Specialty Medicine Compounding Pharmacy, P.C. 8/31/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Detroit District
300 River Place
Suite 5900
Detroit, Ml 48207
Telephone: 313-393-8100
FAX: 313-393-8139

Warning Letter
2015-DET-19

VIA UPS

August 31, 2015

Kenny R. Walkup Jr., President
Specialty Medicine Compounding Pharmacy, P.C.
517 N. Reese Street
South Lyon, MI 48178

Dear Mr. Walkup:

From October 21 to November 5, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Specialty Medicine Compounding Pharmacy, P.C., located at 350 S. Lafayette St., South Lyon, MI 48178-1814. During the inspection, the investigators noted that you were not receiving valid prescriptions for individually-identified patients for a portion 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, gowning practices resulted in exposed skin on operators' faces. In addition,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 have been produced in an environment that poses a significant contamination risk. Also, FDA tested samples of dextrose 50% injectable produced by your firm and collected from a health care facility. FDA testing revealed mold in several of the

unopened vials tested. A Form FDA 483 was issued to your firm on November 5, 2013. FDA acknowledges receipt of your firm's response to the Form FDA 483 dated November 22, 2013, and your statement in that response that the clean room facility was shut down on October 17, 2013. Furthermore, your firm recalled certain products intended or expected to be sterile on October 19, 2013, and October 23, 2013.

Based on this inspection, it appears that you have produced 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 produced. 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 the 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

The drug products you manufacture and distribute without valid prescriptions 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 dextrose 50% injectable product was adulterated within the meaning of sections 501(a)(1) [21 U.S.C. § 351(a)(1)] and 501(b) [21 U.S.C. § 351(b)] of the FDCA and your drug products that are intended or expected to be sterile were 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 causing them to be 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 a portion of your drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs is 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 your 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[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 , 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 and results in the drug being misbranded.

Adulterated Drug Products

Additionally, FDA investigators noted that your drug products that are intended or expected to be sterile 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 noted that gowning practices result in exposed skin on operators' faces. In addition,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 also tested samples of dextrose 50% injection produced by your firm and collected from a health care facility. FDA testing revealed mold in several of the vials tested. These findings demonstrate that these drug products were adulterated within the meaning of section 501(a)(1) of the FDCA, in that they consist in whole or in part of any filthy, putrid, or decomposed substance. Under section 501(b) of the FDCA, a drug is adulterated if it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standards set forth in such compendium. The quality and purity of your dextrose injection fell below the standards set for the drug in the official USP Dextrose Injection monograph and USP General Chapter <1> "Injections." Specifically, it failed sterility testing, causing it to be adulterated under section 501(b) of the FDCA.

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

3. Your firm failed to clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(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 an adequate system for cleaning and disinfecting the room and equipment to produce aseptic conditions (21 CFR 211.42(c)(10)(v)).

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)).

7. 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)).

8. 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)).

C. Corrective Actions

We acknowledge your action on October 19, 2013, to recall a limited amount of products and on October 23, 2013, to extend the recall to all sterile products within expiry. We are also aware that the Michigan Board of Pharmacy suspended your pharmacy license on October 29, 2013, and you voluntarily surrendered your pharmacy license on April 9, 2014.

In your November 22, 2013, response to the Form FDA 483, you reference your purported compliance with United States Pharmacopeia (USP)-National Formulary (NF) General Chapter <797> Pharmaceutical Compounding-- Sterile Preparations and the standards of the Pharmacy Compounding Accreditation Board (PCAB). However, as noted above, your firm manufactured and distributed a portion of your 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).

FDA strongly recommends that if you decide to resume production of sterile drugs, 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. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation. You should fully implement corrections that meet the minimum requirements of 21 CFR 211 to provide assurance that the drug products produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

In addition, you should also correct the violations of FDCA sections 501(a)(1), 501(b), 501(a)(2)(A) and 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 ensure that your firm complies with all requirements of federal law and FDA regulations.

If you decide to resume sterile operations, 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, or you may inform us that you do not intend to resume production of sterile drugs. If you intend to resume production of sterile drugs in the future, please include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. In addition to taking appropriate corrective actions, you should notify this office prior to resuming production of any sterile drugs. 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. Please address your reply to Dr. Tina Pawlowski, Compliance Officer, at the following address.

Tina Pawlowski, Ph.D., Compliance Officer
FDA Detroit District Office
U.S. Food and Drug Administration
300 River Place, Suite 5900
Detroit, MI 48207

If you have questions regarding any issues in this letter, please contact our office at 313-393-8217.

Sincerely,
/S/
Art O. Czabaniuk
District Director
Detroit District

[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 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.

[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 and/or because they are intended to affect the structure or any function of the body. Further, they are "new drugs" within the meaning of section 201(p) [21 U.S.C. 321(p)] of the FDCA because they are not generally recognized as safe and effective for their labeled uses.