Inspections, Compliance, Enforcement, and Criminal Investigations

Lee and Company 6/6/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Dallas District
4040 North Central Expressway,
Suite 300
Dallas, TX 75204
Telephone: 214-253-5200
Facsimile: 214-253-5314

June 6, 2014

Ref: 2014-DAL-WL-08

WARNING LETTER

UPS OVERNIGHT

Dr. Warren B. Lee, President and Owner
Sunnymede Pharmacy, Inc. dba Lee and Company and Lee Pharmacy
4300 Grand Ave
Fort Smith, AR 72904-7028

Dear Dr. Lee:

Between February 19, 2013 and February 21, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Sunnymede Pharmacy, Inc., dba Lee and Company and Lee Pharmacy, located at 4300 Grand Ave, Fort Smith, AR 72904-7028. During the inspection, investigators noted that you were not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. In addition, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigators found that your firm failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 area in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk. These observations and others were noted on Form FDA 483, issued on February 21, 2013. We acknowledge receipt of your firm's response to the Form FDA 483 dated March 14, 2013.

Based on this inspection, it appears your firm is 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 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 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***

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 section 503A, including the requirement of valid prescriptions for individually-identified patients, is applicable in every federal judicial circuit. Accordingly, the drugs you compound without valid prescriptions for individually-identified patients 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 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 section 505(a) and 502(f)(1) (21 U.S.C. §§ 355(a) and 352(f)(1)] of the FDCA, respectively. 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, all 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. 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. Your marketing of these products, or other applicable products, without an approved application violates these provisions of the FDCA.

Misbranded Drug Products

Because the drug products***7*** 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 section 301 (a) of the FDCA. 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. For example, our investigators found that your firm failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 area in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

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

C. Corrective Actions

In your March 14, 2013 response to the Form FDA 483, you referenced your purported compliance with the United States Pharmacopeia (USP)-National Formulary (NF) General Chapter <797> Pharmaceutical Compounding - Sterile Preparations, and you objected to most of the findings of deficiencies in relation to your operations. As discussed 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.

FDA strongly recommends 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 your aseptic processing operations and design. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation. Your firm's planned corrections do not meet the minimum requirements of 21 CFR 211 and there is no assurance that the human drug products produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

D. Conclusion

Please note 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.

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 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 the corrective actions cannot be completed within fifteen working days, state the reason for the delay and the time frame within which the corrections will be implemented. 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. Please address your reply to Rose Ashley, Compliance Officer, at the address above.

If you have questions regarding the contents of this letter, please contact Rose Ashley at (210)-308-1407.

Sincerely,
/S/
Renaldo R. Rodriguez, Jr.
Dallas District Director

cc:
John C. Kirtley, P.D., Executive Director
Arkansas State Board of Pharmacy
322 South Main Street, Suite 600
Little Rock, AR 72201

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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 Jist 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[1].

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)J because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases.

Links on this page:

1. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm