Inspections, Compliance, Enforcement, and Criminal Investigations

Total Pharmacy Services, Inc. 2/28/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
New Orleans District
404 BNA Drive, Building 200
Suite 500
Nashville, TN 37217

UNITED PARCEL SERVICE
DELIVERY SIGNATURE REQUESTED

AMENDED
(This letter replaces Warning Letter No. 2014-NOL-12 dated February 24, 2014)

WARNING LETTER 2014-NOL-12

February 28, 2014

Peter H. Wolfe, Jr., RPh
Owner and Pharmacist-in-Charge
Total Pharmacy Services, Inc.
7806 Park Avenue
Houma, LA 70364

Dear Mr. Wolfe:

U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Total Pharmacy Services, Inc., located at 7806 Park Avenue, Houma, Louisiana, on May 13 - 22, 2013. During the inspection, the investigators noted you were not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. It was also noted 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 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. Our investigators found 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. In addition, our investigators found your operators did not sanitize components which were transferred into the ISO 5 area. Furthermore, operators were observed wearing non-sterile gowning and performing aseptic operations with their arms resting on the work surface of the ISO 5 area. These observations and others were noted on a Form FDA 483 issued to you on May 22, 2013.

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

A. Compounded Drugs Under the FDCA

Section 503A of the FDCA exempts compounded drugs from several key statutory requirements if certain conditions are met, including receipt of valid prescriptions for individually-identified patients prior to distribution of compounded drugs.[1] During the FDA inspection, investigators observed 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.[2]

In addition, 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 Drug Quality and Security Act, which contained 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, including the requirement for 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 human 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.[4]

In addition, we remind you there are a number of other conditions that must be satisfied to qualify for the exemptions in Section 503A of the FDCA.[5]

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 misbranded drugs in violation of Section 502(f)(1) [21 U.S.C. §§ 352(f)(1)] of the FDCA. 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, 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 are 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)].

Misbranded Drug Products

Because the domperidone products and 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 C.F.R. § 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 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)]. The conditions include your firm's failure 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. In addition, our investigators found your operators did not sanitize components that were transferred into the ISO 5 area. Furthermore, operators were observed wearing non-sterile gowning and performing aseptic operations with their arms resting on the work surface of the ISO 5 area.

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 ensure manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).
3. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).
4. 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)).
5. Your firm did 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)).
6. Your firm did not have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release (21 CFR 211.165(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 of the components used to make the drug and results in the drug being adulterated.

C. Corrective Actions

You failed to provide a formal response to the observations noted in the Form FDA 483. We acknowledge your written statement received on May 22, 2013, that you "will no longer engage in any non-patient-specific 'For Office Use' compounding, effective immediately," and have "no intention to engage in re-packing, manufacturing or any other business, other than the practice of pharmacy." Regardless, FDA strongly recommends that you 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.

As noted above, your firm has manufactured and distributed drugs without valid prescriptions for individually-identified patients, and the manufacture of such drugs is subject to FDA's drug CGMP regulations, 21 CFR Parts 210 and 211. 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 the drug product(s) produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

In addition, you should correct the violations of FDCA Section 502(f)(1) noted above.

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 assure that your firm complies with all requirements of federal law and FDA regulations.

You must 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 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. 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.

Please send your reply to the U.S. Food and Drug Administration, Attention: Mark Rivero, Compliance Officer, at the address above. If you have questions regarding any issues in this letter, please contact Mr. Rivero via 504-832-1290, extension 1103.

Sincerely,
/S/
Patricia K. Schafer
District Director

cc

Malcolm J. Broussard
Executive Director
Lousiana Board of Pharmacy
3388 Brentwood Drive
Baton Rouge, LA 70809-1700

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[1] While there were conflicting judicial decisions regarding the applicability of Section 503A at the time FDA inspected your facility, your firm resided in the Fifth Circuit where Section 503A of the FDCA applied. *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] *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).
[3] Drug Quality and Security Act, Public Law 113-54, 127 Stat. 587 (Nov. 27, 2013).
[4] 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]
[5] For example, Section 503A also addresses anticipatory compounding, which includes compounding (not distribution) before receipt of a valid prescription order for an individual patient; it also addresses compounding "any drug products that are essentially copies of a commercially available drug product." 21 U.S.C. § 353a(b)(1)(D). We are not addressing these conditions or any of the other conditions in Section 503A here.

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Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

Links on this page:

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