U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations I
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February 13th, 2019

VIA UPS OVERNIGHT
Robert F. Keem
General Manager
Athenex Pharma Solutions, LLC
11342 Main Street
Clarence, NY 14031-1718
Email: rkeem@athenex.com

Dear Mr. Keem:

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 April 10, 2017, and most recently on October 18, 2017. From December 5, 2017, to December 13, 2017, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, Athenex Pharma Solutions, LLC, located at 11342 Main Street, Clarence, NY 14031-1718.

During the inspection, the investigator observed that you 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 requirements under the FDCA. FDA issued a Form FDA 483 to your facility on December 13, 2017. FDA acknowledges receipt of your facility's response, dated January 4, 2018.

Based on this inspection, it appears your facility is producing drugs that violate the FDCA.

A. Compounded Drugs under the FDCA

Under section 503B(b), 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 outsourcing facility can 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]

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

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 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.

For a compounded drug product to qualify for the exemptions under section 503B, the labeling of the drug must include certain information (section 503B(a)(10) of the FDCA [21 U.S.C. §353b(a)(10)]).

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, the FDA investigator noted that drug products produced by your facility failed to meet the conditions of section 503B. For example, the investigator noted:

1. Some of your facility's drug product labels did not include the dosage form, as well as a list of active and inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

2. Your facility failed to submit a report to FDA upon initial registration as an outsourcing facility in April 2017 and also failed to submit a complete report in June 2017, and again in December 2017, identifying the drug products that you compounded during the previous 6-month period. These Product Reports only appear to report distributed products and not all products compounded during the reporting period as required by section 503B(b)(2) of the FDCA.

Because your compounded drug products have not met all of the conditions in section 503B, they are not eligible for the exemptions under section 503B from the FDA approval requirements in 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

Unapproved New Drug Products

You do not have any FDA-approved applications on file for drug products that you compound.[3] Under sections 301(d) and 505(a) of the FDCA [21 U.S.C. §§ 331(d) and 355(a)] a new drug may not be introduced into or delivered for introduction into interstate commerce unless an application approved by 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

You compound drug products that 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 causing them to be misbranded under section 502(f)(1) of the FDCA.[4] The introduction or delivery for introduction into interstate commerce of these products therefore violates section 301(a) of the FDCA. Further, 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.

Failure to Report Drugs

As noted above, your facility failed to submit a report to FDA upon initial registration as an outsourcing facility in April 2017, and also failed to submit a complete report in June 2017, and again in December 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

Regarding observations related to the conditions of section 503B of the FDCA, your corrective actions on labeling appear adequate:

> You provided copies of labels that now include all required information. Specifically, your labels now include dosage forms and a list of active and inactive ingredients.

Should you continue to compound and distribute 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.

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[3] The specific products made by your firm are drugs within the meaning of section 201(g) of the Act, [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.

[4] 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).

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, you should notify this office in writing of the specific steps 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 the corrective actions cannot be completed within thirty (30) working days, state the reason for the delay and the time frame within which the corrections will be completed.

Please address your (electronic) reply to:

Stephanie Durso
Director of Compliance
Office of Pharmaceutical Quality Operations, Division I
10 Waterview Blvd 3rd FL
Parsippany, NJ 07054
Email: ORAPHARM1_RESPONSES@fda.hhs.gov

If you have questions regarding the contents of this letter, please contact James Mason, Compliance Officer by phone at 570-262-0519 or by email at james.mason@fda.hhs.gov.

Sincerely,

Diana Amador-toro -S

Digitally signed by Diana Amador-toro -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300011579, cn=Diana Amador-toro -S
Date: 2019.02.13 10:20:53 -05'00'

Diana Amador-Toro
Program Division Director
Office of Pharmaceutical Quality Operations, Division I