Eagle Pharmacy, Inc. 10/13/16

New Orleans District
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October 13, 2016

WARNING LETTER NO. 2017-NOL-01

UNITED PARCEL SERVICE
Delivery Signature Requested

Brad Johnson, Owner
Eagle Pharmacy, Inc.
2200 Riverchase Center, Suite 675
Hoover, Alabama 35244-2918

Dear Mr. Johnson:

You 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 *United States Code* (USC) 353b] **[1]** on June 16, 2015, and again on November 23, 2015. From August 3, 2015, to August 21, 2015, an FDA investigator inspected your facility, Eagle Pharmacy, Inc., 2200 Riverchase Center, Suite 675, Hoover, Alabama. During the inspection, the investigator observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, the investigator observed an operator moving their arm over open vials during aseptic filling. In addition, the investigator observed an operator transferring materials onto the critical work surface without first disinfecting the materials. The investigator also noted that your media plates used for personnel and environmental monitoring did not contain disinfectant neutralizers, which could potentially bias results. Furthermore, your firm failed to demonstrate through appropriate studies which your aseptic processing area is able to provide adequate protection of the ISO 5 area in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk. In addition, 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 August 21, 2015. FDA acknowledges receipt of your facility's response, dated September 9, 2015.

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

A. Compounded Drugs under the FDCA

The Drug Quality and Security Act (DQSA) was enacted on November 27, 2013. Title I of the DQSA, the Compounding Quality Act (CQA), added a new Section 503B to 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 USC 355(a)], the requirement in Section 502(f)(1) of the FDCA [21 USC 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 USC 360eee-1] if the conditions in Section 503B of the FDCA are met.

An outsourcing facility, which is defined in Section 503B(d)(4) of the FDCA [21 USC 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 USC 351(a)(2)(B)], regarding current good manufacturing practice (CGMP), and Section 501(a)(2)(A) [21 USC 351(a)(2)(A)], regarding insanitary conditions. Generally, CGMP requirements for the preparation of drug products are established in Title 21, *Code of Federal Regulations* (CFR) Parts 210 and 211.

B. Violations of the FDCA

The FDA investigator noted that drug products that were intended or expected to be sterile were prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health, causing them to be adulterated within the meaning of Section 501(a)(2)(A) of the FDCA. Furthermore, the FDA investigator observed significant CGMP violations at your facility, causing your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the FDCA.

In addition, the FDA investigator observed your facility failed to meet the conditions of Section 503B. For example, during the inspection, the FDA investigator noted:

1. The initial product report submitted to FDA by your facility in June 2015 failed to identify all the drug products that you compounded during the previous six-month period [Section 503B(b)(2) of the FDCA [21 USC 353b(b)(2)].

2. Some of your facility's drug products do not include the following required information on the label: the statement "This is a compounded drug," the address

and phone number of the outsourcing facility, and the strength (of each active ingredient). [Section 503B(a)(10) of the FDCA [21 USC 353b(a)(10)].

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.[2]

Specific violations are described below.

Adulterated Drug Products

The FDA investigator noted that drug products compounded in your facility that were intended or expected to be sterile 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 an operator moving their arm over open vials during aseptic filling. In addition, the investigator observed an operator transferring materials onto the critical work surface without first disinfecting the materials. The investigator also noted that your media plates used for personnel and environmental monitoring did not contain disinfectant neutralizers, which could potentially bias results. Furthermore, your firm failed to demonstrate through appropriate studies that your aseptic processing area is able to provide adequate protection of the ISO 5 area in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

The FDA investigator also noted CGMP violations at your facility, causing your drug product(s) 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 thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed [21 CFR 211.192].

3. 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 210 and 211. FDA intends to promulgate more specific CGMP regulations for outsourcing facilities. FDA has issued a draft guidance, *Current Good Manufacturing Practice — Interim 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 210 and 211 until more specific CGMP regulations for outsourcing facilities are promulgated.

Under Section 301(a) of the FDCA [21 USC 331(a)], the introduction or delivery for introduction into interstate commerce of any drug that is adulterated is a prohibited act. Further, it is a prohibited act under Section 301(k) of the FDCA [21 USC 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.

Unapproved New Drug Products

You do not have any FDA approved applications on file for your drug products.[3] Under Sections 301(d) and 505(a) of the FDCA [21 USC 331(d) and 355(a)], a new drug may not be introduced 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.

Misbranded Drug Products

You compound drug products which 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 Section 502(f)(1) of the FDCA, and they are not exempt from the requirements of Section 502(f)(1) of the FDCA (*see, e.g.,* 21 CFR 201.115). The introduction or delivery for introduction into interstate commerce of these products therefore violates Section 301(a) of the FDCA. Further, 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.

Failure to Report Drugs

As noted above, the initial product report submitted by your facility in June 2015 failed to identify all the drug products that you compounded during the previous six-month period Section 503B(b)(2) of the FDCA [21 USC 353b(b)(2)]. 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 USC 331(ccc)(3)].

C. Corrective Actions

We acknowledge your firm's action on August 28, 2015, to voluntarily recall a lot of Lipo B injection, 10 mL vials, due to undetectable amounts of methylcobalamin in the product. However, from review of your responses, it is not clear if your firm has discontinued production of this formulation.

We further acknowledge your response to the Form FDA 483, dated September 9, 2015. In your response, you describe corrective actions you have taken to address the observed 503B labeling deficiencies. The corrective actions you have made in response to the address and phone number of your facility, and the strength (of each active ingredient), appear to be adequate. However, we note your use of the statement “This is a compounded medication” is not adequate, as the statement required under 503B(a)(10) is “This is a compounded drug.” Furthermore, please note that some of the labels submitted with your September 9, 2015, response do not include the established name of the drug as required by Section 503B(a)(10) of the FDCA [21 USC 353b(a)(10)], but rather use ambiguous abbreviations. For example, the label for your “Keprocaine” product lists the established names of the active ingredients as “Keto/Cycl/Bacl/Lido.”

The corrective action made in response to the observed deficiency regarding your June 2015 product report appears adequate.

In addition, your September 9, 2015, response states you will take or have taken certain corrective actions in response to the Form FDA 483 inspectional observations. Although several of your proposed corrective actions appear adequate, some of the supporting documents do not contain sufficient information for us to make a complete evaluation. For example, in response to our observation of poor aseptic practices, you provided your new SOP entitled, Aseptic Technique (Policy 2.28). However, this document does not contain sufficient detail to allow for complete evaluation of your corrective actions. Specifically, it is not clear from your description how the process of using **(b)(4)** will prevent contamination of open vials. Moreover, your response does not include documentation to show that personnel have been instructed on this new procedure.

In response to our observation of inadequate media plates, you stated “Eagle Pharmacy has purchased contact and air sampling TSA and Sabouraud Dextrose plates with neutralizers to prevent false negatives.” However, your response does not include supporting documentation for our review, such as purchase records or your updated sampling procedure.

FDA strongly recommends that your management immediately undertake a comprehensive assessment of your operations, including facility design, procedures, personnel, processes, materials, and systems. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation. You should fully implement necessary corrections in order to ensure that the drug products produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

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, as amended by the Food and Drug Administration Safety and Innovation Act (Pub.L. 112-144, Title VII, section 711). We note you have chosen to **(b)(4)**. If you choose to contract with a laboratory to perform some functions required by CGMP, it is essential you select a qualified

contractor and you maintain sufficient oversight of the contractor's operations to ensure it is fully CGMP compliant. Regardless of whether you rely on a contract facility, you are responsible for assuring that drugs you introduce into interstate commerce are neither adulterated nor misbranded. [*See* 21 CFR 210.1(b), 21 CFR 200.10(b)].

D. 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 your firm complies with all requirements of federal law, including FDA regulations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction. FDA intends to re-inspect your facility to verify corrective actions have been completed.

Within 15 working days of receipt of this letter, please 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 15 working days, state the reason for the delay and the time frame within which the corrections will be completed. Your written notification should refer to the Warning Letter No. 2017-NOL-01. Please address your reply to Rebecca Asente, Compliance Officer, at the address above.

If you have questions regarding the contents of this letter, please contact Rebecca Asente at (504) 846-6104.

Sincerely,
/S/
Ruth Dixon
District Director
New Orleans District

cc: Tim Martin, President
Alabama Board of Pharmacy
111 Village Street
Birmingham, AL 35242

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

[2] See, e.g., section 503B(a)(11) of the FDCA [21 U.S.C. § 353b(a)(11)].

[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.