Inspections, Compliance, Enforcement, and Criminal Investigations

Grandpa's Compounding Pharmacy, Inc. 5/2/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
San Francisco District
1431 Harbor Bay Parkway
Alameda, CA 94501-7070
Telephone (510) 337-6700

Warning Letter

WL: 423162

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

May 2, 2014

Daniel R. Wills
General Business Manager
Grandpa's Compounding Pharmacy, Inc.
7563 Green Valley Road
Placerville, CA 95667-3917

Dear Mr. Wills:

Between September 3, 2013 and September 10, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Grandpa's Compounding Pharmacy, Inc., 7563 Green Valley Road, Placerville, CA 95667-3917. During the inspection, FDA's investigators were accompanied by California State Board of Pharmacy (BOP) inspectors. At that time, the 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 and flaws in the design of your aseptic processing areas, which could lead to contamination of the products, potentially putting patients at risk. For example, we observed that the air supply duct work for the cleanroom consists of, in part, a **(b)(4)** held together, in part, with duct tape. We also observed that the cleanroom contained an in-wall air conditioner bringing outside air into the room where aseptic manipulations are occurring. These items are difficult to clean and could allow for air to enter the cleanroom that has unacceptable microbial and particulate levels. Furthermore, we observed operators with exposed wrist and forearm skin engaging in aseptic manipulations. In addition, we observed that your firm uses tap water and a **(b)(4)** to clean and depyrogenate containers and closures; these are not suitable to depyrogenate the containers and closures intended for injectable drug products. Therefore, your products may be produced in an environment that poses a significant contamination risk. These observations and others were noted on a Form FDA 483, issued on September 10, 2013. We acknowledge receipt of your firm's response to the Form FDA 483 dated September 20, 2013, in which your firm stated it would cease all sterile compounding.

Based on this inspection, it appears that you are 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 (CPG) (2002).[2] During the inspection, investigators observed that 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 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

The drug products that 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 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 layperson can use these drug 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)]. Examples of these conditions include an air supply system that is composed of, in part, a **(b)(4)** held together, in part, with duct tape; an in-wall air conditioner; operators performing aseptic manipulations with exposed wrist and forearm skin; and the use of tap water and a **(b)(4)** to clean and depyrogenate containers and closures intended for injectable drug products.

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 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 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)).

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 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)).

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 California State BOP issued a Notice of Violation and Embargo Notice to your firm on September 6, 2013. Additionally, on September 10, 2013, the California State BOP issued another Embargo Notice to recall all sterile drug products due to a lack of viable sterility and endotoxin testing, ordered your firm to immediately cease and desist the compounding of injectable sterile drug products (effective until October 31, 2013), and cancelled your firm's sterile compounding license. In a letter to the BOP dated September 16, 2013 (and referenced in your response to the Form FDA 483 dated September 20, 2013), you agreed to voluntarily relinquish your State of California Sterile Compounding License (LSC 99109) to the BOP.

In your September 20, 2013 response to the Form FDA 483, you stated that you had decided at that time to no longer continue sterile compounding. In addition, you stated that your lawyer was "looking over the observations and may have a further response, but he is currently on vacation." No other responses from your firm have been received by FDA since that time. In your letter to the California State BOP dated September 16, 2013, you stated you would continue to compound products that do not require you to have the licensed sterile compounding permit, as well as all other operations as a retail pharmacy.

FDA strongly recommends that if you decide to resume production of sterile drugs, 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.

As noted above, your firm has manufactured and distributed drug products 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 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, if you resume sterile compounding, you should also 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 ensure that your firm complies with all requirements of federal law and FDA regulations.

If you decide to resume sterile drug 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 if you have taken specific steps 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. 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. In addition to taking appropriate corrective actions, you should notify this office prior to resuming production of any sterile drugs in the future. Your written reply should be addressed to:

Lawton Lum
Director, Compliance Branch
U.S. Food and Drug Administration
1431 Harbor Bay Parkway
Alameda, CA 94502

If you have questions regarding any issues in this letter, please contact Mr. Russell Campbell, Compliance Officer, at 510-337-6861.

Sincerely,
/S/

Kathleen M. Lewis, J.D.
District Director

cc:
Virginia Herold, Executive Officer
California State Board of Pharmacy
1625 N Market Street
Sacramento, CA 95834

---

[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 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.

Page Last Updated: 05/19/2014
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.