Jeffreys Drug Store 8/25/16

Department of Health and Human Services

Public Health Service
Food and Drug Administration
PHILADELPHIA DISTRICT
900 U .S. Customhouse
2nd and Chestnut Streets
Philadelphia, PA 19106
Telephono: 215-597-4390

WARNING LETTER
16-PHI-12

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

August 25, 2016

Gerard E. O'Hare, President
Jeffreys Drug Store
1 N. Central Ave
Canonsburg, PA 15371-1301

Dear Mr. O'Hare:

From February 1, 2016, to February 9, 2016, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Jeffreys Drug Store, located at 1 N. Central Ave, Canonsburg PA 15371-1301.

During the inspection, the investigators noted that you were not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. It was also noted that your firm produces domperidone products. Domperidone is not the subject of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, nor is it a component of an FDA-approved human drug product, nor does it appear on a list developed by the Secretary under section 503A(b)(1)(A)(i)(III) of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353a]. In addition, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigators observed that your firm did not use a sporicidal agent as part of the disinfection program for the aseptic processing areas. Moreover, our investigators observed dirt and grime on the plastic separation flaps between the anteroom and the ISO 6 cleanroom. Also, pre-sterilized stoppers were observed to be left uncovered in the ISO 5 hood overnight. Furthermore, our investigators observed that 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 February 9, 2016. FDA acknowledges receipt of your firm's response to the Form FDA 483, dated February 23, 2016. 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. During the FDA inspection, the investigators observed that your firm does not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce.

Another condition that must be met for a compounded drug to qualify for the exemptions under section 503A is that it is compounded using bulk drug substances that: (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, are 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, that appear on a list developed by the Secretary through regulation (section 503A(b)(1)(A)(i)).

Compounded drug products containing domperidone are not eligible for the exemptions provided by subsection (a) of 503A of the FDCA because domperidone is not the subject of an applicable USP or NF monograph, is 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.[1]

Accordingly, the drugs you compound without valid prescriptions for individually-identified patients and any drug products you compound using domperidone are not entitled to the exemptions in section 503A.

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

B. Violations of the FDCA

The drug products that you manufacture and distribute without valid prescriptions for individually-identified patients and the domperidone drug products you manufacture and distribute are misbranded drugs in violation of section 502(f)(1) of the FDCA.

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.

Misbranded Drug Products

You compound domperidone drug products and drug products for which you have not obtained valid prescriptions for individually-identified patients and that are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not

medical practitioners; 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].

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 investigators observed that your 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:

1. Your firm did not use a sporicidal agent as part of the disinfection program for the aseptic processing areas;
2. Dirt and grime were on the plastic separation flaps between the anteroom and the ISO 6 cleanroom;
3. Pre-sterilized stoppers were left uncovered in the ISO 5 hood overnight, with no additional processing to ensure sterility of the component;
4. Your firm failed to demonstrate through appropriate studies that your aseptic processing areas are able to provide adequate protection of the ISO 5 area in which sterile products are processed.

Under section 301(k) of the FDCA, it is a prohibited act 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 have reviewed your firm's planned corrective actions, as documented in your February 23, 2016, response to the Form FDA 483 inspectional observations issued at the close of the inspection. Regarding observed insanitary conditions, some proposed corrective actions appear to be adequate, but could not be fully evaluated, because your response did not include sufficient information or supporting documentation. For example, your firm's response dated February 23, 2016, indicated that smoke studies will be requested and completed within six months. However, your response did not include an adequate description of the conditions under which the study will be performed. Furthermore, the response did not include any interim controls or an assessment of potential product impact until the corrective action is implemented. In addition, your February 23, 2016, response states that you will incorporate bleach into your daily cleaning procedures as a sporicidal agent. However, you did not provide sufficient specifics regarding the concentration of the bleach intended for use or documentation supporting its effectiveness as a sporicidal agent. Moreover, no specific contact/dwell times were included in your response.

You should correct the violations of sections 501(a)(2)(A) and 502(f)(1) of the FDCA noted above. 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 valid prescription for an identified-individual patient. In addition, should you continue to manufacture and distribute drug products without valid prescriptions for individually-identified patients or drug products containing domperidone, the manufacture of such drugs would be subject to FDA's Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals (21 CFR Parts 210 and 211), among other

requirements, and, before doing so, you should fully implement corrections that meet the minimum requirements of 21 CFR Part 211 in order to provide assurance that the drug products produced by your firm conform to the basic quality standards regarding safety, identity, strength, quality, and purity.

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 aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation.

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 the reference number listed above and 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 actions within 15 working days, state the reasons for the delay and the time within which you will complete the correction. Your written notification should be addressed to:

Yvette Johnson, Compliance Officer
Food and Drug Administration
Philadelphia District
Central Region
US Custom House, Room 900
200 Chestnut Street
Philadelphia, PA 19106

If you have questions regarding any issues in this letter, please contact Ms. Yvette Johnson via email at Yvette.Johnson@fda.hhs.gov or by phone at 215-717-3077.

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

[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 FDCA (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 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.