September 21, 2018

Dockets Management Staff (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA 2018-N-2689 for "Facilitating Competition and Innovation in the Biological Products Marketplace; Public Hearing; Request for Comments"

On behalf of our 135 members worldwide, the Alliance for Safe Biologic Medicines (ASBM) respectfully submits this letter to the Food and Drug Administration (FDA) in response to the Agency's request for comments on "Facilitating Competition and Innovation in the Biological Products Marketplace." Since its inception in 2010, ASBM has been focused on increasing access to biosimilars and ensuring patient safety is at the forefront of the regulatory and policy discussion. Our Steering Committee, composed of entirely patient and physician groups, has been leading these efforts.

ASBM firmly believes that patients are entitled to expect quality drug products, irrespective of whether the product is the branded biologic or a biosimilar, and regardless of price. While it is important to find a balance between producing economical drugs for our patients and respecting the drug-discovery process, patient safety should always be paramount. The choice between originator biologics and biosimilars should remain as a discussion point between patients and their healthcare providers. To ensure informed decision-making, patients need comprehensive information about how biosimilars work.

ASBM applauds the FDA for its commitment and arduous efforts in advancing biosimilars in the market. Specifically, we commend the FDA for its rigorous scientific standards in the biosimilar approval process and applaud its work in approving 12 biosimilars to date. We also appreciate the opportunity FDA afforded ASBM to present comments during the FDA's Public Hearing held September 4, 2018 on how FDA can achieve the Biologics Price Competition and Innovation Act's (BPCIA's) objective to balance competition and innovation. Below we provide our comments to address questions posed by FDA in its Federal Register notice posted July 25, 2018.

What can FDA do to help biosimilars and interchangeable products reach patients more quickly after these products are licensed?

ASBM believes increased accessibility of biosimilars in the marketplace will lead to greater confidence in biosimilars among patients, healthcare providers, pharmacists, and other stakeholders. Healthcare providers in particular are generally unfamiliar with biosimilars. Few have ever heard of the Purple Book. Such unfamiliarity puts biosimilars, and thus patients, at a disadvantage. More patient and provider education is needed to facilitate familiarity and access.

One way to raise the profile of biosimilars is to utilize distinct biosimilar naming, which would enable maintenance of a robust pharmacovigilance database. We support FDA's efforts to enhance the pharmacovigilance of biological products via its Nonproprietary Naming of Biological Products guidance

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document.[1] ASBM surveyed physicians globally as well as U.S. pharmacists and found consensus that a robust and active pharmacovigilance database would build confidence in the safety and efficacy of biosimilars. A majority of physicians (66%) and pharmacists (68%) in the U.S. supported the use of distinct nonproprietary names to ensure clear communication among manufacturers, regulators, physicians, pharmacists, and patients.

While distinct nonproprietary naming ensures precise product identification and avoids pooling of adverse events, the current approach uses random four-letter suffixes to accomplish this. In contrast, our survey data shows a strong preference among physicians (60%) and pharmacists (77%) for distinguishing suffixes to be meaningful and more memorable. Despite this potential for improvement in suffix content, ASBM continues to strongly support the FDA in its currently implemented system of distinguishing suffixes.

We also encourage FDA to work more closely with international organizations, such as the World Health Organization (WHO), to achieve international harmonization of nomenclature and advance the use of distinct naming systems worldwide. These changes will ensure greater familiarity with available biologics, strengthen the system of global pharmacovigilance, and increase confidence in the use of biological products among healthcare providers.

What additional information or features could be incorporated into the Purple Book to make it more useful to stakeholders, including patients, healthcare providers, pharmacists, and manufacturers?

The Purple Book is a useful reference. Its existence is not well known. We urge FDA to increase promotion of the Purple Book to physicians, patients, pharmacists, and other healthcare stakeholders.

FDA expects that the number of licensed biosimilar and interchangeable products will continue to increase in the coming years. In many, if not most, cases, FDA anticipates that multiple products will be licensed as biosimilar to, or interchangeable with, a given reference product. What additional steps can FDA take to facilitate the evolution of the biosimilar and interchangeable product marketplace? What can FDA do to ensure that confidence in these products among patients, healthcare providers, pharmacists, and other stakeholders will continue to grow?

1. *Multiple biosimilars for one reference product*

ASBM believes the marketability of biosimilars depends on high scientific standards and urges FDA not to sacrifice or diminish quality, safety, or effectiveness standards in the biosimilar approval process.

We are particularly concerned about the possibility of substitution between two biosimilars if each biosimilar is approved to be interchangeable with the same reference product. To facilitate the efficient development of biosimilars and interchangeable products, it is critical to require a demonstration of interchangeability between the two biosimilars before automatic substitution is permitted. The

[1] *See* Guidance for Industry: Nonproprietary Naming of Biological Products (January 2017), available at, https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf

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interchangeability assessment must be based on evidence that an interchangeable product will produce the same clinical result as the reference product in any given patient.

Given their molecular complexity, structural differences inherently exist between a reference product and a biosimilar. Inherent differences would also exist between two biosimilars of the same reference product. Even if two biosimilars are approved as interchangeable with the reference product, they too can be expected to have differences between each other that neither has with the reference product. Therefore, the substitution of one biosimilar interchangeable product for the other biosimilar interchangeable product would very likely expose patients to an unreasonable risk of adverse events in the absence of direct safety data. Specifically, clinical trials studying the safety of such substitution are needed before any substitution is considered.

We urge FDA to require clinical studies to demonstrate that two biosimilars that are interchangeable with the same reference product can be safely substituted for each other. Unless and until such studies are successfully conducted and safety is demonstrated to FDA's satisfaction, we urge FDA to require labeling on interchangeable biosimilars that explicitly warns against the interchangeability between biosimilars.

2. Patient Education

Biosimilars are new and the general public has very little familiarity with them. ASBM believes direct-to-consumer (DTC) education by FDA and advertising by the industry would be an effective means for disseminating important information about biosimilars. We believe FDA can and should actively encourage DTC outreach about biosimilars, their benefits as new treatment options, and their lower cost.

What can FDA do to help reduce development costs arising from analytical studies of the reference product without compromising FDA's robust scientific standards for licensure of products under section 351(k) of the PHS Act?

ASBM firmly believes that short cuts are potentially dangerous and could lead to serious patient harm. Such unwanted and avoidable outcomes would significantly undermine confidence in biosimilars. Extensive analytical studies are needed. The actual number of lots tested should be based on sound statistical methodology. We strongly recommend that short cuts not be taken.

What other challenges have the potential to disrupt the balance between innovation and competition in the biological product marketplace and how can FDA or other stakeholders address these challenges?

The marketability of biosimilars depends in great measure on the removal of commercial barriers to access. In his presentation at the Brookings Institution in July 2018,[2], Dr. Gottlieb announced FDA's Biosimilars Action Plan and highlighted obstruction by payors who require step-therapy or prior authorization for reference biologic products before permitting patients access to a biosimilar. He noted

[2] See *Remarks from FDA Commissioner Scott Gottlieb, M.D., as prepared for delivery at the Brooking Institution on the release of the FDA's Biosimilars Action Plan*, available at, https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm613881.htm

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there is "no clinical rationale for these practices, since a biosimilar must demonstrate, among other things, that it has no clinically meaningful differences from the reference product as a part of demonstrating biosimilarity."

ASBM believes that these commercial barriers present more challenges for marketability than do the current scientific standards for approval. Although FDA has approved 12 biosimilars, only four are currently on the market primarily because pharmacy benefit managers (PBMs) and manufacturers negotiate high rebates and deep discounts to deter the entry of approved biosimilars. Notably, the top three PBMs cover 80% of the prescription medications for Americans. Their formularies determine which medicines are included and excluded from a healthcare plan.

In short, PBM's are interfering with the doctor's best medical judgment. They often make it impossible, for all practical purposes, to choose the best drug therapy for the patient. Instead of using their best medical judgment, doctors are forced to use their second, third, or fourth best medical judgment. Thus, only 35% of patients submitting drug prescriptions are getting the drug the doctor felt was best. One way to address the negative impact of PBMs is to remove rebates, which create a perverse incentive for higher list prices. Therefore, we urge FDA to work with agencies such as the Centers for Medicare and Medicaid Services (CMS) and the consumer protection division of the Federal Trade Commission (FTC) to remove commercial obstacles and prevent gaming of FDA requirements to delay biosimilar access unfairly.

Finally, we note that patients are being harmed by PBMs who drop drugs from their formularies mid-cycle, which is nothing more than a disingenuous bait-and-switch. The formulary should carry the listed set of drugs for the entire term of the plan. A Medicare patient who joins the drug benefit plan should have access to the drug at the plan's price effective at the time of enrollment through the completion of the plan term.

What else can FDA do to provide additional scientific or regulatory clarity regarding FDA's regulation of biological products?

The BPCIA included a "Deemed to be a License" provision for biologics previously approved through a new drug application (NDA) under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA). Under the Deemed to be a License provision, a biological product approved under section 505 would be deemed to be a licensed biological product under section 351 of the Public Health Services Act (PHSA), which requires the submission of a Biological License Application (BLA) to obtain marketing authorization for a biological product. In March 2016, FDA issued a draft guidance discussing its implementation of this BPCIA provision, which would become effective on March 23, 2020.[3]

There remains uncertainty, however, as to whether biological products approved via an NDA submitted under section 505(b)(2) of the FDCA would be deemed a licensed biologic under section 351(a) of the PHSA as an originator biologic or section 351(k) of the PHSA as a biosimilar. For example, the product Basaglar is a "follow-on biologic" to Lantus; however, it was found to be a new chemical entity and

[3] *See* Draft Guidance for Industry: Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009 (March 2016), at *1, *available at*, https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM490264.pdf

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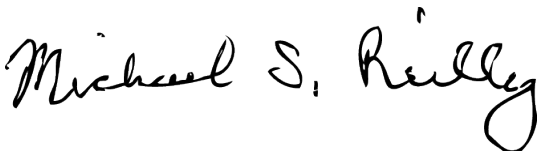
approved via the 505(b) (2) pathway. We ask FDA to clarify how products such as Basaglar will be classified when it is transitioned to a licensed biological product after March 23, 2020.

We appreciate your consideration of ASBM's comments and look forward to working with FDA in the future on these important policy issues.

Sincerely,



Michael S. Reilly
Executive Director,
Alliance for Safe Biologic Medicines

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