First Pharma Associates LLC dba Riverpoint Pharmacy 9/12/17

Division of Pharmaceutical
Quality Operations IV
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WARNING LETTER

VIA UNITED PARCEL SERVICE
SIGNATURE REQUIRED

September 12,
2017

WL#: CMS 522020

Catherine M. Hudek, RPh, NCMP
Director of Pharmacy
First Pharma Associates, LLC DBA Riverpoint Pharmacy
528 E. Spokane Falls Blvd, Suite 110
Spokane, WA 99202

Dear Ms. Hudek:

From December 6, 2016, to December 16, 2016, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, First Pharma Associates, LLC, dba Riverpoint Pharmacy, located at 528 E. Spokane Falls Blvd, Suite 110, Spokane, WA 99202. 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 serious deficiencies in your practices for producing non-sterile drug products, which put patients at risk.

FDA issued a Form FDA 483 to your firm on December 16, 2016. FDA acknowledges receipt of your facility's response, dated January 9, 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 practices (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.

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 noted that drug products produced by your firm failed to meet the conditions of section 503A. Specifically, the investigator noted that your firm compounded drug products using peruvian balsam and zinc picolinate. Drug products compounded using peruvian balsam and zinc picolinate are not eligible for the exemptions provided by section 503A(a), because peruvian balsam and zinc picolinate are not the subject of an applicable USP or NF monograph, are not a component of an FDA-approved human drug, or do 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 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 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 that your firm's ISO-classified areas have difficult to clean, particle-generating, or visibly dirty equipment or surfaces. Our investigator also observed that your ISO 5 **(b)(4)** is located in the Prep Room which is an unclassified area that is not supplied by HEPA filtered air, and this area also contains a **(b)(4)** sink. Furthermore, your firm failed to demonstrate, through appropriate studies, that your laminar flow hood is able to provide adequate protection of the ISO 5 area in which products intended to be sterile are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

Under section 301(a) of the FDCA [21 U.S.C. § 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 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.

We acknowledge your response to the Form FDA 483 inspectional observations, dated January 9, 2017. We are unable to fully evaluate your corrective actions due to the lack of adequate supporting documentation. Specifically, we remain concerned that your ISO 5 **(b)(4)** is located in an unclassified area. Your response states that the Prep Room, where the **(b)(4)** is located, has never failed to qualify as an ISO 8 room. However, the certification report provided with your response, dated December 14, 2016, states that due to the lack of HVAC system in place for the Prep Room, "it will be difficult to generate any airflow cascade or direction within the space". It is essential that a positive pressure differential be maintained between rooms of higher and lower air cleanliness to achieve and sustain ISO-classified conditions within a cleanroom. In addition, the report does not indicate if viable air monitoring was performed in your Prep Room to support an ISO 8 classification of the area. Please note, as currently constructed, your Prep Room is not physically separated from the unclassified Laboratory environment. Furthermore, there is a **(b)(4)** sink in close proximity to the ISO 5 **(b)(4)**. Sinks are sources of microbial contamination, and your

response does not adequately address this deficiency. Furthermore, the documentation provided by your firm to support dynamic smoke studies in ISO 5 areas does not include a description of how dynamic conditions were simulated for the studies performed, or a video for our review.

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 that bulk drug substances used to compound 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 503A bulks list.

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 meet the minimum requirements of the CGMP regulations.

FDA strongly recommends that your management undertake a comprehensive assessment of operations, including facility design, procedures, personnel, processes, maintenance, materials, and systems. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise should assist you in conducting this comprehensive evaluation.

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.

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.

Within fifteen (15) 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 15 working days, state the reason for the delay and the time within which you will complete the correction.

Your written notification should refer to the Warning Letter Number above (CMS 522020)

Please address your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
United States Food and Drug Administration
19701 Fairchild Road
Irvine, California 92612

If you have any questions regarding any issues in this letter, please contact Mrs. Mariza Jafary, Compliance Officer via email at Mariza.Jafary@fda.hhs.gov by phone at (949) 608-2977 and reference unique identifier CMS 522020.

Sincerely,
/S/
Acting for CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV

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[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.

[2] On June 9, 2016, FDA issued a final guidance titled, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. This guidance describes FDA's interim regulatory policy for State-licensed pharmacies, Federal facilities, and licensed physicians that compound human drug products using bulk drug substances that do not otherwise meet the conditions of section 503A(b)(1)(A)(i) while the 503A bulks list is being developed. Specifically, the guidance sets out the conditions under which FDA does not intend to take action against a State-licensed pharmacy, Federal facility, or licensed physician for compounding a drug product using a bulk drug substance that is not the subject of an applicable USP or NF monograph or a component of an FDA-approved drug, until the substance is identified in a final rule as included or not included on the 503A bulks list. These conditions include that the substance may be eligible for inclusion on the 503A bulks list, was nominated with adequate support for FDA to evaluate it, and has not been identified by FDA as a substance that appears to present significant safety risks pending further evaluation. Peruvian Balsam and Zinc Picolinate were nominated for inclusion on the 503A bulks list, however, neither of these bulk drug substances were nominated with adequate support for FDA to evaluate the substance. For additional information, see the guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469120.pdf.

[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).