Custom Compounding Center 3/16/16

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Dallas District Office
4040 North Central Expressway
Suite 300
Dallas, Texas 75204-3128

March 16, 2016

2016-DAL-WL-14

WARNING LETTER

UPS Overnight

Mark W. Shinabery, Owner/Pharmacist-in-Charge
Custom Compounding Center
11700 Kanis Road, Suite 1
Little Rock, Arkansas 72211-3745

Dear Mr. Shinabery:

From March 30, 2015 to April 9, 2015, U.S. Food and Drug Administration (FDA) Investigators conducted an inspection of your facility, Custom Compounding Center, located at 11700 Kanis Road, Little Rock, Arkansas 72211-3745. During this 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, our Investigators observed operators processing sterile drug products in ISO 5 areas with exposed neck and facial skin. Also, our Investigators observed the facility is not designed in a manner to ensure substantial pressure differentials between higher and lower air cleanliness; specifically, rooms with different classifications are not properly separated by a physical door. Furthermore, your firm failed to demonstrate through appropriate studies that the **(b)(4)** are able to provide adequate protection of the ISO 5 area in which sterile products are manufactured. Therefore, your products may be produced in an environment that poses a significant contamination risk.

FDA issued an FDA 483 to your firm on April 9, 2015. FDA acknowledges receipt of your facility's responses dated April 29, 2015, July 1, 2015, and September 23, 2015.

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

Section 503A of the FDCA [21 U.S.C. § 353a] describes the conditions under which certain compounded human drug products may 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 there are a number of 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 those drugs is subject to FDA's 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.

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] Under Sections 505(a) and 301(d) of the FDCA [21 U.S.C. §§ 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.

Misbranded Drug Products

You compound drug products for which you have not obtained valid prescriptions for individually-identified patients, which 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 U.S.C. § 331(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 and results in the drug being misbranded.

Adulterated Drug Products

The FDA Investigators noted that 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 the drug products to be adulterated under Section 501(a)(2)(A) of the FDCA [21 USC § 351(a)(2)(A)]. For example, our Investigators observed operators processing sterile drug products in ISO 5 areas with exposed facial skin. In addition, our Investigators observed the facility is not designed in a manner to ensure substantial pressure differentials between higher and lower air cleanliness, specifically rooms with different classifications are not properly separated by a physical door. Furthermore, your firm failed to demonstrate through appropriate studies that the **(b)(4)** are able to provide adequate protection of the ISO 5 area in which sterile products are manufactured. Therefore, your products may be produced in an environment that poses a significant contamination risk.

The 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 USC § 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 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)]
5. Your firm failed to ensure that each person engaged in the manufacture, processing, packing, or holding of a drug product has the education, training, and

experience, or any combination thereof, to enable that person to perform his or her assigned functions. [21 CFR 211.25(a)]

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 and results in the drug being adulterated.

D. Corrective Actions

We have reviewed your firm's planned corrective actions, as documented in your April 29, 2015, July 1, 2015, and September 23, 2015 responses to the FDA 483, Inspectional Observations, issued at the close of the inspection and determined that, although several of your corrective actions appear adequate, others are deficient. For example, you commit to recertify the hoods after **(b)(4)**. However, you do not note any interim measures in place prior to the **(b)(4)**.

FDA strongly recommends that 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.

In addition, in your response to the FDA 483 dated April 29, 2015, you committed to cease compounding of drug products for office stock and to only furnish compounded drug products upon receipt of a patient-specific prescription. You also stated that as a "traditional pharmacy," Custom Compounding Center is not required to register with the FDA or comply with CGMP. However, 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 parts 210 and 211. Furthermore, please note 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 prescription for an identified individual patient. You should correct all insanitary conditions at your firm.

In addition, you should also correct the violations of Sections 505(a) and 502(f)(1) of the FDCA, noted above.

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 that 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.

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 corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the correction will be completed.

Your firm's response to this letter should be sent to: Dallas District Office, ATTN: John W. Diehl, 4040 North Central Expressway, Suite 300, Dallas, Texas 75204.

If you have any questions about the contents of this letter, please contact John W. Diehl, Compliance Officer, at 214-253-5288.

Sincerely,
/S/
Reynaldo R. Rodriguez, Jr.
Dallas District Director

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[1] For example, Section 503A of the FDCA 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 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) of the FDCA [21 U.S.C. § 321(p)] because they are not generally recognized as safe and effective for their labeled uses.