FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS

VIA EMAIL CONFIRMED DELIVERY
RETURN RECEIPT REQUESTED

September 14, 2023

Sean M. Barclay, Pharm. D.
Owner
Barclay, Luke, and Pillai Specialty Pharmacy, PLLC, dba Meta Pharmacy Services
8352 W. Warm Springs Road, Suite 120
Las Vegas, NV 89113-3629
sean@metapharmacyservices.com

Dear Dr. Barclay:

From November 28, 2022, to December 9, 2022, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, Barclay, Luke, and Pillai Specialty Pharmacy, PLLC, dba Meta Pharmacy Services, located at 8352 W. Warm Springs Road, Suite 120, Las Vegas, NV 89113. During the inspection, the investigator noted that drug products you produced failed to meet the conditions of section 503A of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353a] for exemption from certain provisions of the FDCA. In addition, the investigator noted deficiencies in your practices for producing non-sterile drug products and drug products intended or expected to be sterile, which put patients at risk.

The FDA issued a Form FDA 483 on December 9, 2022, and an amended Form FDA 483 to your firm on December 13, 2022. The FDA acknowledges receipt of your facility's responses, dated January 3, 2023, March 6, 2023, and March 8, 2023. Based on this inspection, it appears that you produced drug products that violate the FDCA.

A. Compounded Drug Products Under the FDCA

Section 503A of the FDCA describes the conditions under which human drug products compounded by a licensed pharmacist in a state licensed pharmacy or a federal facility, or a licensed physician, qualify for exemptions from three sections of the FDCA: compliance with current good manufacturing practice (CGMP) (section 501(a)(2)(B)); labeling with adequate directions for use (section 502(f)(1)); and FDA approval prior to marketing (section 505) [21 U.S.C. §§ 351(a)(2)(B), 352(f)(1) and 355(a)].[1] Receipt of

[1] We remind you that there are conditions other than those discussed in this letter that must be satisfied to qualify for the exemptions in section 503A of the FDCA.

valid prescriptions for individually-identified patients is one of the conditions for the exemptions under section 503A.

In addition, for a compounded drug product to qualify for the exemptions under section 503A, bulk drug substances used to compound it must: (I) comply with the standards of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, if a monograph exists, and the USP chapter on pharmacy compounding; (II) if such a monograph does not exist, be components of drugs approved by the Secretary; or (III) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appear on a list developed by the Secretary through regulation ("503A bulks list") (section 503A(b)(1)(A)(i) of the FDCA).

B. Failure to Meet the Conditions of Section 503A

During the inspection, the FDA investigator noted that drug products produced by your firm failed to meet the conditions of section 503A. For example, the investigator noted:

1. Your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced, including dyclonine oral suspension and lidocaine 5% topical solution.

2. Your firm compounded drug products using ibutamoren mesylate, BPC-157 acetate and theanine, that are not eligible for the exemptions provided by section 503A(a), because the bulk drug substances are not the subject of applicable USP or NF monographs, not components of FDA-approved human drugs, and do not appear on the 503A bulks list.[2]

Therefore, you compounded drug products that do not meet the conditions of section 503A and are not eligible for the exemptions in that section, including the FDA approval requirement of section 505 of the FDCA, the requirement under section 502(f)(1) of the FDCA that labeling bear adequate directions for use, and the requirement of compliance with CGMP under section 501(a)(2)(B) of the FDCA. In the remainder of this letter, we refer to your drug products that do not qualify for exemptions under section 503A as the "ineligible drug products."

Specific violations are described below.

[2] These substances are also not eligible for the policy applicable to certain bulk drug substances described in the final guidance titled, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. This guidance describes the FDA's interim regulatory policy for State-licensed pharmacies, Federal facilities, and licensed physicians that compound human drug products using bulk drug substances that do not otherwise meet the conditions of section 503A(b)(1)(A)(i) while the 503A bulks list is being developed. Specifically, the guidance sets out the conditions under which the FDA does not intend to take action against a State-licensed pharmacy, Federal facility, or licensed physician for compounding a drug product using a bulk drug substance that is not the subject of an applicable USP or NF monograph or a component of an FDA-approved drug, until the substance is identified in a final rule as included or not included on the 503A bulks list. These conditions include that the substance may be eligible for inclusion on the 503A bulks list, was nominated with adequate support for the FDA to evaluate it, and has not been identified by the FDA as a substance that appears to present significant safety risks pending further evaluation. For additional information, see the guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469120.pdf.

C. Violations of the FDCA

Adulterated Drug Products

The FDA investigator noted that drug products intended or expected to be sterile were prepared, packed, or held under insanitary conditions, whereby they may have become contaminated with filth or rendered injurious to health, causing your drug products to be adulterated under section 501(a)(2)(A) of the FDCA. For example, the investigator observed that:

1. The ISO 5 Classified aseptic processing areas had difficult to clean and visibly dirty equipment or surface.

2. Non-microbial contamination was observed in your production area.

3. Unsealed, loose ceiling tiles were observed in your cleanroom.

4. Media fills do not adequately simulate the most challenging or stressful conditions. This is a repeat observation from the FDA inspection in 2016.

Furthermore, the manufacture of the ineligible drug products is subject to the FDA's CGMP regulations, Title 21, Code of Federal Regulations (CFR), parts 210 and 211. The FDA investigator observed significant CGMP violations at your facility, causing the ineligible drug products to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA. The violations included, for example:

1. Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release (21 CFR 211.165(a)).

2. The identity of each component of a drug product is not verified by conducting at least one test to verify the identity, using specific identity tests if they exist (21 CFR 211.84(d)(1)).

It is a prohibited act under section 301(k) of the FDCA [21 U.S.C. § 331(k)] to do any act with respect to a drug, if such act is done while the drug is held for sale after shipment in interstate commerce and results in the drug being adulterated.

Unapproved New Drug Products

You do not have any FDA-approved applications on file for the ineligible drug products that you compounded.[3] Under sections 505(a) and 301(d) of the FDCA [21 U.S.C. §

[3] The specific products made by your firm are drugs within the meaning of section 201(g) of the FDCA [21 U.S.C. § 321(g)] because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases and/or because they are intended to affect the structure or any function of the body. Further, they are "new drugs" within the meaning of section 201(p) of the FDCA [21 U.S.C. 321(p)] because they are not generally recognized as safe and effective for their labeled uses.

331(d)], a new drug may not be introduced into or delivered for introduction into interstate commerce unless an application approved by the FDA under section 505 of the FDCA is in effect for the drug. Marketing of these products, or other applicable products, without an approved application violates these provisions of the FDCA.

Misbranded Drug Products

The ineligible drug products you compounded are intended for conditions not amenable to self-diagnosis and treatment by individuals who are not medical practitioners; therefore, adequate directions for use cannot be written so that a layman can use these products safely for their intended uses. Consequently, their labeling fails to bear adequate directions for their intended uses.[4] Accordingly, these ineligible drug products are misbranded under section 502(f)(1) of the FDCA. The introduction or delivery for introduction into interstate commerce of these products therefore violates section 301(a) of the FDCA. It is also a prohibited act under section 301(k) of the FDCA to do any act with respect to a drug, if such act is done while the drug is held for sale after shipment in interstate commerce and results in the drug being misbranded.

D. Corrective Actions

We have reviewed your firm's responses to the Form FDA 483.

Regarding your responses related to the insanitary conditions, some of your corrective actions appear adequate; however, we cannot fully evaluate the adequacy of the following corrective actions described in your response because you did not include sufficient information or supporting documentation:

1. You provided photo evidence of your corrective cleaning actions in the ISO 5 Classified aseptic processing areas but did not provide details of the cleaning process and how/if your new (b) (4) cleaning process will sufficiently prevent further residue buildup.

2. You provided some photo evidence of your corrective cleaning actions in your production areas, but you did not include photos of all areas shown to be visibly dirty. You did not provide details on the process, date, or personnel conducting the corrective actions or how cleaning would be maintained in the future. For example, the chipped wood was stated to be repaired, but no description was provided. In addition, your "(b) (4)" was replaced but the replacement screw appears to be a difficult to clean surface.

3. You provided one photo of one ceiling tile as evidence of corrective action, but there were two tiles which appeared unsealed. In addition, you did not provide any details regarding who performed the corrective actions or date of completion.

[4] Your ineligible drug products are not exempted from the requirements of section 502(f)(1) of the FDCA by regulations issued by the FDA (see, e.g., 21 CFR 201.115).

4. You provided that media fills would be increased to (b) (4) mL, but you did not provide explanation why it would not be increased to your largest batch size of at least (b) (4) mL.

Please be aware that section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether drug products you compound meet the conditions of section 503A, including the condition on receipt of a prescription for an identified individual patient prior to compounding and distributing drug products.

In addition, regarding issues related to the conditions of section 503A of the FDCA, some of your corrective actions appear adequate. You state that "all compounding prescriptions moving forward will […] need a patient specific prescription" and that "there will be a large focus not to allow any office use prescriptions from [your] pharmacy."

However, you have not addressed the compounding of drug products using ineligible bulk drug substances, including ibutamoren mesylate, BPC-157 acetate and theanine. As explained above, drug products compounded using these bulk drug substances are not eligible for the exemptions provided by section 503A(a) because they are not the subject of applicable USP or NF monographs, are not components of FDA-approved human drugs, and do not appear on the 503A bulks list.

Should you continue to compound and distribute drug products that do not meet the conditions of section 503A, the compounding and distribution of such drugs would be subject to the new drug approval requirement, the requirement to label drug products with adequate directions for use, and the drug CGMP regulations. Before doing so, you must comply with the requirements of section 505 and 502(f)(1) and fully implement corrections that meet the minimum requirements of the CGMP regulations.[5]

In addition to the issues discussed above, you should note that CGMP requires the implementation of quality oversight and controls over the manufacture of drugs, including the safety of raw materials, materials used in drug manufacturing, and finished drug products. See section 501 of the FDCA. If you choose to contract with a laboratory to perform some functions required by CGMP, it is essential that you select a qualified contractor and that you maintain sufficient oversight of the contractor's operations to ensure that it is fully CGMP compliant. Regardless of whether you rely on a contract facility, you are responsible for assuring that drugs you produce are neither adulterated nor misbranded. [*See* 21 CFR 210.1(b), 21 CFR 200.10(b)].

E. Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations at your facility. You are responsible for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other

[5] In this letter we do not address whether your proposed corrective actions would resolve the CGMP violations noted above.

violations. It is your responsibility to ensure that your firm complies with all requirements of federal law, including the FDA regulations.

Within thirty (30) working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to address any violations. Please include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. This letter notifies you of our concerns and provides you an opportunity to address them. If you believe your products are not in violation of the FDCA, include your reasoning and any supporting information for our consideration. If you cannot completely address this matter within thirty (30) working days, state the reason for the delay and the time within which you will do so.

Your written notification should refer to the CMS Number above (CMS 402230). Please address your reply to ORAPHARM4_Responses@FDA.HHS.GOV with ATTN: CDR Steven E. Porter, Jr. or mail your written response to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
U.S. Food & Drug Administration
19701 Fairchild Road
Irvine, CA 92612-2506

If you have questions regarding the contents of this letter, please contact LCDR Rumany Penn, compliance officer, at (949) 608-4409 or Rumany.Penn@FDA.HHS.GOV.

Sincerely,

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV

SP:rp