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

October 4, 2019

VIA UNITED PARCEL SERVICE
Charles J. Fanaras
President
Mytilini Enterprises, LLC
dba Bedford Pharmacy
209 Route 101
Bedford, NH 03110-5440

Dear Mr. Fanaras:

From August 2, 2017, to August 17, 2017, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, Mytilini Enterprises, LLC dba Bedford Pharmacy, located at 209 Route 101, Bedford, NH 03110-5440. 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. Additionally, 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 August 17, 2017. FDA acknowledges receipt of your facility's response, dated September 22, 2017. 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].[1] Receipt of valid prescriptions for individually-identified patients is one of the conditions for the exemptions under section 503A.

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.

[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.

Therefore, you compounded drug products that do not meet the conditions of section 503A and are not eligible for the exemptions in that section from 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 your firm handled hazardous drug products without providing adequate containment, segregation, or cleaning of work surfaces and utensils to prevent contamination. Specifically, your firm utilized non-dedicated equipment and utensils to produce drug products with no assurance that your cleaning process can deactivate and remove residual drug product. In addition, you failed to confirm that the quality of water was suitable for its intended use in producing numerous drug products.

Furthermore, 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 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 clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).

2. Your firm failed to test samples of each component for conformity with all appropriate written specifications for purity, strength, and quality (21 CFR 211.84(d)(2)).

3. Your firm does not 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)).

4. Your firm failed to establish a laboratory control mechanism providing for the calibration of instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met (21 CFR 211.160(b)(4)).

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. Corrective Actions

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

Regarding the insanitary condition observations in the Form FDA 483, we cannot fully evaluate the adequacy of your corrective actions described in your response because you did not include sufficient information or supporting documentation:

1. Your response includes your updated cleaning procedure that requires the use of (b) (4) (b) (4) or another appropriate cleaning solution." However, you did not provide supporting documentation, such as product labels and required contact times. Therefore, we cannot evaluate whether your firm's procedure is adequate to clean work surfaces and utensils to prevent cross-contamination.

2. Your response states that your firm has "contracted with Fillmaster to perform annual maintenance" and that you have "also contracted with a local water testing firm to perform bi-annual water testing." However, you did not provide documentation that the water you utilize in drug production meets, at minimum, the specifications of Purified Water, USP. In addition, it is the Agency's policy that any action limit over 100 CFU/mL for a purified water system would be unacceptable (see inspection guide at https://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074905.htm).

Regarding issues related to the conditions of section 503A of the FDCA, the following corrective action appears adequate:

1. Your response states that your firm is only engaged in patient-specific, pharmacy-based compounding.

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.[3]

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

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 the corrective actions within 30 working days, state the reason for the delay and the time within which you will complete the correction.

Your written response should reference CMS Case# 552176 and be electronically sent to the U.S. Food and Drug Administration at ORAPharm1_Responses@fda.hhs.gov. If you have questions regarding the contents of this letter, please contact Compliance Officer, Juan Jimenez at email, juan.jimenez@fda.hhs.gov or by phone at 1-518-453-2314 ex. 1014.

Sincerely,

Craig W. Swanson -S

Digitally signed by Craig W. Swanson -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300092363, cn=Craig W. Swanson -S
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Craig Swanson
For Diana Amador-Toro
Program Division Director/District Director
Division of Pharmaceutical Quality Operations