Inspections, Compliance, Enforcement, and Criminal Investigations

Medi-Fare Drug and Home Health Center 3/7/13

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Atlanta District
60 Eighth Street, NE
Atlanta, GA 30309

March 7, 2013

VIA UNITED PARCEL SERVICE

WARNING LETTER
(13-ATL-12)

Patricia Stevens, Pharm. D.
Owner and Pharmacist in Charge
Medi-Fare Drug & Home Health Center, Inc.
300 W. Pine Street
Blacksburg, SC 29702

Dear Ms. Stevens:

Between December 10, 2012, and January 18, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Medi-Fare Drug and Home Health Center, Inc., located at 300 W. Pine Street in Blacksburg, South Carolina 29702. During the inspection, the investigator noted that you were not receiving valid prescriptions for individually-identified patients for a significant number of drug products you were producing. In addition, the investigator observed serious deficiencies in your practices for producing sterile drug product, which could lead to contamination of the products, potentially putting patients at risk. These observations and others were noted on an FDA Form 483 issued on January 18, 2013. We acknowledge receipt of your firm's letter to FDA dated December 12, 2012, as well as your firm's response to the FDA Form 483 dated January 29, 2013.

On February 28, 2013, we held a teleconference with you. Among other issues discussed, we expressed our concerns related to the design of your firm's aseptic fill areas, which places sterile products at considerable risk of microbial contamination. As evidenced by photographs taken by the FDA investigator during the inspection your firm's aseptic fill area is **(b)(4)** In addition, other activities, including labeling and weighing of non-sterile ingredients, are performed in this same room where sterile product is manipulated, creating a risk of contamination.

We are aware that the South Carolina Board of Pharmacy has recently lifted a suspension of your pharmacy license to produce sterile products. During our February 28, 2013 teleconference, we informed you that you should not resume production of sterile drugs until you implement appropriate corrective actions. You stated that you did not intend to resume production of sterile drugs until appropriate corrective actions have been implemented. We expect that you will notify this office before resuming production of sterile drugs.

Based on this inspection, it appears that you are producing drugs that do not fall within the exemptions for compounded drugs described in section 503A of the Federal Food, Drug, and Cosmetic Act (FDCA) or within the agency's exercise of enforcement discretion set forth in Compliance Policy Guide 460.200 on Pharmacy Compounding (CPG) (2002).**1**

A. Compounded Drugs Under the FDCA

Currently, there are 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.**2** Nevertheless, receipt of valid prescriptions for individually-identified patients prior to distribution of compounded drugs is relevant for both section 503A of the FDCA and the agency's CPG. During the FDA inspection, the investigator observed that your firm does not receive valid prescriptions for individually-identified patients for a significant number of the drug

products you produce. Based on this factor alone, those drugs are not entitled to the statutory exemptions for compounded drugs described in section 503A of the FDCA and do not qualify for the agency's exercise of enforcement discretion set forth in the CPG.**3** In addition, we remind you that there are other conditions that must be satisfied to qualify for the exemptions in section 503A of the FDCA, as well as other factors that FDA considers in determining whether to exercise enforcement discretion under the CPG.**4**

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. In addition, because you manufacture and distribute drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs remains 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)].

B. Violations of the FDCA

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.**5** 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

Additionally, because 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)]. Because your products lack required approved applications, they are not exempt under 21 CFR § 201.115 from the requirements of section 502(f)(1) of the FDCA. 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)].

Adulteration Charges

Additionally, the FDA investigator 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 an adequate air supply filtered through high-efficiency particulate air filters under positive pressure in the aseptic processing areas (21 CFR 211.42(c)(10)(iii)).

2. Your firm failed to establish or follow appropriate written procedures 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)).

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

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

5. 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)).

6. 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)).

C. Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations that exist 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 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. Other federal agencies may take this Warning Letter into account when considering the award of contracts.

In your response to the FDA-483 dated January 29, 2013, your firm indicates plans to address our inspectional findings with certain corrective actions. In your letter, 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 manufactures and distributes a significant number 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 Parts 210 and 211. Your firm's planned corrections should meet the minimum requirements of 21 CFR Part 211 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. As part of your comprehensive assessment of your operations, you should address the design of the aseptic fill area. FDA strongly recommends that your management immediately undertake a comprehensive assessment of your manufacturing 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.

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 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. Your written reply should be addressed to:

Marie Mathews, Compliance Officer
FDA Atlanta District Office
U.S. Food and Drug Administration
60 8th Street, N.E.
Atlanta, GA 30309

If you have questions regarding any issues in this letter, please contact our office at 404-253-1279.

Sincerely,
/S/
John R. Gridley
District Director

1 The CPG sets forth a non-exhaustive list of factors that FDA considers in determining whether to take enforcement action when the scope and nature of a pharmacy's activities raise concerns. The CPG is available at: http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm[1].

2 *Compare Western States Med. Ctr. v. Shalala*, 238 F.3d 1090 (9th Cir. 2001) (holding that the solicitation and advertising prohibitions in section 503A are an impermissible regulation of commercial speech and that those provisions are unconstitutional and cannot be severed from the rest of section 503A, causing all of section 503A to be invalid); *with Medical Ctr. Pharm. v. Mukasey*, 536 F.3d 383 (5th Cir. 2008) (compounded drugs are "new drugs" and "new animal drugs" within the meaning of the FDCA and therefore are subject to regulation by the FDA.
and the advertising prohibitions in section 503A previously found to be unconstitutional can be severed from section 503A, leaving the remaining parts of that section valid and effective).

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 For example, section 503A and the CPG also address 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 because you fail to obtain valid prescriptions for individually-identified patients at any time prior to distribution of a significant number of drugs you produce.

5 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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1. http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm