October 11, 2016

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

Re: Docket No. FDA-2016-D-1309: Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry; and FDA-2016-D-1267: Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the Draft Guidances entitled "*Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act*" (503A Draft Guidance) and "*Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act*" (503B Draft Guidance).

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products.

As articulated in previous comments and meetings, BIO strongly believes that the drug compounding provisions of the Drug Quality and Security Act (DQSA) did not alter current law with regard to biologics; therefore, there are still no applicable exemptions under the Food, Drug, and Cosmetic Act (FD&C Act) compounding provisions for entities that compound or repackage biological products. Additionally, due to special manufacturing challenges and heightened patient safety concerns, all drug products with a narrow therapeutic index should not be compounded.

GENERAL COMMENTS:

BIO thanks FDA for the release of the two Draft Guidances regarding compounded drug products that are essentially copies of commercially available drug products. BIO fully supports policies that facilitate timely entry of safe, effective, and high-quality medicines and recognizes that access to medically-needed compounded medicines is highly important; but access cannot and should not come at the expense of product quality and patient safety. BIO has long supported the prohibition on compounding of commercially available FDA-approved products, unless the products are medically necessary to address a unique

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individual patient need not met by the approved drug, and when supported by a valid prescription. As such, we are we are pleased to see FDA incorporate this idea in both the Draft Guidances; stating "The restrictions on making drugs that are essentially copies ensure that pharmacists and physicians do not compound drug products under the exemptions for patients who could use a commercially available drug product" in its 503A Draft Guidance, and "The restrictions on compounding drugs that are essentially copies of approved products ensure that outsourcing facilities do not compound drug products under the exemptions in section 503B for use in patients who could use an approved product" in its 503B Draft Guidance. Both Draft Guidances go on to discuss the inherent safety risks of compounded products that have not been approved by FDA and thus have not been shown to be safe and effective. Because of this inherent risk, it is critical that only patients that have a medical need that cannot be met by an approved product receive a compounded product, and only at the direction of a physician.

BIO also believes that when unauthorized versions of drugs - including drugs subject to patent protection – are compounded, it weakens incentives for companies to conduct clinical testing and bring a new drug to market via the traditional FDA-approval pathways for innovative and even generic drugs. Over the long term, this can lead to fewer new drugs, less clinical information available to prescribers about the safety and effectiveness of these products, and fewer approved medical options for patients. As such, we are also pleased to see FDA discuss in both Draft Guidances that, in addition to protecting patient safety and reducing public health risks, the prohibition on compounding products that are essentially a copy "protects the integrity and effectiveness of the new drug and abbreviated new drug approval processes."

However, we are concerned that the definition of "essentially a copy of an approved drug" in the 503B is inconsistent with the definition of "essentially a copy of a commercially available drug product." The definition for 503B outsourcing facilities could lead to large volume production of compounded drugs with slight alterations in strength and/or concentration without the necessary confirmation of clinical safety and effectiveness. This would essentially bypass the regulatory approval system and produce an unapproved drug under the guise of compounding. As such, we suggest the definition of "essentially a copy of an approved drug" in the 503B Guidance be amended to read, "the compounded drug product and the FDA-approved drug have the same: active ingredient(s) in the same, similar or easily substitutable dosage strength, route of administration and dosage form," thus bringing it in line with this portion of the definition in the 503A Guidance. Both compounding facilities and outsourcing facilities should be prohibited from changing dosage strength from an FDA-approved product simply to justify compounding and then promoting an unapproved version of an FDA-approved and commercially available product. Again, patient safety should be paramount.

While we are encouraged by and supportive of these Draft Guidances, it is critically important that FDA use its full range of regulatory and enforcement authorities to ensure that compounding does not endanger the public health or the safety of patients that rely on these products. Without adequate regulation (and vigilant oversight and enforcement), compounding under both 503A and 503B may undermine patient safety, and also the integrity of the traditional New Drug Application (NDA), supplemental New Drug Application (sNDA), and Abbreviated New Drug Application (ANDA) approval processes, by providing a far less regulated alternative pathway.

To ensure that there is not confusion about compounded drugs with components of FDA-approved products and products that are "essentially a copy," FDA should issue strong additional guidance regarding the Compounding Quality Act's (CQA) prohibition on false and misleading promotion of compounded products. In particular, compounders should not be permitted to lead patients to believe that FDA has either in part or in whole approved the compounded formulation, which is not the case as discussed by FDA in these Draft Guidances. Further, while compounding pharmacies can make physicians aware of their ability to compound for specific patient clinical needs, it is quite another issue to allow these entities which are not required to register with the FDA to produce a mass volume of compounded drugs and promote the availability of their unapproved formulations for no particular patient. In fact, this would go against the intent of the CQA, which established meaningful systems to protect patients.

To be compounded in accordance with section 503A, a drug product that is essentially a copy of a commercially available drug cannot be compounded "regularly or in inordinate amounts" In the 503A Draft Guidance, FDA lays out four examples of factors that may support a conclusion that a compounded drug product has been compounded regularly or in inordinate amounts. The FDA notes that this list is not intended to be exhaustive, and that other factors may be appropriate for consideration in a particular case. In general, BIO believes the four examples are appropriate for use in considering whether a product has been compounded regularly or in inordinate amounts.

Insofar as a compounded drug that is essentially a copy of a commercially available drug may not be compounded regularly or in inordinate amounts, BIO believes that the FDA should also require that no individual commercially available product, type of commercially available product, or class of commercially available product comprises a substantial portion of a compounder's business.

Finally, to further protect patients, we urge that the FDA's four part test, Appendix A, regarding "How FDA Intends to Determine Whether a Compounded Drug Product is Essentially a Copy of an Approved Drug Under Section 503B" should commence with, rather than conclude with, the question on prescriber requested individual clinical difference. While we recognize that the appendix is not necessarily a prioritization list, to avoid confusion and highlight importance, FDA may consider including language at the beginning emphasizing the clinical difference requirement. Limiting risk exposure to only those patients who have an unmet clinical need should be the first test, not the last. We believe it would also be helpful to include a similar flow chart in the 503A Guidance to illustrate how FDA determines whether a compounded product meets the condition in section 503A regarding essentially copies.

CONCLUSION:

BIO appreciates this opportunity to comment on the FDA Draft Guidances entitled "*Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act*" and "*Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act*." BIO fully supports policies that

facilitate timely entry of safe, effective, and high-quality medicines and recognizes that access to medically-needed compounded medicines is highly important; but access cannot and should not come at the expense of product quality and patient safety. We are pleased to see FDA acknowledge that compounded products should not be given to patients that could use a commercially available drug product and that producing a drug product that is essentially a copy of an approved drug product could undermine the regulatory approval process for both new and generic drugs.

We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/s/

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