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August 21, 2019

VIA PARCEL CARRIER

Michael Souza, CEO
New England Life Care, Inc.
dba Advanced Compounding Solutions
4 Constitution Way, Suite L
Woburn, MA 01801

FEI #3010371376

Dear Mr. Souza:

You originally registered with the U.S. Food and Drug Administration (FDA) as an outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353b][1] on March 2, 2017, and most recently on January 24, 2018. From August 2, 2017, to August 22, 2017, U.S. Food and Drug Administration (FDA) investigators inspected your facility, New England Life Care, Inc., dba Advanced Compounding Solutions, located at 4 Constitution Way, Suite L, Woburn, MA 01801. During the inspection, the investigators noted serious deficiencies in your practices for producing sterile drug products, which put patients at risk. In addition, the investigators observed that drug products you produced failed to meet the conditions under section 503B of the FDCA necessary for drugs produced by an outsourcing facility to qualify for exemptions from certain provisions of the FDCA.

FDA issued a Form FDA 483 to your firm on August 22, 2017. FDA acknowledges receipt of your firm's responses, dated September 8, 2017, December 14, 2017, and January 5, 2018, as well as your subsequent correspondence.

Based on this inspection, it appears your firm produced drugs that violate the FDCA.

A. Compounded Drug Products under the FDCA

Under section 503B(b) of the FDCA, a compounder can register as an outsourcing facility with FDA. Drug products compounded by or under the direct supervision of a licensed pharmacist in an

[1] *See* Pub. L. No. 113-54, § 102(a), 127 Stat. 587, 587-588 (2013).

outsourcing facility qualify for exemptions from the drug approval requirements in section 505 of the FDCA [21 U.S.C. § 355(a)], the requirement in section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] that labeling bear adequate directions for use, and the Drug Supply Chain Security Act requirements in section 582 of the FDCA [21 U.S.C. § 360eee-1] if the conditions in section 503B of the FDCA are met.[2]

An outsourcing facility, which is defined in section 503B(d)(4) of the FDCA [21 U.S.C. § 353b(d)(4)], is a facility at one geographic location or address that — (i) is engaged in the compounding of sterile drugs; (ii) has elected to register as an outsourcing facility; and (iii) complies with all of the requirements of this section. Outsourcing facilities must comply with other applicable provisions of the FDCA, including section 501(a)(2)(B) [21 U.S.C. § 351(a)(2)(B)], regarding current good manufacturing practice (CGMP), and section 501(a)(2)(A) [21 U.S.C. § 351(a)(2)(A)], regarding insanitary conditions. Generally, CGMP requirements for the preparation of drug products are established in Title 21 of the Code of Federal Regulations (CFR) parts 210 and 211.

In addition, for a compounded drug product to qualify for the exemptions under section 503B, it must be compounded in an outsourcing facility that is in compliance with the registration and reporting requirements in section 503B(b) including the requirement to submit a report to FDA upon initially registering as an outsourcing facility, once in June of each year, and once in December of each year identifying the drug products compounded during the previous 6-month period (section 503B(b)(2) of the FDCA [21 U.S.C. §353b(b)(2)]).

B. Failure to Meet the Conditions of Section 503B

During the inspection, FDA investigators noted that drug products produced by your facility failed to meet the conditions of section 503B. For example, the investigators noted your facility failed to submit a report to FDA upon initial registration as an outsourcing facility, and again in June 2017, identifying the drug products that you compounded during the previous 6-month period.

Because your compounded drug products have not met all of the conditions of section 503B, they are not eligible for the exemptions in that section from the FDA approval requirements of section 505, the requirement under section 502(f)(1) that labeling bear adequate directions for use, and the Drug Supply Chain Security Act requirements described in section 582 of the FDCA.

Specific violations are described below.

C. Violations of the FDCA

Misbranded Drug Products

You compound drug products that are intended for conditions that are 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, causing them to be misbranded under

[2] 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 503B of the FDCA.

section 502(f)(1) of the FDCA, and they are not exempt from the requirements of section 502(f)(1) of the FDCA.[3] 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.

Adulterated Drug Products

FDA investigators noted CGMP violations at your facility, that caused your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA. The violations include, for example:

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

2. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

Outsourcing facilities must comply with CGMP requirements under section 501(a)(2)(B) of the FDCA. FDA's regulations regarding CGMP requirements for the preparation of drug products have been established in 21 CFR parts 210 and 211. FDA intends to promulgate more specific CGMP regulations for outsourcing facilities. FDA has issued a revised draft guidance, *Current Good Manufacturing Practice — Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act*. This draft guidance, when finalized, will describe FDA's expectations regarding outsourcing facilities and the CGMP requirements in 21 CFR parts 210 and 211 until more specific CGMP regulations for outsourcing facilities are promulgated.

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.

Failure to Report Drugs

As noted above, your facility failed to submit a report to FDA upon initial registration as an outsourcing facility, and again in June 2017, identifying the drug products that you compounded during the previous 6-month period (section 503B(b)(2) of the FDCA). The failure to report drugs by an entity that is registered with FDA in accordance with section 503B(b) is a prohibited act under section 301(ccc)(3) of the FDCA [21 U.S.C. § 331(ccc)(3)].

D. Corrective Actions

We have reviewed your facility's responses dated September 8, 2017, December 14, 2017, and January 5, 2018, as well as your subsequent correspondence. It appears you have corrected most of the violations. However, we have the following concerns:

[3] Your compounded 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).

1. You stated that you made changes to the "media challenge" process and submitted an updated SOP; however, your firm failed to describe in detail how the process is simulating the most challenging and stressful conditions. For example, it is not clear that your firm is simulating your full production batch sizes. Therefore, we cannot fully evaluate the adequacy of your corrective actions.

2. Your firm's SOP PP#: 03-01.02 "Environmental Monitoring Program" states that "Personnel will be monitored for finger tips(b)(4) " However, it does not specifically state you monitor both hands and other critical areas of the operator. Also, your firm's SOP states that "If there is an action level result, perform a re-test to confirm. If the re-test passes, record the passing result." As written, this practice is concerning. It is unacceptable to invalidate an action level result if you lack a documented investigation that scientifically supports such a conclusion. It is essential that you conduct a thorough investigation of all potential causes and implement appropriate corrective and preventive actions.

3. We remain concerned with your environmental monitoring alert and action limits. For example, your action level for the ISO 5 work surface is(b)(4) CFU per plate. As an outsourcing facility, you must comply with CGMP requirements under section 501(a)(2)(B) of the FDCA. Samples from the ISO 5 environments should normally yield no microbiological contaminants. Your firm's current limits do not require action, including assessment of product impact, when any microbial contamination is recovered on the ISO 5 surface or on aseptic operators' gloved fingertips. You should address this concern and perform an impact assessment to evaluate any risk to product intended to be sterile currently on the market.

In addition to the issues discussed above, please 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).

In addition, regarding observations related to the conditions of section 503B of the FDCA, we acknowledge that, during the inspection, you provided a copy of an email, addressed to FDA's ESG helpdesk, stating you were not "aware that [your firm] needed an ESG account in order to complete Electronic Drug Reporting." We acknowledge that, since the inspection, your firm has submitted adequate product reports to FDA. Should you resume compounding and distributing drug products that do not meet the conditions of section 503B of the FDCA, the compounding and distribution of your drugs would be subject to the new drug approval requirement, the requirement to label drug products with adequate directions for use, and the Drug Supply Chain Security Act requirements.

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 if you have taken any steps to correct the violations. Please include an explanation of each step being taken to prevent the recurrence of the 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 30 (thirty) working days, state the reason for the delay and the time within which you will complete the correction.

If you have any questions, please send your inquiry to orapharm1_responses@fda.hhs.gov and contact Compliance Officer Juan Jimenez at juan.jimenez@fda.hhs.gov or call to 518-453-2314 X-1014.

Diana Amador-toro -S

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