Complete Pharmacy and Medical Solutions LLC 3/10/16

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Florida District
555 Winderley Place, Suite 200
Maitland, Florida 32751
Telephone: 407-475-4700
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VIA UPS NEXT DAY AIR
w/ DELIVERY CONFIRMATION

WARNING LETTER
FLA-16-10
March 10, 2016

Gregory G. Gaiser, RPh, DPh, President and Owner
Complete Pharmacy and Medical Solutions, LLC
5829 NW 158th St.
Miami Lakes, FL 33014

Dear Mr. Gaiser:

You registered with the U.S. Food and Drug Administration (FDA) as an outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353b] **[1]** on June 6, 2014, and again on December 31, 2015. From August 4, 2014, to August 12, 2014, FDA investigators inspected your facility, Complete Pharmacy and Medical Solutions, LLC, located at 5829 NW 158th St., Miami Lakes, FL 33014. During the inspection, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, the investigators noted that your firm did not use an effective sporicidal agent as part of the disinfection program for the clean room and the ISO-5 area. In addition, your firm did not have adequate procedures to ensure glass vials and rubber stoppers were properly sterilized and depyrogenated. Furthermore, 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 being produced. Therefore, your products may be produced in an environment that poses a significant contamination risk. In addition, the investigators observed that you failed to meet the conditions under section 503B of the FDCA necessary for drugs produced by an outsourcing facility to qualify for exemptions from certain

requirements under the FDCA. FDA issued a Form FDA 483 to your facility on August 12, 2014. FDA acknowledges receipt of your facility's responses, dated August 26, 2014 and December 12, 2014.

Based on this inspection, it appears your facility is producing drugs that violate the FDCA.

A. Compounded Drugs under the FDCA

The Drug Quality and Security Act (DQSA) was enacted on November 27, 2013. Title I of the DQSA, the Compounding Quality Act (CQA), added a new section 503B to the FDCA. Under section 503B(b), a compounder can register as an outsourcing facility with FDA. Drug products compounded by or under the direct supervision of a licensed pharmacist in an outsourcing facility can qualify for exemptions from the drug approval requirements in section 505 of the FDCA [21 U.S.C. § 355(a)], the requirement in section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] that labeling bear adequate directions for use and the Drug Supply Chain Security Act requirements in section 582 of the FDCA [21 U.S.C. § 360eee-1] if the conditions in section 503B of the FDCA are met.

An outsourcing facility, which is defined in section 503B(d)(4) of the FDCA [21 U.S.C. § 353b(d)(4)], is a facility at one geographic location or address that — (i) is engaged in the compounding of sterile drugs; (ii) has elected to register as an outsourcing facility; and (iii) complies with all of the requirements of this section. Outsourcing facilities must comply with other provisions of the FDCA, including section 501(a)(2)(B) [21 U.S.C. § 351(a)(2)(B)], regarding current good manufacturing practice (CGMP), and section 501(a)(2)(A) [21 U.S.C. § 351(a)(2)(A)], regarding insanitary conditions. Generally, CGMP requirements for the preparation of drug products are established in Title 21 of the Code of Federal Regulations (CFR) parts 210 and 211.

B. Violations of the FDCA

The investigators noted that drug products that were 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. Furthermore, 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.

In addition, the FDA investigators also observed that your facility failed to meet the conditions of section 503B. For example, during the inspection, the FDA investigators noted:

Your facility's drug products do not include a list of inactive ingredients, identified by established name and the quantity or proportion of each ingredient, either on the label or container for such drug products. Furthermore, the containers for some of your facility's drug products do not include the following information to facilitate adverse event reporting: www.fda.gov/medwatch; and 1-800-FDA-1088. [Section 503B(a)(10) of the FDCA [21 U.S.C. §353b(a)(10)]].

In addition, your facility submitted a report to FDA two months after initial registration and failed to submit a report to FDA in December 2014 identifying the drug products that you compounded during the previous 6-month period [Section 503B(b)(2) of the FDCA [21 U.S.C. §353b(b)(2)]].

Because your compounded drug products have not met all of the conditions in section 503B, they are not eligible for the exemptions under section 503B from the FDA approval requirements in section 505, the requirement under section 502(f)(1) that labeling bear adequate directions for use, and the Drug Supply Chain Security Act requirements described in section 582 of the FDCA.[2]

Specific violations are described below.

Adulterated Drug Products

The FDA investigators noted that drug products compounded 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, the investigators observed that your firm did not use an effective sporicidal agent as part of the disinfection program for the clean room and the ISO-5 area. In addition, your firm did not have adequate procedures to ensure glass vials and rubber stoppers were properly sterilized and depyrogenated. Furthermore, 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 being produced. 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 your drug product(s) to be adulterated within the meaning of 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. The 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)).

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, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product (21 CFR 211.165(a)).

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)).

6. Your firm failed to carefully examine batch labeling materials for identity and conformity to the labeling specified in the batch production records. Specifically, the firm does not exercise sufficient control over the preparation and application of labels (21 CFR 211.125 (b)).

Outsourcing facilities must comply with CGMP requirements under section 501(a)(2)(B) of the FDCA. FDA's regulations regarding CGMP requirements for the preparation of drug products have been established in 21 CFR parts 210 and 211. FDA intends to promulgate more specific CGMP regulations for outsourcing facilities. FDA has issued draft guidance, *Current Good Manufacturing Practice — Interim Guidance for Human Drug Compounding Outsourcing Facilities under Section 503B of the FD&C Act*. This draft guidance, when finalized, will describe FDA's expectations regarding outsourcing facilities and the CGMP requirements in 21 CFR parts 210 and 211 until more specific CGMP regulations for outsourcing facilities are promulgated.

Under section 301(a) of the FDCA [21 U.S.C. § 331(a)], 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 [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 adulterated.

Unapproved New Drug Products

You do not have any FDA-approved applications on file for your drug products.[3] Under sections 301(d) and 505(a) of the FDCA [21 U.S.C. §§ 331(d) and 355(a)], a new drug may not be introduced 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.

Misbranded Drug Products

You compound drug products 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. 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 misbranded.

Failure to Report Drugs

As noted above, your facility failed to submit a report to FDA in December 2014 identifying the drug products that you compounded during the previous 6-month

period. (Section 503B(b)(2) of the FDCA [21 U.S.C. § 353b(b)(2)]). The failure to report drugs by an entity that is registered with FDA in accordance with section 503B(b) is a prohibited act under section 301(ccc)(3) of the FDCA [21 U.S.C. § 331(ccc)(3)].

C. Corrective Actions

In your August 26, 2014 and December 12, 2015 responses to the Form FDA 483 issued at the close of FDA's inspection of your facility, you describe certain corrective actions taken in response to the Form FDA 483 observations. Although several of your corrective actions appear adequate, others are deficient. For example, your response addressing the observation for the inadequate depyrogenation of glassware use in aseptic operations did not include scientific justification to demonstrate that the newly implemented depyrogenation procedure using **(b)(4)** will effectively remove endotoxins. In addition, your firm's viable air particle monitoring program does not include active air monitoring. Moreover, we cannot evaluate your response addressing the inadequate inspection of finished products because you did not provide adequate documentation that you have successfully implemented the corrective actions, such as revised standard operating procedures or any other supporting documentation.

We acknowledge your revised SOP addressing the observed failure to meet 503B conditions, specifically, to include a list of active ingredients on the immediate drug container label or the secondary packaging label, and inactive ingredients as well as information to facilitate adverse event reporting on the containers for your facility's drug products.

In addition to the issues discussed above, you should note that CGMP requires the implementation of quality oversight and controls over the manufacture of drugs, including the safety of raw materials, materials used in drug manufacturing, and finished drug products. *See* section 501 of the FDCA, as amended by the Food and Drug Administration Safety and Innovation Act (Pub.L. 112-144, Title VII, section 711). We note that you have chosen to hire contract testing laboratories to perform some of the required testing of your finished drug products. If you choose to contract with a laboratory to perform some functions required by CGMP, it is essential that you select a qualified contractor and that you maintain sufficient oversight of the contractor's operations to ensure that it is fully CGMP compliant. Regardless of whether you rely on a contract facility, you are responsible for assuring that drugs you introduce into interstate commerce are neither adulterated nor misbranded. [*See* 21 CFR 210.1(b), 21 CFR 200.10(b).]

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. FDA intends to re-inspect your facility to verify corrective actions have been completed.

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. 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 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 completed. Your written notification should refer to the Warning Letter Number above (FLA-16-10). Please address your reply to Andrea Norwood, Compliance Officer, at the address above.

If you have questions regarding the contents of this letter, please contact Andrea Norwood at 407-475-4724.

Sincerely,
/S/
Susan M. Turcovski
District Director
Florida District

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[1] *See* Pub. L. No. 113-54, § 102(a), 127 Stat. 587, 587-588 (2013).

[2] See, e.g., section 503B(a)(11) of the FDCA [21 U.S.C. § 353b(a)(11)].

[3] 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.