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

VIA EMAIL CONFIRMED DELIVERY

October 20, 2021

Samih N. Botros
Owner and Pharmacist-In-Charge
Botrosons Pharmaceutical Inc.
dba Tower Pharmacy
26732 Crown Valley Pkwy
Mission Viejo, CA 92691

Dear Mr. Botros:

From September 9, 2019, to September 19, 2019, a U.S. Food and Drug Administration investigator inspected your facility, Botrosons Pharmaceutical Inc. dba Tower Pharmacy, located at 26732 Crown Valley Pkwy, Mission Viejo, CA 92691. 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 drug products, which put patients at risk.

The FDA issued a Form FDA 483 to your firm on September 19, 2019. The FDA acknowledges receipt of your facility's response, dated October 1, 2019. 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 valid prescriptions for individually-identified patients is one of the conditions for the exemptions under section 503A.

[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.

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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 that your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced.

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.

C. Violations of the FDCA

Adulterated Drug Products

The FDA investigator noted that drug products 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. Your firm handled hazardous drug products without adequate containment, segregation, or cleaning of work surfaces and utensils to prevent cross-contamination.

2. Your firm produced drug products with soiled and deteriorated equipment.

3. Your firm used (b) (4) that was not labeled or intended for use in the production of non-sterile drug products and whose quality you did not confirm.

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.

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.[2] Accordingly, these ineligible drug products are misbranded under section 502(f)(1) of the FDCA. It is 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. Domperidone

During the inspection, the FDA investigator noted that your firm stored multiple expired reagents and containers of empty capsules of domperidone on the active reagent shelves in the compounding area. The investigator did not determine whether you have used domperidone to compound drug products. Please be aware that for a compounded drug product to qualify for the exemptions under section 503A of the FDCA, 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). We note that drug products compounded using domperidone are not eligible for the exemptions provided by section 503A(a) because domperidone is not the subject of an applicable USP or NF monograph, is not a component of an FDA-approved human drug and does not appear on the 503A bulks list.[3]

E. Corrective Actions

We have reviewed your firm's response to the Form FDA 483. Regarding your responses related to the insanitary conditions, some of your corrective actions appear adequate. However, you did not address an observation related to insanitary

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[2] 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).

[3] On June 9, 2016, the FDA issued a 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 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. Domperidone was nominated for inclusion on the 503A bulks list. It has been identified as a substance that appears to present significant safety risks. For additional information, see the guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469120.pdf.

conditions. Specifically, your response did not address any containment, segregation, or cleaning for handling hazardous drugs to prevent cross-contamination of these substances in other drug products, including any controls you have implemented to prevent cross-contamination and any cleaning agents and methods used to clean shared equipment and utensils for hazardous and non-hazardous drugs.

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, the FDA acknowledges your letter, dated September 23, 2019, in which you state that "any compounding order received from a physician has to be prescription specific for a particular patient."

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.

We also note that, during the inspection, the FDA investigator collected evidence indicating that on at least some occasions, your firm compounded drug products, including testosterone gel, estradiol cream, and progesterone suppositories, that had the same active pharmaceutical ingredients (APIs) in the same, similar, or easily substitutable strengths as commercially available drug products. Furthermore, evidence collected indicates that the commercially available drug products can be used by the same route of administration prescribed for the compounded drug products. Please note that one of the conditions for a compounded drug product to qualify for the exemptions under section 503A of the FDCA is that the licensed pharmacist or physician "does not compound regularly or in inordinate amounts (as defined by the Secretary) " any drug products that are essentially copies of a commercially available drug product" (section 503A(b)(1)(D) of the FDCA).[4] For more information on the "essentially a copy" condition, please see FDA's guidance, "Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act."

F. 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

[4] For purposes of section 503A(b)(1)(D), "the term 'essentially a copy of a commercially available drug product' does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product" (section 503A(b)(2) of the FDCA).

causes of any violations and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all requirements of federal law, including 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 correct violations. Please include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you do not believe that the products discussed above are in violation of the FDCA, include your reasoning and any supporting information for our consideration. If you cannot complete corrective action within thirty (30) working days, state the reason for the delay and the time within which you will complete the correction.

Send your electronic reply to ORAPharm4_responses@fda.hhs.gov or mail your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
19701 Fairchild Road
Irvine, CA 92612-2506

Please identify your response with unique identifier CMS 609301.

If you have questions regarding any issues in this letter, please contact Andrew Haack, Compliance Officer via email at Andrew.Haack@fda.hhs.gov or by phone at 206-340-8212.

Sincerely,

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

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