Inspections, Compliance, Enforcement, and Criminal Investigations

Lowlite Investments, Inc. D/B/A Olympia Pharmacy 2/18/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Florida District
555 Winderley Place, Suite 200
Maitland, Florida 32751

Telephone: 407-475-4700
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VIA UPS
w/ DELIVERY CONFIRMATION

WARNING LETTER
FLA-14-04
February 18, 2014

Marco Loleit, CEO
Lowlite Investments, Inc., D/B/A Olympia Pharmacy
6700 Conroy Windermere Rd, Suite 140
Orlando, FL 32835-3500

Dear Mr. Loleit:

From March 4 to March 21, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility at 6700 Conroy Windermere Rd, Suite 140, Orlando, FL 32835. 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 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, nor does it appear on a list developed by the Secretary under 503A(b)(1)(A)(i)(III). In addition, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. All sterile products produced before March 27, 2013, were recalled as a result of these observations. These observations were noted on a Form FDA 483, issued on March 21, 2013.

During teleconferences with your firm on May 9 and May 16, 2013, we expressed our concerns about multiple observations made during our inspection of your firm. For example, we observed personnel with torn gloves and exposed skin reaching over and touching uncapped vials containing sterile drug products and container-closures during aseptic filling and stoppering operations. We also observed personnel opening a bag of vial stoppers onto the non-sterile work surface of an ISO-5 area and transferring in-process sterile products to the lyophilizer without ISO-5 protection. Furthermore, your firm used only non-sterile **(b)(4)** solutions to disinfect ISO-5 areas; no sporicidal agents were used. In addition, your firm did not routinely disinfect equipment or supplies used during aseptic processing.

Based on this inspection, it appears that you are producing drugs that violate the Federal Food, Drug, and Cosmetic Act (FDCA).

A. Compounded Drugs Under the FDCA

At the time FDA inspected your facility, 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] Nevertheless, 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.[2] During the FDA inspection, investigators observed that your firm does not

receive valid prescriptions for individually-identified patients for a portion of the drug products you produce. Based on this factor alone, those drugs were not entitled to the statutory exemptions for compounded drugs described in section 503A of the FDCA and did not qualify for the agency's exercise of enforcement discretion set forth in the CPG.[3]

In addition, under the CPG, when determining whether enforcement discretion is appropriate, 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 subsection (a) of 503A did not apply to compounded drug products containing domperidone because domperidone was not the subject of an applicable USP or NF monograph, was not a component of an FDA-approved human drug, and it did not appear on a list of bulk drug substances that may be used for compounding developed by the Secretary [21 U.S.C. § 353a(b)(1)(A)(i)(I)-(III)].

Since FDA inspected your facility, Congress enacted and the President signed into law the Compounding Quality Act (CQA)[4], 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 the requirements in section 503A are applicable in every federal judicial circuit, including the requirement of valid prescriptions for individually identified patients, and the requirement to compound drug products using bulk drug substances that are the subject of an applicable USP or NF monograph or are a component of an FDA-approved drug or that appear on a list developed by the Secretary under 503A(b)(1)(A)(i)(III). Accordingly, the drugs you compound without valid prescriptions for individually identified patients and the drug products you compound with domperidone, which is not the subject of an applicable USP or NF monograph, not a component of an FDA-approved human drug, and did not appear on a list developed by the secretary under 503A(b)(1)(A)(i)(III), 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 that you manufacture and distribute without valid prescriptions for individually-identified patients 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. Furthermore, the domperidone products you produce are misbranded drugs under section 502(f)(1) [21 U.S.C. § 352(f)(1)] of the FDCA.

In addition, your sterile drug products are 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. As such, the sterile products you manufacture are 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 drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs is also 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 such drug product(s) 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.[7] Under sections 301(d) and 505(a) of the FDCA [21 U.S.C. §§ 331(d) and 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 [21 U.S.C. § 355] 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

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 [21 U.S.C. § 352(f)(1)], 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 of the components used to make the drug 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 [21 U.S.C. § 351(a)(2)(A)]. For example, during aseptic filling and stoppering operations, personnel with torn gloves and exposed skinwere observed reaching over and touching uncapped vials containing sterile drug products and container-closures. Personnel were also observed opening a bag of vial stoppers onto the non-sterile work surface of the ISO- 5 area and transferring in-process sterile products to the lyophilizer without ISO 5 protection. Additionally, non-sterile **(b)(4)** solutions were used to disinfect the ISO-5 areas, and no sporicidal agents were used and the equipment or supplies used during aseptic processing were not routinely disinfected.

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 [21 U.S.C. § 351(a)(2)(B)]. 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 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)].

3. Your firm does not have, for each batch of drug product purporting to be sterile and/or pyrogen-free, an 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 products from contamination [21 CFR 211.28(a)].

5. Your firm failed to establish an adequate system for cleaning and disinfecting the room and equipment to product aseptic conditions [21 CFR 211.42(c)(10)(v)].

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

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 of the components used to make the drug and results in the drug being adulterated.

C. Corrective Actions

In your response to the Form FDA 483, you referenced your purported compliance with United States Pharmacopeia (USP)-National Formulary (NF) General Chapter <797> Pharmaceutical Compounding--Sterile Preparations. However, as noted above, your firm has manufactured and distributed drugs without valid prescriptions for individually-identified patients. As stated above, your manufacture of such drugs is subject to FDA's drug CGMP regulations, 21 C.F.R. Parts 210 and 211.

Your firm's planned corrections do not meet the minimum requirements of 21 CFR Part 211, and there is no assurance that these drug product(s) produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity. To address this issue, and also to ensure compliance with section 501(a)(2)(A), FDA strongly recommends that your management 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.

In addition, you should correct the violations of FDCA sections 502 and 505 noted above.

D. Conclusion

Please note that 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 and 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. 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 notification should be addressed to:

Andrea Norwood, Compliance Officer
FDA Florida District Office
U.S. Food and Drug Administration
555 Winderley Place, Suite 200
Maitland, FL 32751

If you have questions regarding any issues in this letter, please contact our office at 407-475-4700.

Sincerely,
/S/
Elizabeth W. Ormond
Acting Director, Florida District

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[1] *Compare Western States Med. Ctr. v. Shalala*, 238 F.3d 1090 (9th Cir. 2001) *with Medical Ctr. Pharm. v. Mukasey*, 536 F.3d 383 (5th Cir. 2008).
[2] The CPG set forth a non-exhaustive list of factors that FDA considered in determining whether to take enforcement action when the scope and nature of a pharmacy's activities raised concerns. This CPG has been withdrawn in light of new legislation. See below.
[3] *See* 21 U.S.C. § 353a(a) (granting compounded drugs statutory exemptions if, among other things, "the drug product is compounded for an identified individual patient based on the . . . receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient . . . ."); CPG at 2 ("FDA recognizes that pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of human drugs upon receipt of a valid prescription for an individually-identified patient from a licensed practitioner. This traditional activity is not the subject of this guidance.").
[4] Drug Quality and Security Act, Public Law 113-54, 127 Stat. 587 (Nov. 27, 2013).
[5]The CQA contains a number of other provisions, including new exemptions and requirements for compounders seeking to operate as outsourcing facilities. A discussion of the CQA and the agency's plans to implement the new law may be found at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm.
[6] 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.
[7] 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. 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.

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