October 11, 2016

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

Re: Biocom Response to Industry Guidance Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act [Docket Number: FDA-2016-D-1267]

To whom it may concern,

Biocom is the largest, most experienced leader and advocate for California's life science sector, which includes biotechnology, pharmaceutical, medical device, genomics and diagnostics companies of all sizes, as well as research universities and institutes, clinical research organizations, investors and service providers. With more than 800 members dedicated to improving health and quality of life, Biocom drives public policy initiatives to positively influence the state's life science community in the research, development, and delivery of innovative products.

In our mission of providing feedback and communication between the industry and regulators, we write in response to the Draft Guidance *Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act ("draft guidance")*. Biocom commends the agency on releasing the aforementioned draft guidance, which sets clear standards for determining whether a compounded product is essentially a copy of an FDA-approved product, which will guarantee patient safety, drug efficacy, and fairness in the drug approval process. Biocom thanks the agency for the opportunity to provide comments on areas where we believe further clarification is warranted.

Section III, A, 1, a, i

Section III, A, 1, a, i states, *"FDA intends to consider a compounded drug product to be identical or nearly identical to an approved drug if the compounded drug product and the FDA-approved drug have the same:*

- *active ingredient(s),*
- *route of administration,*
- *dosage form,*
- *dosage strength, and*
- *excipients.*

A compounded drug product that has all of these characteristics in common with an FDA-approved drug product is essentially a copy of an approved drug."

We believe that the five criteria to be considered "essentially a copy of an approved drug" are not sufficiently detailed to prevent compounding pharmacies from creating drugs nearly identical to approved drugs.

Dosage Strength

We support FDA's position that minor changes in dosage strength should not exempt a drug from being "essentially a copy," but encourage stronger language to further protect patients.

Clarification on the dosage strength criterion is needed otherwise compounding of any FDA-approved drug would be allowable as long as the dosage strength was different. For example:

- If an FDA-approved drug has a dosage strength in a 100mg/ml vial, an outsourcing facility could make this same product with a dosage strength of 125mg/ml or 100mg/1.25ml.
- If an FDA-approved drug has a dosage strength in 50mg capsules, an outsourcing facility could make 25mg capsules.

This ambiguity in the dosage strength criterion could be clarified with specific language stating that altering the dosage strength does not allow for the compounding of FDA-approved drugs except for the rare circumstance in which the FDA-approved drug cannot be administered to the patient in its current dosage strength (i.e., using half of the vial, using two vials, breaking the tablet, mixing a tablet with water). Changes in dosages must be explicitly linked by a prescriber to a clinical need of an individual patient. As a matter of patient safety, outsourcing facilities should not be permitted to promote product claims unrelated to a specific prescriber-identified clinical need or change dosage strength from an FDA-approved product simply to justify compounding.

Excipients

Clarification on the excipients criterion is needed otherwise compounding of any FDA-approved drug would be allowable by changing the excipients used in the compounded drug product. The excipients used in an FDA-approved drug have been determined by the manufacturer and FDA to be essential to maintaining the safety, efficacy, and stability attributes of the drug. Allowing compounding pharmacies to produce drug products without excipients or with different excipients that have not been adequately studied with the active pharmaceutical ingredient has the potential to pose a public health risk.

This ambiguity in the excipients criterion could be clarified with specific language stating that an outsourcing facility should only be allowed to compound a copy of an FDA-approved drug using different excipients if the patient is known to have an allergy or contraindication to the excipients used in the FDA-approved drug.

Section III, A, 1, b, ii

Clinical Difference

Section III, A, 1, b, ii states, *"If an outsourcing facility compounds a drug, the component of which is a bulk drug substance that is a component of an approved drug, there must be a change that produces a clinical difference for an individual patient as determined by the prescribing practitioner...Note also that the clinical difference identified on either a patient-specific prescription or order, or non-patient specific order, must be produced by the "change" between the outsourcing facility's product and the approved drug (i.e., a change in product formulation)."*

We believe that the concept of "clinical difference" is of utmost importance when determining whether a compounded product is essentially a copy of an approved product. Therefore, it should apply to compounded drugs that are identical or nearly identical to an approved drug (Section III, A, 1, a), in addition to compounded drugs that contain a bulk drug substance that is a component of an approved drug (Section III, A, 1, b).

Second, FDA's definition of clinical difference should be explicitly stated in the guidance. A potential definition could be documented improved efficacy or a measurable reduction in side effects.

Third, outsourcing facilities must – rather than should - ensure that a prescription or order clearly states a clinical need in order to justify relying on clinical differences to establish that a compounded drug is not essentially a copy of an FDA-approved drug. We urge the FDA to tighten format requirements for office stock orders so that practitioners must provide more details regarding the patient population in need of a compounded drug, and consider whether there is a public health benefit to tracking this information. Practitioners should be strongly encouraged to provide background data indicating a need for a compounded drug. Where a hospital is ordering office stock for practitioners to prescribe, it would be useful that both the hospital and practitioner produce statements of clinical difference.

Lower Cost

Section III, A, 1, b, ii states, "Other factors such as a lower price are not sufficient to establish that the compounded product is not essentially a copy of the approved drug."

We believe that this statement is one of the most important statements in the draft guidance and should be applicable to all sections of the guidance, not just compounded drugs that contain a bulk drug substance that is a component of an approved drug (Section III, A, 1, b). Lower cost is frequently used as justification by compounding pharmacies and physicians for the use of compounded drugs today and does not reflect the time and resources needed to bring new products to patients. Drug manufacturers bear the cost of research and development (R&D), in addition to a comprehensive review and approval process at the Food and Drug Administration (FDA). It takes an average of 15 years and $2 billion to bring a new drug to market. Making the aforementioned statement more prominent in the guidance will help eliminate this justification in the future.

Misleading Labeling

Unfortunately, some compounding pharmacies are using the phrase "FDA-approved" in conjunction with their formulations, referring to specific components of their products and suggesting that the FDA has, either in part or in whole, approved the compounded formulation. FDA should take appropriate steps to eliminate this misleading sense of security, which jeopardizes patient safety by suggesting that there is a lower level of risk.

Biocom recommends that the FDA adds a section about misleading promotion of compounded products to clarify that outsourcing facilities manufacturing compounded drugs with components of FDA-approved products should not use "FDA-approved" on their labels and promotion materials. In addition, outsourcing facilities should not be permitted to lead patients to believe that compounded drugs are either, in whole or in part, essentially a copy of an FDA-approved drug.

Appendix A

Finally, to further protect patients, we urge the FDA's four-part test, Appendix A, "How FDA Intends to Determine Whether a Compounded Drug Product is Essentially a Copy of an Approved Drug Under Section 503B" to commence with, rather than conclude with, the question about patient 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 emphasizing the clinical difference requirement at the beginning of its model. Outsourcing facilities should consider first whether it is necessary and legal to make the compounded drug before exploring other criteria. Limiting risk exposure to only those patients who have an unmet clinical need should be tested first, not last.

We thank you for your time and diligence in examining our comments related to the Draft Guidance *Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act*. Our industry is committed to investing time and financial resources to research and develop new drugs that are deemed safe and effective by the FDA. Our suggested changes to the guidance will help ensure that biopharmaceutical companies can continue to innovate and bring life-saving products to patients in need.

Sincerely,

Joe Panetta
President and CEO
Biocom