



July 18, 2016

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

Re: Docket No. FDA-2016-D-0269: Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the Draft Guidance "Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act" (Draft Guidance).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.

GENERAL COMMENTS:

BIO applauds the issuance by the FDA of this Draft Guidance as it recognizes the importance of the prescription requirement under Section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act). BIO 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 agrees with the assertion that the prescription requirement is critical in differentiating between compounding by a pharmacist or physician from conventional manufacturing and from compounding by an outsourcing facility. We believe that the Draft Guidance appropriately provides recommendations for compounding in the traditional pharmacy setting either upon receipt of a prescription for an individual patient, or in anticipation of receiving such a prescription but correctly does not allow for distribution of a compounded drug product *before* receiving a valid patient-specific prescription.

Congress recognized that supplies of drugs compounded without patient-specific prescriptions are sometimes needed by providers when an FDA-approved product is not available. However, the need to better ensure the quality of these drugs should not be ignored. If traditional pharmacies under Section 503A are permitted to supply compounded drugs without prescriptions outside of these new quality requirements, they will have little to no incentive to register with the FDA nor to adhere to the more rigorous quality standards that are appropriate for compounding at that scale.



As BIO has noted in previous comments to FDA regarding compounding¹, we strongly believe that the drug compounding provisions of the Drug Quality and Security Act (DQSA) did not alter current law with regard to biologics and that therefore there is still no applicable exemption in the FD&C Act compounding provisions for entities that compound or repackage biological products. We are pleased to see this Draft Guidance contains a footnote (footnote 2) that states this Guidance does not apply to biological products subject to licensure in a biologics license application.

More broadly, BIO asks that FDA include a statement in this Guidance, as well as all other applicable FDA regulations and guidance², that compounding of commercially available, FDA-approved products is not allowed. The only exception being when such products are medically necessary to address a unique individual patient need not met by the approved drug, and when supported by a valid prescription. We acknowledge and appreciate FDA's recent release of the two Draft Guidances on compounded products that are essentially copies of a commercially available drug product³ but believe it would be helpful for all guidances and relevant compounding documents to include a statement barring the compounding of such products as well as reference to the appropriate guidances. We also believe FDA should articulate penalties for compounding of commercially available, FDA-approved drug products.

A. Anticipatory Compounding

While BIO appreciates the need for some anticipatory compounding, the Draft Guidance's proposed 30-day supply exception for compounding in advance of receipt of a prescription (*i.e.*, anticipatory compounding) does not sufficiently ensure that "entities purportedly operating under section 503A are not actually operating as conventional manufacturers." Missing from the scope of the Draft Guidance is any consideration of the overall scope of the compounder's operations. While compounding a 30-day anticipatory supply of a drug for a single patient is not analogous to manufacturing, compounding hundreds or thousands of doses in advance for numerous patients does appear to be conventional manufacturing.

The Draft Guidance on whether a compounder will be considered to have exceeded the limited quantity condition should be modified to require that the compounder hold for distribution no more than the lesser of (1) a 30-day supply of a particular compounded drug or (2) an FDA specified amount, for example 500 dosage units, per therapeutic category

¹ "BIO Comments on FDA Draft Guidance: Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act" February 3, 2014 located [here](#). "BIO Comments on FDA Draft Guidance for Industry on Current Good Manufacturing Practices—Interim Guidance for Human Drug Compounding Outsourcing Facilities Under the Federal Food, Drug and Cosmetic Act" September 2, 2014 located [here](#). "BIO Comments on FDA Draft Guidance for Industry on Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application" May 20, 2015 located [here](#).

² Including FDA Draft Guidances for Industry on "Facility Definition Under Section 503B of the Federal Food, Drug and Cosmetic Act" and "Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act" (April 2016).

³ FDA Draft Guidance for Industry "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 FDA Draft Guidance for Industry "Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503B of the Federal Food, Drug, and Cosmetic Act" (July 2016).



which contemplates inherent patient safety risks and reflects the limited quality intent within the statute.

BIO notes that the timeframe in the Draft Guidance associated with anticipatory compounding is the same for all products. However, not all products are stable, even for short timeframes, particularly when no evaluation of packaging requirements or container-closure systems has been performed. This could adversely impact the potency of the drug ultimately administered to a given patient. Therefore, BIO suggests that some limitation should be placed on how far in advance anticipatory compounding can be done.

Additionally, the Draft Guidance acknowledges that anticipatory compounding has risks and because drug products compounded in accordance with section 503A are exempt from current good manufacturing practice (CGMP) requirements, there is an inherently greater chance of a production mistake or contamination. While we appreciate that this concern for patient safety has informed FDA's set of conditions for anticipatory compounding we find that merely stating that the risks are acknowledged in this Draft Guidance seems insufficient. Therefore, BIO suggests that the Guidance stipulate the expiry dating for anticipatory compounded products by type of dosage form and require a record of destruction for any product that exceeds the prescribed time. For example, 30 days for solid oral dosage forms, 15 days for oral liquids and 24 hours for any sterile formulation.

B. Adherence to United States Pharmacopeia Guidelines

The United States Pharmacopeia (USP) has guidelines addressing compounding of both sterile⁴ and nonsterile products⁵. These guidelines contain information on the types of products; levels of risk and general compounding principles; responsibilities of the compounder; facility requirements; stability and beyond use dating; requisite documentation; quality standards; and training. BIO believes that adherence to both these USP Chapters should be mandated in the Final Guidance given the explicit link to compounding requirements and patient safety.

For sterile preparations, the USP testing requirements "describe conditions and practices to prevent harm, including death, to patients that could result from (1) microbial contamination (nonsterility), (2) excessive bacterial endotoxins, (3) variability in the intended strength of correct ingredients that exceeds either monograph limits for official articles⁶ or 10% for nonofficial articles, (4) unintended chemical and physical contaminants, and (5) ingredients of inappropriate quality in compounded sterile preparations (CSPs)."⁷ The chapter provides minimum requirements and quality standards for CSPs based on current scientific information and best sterile compounding practices, which includes specific environmental conditions (minimum air handling depending on level of risk associated with

⁴USP <797> General Chapters: Pharmaceutical Compounding- Sterile Preparations (2016 USPC Official 5/1/2016-7/31/2016).

⁵ USP <795> General Chapters: Pharmaceutical Compounding- Nonsterile Preparations (2016 USPC Official 5/1/2016-7/31/2016).

⁶ See "official" and "article" in the General Notices and Requirements

⁷USP <797> General Chapters: Pharmaceutical Compounding- Sterile Preparations (2016 USPC Official 5/1/2016-7/31/2016).



a given CSP to ensure sterility). There are specific timeframes established for final sterilization of water-containing CSPs that are nonsterile during any phase of compounding, as well as those for use of compounded products. Following these requirements will be critical to ensure patient safety.

CONCLUSION:

BIO appreciates this opportunity to comment on the Draft Guidance "Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act". We recognize 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 believe that the Draft Guidance appropriately provides recommendations for compounding in the traditional pharmacy setting either upon receipt of a prescription for an individual patient, or in anticipation of receiving such a prescription but correctly does not allow for distribution of a compounded drug product *before* receiving a valid patient-specific prescription. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

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Biotechnology Innovation Organization