Pharmakon Compounding Pharmacy, Inc. 9/7/17

Division of Phannaceutical
Quality Operations III
300 River Place. Suite 5900
Detroit, Ml 48207
Telephone: (313) 393-8100
Fax: (313) 393-8139

September 7, 2017

WARNING LETTER

Case# 523191

UPS NEXT DAY
SIGNATURE REQUIRED

Paul J. Elmer, R.Ph., Owner
Pharmakon Compounding Pharmacy. Inc.
14460 Getz Road, Suite 300
Noblesville, IN 46060-3303

Dear Mr. Elmer:

From April 18, 2016, to May 6, 2016, U.S. Food and Drug Administration (FDA) investigators inspected your facility, Pharmakon Compounding Pharmacy, Inc., located at 14460 Getz Road, Suite 300, Noblesville, IN 46060-3303. During the inspection, the investigators 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 investigators noted serious deficiencies in your practices for producing sterile drug products, which put patients at risk.

FDA issued a Form FDA 483 to your firm on May 6, 2016. FDA acknowledges receipt of your facility's responses, received on May 27, 2016, June 9 and 21, 2016, and July 21, 2016. FDA also acknowledges that your firm was sold in December 2016 and under new ownership as Medscript Compounding Pharmacy. 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.

B. Failure to Meet the Conditions of Section 503A

During the inspection, the FDA investigators noted that drug products produced by your firm failed to meet the conditions of section 503A. For example, the investigators noted that your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced.

Therefore, you compounded drug products that do not meet the conditions of section 503A and are not eligible for the exemptions 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 investigators 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, our investigators observed that materials and components were not disinfected prior to being transferred from the **(b)(4)** to the **(b)(4)** of the isolator. The **(b)(4)**(ISO 5), used in aseptic processing of sterile drug products, are located in an unclassified room/area. Additionally, the certification for the ISO 5 isolator dated December 2015 showed that airflow as observed in the smoke studies may be turbulent in both isolators.

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 investigators observed significant 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 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 maintaining equipment used to control the aseptic conditions. 21 CFR 211.42(c)(10)(vi).

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

4. 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).

5. Your firm does not have, for each batch of drug product purporting to be sterile and/or pyrogen-free, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product. 21 CFR 211.167(a).

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.

Unapproved New Drug Products

You do not have any FDA-approved applications on file for the ineligible drug products that you compounded.[2] Under sections 505(a) and 301(d) of the FDCA [21 U.S.C. § 331(d)], 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

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. The introduction or delivery for introduction into interstate commerce of these products therefore violates section 301(a) of the FDCA. 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.

D. Corrective Actions

We have reviewed your firm's responses to the Form FDA 483. FDA acknowledges that Pharmakon Compounding Pharmacy, Inc., is no longer listed on the Indiana Board of Pharmacy (INBOP) website. Further, we acknowledge that your firm was

sold in December 2016 and under the new ownership as Medscript Compounding Pharmacy.

Corrective actions regarding the insanitary condition observations in the Form FDA 483 appear to be adequate. However, certain corrective actions cannot be fully evaluated as your firm did not provide sufficient supporting documentation. For example, in response to our observation that your firm failed to adequately clean/disinfect materials/components prior to the introduction of these items within the ISO 5 environment, you indicated that your procedure will require employees to take steps to disinfect supplies prior to introduction into the isolators for use during the production of sterile products. However, your firm failed to address the concerns regarding the cleaning/disinfection of **(b)(4)** exposed to an unclassified environment prior to transferring to an isolator (ISO 5) for further sterile filtration.

Additionally, in response to our observation that smoke studies performed in December 2015 for the **(b)(4)**(ISO 5) showed turbulent airflow, you indicated that your firm recertified the isolators on June 2, 2016. This report states that the smoke studies showed some reflux inside the isolators on both chambers. However, your firm failed to address the concerns noted in this certification and provided no corrective actions. Additionally, this report states that your firm did not perform any **(b)(4)** testing within your **(b)(4)** room.

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 on receipt of a prescription for an identified individual patient prior to compounding and distributing drug products.

As explained above, receipt of valid prescriptions for individually-identified patients is a condition of section 503A, which your firm failed to meet for a portion of the drug products you produced. 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.[4]

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 introduce into interstate commerce are neither adulterated nor misbranded. [*See* 21 CFR 210.1(b), 21 CFR 200.10(b)].

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. Please confirm whether you still own this firm or if it is under new ownership. The owner of the pharmacy is 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 the owner's responsibility to ensure that the firm complies with all requirements of federal law, including FDA regulations.

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

Please address your reply to:

Tina M. Pawlowski, Compliance Officer
U. S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III
Detroit Office
300 River Place, Suite 5900
Detroit, MI 48207-5057

Refer to the Unique Identification Number (Case# 523191) when replying. If you have questions regarding the contents of this letter, please contact Tina M. Pawlowski by phone at (313) 393-8217 or via email at Tina.Pawlowski@fda.hhs.gov.

Sincerely,
/S/
Art O. Czabaniuk
Division Director
Division of Pharmaceutical Operations III

---

[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] 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) [21 U.S.C. 321(p)] of the FDCA because they are not generally recognized as safe and effective for their labeled uses.

[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).

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