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

**August 21, 2020**

**Case #: 610189**

**VIA ELECTRONIC MAIL**

Derek R. Sien, President
Claremore Compounding Center, Inc.
1151 N. Lynn Riggs Blvd.
Claremore, Oklahoma 74017-3068

Mr. Sien:

From January 13, 2020, to January 24, 2020, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, Claremore Compounding Center, Inc., located at 1151 N. Lynn Riggs Blvd., Claremore, Oklahoma 74017. 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.

FDA issued a Form FDA 483 to your firm on January 24, 2020. FDA acknowledges receipt of your facility's response, signed January 24, 2020. FDA also acknowledges that effective September 12, 2019 you discontinued the production of products containing tranilast. 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.

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 collected evidence indicating that drug products produced by your firm failed to meet the conditions of section 503A. For example, the investigator collected evidence indicating that:

1. Your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced, including CCC Cold Max 100-5-10-2 mg per 5 mL Suspension, CCC Coughist PE 100-5-2 mg per 5 mL Suspension and Jungle Juice (NF) Liquid.

2. Your firm compounded a drug product using tranilast. Drug products compounded using tranilast are not eligible for the exemptions provided by section 503A(a), because tranilast 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.[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.

**C. Violations of the FDCA**

**Adulterated Drug Products**

The manufacture of the ineligible drug products is subject to FDA's CGMP regulations, Title 21, Code of Federal Regulations (CFR), parts 210 and 211. The FDA investigator

[2] Tranilast was nominated for inclusion on the 503A bulks list and after evaluating it FDA determined that Tranilast would not be placed on the 503A bulks list, found at 21 C.F.R. 216.23(a). *See* 21 C.F.R. 216.23(b).

observed 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. Your firm failed to have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release (21 CFR 211.165(a)).

2. Your firm failed to follow an adequate written testing program designed to assess the stability characteristics of drug products and to use results of such stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).

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.[3] 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. Corrective Actions**

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

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 and the condition on compounding drug products using a bulk drug substance that complies with an applicable USP or NF monograph, is a component of an FDA-approved human drug, or appears on the 503A bulks list.

[3] 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).

In addition, regarding issues related to the conditions of section 503A of the FDCA, your corrective actions appear adequate:

1. You state that your facility "will ensure that all compounded products require a patient specific prescription, including over the counter strength compounds."

2. You state that your facility "has discontinued compounding medications with *Tranilast* effective on 9-12-2019."

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.[4]

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 the violations identified above 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.

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

Your written notification should refer to case # 610189. Please electronically submit your reply, on company letterhead, to Mark W. Rivero, Compliance Officer, at ORAPHARM2_RESPONSES@fda.hhs.gov. In addition, please submit a signed copy of your response to mark.rivero@fda.hhs.gov.

If you have questions regarding the contents of this letter, please contact Mr. Rivero at (504) 846-6103.

Sincerely,


Monica R. Maxwell
Program Division Director
Office of Pharmaceutical Quality Operations, Division II

Cc: Larry D. Brim, II, DPh, Vice President, Secretary
Claremore Compounding Center, Inc.
1151 N. Lynn Riggs Blvd.
Claremore, OK 74017-3068
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