VIA EMAIL
Receipt Acknowledgement Requested

9/27/2024

James P. Cangelosi, President
Brookfield Medical Surgical Supply, Inc.
60 Old New Milford Road, Suite 1B
Brookfield, CT 06804-2430

Dear Mr. Cangelosi:

You registered your facility 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 January 12, 2015 and most recently, on January 2, 2024. From April 22, 2024 to May 10, 2024, FDA investigators inspected your facility, Brookfield Medical Surgical Supply, Inc., located at 60 Old New Milford Road, Suite 1B, Brookfield, CT, 06804. During the inspection, the investigators noted that drug products you produced failed to meet the conditions of section 503B of the FDCA necessary for drugs produced by an outsourcing facility to qualify for exemptions from certain provisions of the FDCA. In addition, the investigators noted deficiencies in your practices for producing drug products intended or expected to be sterile, which put patients at risk.

FDA issued a Form FDA 483 to your facility on May 10, 2024. FDA acknowledges receipt of your facility's responses, dated May 31, 2024 and August 31, 2024. Based on this inspection, it appears you produced drugs that violate the FDCA.

A. Compounded Drug Products under the FDCA

Under section 503B(b) of the FDCA, 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 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.[2]

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

[1] *See* Pub. L. No. 113-54, § 102(a), 127 Stat. 587, 587-588 (2013).
[2] We remind you that there are conditions, other than those discussed in this letter, that must be satisfied to qualify for the exemptions in section 503B of the FDCA.

other applicable 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.

In addition, for a compounded drug product to qualify for the exemptions under section 503B, the labeling of the drug must include certain information (section 503B(a)(10) of the FDCA [21 U.S.C. §353b(a)(10)]).

B. Failure to Meet the Conditions of Section 503B

During the inspection, FDA investigators noted that drug products produced by your facility failed to meet the conditions of section 503B. For example, the investigators noted that some of your facility's drug products, such as Betamethasone Sodium Phosphate 3mL single use vial 6mg/mL Injection, Methylprednisolone Acetate Suspension 5mL single use vial 40mg/mL Injection, Morphine Sulfate Solution 10mL single use vial 25mg/mL Injection, and Triamcinolone Acetonide Suspension 3mL single use vial 40mg/mL Injection, did not include the following information on the container: 1) information to facilitate adverse event reporting: www.fda.gov/medwatch and 1-800-FDA-1088 as required by Section 503B(a)(10)(B)(ii) of the FDCA and 2) directions for use, including, as appropriate, dosage and administration as required by Section 503B(a)(10)(B)(iii) of the FDCA.

Additionally, the investigators collected evidence indicating that some of your facility's drug products, such as Betamethasone Sodium Phosphate 3mL single use vial 6mg/mL Injection, Methylprednisolone Acetate Suspension 5mL single use vial 40mg/mL Injection, Morphine Sulfate Solution 10mL single use vial 25mg/mL Injection, and Triamcinolone Acetonide Suspension 3mL single use vial 40mg/mL Injection, did not include the following information on the label: inactive ingredients, identified by established name as required by Section 503B(a)(10)(A)(iii)(X) of the FDCA.

Because your compounded drug products have not met all of the conditions of section 503B, they are not eligible for the exemptions in that section from the FDA approval requirements of 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.

Specific violations are described below.

C. Violations of the FDCA

Adulterated Drug Products

FDA investigators noted that drug products 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:

1. Your firm failed to perform adequate smoke studies under dynamic conditions to demonstrate that the manipulations performed by the operator do not interfere with the unidirectional airflow within the ISO 5 area. Specifically, your firm's dynamic smoke studies were conducted using an inadequate quantity of generated smoke, which does not allow for an adequate determination that the manipulations performed by the operator do not interfere with the unidirectional airflow over and away from the product during manufacturing operations. Therefore, your products intended to be sterile are produced in an environment that may not provide adequate protection against the risk of contamination.

2. Your firm failed to appropriately clean equipment located in the ISO 5 area. Specifically, your firm failed to perform a (b) (4) clean after a sample taken from a settle air plate in the ISO 5 area had 1 CFU of an objectionable organism identified. Your firm's procedure requires a (b) (4) clean when environmental monitoring excursions involve objectionable organisms being recovered in the ISO 5, ISO 7, or ISO 8 areas; however, only a standard cleaning was performed.

FDA investigators also noted CGMP violations at your facility, that caused 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 follow procedures designed to prevent microbiological contamination of drug products purporting to be sterile (21 CFR 211.113(b)).

2. Your firm failed to follow written procedures for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product (21 CFR 211.67(b)).

3. Your firm failed to establish adequate written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess (21 CFR 211.100(a)).

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 a revised draft guidance, *Current Good Manufacturing Practice — 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 drug products that you compound.[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. 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 that are intended for conditions 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.[4] The introduction or delivery for introduction into interstate commerce of these products therefore violates section 301(a) of the FDCA. Further, 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 and results in the drug being misbranded.

D. Corrective Actions

We have reviewed your firm's responses to the Form FDA 483.

Some of your corrective actions appear adequate; however, we cannot fully evaluate the adequacy of the following corrective actions described in your responses because you did not include sufficient information or supporting documentation:

1. You state in your May 31, 2024 and August 31, 2024 responses that a vendor will be sourced to perform a smoke study and acknowledge that this is a repeat observation. However, you did not provide a timeline for when smoke studies will be completed and for when reports of the testing and smoke study videos will be provided.

2. You state that procedures will be reviewed with all employees on the proper time to perform a (b) (4) clean, but it is unclear if a (b) (4) clean was ever performed as a corrective action.

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*

[3] The specific products made by your firm are drugs within the meaning of section 201(g) of the FDCA [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.

[4] Your compounded drug products are not exempted from the requirements of section 502(f)(1) of the FDCA by regulations issued by the FDA (see, e.g., 21 CFR 201.115).

section 501 of the FDCA. 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 produce are neither adulterated nor misbranded. [*See* 21 CFR 210.1(b), 21 CFR 200.10(b).]

In addition, regarding observations related to the conditions of section 503B of the FDCA, some of your corrective actions appear adequate: you state that "a new procedure has been implemented to apply a finished product label on the outside of each container prior to shipment." However, you have not addressed your facility's failure to include the following information on the label of your facility's drug product: inactive ingredients identified by established name.

Should you continue to compound and distribute drug products that do not meet the conditions of section 503B, the compounding and distribution of your drugs would be subject to the new drug approval requirement, the requirement to label drug products with adequate directions for use, and the Drug Supply Chain Security Act requirements.

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 any violations 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.

Within thirty (30) working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to address any violations. Please include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. This letter notifies you of our concerns and provides you an opportunity to address them. If you believe your products are not in violation of the FDCA, include your reasoning and any supporting information for our consideration. If you cannot completely address this matter within thirty (30) working days, state the reason for the delay and the time within which you will do so.

All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. If you have questions regarding the contents of this letter, please contact compoundinginspections@fda.hhs.gov.

Sincerely,

Craig W. Swanson -S

Digitally signed by Craig W. Swanson -S
Date: 2024.09.27 13:53:03 -04'00'

Craig Swanson
Deputy Program Division Director
US Food and Drug Administration
Office of Pharmaceutical Quality Operations Division I