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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

RE: Nonproprietary Naming of Biological Products: Draft Guidance for Industry; Availability [Docket No. FDA-2013-D-1543]

To Whom It May Concern:

Allergan plc ("Allergan") is pleased to submit comments to the U.S. Food and Drug Administration ("FDA") in response to the Agency's request regarding the above-captioned draft guidance. Allergan is the manufacturer of BOTOX® (onabotulinumtoxinA), a biological product licensed under section 351(a) of the Public Health Service Act, and is developing several biosimilar products for intended commercialization in the United States.

Allergan supports the proposal outlined in the draft guidance insofar as it would result in the establishment of proper names that include a designated, meaningful suffix for all licensed originator, related, and biosimilar biological products. Allergan also encourages the Agency to assign designated, meaningful suffixes for biological products that are determined to be interchangeable with a reference product.

In support of our position, we offer the following for your consideration:

- General rationale for our position
- Observations and insights based on our experience when the proper name for BOTOX® was changed in 2009
- Response to specific questions posed in the draft guidance

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General rationale

Allergan supports the proposal outlined in the draft guidance to the extent it would allow FDA to establish proper names that include a designated, meaningful suffix for all licensed originator, related, and biosimilar biological products. Allergan also encourages the Agency to assign designated, meaningful suffixes for interchangeable biological products. Allergan takes this position because the addition of a designated, meaningful suffix to the proper name will promote safe use by preventing inadvertent substitution and support accurate pharmacovigilance.

Related biological products may differ in terms of licensed indications, routes of administration, and delivery systems (among other aspects relevant to clinical use). If a group of related biological products is assigned the same proper name, however, providers may incorrectly assume that the Agency has determined that the products are interchangeable. The inadvertent substitution of a specific product for a related product may lead to confusion and dosing errors if, for example, a patient receives a product with

a different route of administration than the prescriber intended. Distinct naming will help ensure that patients receive the specific biological product that their providers intended to prescribe.

The establishment of designated, meaningful suffixes would also enhance pharmacovigilance efforts. Distinct naming will make it easier for drug safety authorities, patients and providers to attribute adverse events to the correct biological product, and will facilitate the identification of differences between and among biological products.

Observations and insights based on our experience when the proper name for BOTOX® was changed in 2009

In 2009, Allergan, in conjunction with the FDA and the United States Adopted Names Council (USAN), adopted the proper name "onabotulinumtoxinA" for BOTOX®. This uniquely established name replaced the previous common term "botulinum toxin type A" and differs from the proper names adopted for the three other FDA-approved botulinum toxin products (DYSPORT® (abobotulinumtoxinA), XEOMIN® (incobotulinumtoxinA), and MYOBLOC® (rimabotulinumtoxinB)). The impetus for the name change was that approximately 20 years after BOTOX® was first approved under the common name "botulinum toxin type A", a new botulinum toxin serotype A product was coming to market with different units of biological activity. Insofar as units of activity of the new botulinum toxin type A product could not be compared to nor converted into units of BOTOX® or any other botulinum toxin product, FDA recognized the importance of assigning a new proper name to BOTOX® and to establishing a new nomenclature stem for new botulinum toxin products. Based upon that unique experience, Allergan is well-positioned to comment on issues related to the proper naming of biological products and how to adopt and implement changes in proper names for biological products. Our observations and insights include the following:

- **Many of the same issues the FDA hopes to address with the proposed proper naming scheme for biological products – i.e., inadvertent substitution, pharmacovigilance, and provider confusion – were concerns with the botulinum toxin class, and these were addressed effectively with the establishment of unique proper names for each biological in the botulinum toxin class.** Before BOTOX® had a specific proper name (onabotulinumtoxinA) that distinguished it from other botulinum toxin products, Allergan identified the following concerns with respect to shared proper names: risks related to inadvertent substitution (e.g., medication errors), difficulty tracking products for pharmacovigilance purposes or tracing inappropriate use, and confusion in the medical literature, which hampered scientific consideration and provider education on the correct use of biological products. In our experience, these problems were addressed effectively when the FDA assigned each of the botulinum toxin products a unique proper name. This suggests that the establishment of distinct proper names for reference biologicals and biosimilars will have a similar positive effect with biological products generally.

- **We spent substantial time and expended substantial resources to educate and inform stakeholders about the new proper name.** To facilitate uptake of the new proper name, Allergan engaged in a range of activities, including:
    - Updating product labeling, advertisements, and directions for use;
    - Educating internal stakeholders (e.g., account representatives, Medical Affairs);
    - Educating providers (physician and institutional providers);
    - Contacting a broad range of external stakeholders, including the National Library of Medicine (to alert for changes in search terms for clinical literature), clinical compendia, the Centers for Medicare and Medicaid Services (CMS), the Centers for Disease Control and Prevention (CDC), the Agency for Healthcare Research and Quality (AHRQ), the

National Institutes of Health (NIH [outside of the National Library of Medicine]), third party payers, state public health agencies, pricing compendia, group purchasing organizations, pharmacy benefit managers, retailers, specialty pharmacy providers, wholesalers, consultants, and medical school librarians, among others; and

- Monitoring third-party communications (e.g., payer policies) to assess uptake of the new proper name

Response to specific questions posed in the draft guidance

In the *Federal Register* notice that announced the availability of the draft guidance, the FDA posed several questions on which the Agency specifically requested public comment.[1] Below, please find Allergan's response to each of these questions. (For ease of reference, the questions from the *Federal Register* notice are provided in bold text.)

1. **What are the potential benefits and challenges of designating a suffix in the proper name of a biological product that is:**
    a. **Devoid of meaning versus meaningful (e.g., a suffix derived from the name of the license holder)**
    b. **Unique to each biological product versus unique to each license holder and shared by each biological product manufactured by that license holder.**

    In your comments, please address how each option would impact the following: Safe use of biological products; pharmacovigilance; and market acceptance and uptake for certain products.

    Allergan response: Allergan strongly supports the designation of meaningful suffixes. A suffix that is devoid of meaning may be difficult for medical professionals and/or consumers to remember, inhibiting the identification of the biological during ordering, prescribing, dispensing, recordkeeping, and/or adverse event reporting. A suffix that is devoid of meaning may also lead to transcription errors. A meaningful suffix, however, would likely be easier for health care professionals and consumers to remember and/or properly use.

    Allergan also strongly supports the designation of a suffix that is unique to each license holder and is shared by each licensed biological product of that license holder (e.g., a suffix based on the license holder's company name). The designation of a suffix that is the same for all of a license holder's products would reduce the number of suffixes that health care professionals must remember, facilitating the appropriate and correct use of the suffixes.[2] The designation of a suffix based on the license holder's name would not be expected to meaningfully impact the acceptance and uptake of biosimilars because the name merely reinforces information (e.g., the license holder's name) that is already included in FDA-approved product labeling.

2. **What would be the potential benefits and challenges for an interchangeable product to share the same suffix as designated in the proper name of the reference product? Your response should consider that FDA's publicly available electronic resource, the Purple Book, will identify biological products determined by FDA to be biosimilar to or**

[1] 80 Fed. Reg. 52,296 (Aug. 28, 2015).

[2] Although Allergan supports the designation of a meaningful suffix that is based on each licensed holder's name, there are several issues that the FDA will need to consider before implementing this system. For example, how does the FDA intend to address situations where there is a change in ownership or a change in the name of the license holder? What if the same company is the license holder for a reference product and its biosimilar? What is the same company is the license holder for two reference products licensed under distinct BLAs that have the same proper name?

interchangeable with a reference product. If an interchangeable product does share the same suffix as the reference product, how would this impact your responses to question 1, including pharmacovigilance?

Allergan response: An interchangeable biological product should not share the same suffix as its reference product. A suffix will not facilitate the identification of a specific biological product produced by a specific license holder if an interchangeable product is assigned the same suffix (and therefore has the same proper name) as its reference product.

If the FDA decides to designate meaningful suffixes that incorporate license holder names, an interchangeable product should never be assigned the same suffix as its reference product because the identification of multiple license holders' products with a suffix based on the reference license holder's name may create confusion and uncertainty, particularly with respect to the attribution of adverse events. This would negate the pharmacovigilance benefits associated with the use of the suffix.

3. **Would there be additional benefits or challenges if the suffix designated in the proper name of a biosimilar product that is subsequently determined to be interchangeable were changed to that of the reference product upon a determination of interchangeability? Would there be benefits or challenges to allowing the manufacturer of the biosimilar product that is subsequently determined to be interchangeable to have the option of retaining its original suffix or adopting the same suffix as the reference product?**

Allergan response: The FDA has noted that it would be difficult for a biosimilar manufacturer to establish interchangeability at the time of an initial 351(k) application.[3] Therefore, most products meeting approval criteria will likely initially be licensed as biosimilars and will not be considered interchangeable. Hence, under the proposed policy, most biosimilar products will have their own unique name. If a biosimilar is later determined to be interchangeable, requiring the biosimilar to change its suffix may create confusion for providers, patients and pharmacists, and will impose substantial administrative and logistical burdens on the product's sponsor.

4. **How could FDA and/or other Federal partners improve active pharmacovigilance systems for purposes of monitoring the safety of biological products? For example, because NDC numbers are not routinely recorded in billing and patient records in many clinical settings in which biological products are dispensed and administered, are there other identifiers besides distinguishable nonproprietary names that are routinely accessible by active pharmacovigilance systems and could enable as good as or better pharmacovigilance? How can FDA and/or other Federal partners help ensure that a distinguishable identifier for each biological product would be captured at the point of dispensing or administration to the patient and be routinely accessible in systems used for pharmacovigilance?**

Allergan response: Proper names are routinely-used identifiers for biological products. As such, distinguishable proper names offer a relatively simple way to facilitate the identification of a specific marketed product for purposes of pharmacovigilance. Allergan is not aware of any other identifier that is as routinely accessible by active pharmacovigilance systems and could enable as good as or better pharmacovigilance.

[3] *See* Biosimilars: Additional Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (Draft Guidance), at 6-7 ("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.")

To ensure that a distinguishable identifier for each biological product will be captured at the point of dispensing or administration to the patient and be routinely accessible in systems used for pharmacovigilance, the FDA should encourage CMS to require the inclusion and recognition of the new proper names as a condition of electronic health record ("EHR") certification.[4] Moreover, because certain biological products may be reported using Healthcare Common Procedure Coding System ("HCPCS") codes (e.g., to report the provision of a physician-administered biological product in a physician office or hospital setting), FDA should also encourage CMS to assign a unique HCPCS code to each biological product and to incorporate the product's unique proper name in the code's descriptor.

5. **What process and reasonable timeframe should FDA use to designate a suffix to include in the nonproprietary name of a previously licensed biological product?**

Allergan response: Consistent with the approach taken when Allergan changed BOTOX®'s proper name from "botulinum toxin type A" to "onabotulinumtoxinA", the sponsor should propose a preferred suffix (or suffixes) in a prior approval labeling supplement, and if appropriate, the Agency should approve one of these suffixes. The Agency's prior approval of a suffix will prevent license holders from taking steps (and expending substantial resources) to implement a suffix that the Agency later determines is unacceptable (e.g., due to the potential for confusion with the name of another product or product's sponsor).

To review proposed meaningful suffixes, the Agency should institute a fair, equitable, and reliable procedure that ensures that a suffix requested by one company cannot be confused with a suffix requested by another company.

However, the exact process and, therefore, the timeframe required to assign a suffix to the nonproprietary name of a previously licensed biological product cannot be defined until a thorough evaluation of the required logistical and operational steps is conducted. Allergan recommends that the Agency convene a series of multi-stakeholder meetings to accurately inform this assessment.

6. **What criteria should FDA use to prioritize retrospective application of this naming convention to previously licensed biological products?**

Allergan response: Consistent with the approach outlined in the proposed rule that accompanied this draft guidance, the FDA should prioritize previously-licensed biological products that have been identified as a reference product in an approved or pending 351(k) application, as well as "related products" to such reference products. Whenever possible, the FDA should establish revised proper names for reference and related biological products effective no later than the date on which the Agency approves the relevant 351(k) application.

7. **What are the expected time frames for sponsors of previously licensed biological products to distribute products that conform to this naming convention after approval of a labeling supplement?**

Allergan response: It may take manufacturers of certain products more or less time to conform to the new naming convention. Allergan, therefore, reiterates its suggestion that the Agency

[4] Certified EHR Technology (February 12, 2015), https://www.cms.gov/Regulations-and-Guidance/Legislation/EHRIncentivePrograms/Certification.html.

convene a series of multi-stakeholder meetings to fully evaluate the process and the timeframe required to assign a suffix to the nonproprietary name of a previously licensed biological product.

8. **What strategies could FDA use to enhance stakeholders' understanding of and education about this naming convention?**

   Allergan response: The FDA should conduct a series of webinars before and after the guidance is finalized) to educate stakeholders about the naming convention. The FDA should also consider creating a dedicated e-mail address (or other contact point) to which interested stakeholders may direct questions specific to the proper naming of biological products.

9. **FDA notes that this naming convention (i.e., use of a suffix) has some similarities to the World Health Organization (WHO) proposal, "Biological Qualifier--An INN Proposal." At the time of publication of this draft guidance, WHO was still evaluating the comments received on its proposal. If WHO adopts a Biological Qualifier proposal, how should the biological qualifiers generated by WHO be considered in the determination of FDA designated proper names for the biological products within the scope of this guidance?**

   Allergan response: Allergan supports the designation of proper names by FDA that incorporate the Biological Qualifiers ("BQs") adopted by WHO – but only insofar as WHO adopts meaningful BQs. If WHO adopts a biological qualifier convention based on a random code (as is currently proposed), we encourage the FDA to adopt its own proper naming convention and not incorporate the WHO BQs.

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Allergan appreciates the opportunity to comment on this draft guidance.

Sincerely yours,

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