Inspections, Compliance, Enforcement, and Criminal Investigations

Brookfield Prescription Center Inc. dba MD Custom Rx 5/2/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Minneapolis District Office
Central Region
250 Marquette Avenue, Suite 600
Minneapolis, MN 55401
Telephone: (612) 334-4100
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May 2, 2014

WARNING LETTER

Via UPS Overnight Delivery

Refer to MIN 14 - 19

Monica M. Zatarski, Pharm.D.
President and Owner
Brookfield Prescription Center Inc. dba MD Custom Rx
19035 W. Capitol Drive, Suite 102
Brookfield, Wisconsin 53045

Dear Dr. Zatarski:

From December 3 - 10, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Brookfield Prescription Center Inc. dba MD Custom Rx, at 19035 W. Capitol Drive, Suite 105, Brookfield, Wisconsin. 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, our investigators observed that operators failed to sanitize components that were transferred into the ISO 5 area and processed sterile drug products with exposed skin on their faces and wearing non-sterile masks. 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 issued a Form FDA 483, Inspectional Observations, to your firm on December 13, 2013. Furthermore, a sterility failure resulted in the recall of product on November 12, 2013.

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 are entitled to exemption from three sections of the FDCA: compliance with current good manufacturing practices (CGMP), section 501(a)(2)(B); labeling with adequate directions for use, section 502(f)(1); and FDA approval prior to marketing, section 505. Receipt of valid prescriptions for individually-identified patients is one of the conditions for the exemptions under section 503A.

During our inspection 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.[1]

In addition, we remind you that there are other conditions that must be satisfied to qualify for the exemptions in section 503A of the FDCA.[2]

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, 21 U.S.C. §§ 355(a) and 352(f)(1), respectively. 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 drug 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 a portion of your drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs are also subject to FDA's Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (21 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.[3] Under sections 505(a) and 301(d) of the FDCA, 21 U.S.C. § 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
Additionally, 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 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 (for example, see 21 CFR 201.115). The introduction or delivery for introduction into interstate commerce of these products therefore violates sections 301(a) of the FDCA. It is also 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 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. For example, our investigators observed that operators failed to sanitize components that were transferred into the ISO 5 area and processed sterile drug products with exposed skin on their faces and wearing non-sterile masks. 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 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 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 ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination, 21 CFR 211.28(a).

4. Your firm did 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).

5. 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).

6. Your firm failed to perform operations related to the manufacture, processing, and packing of penicillin in facilities separate from those used for other drug products for human use, 21 CFR 211.42(d).

7. Your firm did 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).

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

In your responses dated January 2 and 6, 2014, to the Form FDA 483, Inspectional Observations, issued at the close of the inspection you indicated that you discontinued production of sterile drug products at your facility effective December 30, 2013, and you also committed to implementing corrective and preventive actions compliant with United States Pharmacopeia (USP) - National Formulary (NF) General Chapter <795> Pharmaceutical Compounding--Nonsterile Preparations.

If you decide to resume production of sterile drugs, FDA strongly recommends that your management immediately undertakes 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.

As discussed above, your firm has manufactured and distributed 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. Before resuming such operations, you should fully implement corrections 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 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 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 a contract testing laboratory to perform some of the required testing of your finished drug products. **(b)(4).** 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 ensuring that drugs you introduce into interstate commerce are neither adulterated nor misbranded. See 21 CFR 210.1(b) and 21 CFR 200.10 (b).

In addition, if you resume sterile compounding, you should also correct the violations of FDCA sections 502 and 505 noted above.

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 15 working days of receipt of this letter, please notify this office in writing if you have taken any 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 notification should be addressed to Demetria Lueneburg, Compliance Officer, at the address on the letterhead. If you have questions regarding this letter please contact Ms. Lueneburg at (612) 758-7210.

Sincerely,
/S/
Michael Dutcher, DVM
Director
Minneapolis District

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[1]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/[1]PharmacyCompounding/default.htm*.
[2] 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.
[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. 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.

Links on this page:

1. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm