Leiter's Compounding 4/14/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
San Francisco District
Pacific Region
1431 Harbor Bay Parkway
Alameda, CA 94502-7070

Telephone: 510-337-6700
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WARNING LETTER

Via United Parcel Service
Delivery Signature Requested

April 14, 2015

Dr. Charles W. Leiter, CEO
Leiter's Cambrian Park Drugs, Inc. dba Leiter's Compounding
1700 Park Ave
San Jose, CA 95126-2033

Dear Mr. Leiter:

From October 22, 2013 to November 5, 2013, and from February 18, 2014 to March 6, 2014, U.S. Food and Drug Administration (FDA) investigators conducted two inspections of your facility located at Leiter's Cambrian Park Drugs, Inc., 1700 Park Ave, San Jose, CA 95126-2033.

During the inspections, the investigators noted your firm was not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. Investigators also noted that your firm produces domperidone drug 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, and it 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 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, investigators observed that although product that failed sterility testing was rejected, an appropriate investigation was not conducted to determine the possible cause of the contamination and the necessary steps to prevent recurrence. They also observed an operator in the cleanroom who was wearing eye cosmetics (i.e., eye lash extensions) without eye protection and with

exposed skin, while filling injectable drug products. FDA issued two Form FDA-483s to your firm, one on November 5, 2013 and one on March 6, 2014, both for the location at 1700 Park Avenue. We understand that you are no longer compounding drug products at this location.

Based on these inspections, it appears you have produced drugs that violate the FDCA.

FDA acknowledges that on January 31, 2014, Leiter's Cambrian Park Drugs, Inc. registered its facility located at 17 Great Oaks Blvd, San Jose, CA 95119-1359 with FDA as an outsourcing facility under section 503B of the FDCA, and re-registered this facility on January 26, 2015. This letter addresses our inspections of your 1700 Park Avenue location only, and does not address the inspection of Leiter's 503B facility in September-October 2014.

A. Compounded Drugs Under the FDCA

At the time FDA inspected your facility in November, 2013, there were conflicting judicial decisions regarding the applicability of section 503A of the FDCA [21 U.S.C. § 353a], which exempts compounded drugs from several key statutory requirements if certain conditions are met.[1] Because your firm was in the Ninth Circuit, at the time of this inspection, FDA applied the enforcement policy articulated in Compliance Policy Guide 460.200 ["Pharmacy Compounding"], issued by FDA on May 29, 2002, [see Notice of Availability, 67 Fed. Reg. 39, 409 (June 7, 2002)] to your compounding of human drugs. The CPG identified a non-exhaustive list of factors for the FDA to consider in deciding whether to initiate an enforcement action with respect to the compounding of human drugs. Receipt of valid prescriptions for individually-identified patients prior to distribution of compounded drugs was relevant for both section 503A of the FDCA and the agency's Compliance Policy Guide 460.200 on Pharmacy Compounding (CPG) (2002), which was then in effect (CPG) (2002).[2]

Subsequent to the initial FDA inspection your facility, Congress passed and the President signed into law the Compounding Quality Act (CQA)[3], which amended FDCA section 503A by eliminating the advertising restrictions that had been the basis for conflicting judicial decisions. The CQA otherwise left section 503A intact, and so clarified that the remainder of section 503A, is applicable in every federal judicial circuit, including the requirement of valid prescriptions for individually identified patients.

During the FDA inspections, investigators observed that your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce. Based on this factor alone, those drugs did not qualify for the agency's exercise of enforcement discretion set forth in the CPG[4] and are not entitled to the statutory exemptions for compounded drugs described in section 503A of the FDCA. In addition, under the CPG, when determining whether to initiate enforcement action, FDA considered whether a firm compounded finished drugs from bulk active ingredients that were not components of FDA-approved drugs without an FDA sanctioned investigational new drug application. Because domperidone was not a component of an FDA-approved human drug, your compounded drugs containing domperidone would not qualify for the exercise of enforcement discretion set forth in the CPG. Further, the exemptions provided by section 503A(a) of the FDCA do not apply to compounded drug products containing domperidone because domperidone is not the subject of an applicable USP or NF monograph, is not a component of an FDA-approved human drug under section 503A(b)(1)(A)(i) of the FDCA, and it does not appear on a list of bulk drug substances developed by the Secretary under section 503A(b)(1)(A)(i)(III) of the FDCA.

Accordingly, the drugs you compounded without valid prescriptions for individually identified patients and any drug products you compounded using domperidone, are not entitled to the exemptions in section 503A.[5]

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.[6]

B. Violations of the FDCA

Because the drug products your firm manufactured and distributed without valid prescriptions for individually-identified patients and the domperidone products you manufactured 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) [21 U.S.C. §§ 355(a) and 352(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) [21 U.S.C. § 351(a)(2)(A)] of the FDCA. 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 Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (CFR), Parts 210 and 211. FDA investigators 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 [21 U.S.C. § 351(a)(2)(B)].

Unapproved New Drug Products

You do not have any FDA-approved applications on file for the drug products for which you have not obtained valid prescriptions for individually-identified patients or for the domperidone products you manufacture.[7] Under sections 301(d) [21 U.S.C. § 331(d)] and 505(a) of the FDCA [21 U.S.C § 355(a)] 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

Additionally, because the domperidone products and the drug products for which you have not obtained valid prescriptions for individually-identified patients are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners, adequate directions cannot be written for them 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 sections 301(a) of the FDCA [21 U.S.C. § 331(a)]. It is also 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.

Adulteration Charges

Additionally, FDA investigators noted that your sterile drug products 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 an operator in the cleanroom who was wearing eye cosmetics (i.e., eye lash extensions) without eye protection and with exposed skin, while filling injectable drug products.

FDA investigators 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 monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

3. 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)).

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

5. Your firm failed to thoroughly 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).

6. 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)).

Under section 301(a) of the FDCA the 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

As noted above, your firm manufactured and distributed a portion of drugs without valid prescriptions for individually-identified patients, and the manufacture of such drugs is subject to FDA's drug CGMP regulations (21 CFR 210 and 211). During the inspections of your facility from October 22, 2013 to November 5, 2013, and from February 18, 2014, to March 6, 2014, investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. During a teleconference on January 17, 2014, and in your firm's response letters dated November 25, 2013, January 24, 2014, and March 26, 2014, to the observations documented in the Form FDA 483s, you agreed to address the observations and update your firm's Standard Operating Procedures accordingly. Your firm's planned corrective actions, as documented in your response letters, did not meet the minimum requirements of 21 CFR Parts 210 and 211. However, FDA acknowledges that you have discontinued compounding operations at this facility. Therefore, we will not further address the deficiencies in your corrective actions in this letter.

FDA strongly recommends that if you decide to resume production of sterile drugs in this facility in the future, your management first 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 and design. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation.

Before resuming such operations, you should fully implement corrections that meet the minimum requirements of 21 CFR Part 211, in order to provide assurance that such human drug products produced by you firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

D. Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations existing 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 and FDA regulations.

If you decide to resume operations at this facility, 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 may re-inspect to verify corrective actions have been completed.

Within fifteen working days of receipt of this letter, please notify this office in writing if you have taken any specific steps to correct violations or you may confirm that you do not intend to resume production of sterile drugs at this facility. If you intend to resume production of sterile drugs at this facility in the future, 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. In addition to taking appropriate corrective actions, you should notify this office prior to resuming production of any sterile drugs at the facility located at 1700 Park Ave. Please address your reply to:

Lawton Lum
Director, Compliance Branch
U.S. Food and Drug Administration
San Francisco District
1431 Harbor Bay Parkway
Alameda, CA 94502

If you have any questions with regard to this letter, please feel free to contact Compliance Officer Russell A. Campbell at (510) 337-6861 or email at **russella.campbell@fda.hhs.gov**.

Sincerely,
/S/
Kathleen M. Lewis, J.D.
District Director
San Francisco District

cc:
Virginia Herold, Executive Officer
California State Board of Pharmacy
1625 N Market Street
Sacramento, CA 95834