The Compounding Pharmacy of America 6/9/16

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
Telephone: (615) 366-7801
FAX: (615) 366-7802

June 9, 2016

WARNING LETTER No. 2016-NOL-08

UNITED PARCEL SERVICE
Delivery Signature Requested

Vincent Matthew Poteet, PharmD, COO
The Compounding Pharmacy of America, Inc.
6216 Highland Place Way, Suite 201
Knoxville, Tennessee 37919

Dear Dr. Poteet:

From May 12-15 and 21, 2015, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, The Compounding Pharmacy of America, Inc., located at 6216 Highland Place Way, Suite 201, Nashville, Tennessee. This inspection was conducted after receipt of a MedWatch report associated with an intrathecal product of Fentanyl 7,000 mcg and Bupivacaine 40 mg prepared by your firm.

During the inspection, 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, which put patients at risk. For example, during aseptic processing, our investigators observed technicians preparing sterile drugs in street clothes, without doning proper gowning. Furthermore, this process took place in an unclassified room with no HEPA filtration. In addition, your firm did not use a sporicidal agent as part of the disinfection program for the aseptic processing areas. Moreover, 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 issued a Form FDA 483, Inspectional Observations, to your firm on May 21, 2015. FDA acknowledges receipt of your firm's response to the Form FDA 483, dated June 26, 2015.

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

A. Compounded Drugs Under the FDCA

Section 503A of the FDCA [21 *United States Code* (USC) 353a] describes the conditions under which certain compounded human drug products qualify for exemptions from three Sections of the FDCA: compliance with current good manufacturing practices (CGMP), Section 501(a)(2)(B) of the FDCA [21 USC 351(a)(2)(B)]; labeling with adequate directions for use, Section 502(f)(1) of the FDCA [21 USC 352(f)(1)]; and FDA approval prior to marketing, Section 505 of the FDCA [21 USC 355]. Receipt of valid prescriptions for individually-identified patients is one of the conditions for the exemptions under Section 503A of the FDCA.

During the FDA inspection, the investigators observed that your firm does not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce. Accordingly, the drugs you compound without valid prescriptions for individually-identified patients are not entitled to the exemptions in Section 503A of the FDCA.

In addition, we remind you that there are other conditions which must be satisfied to qualify for the exemptions in Section 503A of the FDCA.[1]

B. Violations of the FDCA

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) of the FDCA, respectively.

In addition, 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 rendered injurious to health, causing them to be adulterated within the meaning of Section 501(a)(2)(A) of the FDCA [21 USC 351(a)(2)(A)]. Furthermore, because you manufacture and distribute a portion of your drugs without valid prescriptions for individually-identified patients, the manufacture of such drugs is also subject to FDA's CGMP regulations for Finished Pharmaceuticals, Title 21, *Code of Federal Regulations* (CFR), Parts 210 and 211. The FDA investigators observed significant CGMP violations at your facility, causing your drug products to be adulterated within the meaning of Section 501(a)(2)(B) 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.**[2]** 355(a) and 331(d)], 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 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. Under Sections 505(a) and 301(d) of the FDCA [21 USC

Misbranded Drug Products

You compound drug products for which you have not obtained valid prescriptions for individually-identified patients that are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners; therefore, adequate directions for use cannot be written 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 CFR 201.115]. The introduction or delivery for introduction into interstate commerce of these products therefore violates Section 301(a) of the FDCA [21 USC 331(a)]. It is a also prohibited act under Section 301(k) of the FDCA [21 USC 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

The FDA investigators noted the drug products in your facility that were 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, during aseptic processing, our investigators observed technicians preparing sterile drugs in street clothes, without dooning proper gowning. Furthermore, this process took place in an unclassified room with no HEPA filtration. In addition, your firm did not use a sporicidal agent as part of the disinfection program for the aseptic processing areas. Moreover, 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.

The FDA investigators also observed 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 establish an adequate system for monitoring environmental conditions in aseptic processing areas [21 CFR 211.42(c)(10)(iv)].
3. Failure 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)]
4. 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)].
5. Failure to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination [21 CFR 211.28(a)].
6. 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)].
7. Your firm failed to establish and follow procedure for aseptic processing which includes temperature and humidity controls [21 CFR 211.42(c)(10)(ii)].

Under Section 301(a) of the FDCA, the introduction or delivery for introduction into interstate commerce of any drug that is adulterated is a prohibited Act. Further, it is a prohibited Act under Section 301(k) of the FDCA 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

FDA acknowledges your action on June 2, 2015, to voluntarily recall all sterile drug products distributed between November 2014 and May 2015 within expiry. FDA further acknowledges receipt of your response dated June 26, 2015, to the Form FDA 483, Inspection Observation, in which you state that you have "ceased the practice of 'office use' compounding…and now require a patient-specific prescription for all sterile and non-sterile compounded medications." In addition, you referenced your purported compliance with the United States Pharmacopeia (USP) General Chapter <797> on Pharmaceutical Compounding Sterile Preparations. However, as discussed above, if you continue to manufacture and distribute drugs without valid prescriptions for individually-identified patients, the manufacture of such drugs is subject to FDA's finished drug product CGMP regulations, 21 CFR 210 and 211.

In regards to your response, several of your proposed corrective actions appear to be adequate. The remaining proposed corrective actions either cannot be fully evaluated as your firm did not provide supporting documentation or appear to be defficient. For example, your response indicates that your firm has updated the cleaning and disinfecting SOP. However, the SOP does not appear to be finalized and does not provide specific guidance to carry out the cleaning/disinfecting regimen. In addition, your response states that your facility was recertified on May 15, 2015, and a video was taken to document the smoke study. However, your response did not include a copy of this documentation. Moreover, your response does not address any interim actions to be put into place prior to the full implementation of corrective actions.

FDA strongly recommends 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.

Please be aware that Section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether the drugs are compounded and distributed after receipt of a valid prescription for an individually-identified patient. You must correct all insanitary conditions at your firm.

In addition, should you continue to manufacture and distribute drug products without valid prescriptions for individually-identified patients, the manufacture of such drugs would be subject to FDA's drug CGMP regulations [21 CFR 210 and 211], among other requirements described above, and, before doing so, you should fully implement corrections that meet the minimum requirements of 21 CFR 211, in order 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. You should also correct the volations of FDCA Sections 505(a) and 502(f)(1).

E. 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 your firm complies with all requirements of federal law, including 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.

Within15 working days of receipt of this letter, please notify this office in writing of the specific steps 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 you cannot complete corrective actions within 15 working days, state the reason for the delay and the time frame within which you will complete the corrections.

If you have questions regarding any issues in this letter, please contact Compliance Officer Rebecca Asente via email at Rebecca.Asente@fda.hhs.gov or by phone at 504-846-6104. Please address your reply to Rebecca A. Asente, Compliance Officer, at the address above.

Sincerely,
/S/
Ruth Dixon
District Director
New Orleans District

cc:
Victor A. Poteet, PharmD, CEO
The Compounding Pharmacy of America, Inc.
6216 Highland Place Way, Suite 201
Knoxville, Tennessee 37919

Tennessee Board of Pharmacy
Tennessee Department of Health
Health Related Boards
665 Mainstream Drive
Nashville, Tennessee 37243

---

[1] 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.

[2] The specific products made by your firm are drugs within the meaning of section 201(g) of the FDCA [21 USC 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) of the FDCA because they are not generally recognized as safe and effective for their labeled uses.