SaveWay Compounding Pharmacy, Inc. 10/4/16

U.S. FOOD & DRUG ADMINISTRATION

Philadelphia District Office
900 U.S. Customhouse
200 Chestnut Street
Philadelphia, PA 19106

Telephone: (215) 597-4390
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WARNING LETTER
17-PHI-01

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

October 4, 2016

Brenda L. Pavlic, CPhT/Owner/Director of Sterile Operations
SaveWay Compounding Pharmacy, Inc.
31 Albe Drive, Suite 1
Newark, DE 19702

Dear Ms. Pavlic:

Between August 31, 2015, and October 2, 2015, a U.S. Food and Drug Administration (FDA) investigator conducted an inspection of your facility, SaveWay Compounding Pharmacy, Inc., located at 31 Albe Drive, Suite 1, Newark, DE 19702.

During the inspection, the investigator noted that you were not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. The investigator also noted records showing that your firm produced domperidone drug products. Domperidone is not the subject of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, is not a component of an FDA-approved human drug product, and does not appear on a list

developed by the Secretary under section 503A(b)(1)(A)(i)(III) of the Federal Food, Drug, and Cosmetic (FDCA) [21 U.S.C. § 353a(b)(1)(A)(i)(III)].

In addition, the investigator observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigator noted that your firm did not use sterile wipes and used non-sterile disinfectants as part of your disinfection program for the aseptic processing area. Furthermore, your firm failed to demonstrate through appropriate studies that your aseptic processing areas are able to provide adequate protection of the ISO 5 areas in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

FDA issued a Form FDA 483 to your firm on October 2, 2015. FDA acknowledges your response to the Form FDA 483 dated October 14, 2015.

Based on this inspection, it appears that you are producing drugs that violate the FDCA.

A. Compounded Drugs Under the FDCA

Section 503A of the FDCA [21 U.S.C. § 353a] describes the conditions under which certain compounded human drug products qualify for exemptions from three sections of the FDCA: compliance with current good manufacturing practice (CGMP) requirements, section 501(a)(2)(B) of the FDCA [21 U.S.C. § 351(a)(2)(B)]; labeling with adequate directions for use, section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)]; and FDA approval prior to marketing, section 505 of the FDCA [21 U.S.C. § 355]. Receipt of valid prescriptions for individually-identified patients is one of the conditions for the exemptions under section 503A of the FDCA.

During the FDA inspection, the investigator observed that your firm does not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce. Accordingly, the drugs you compound without valid prescriptions for individually-identified patients are not entitled to the exemptions in section 503A of the FDCA.

In addition, compounded drug products containing the bulk drug substance domperidone**[1]** are not eligible for the exemptions provided by subsection (a) of 503A because domperidone is not the subject of an applicable USP or NF monograph, not a component of an FDA-approved human drug, and does not appear on a list of bulk drug substances that may be used for compounding developed by the Secretary.

Furthermore, another condition that must be met for drug products to qualify for the exemptions under section 503A is that the licensed pharmacist or licensed physician does not compound a drug product that appears on a list published by FDA at 21 CFR Part 216 of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective (section 503A(b)(1)(C) of the FDCA [21 U.S.C. § 353A(b)(1)(C)]) (“withdrawn or removed list”). During the FDA inspection, the investigator noted records showing that your firm produced chlorhexidine

gluconate. All tinctures of chlorhexidine gluconate formulated for use as a patient preoperative skin preparation are included on the withdrawn or removed list published by FDA at 21 CFR 216.24. We do not have specific information regarding the formulation(s) or intended use(s) of your chlorhexidine gluconate products, but you should know that compounded tinctures of chlorohexidine gluconate formulated for use as a patient preoperative skin preparation are not eligible for the exemptions provided by section 503A of the FDCA.

In addition, we remind you there are a number of other conditions which must be satisfied to qualify for the exemptions in section 503A of the FDCA.[2]

B. Violations of the FDCA

Because the drug products you manufactured and distributed without valid prescriptions for individually-identified patients and the domperidone products you manufactured and distributed are not the subject of approved applications, they are unapproved new drugs and misbranded drugs in violation of sections 505(a) and 502(f)(1) of the FDCA, respectively.

In addition, drug products that are intended or expected to be sterile were prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth, or whereby they may have been rendered injurious to health, causing them to be adulterated within the meaning of section 501(a)(2)(A) of the FDCA [21 U.S.C. § 351(a)(2)(A)]. Furthermore, because you manufacture and distribute a portion of your drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs is subject to FDA's CGMP regulations for Finished Pharmaceuticals, 21 CFR Parts 210 and 211. 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.

Unapproved New Drug Products

You did not have any FDA-approved applications on file for the drug products for which you did not obtain valid prescriptions for individually-identified patients or the domperidone drug products.[3] Under sections 301(d) [21 U.S.C. § 331(d)] and 505(a) of the FDCA, 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. Your 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 for which you have not obtained valid prescriptions for individually-identified patients, and drug products in which you used the bulk drug substance domperidone, 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 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 [21 U.S.C, § 331(a)]. 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 misbranded.

Adulterated Drug Products

Additionally, 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 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 investigator noted that your firm did not use sterile wipes and used non-sterile disinfectants as part of your disinfection program for the aseptic processing area. Furthermore, your firm failed to demonstrate through appropriate studies that your aseptic processing areas are able to provide adequate protection of the ISO 5 areas 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 the drug products for which you have not obtained valid prescriptions for individually-identified patients to be adulterated under 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 cleaning and disinfecting the room and equipment to produce aseptic conditions [21 CFR 211.42(c)(10)(v)].

3. Your firm failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination [21 CFR 211.28(a)].

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

5. Your firm failed to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products and to use results of such stability testing to determine appropriate storage conditions and expiration dates [21 CFR 211.166(a)].

6. Your firm failed to review the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed. [21 CFR 211.192].

Under section 301(a) of the FDCA, 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 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.

C. Corrective Actions

We acknowledge your correspondence dated September 3, 2015, which states that you will "immediately discontinue the practice of preparing non-patient-specific compounded preparations for office use or administration." In addition, we acknowledge that you gave the investigator an undated and unsigned correspondence stating that you "will no longer compound Domperidone for human use."

Furthermore, in your response to the Form FDA 483 inspectional observations dated October 14, 2015, you describe certain corrective actions taken to address the observations. Although, several of your proposed corrective actions appear adequate, others are deficient. For example, in your response to our observation regarding cleaning and disinfection, you stated that "Daily, weekly, and monthly cleaning policy and procedures have been rewritten to include contact times per manufacturer guidelines for all cleaning products used throughout the cleanroom suite during routine cleaning and disinfecting." However, it is not clear if your firm will use sterile disinfectants and wipes to disinfect your aseptic processing areas. Furthermore, your response cannot be evaluated due to lack of supporting documentation for some of the corrective actions, such as your firm's updated cleaning policy and procedures.

In your response to our observation regarding smoke studies, you indicated that all future smoke studies will be performed under dynamic conditions. However, we are unable to evaluate this corrective action because you have not provided documentation, such as a description of the conditions at the time of the smoke studies or a video copy of the smoke studies, to show that these studies have been and will be conducted under dynamic conditions. In addition, your firm failed to include any interim controls or a time frame within which the smoke studies will be completed.

FDA strongly recommends that you 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.

Please be aware that section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether the drugs are compounded and distributed after receipt of a prescription for an identified individual patient.

In addition, if you were to continue to manufacture and distribute drug products without valid prescriptions for individually-identified patients, the manufacture of such

drugs would be subject to FDA's drug CGMP regulations (21 CFR Parts 210 and 211), and, before doing so, you should fully implement corrections that meet the minimum requirements of 21 CFR Part 211 to provide assurance that the drug product(s) produced by your firm conform to the basic quality standards regarding safety, identity, strength, quality, and purity. As indicated above, such drug products would also be subject to new drug approval requirements in section 505 and the requirements for adequate directions for use in section 502(f)(1).

Inaddition 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). 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).

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 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 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.

Your written response should be sent to Ms. Yvette Johnson, Compliance Officer, U.S. Food and Drug Administration, 900 U.S. Customhouse, 200 Chestnut Street, Philadelphia, Pennsylvania 19106. If you have any questions about this letter, please contact Ms. Johnson at (215)717-3077 or e-mail at Yvette.Johnson@FDA.HHS.GOV.

Sincerely,
/S/
Anne E. Johnson
District Director
Philadelphia District Office

[1] Domperidone was nominated for inclusion on the list of bulk drug substances that can be used in compounding that must be developed through regulation pursuant to section 503A(b)(1)(A)(i)(III) of the FD&C Act (503A bulks list). 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 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 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 sufficient supporting information for FDA to evaluate it, and that it has not been identified by FDA as a substance that appears to present significant safety risks pending further evaluation. Domperidone has been identified as a substance that appears to present significant safety risks. For additional information, see the guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469120.pdf.

[2] For example, section 503A also addresses anticipatory compounding, which includes compounding (not distribution) before receipt of a valid prescription order for an individual patient. We are not addressing anticipatory compounding here.

[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.