Inspections, Compliance, Enforcement, and Criminal Investigations

Stewart Compounding Pharmacy 8/21/13

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Atlanta District Office
60 Eighth Street N.E.
Atlanta, GA 30309
Telephone: 404-253-1161

August 21, 2013

VIA UNITED PARCEL SERVICE

WARNING LETTER
(13-ATL-20)

Chalmas Craig Stewart, RPh
Owner and Pharmacist in Charge
Stewart Pharmaceuticals, Inc. (dba Stewart Compounding Pharmacy)
101 Broadfoot Avenue
Fayetteville, NC 28305

Dear Mr. Stewart:

From March 18 to March 25, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Stewart Pharmaceuticals, Inc. (dba Stewart Compounding Pharmacy), located at 101 Broadfoot Avenue, Fayetteville, North Carolina 28305. During the inspection, the investigators 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 investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, **(b)(4)** processing and filling of syringes are performed in the general pharmacy (unclassified) area without further sterilization. In addition, smoke studies are not performed, **(b)(4)** used to sterilize drug products were not suitable for pharmaceutical production and not properly **(b)(4)** tested, and personnel do not use sterile garments. These observations and others were noted on a Form FDA 483 issued on March 25, 2013.

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 CPO. During the FDA inspection, investigators 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***

B. Violations of the FDCA

The drug products that you manufacture and distribute without valid prescnptwns for individually-identified patients are misbranded drugs in violation of 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 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)].

Misbranded Drug Products

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)], and they are not exempt from the requirements of section 502(f)(1) of the FDCA (see, e.g., 21 CFR § 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)]. For example, **(b)(4)** processing and filling of syringes are performed in the general pharmacy (unclassified) area without further sterilization. In addition, smoke studies are not performed, **(b)(4)** used to sterilize drug products were not suitable for pharmaceutical production and not properly **(b)(4)** tested, and personnel do not use sterile garments.

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) ofthe 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 that 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 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)].

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, 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

We are aware that the North Carolina Board of Pharmacy suspended your pharmacy license to produce sterile products on March 11, 2013. In your response to the Form FDA 483 received on April 11, 2013, you indicated your plans to address our inspectional findings and described several corrective actions. Because your firm's planned corrections do not meet the minimum requirements of 21 CFR part 211, there is no assurance that the drug product(s) produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

FDA strongly recommends that if you decide to resume production of sterile drugs, your management 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. In your response to the Form FDA 483, you reference compliance with United States Pharmacopeia (USP)-National Formulary (NF) General Chapter <797> Pharmaceutical Compounding-- Sterile Preparations. As noted above, your firm has manufactured and distributed 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. Before resuming such operations, you should fully implement corrective actions that meet the minimum requirements of 21 CFR Part 211.

D. Conclusion

Please note that 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.

If you decide to resume sterile operations, 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. Other federal agencies may take this Warning Letter into account when considering the award of contracts.

In addition to taking appropriate corrective actions, you should notify this office prior to resuming production of any sterile drugs. Your notification 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

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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 ofhuman drugs upon receipt of a valid prescr iption 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.