similar biosimilar product would be sufficient for any given patient.[7] In the event that a prescriber is uncertain whether a highly similar product is appropriate, he or she can refer to the Purple Book and review those biosimilars with the appropriate suffix; the prescriber does not need to look at all of the Purple Book entries listed with the core name to answer this question.

Similarly, a dispenser could easily determine whether the prescription requires the RLB, an interchangeable product, or a highly similar product by using the suggested suffix. We are currently aware of at least sixteen (16) states that allow for the automatic substitution of

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[5] *See, e.g.*, Joseph P Fuhr, Ph.D., Amitabh Chandra, Ph.D., Jacqueline Vanderpuye-Orgle, Ph.D., John Romley, Ph.D., Suepattra May, Ph.D., and Tiffany Shih, Ph.D., *Product Naming, Pricing, and Market Uptake of Biosimilars*, 4(2) GaBI J. 64 (2015) (noting that in a 2012 survey "67% of respondents assumed that shared non-proprietary names implied it was safe for a patient to be switched between products when prescribing").

[6] We advocate using the same proper name for the RLB and biosimilars to show the relationship between the products and to facilitate organization and characterization of biosimilars in databases and the like.

[7] To date, the Purple Book presently includes columns for "BLA STN" [Number], "Product (Proper) Name" [*i.e.*, non-proprietary name], "Proprietary Name", "Date of Licensure", "Date of First Licensure", "Reference Product Exclusivity Expiry Date", "Interchangeable (I) / Biosimilar (B)", and "Withdrawn". Not all RLBs are identified as such in the Purple Book.

interchangeable biosimilar products.[8] In addition, insurers have different reimbursement policies depending on the drug dispersed. Identification of interchangeable products allows pharmacists to more easily and accurately comply with state substitutability laws and insurance plans. Moreover, using a uniform set of codes avoids writing, transcribing, or reading errors that are more likely to occur when the suffix could be an array of any four letters of the alphabet. By using predictable codes, pharmacists are more likely to interpret biological product prescriptions accurately.

Although numerous biosimilars with the same proper name may achieve interchangeability over time, prescribers and insurers can still easily select one biosimilar over another if the manufacturer's name is incorporated into the naming convention. Prescribers will also be able to assess whether the prescription for a biosimilar has deviated for a given patient over time. Should a patient be switched to a different biosimilar, or if a pharmacy stops carrying a biosimilar made by a particular manufacturer, the pharmacist will be able to identify this change immediately and assess whether any notification requirements are triggered. Moreover, pharmacists would be immediately aware of any change in therapeutic similarity status, also triggering additional inspection by a healthcare provider of what the change means.

B. Enhancing Biological Product Pharmacovigilance

The Guidance notes that the FDA must "have the ability to track adverse events to the specific manufacturer" and must be able to identify the manufacturer quickly.[9] When products share the same proper name, identifying the manufacturer becomes difficult. Therefore, we support FDA's efforts to create a unique naming system for biosimilars to facilitate the identification process in adverse event situations.

Although the four letter code suggested in the Guidance will make the name of a manufacturer's biosimilar unique, it will still take time to track the code to the assigned manufacturer. We suggest including the manufacturer's name in the suffix (or a consistent four letter code for each manufacture across biosimilars) to reduce the time needed to identify the manufacture. Moreover, if the name is easily recognizable to the patient or reporting physician, they can relay that information directly when identifying the name of the biosimilar.

An additional benefit to including the manufacturer's name (or a code that correlates to the manufacturer's name) is that it incentivizes manufacturers to make high quality biological products. Over time, goodwill is associated with the biosimilar and the manufacturer when few adverse events are reported. In addition, should the FDA identify issues in the manufacturing process and send an FDA Form 483 or a warning letter, the public at large can associate this information with a given product made by the manufacturer.

[8] States that allow for substitutability include: California, Colorado, Delaware, Florida, Georgia, Indiana, Louisiana, Massachusetts, North Carolina, North Dakota, Oregon, Tennessee, Texas, Utah, Virginia, and Washington.

[9] Guidance at 6.

C. Advancing Appropriate Practices and Perceptions Regarding Biological Products

The Guidance relays issues raised by industry participants that distinguishing RLBs from biosimilars will disincentivize the use of biosimilars. Certainly, there are competing concerns in this regard: on the one hand, we should encourage the use of biosimilars to facilitate further entry and competition; on the other hand, we need to prevent the improper use of biosimilars. Unfortunately, even in the small molecule space, there is a common perception that branded pharmaceutical products are superior to generic brands.[10] Therefore, this perception is likely to transcend to the biosimilar space no matter what naming convention is used.

A potential upside to distinguishing highly similar and interchangeable biologics is that manufacturers will be encouraged to achieve interchangeability under 351(k)(4) of the PHS Act. One of the metrics a manufacturer must prove before obtaining interchangeability is a demonstration that "for a product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the product and its reference product is not greater than the risk of using the reference product without such alternation or switch."[11] Such as demonstration can only be proven over time. Therefore, highly similar biosimilars could potentially enter the market and prove interchangeability at a later date. Once interchangeability is achieved, the designation will change, and prescribers and pharmacists will be more apt to prescribe and dispense the manufacturer's drug.

D. Prospective and Retrospective Application of Naming Convention

We agree with the Guidance's approach to applying the naming convention prospectively and retroactively, but have no comment as to what would be a reasonable timeframe to designate a previously-designated biosimilar and defer to the FDA.

We thank you for the opportunity to submit these comments and look forward to a continued discussion.

Submission by the New York Bar Association Food, Drug and Cosmetic Law Section (Chair, Brian Malkin) (Biologics Law Committee Co-Chairs, Brian Malkin and Karl Williams) and Health Law Section Committee on Medical Research and Biotechnology (Committee Co-Chairs, Alex Brownstein and Sam Servello).

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[10] *See, e.g.*, Joseph P Fuhr, Ph.D, Amitabh Chandra, Ph.D, Jacqueline Vanderpuye-Orgle, Ph.D, John Romley, Ph.D, Suepattra May, Ph.D, and Tiffany Shih, Ph.D, *Product Naming, Pricing, and Market Uptake of Biosimilars*, 4(2) GaBI J. 64 (2015) ("In the case of generics, shared non-proprietary names have not resolved consumer perceptions around whether drugs are identical; yet the market for generics remains substantial because generics are priced lower"); *see also*, S. Fernandez-Lopez, D. Kazzaz, and T. Bashir M, McLaughlin, *Assessment of pharmacist' views on biosimilar naming conventions*, 21(3) J. Managed Care Spec. Pharm. 188 (2015) (indicating that "74.6% of pharmacists indicated that they would be confident or very confident in substituting an interchangeable biosimilar with the reference product if both shared the same active ingredient or nonproprietary name of the reference biologic").

[11] Public Health Service Act, 42 U.S.C. § 262(k)(4).