FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS

VIA EMAIL CONFIRMED DELIVERY

April 25, 2024

Marcy Bliss, Chief Executive Officer
Wedgewood Pharmacy
405 Heron Drive, Suite 200
Swedesboro, NJ 08085
mbliss@wedgewoodpharmacy.com

Dear Ms. Bliss:

You registered your facility with the U.S. Food and Drug Administration as an outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353b][1] on January 31, 2014, and most recently on December 8, 2023. From November 1, 2023, to November 17, 2023, FDA investigators inspected your facility, Wedgewood Connect, LLC located at 17 Great Oaks Blvd., San Jose, CA 9511. 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.

The FDA issued a Form FDA 483 to your facility on November 17, 2023. The FDA acknowledges receipt of your facility's response, dated December 7, 2023. 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 the 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]

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[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.

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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 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 Moxifloxacin 1mg/ml in Balanced Salt Solution, did not include the following information on the label: the name of the outsourcing facility as required by section 503B(a)(10)(A)(ii) 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:

Your firm failed to perform adequate smoke studies under dynamic conditions to demonstrate unidirectional airflow within the ISO 5 area. Therefore, your products intended to be sterile are produced in an environment that may not provide adequate protection against the risk of contamination.

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 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 acceptance criteria for the sampling and testing conducted by the quality control unit that are adequate to assure that batches of drug products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release (21 CFR 211.165(d)).

3. Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed (21 CFR 211.192).

4. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

5. 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)).

6. Your firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products (21 CFR 211.22(a)).

7. 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)).

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. The FDA intends to promulgate more specific CGMP regulations for outsourcing facilities. The 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 the 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 facility's response to the Form FDA 483. Some of your corrective actions appear adequate; however, we are unable to fully evaluate some of your corrective actions due to lack of adequate supporting documentation:

1. Your response to surface sampling locations within your ISO 5 areas indicated plans to perform Environmental Monitoring Performance Qualification (EMPQ) for the ISO 5 areas by the end of December 2023, but no data for these studies has been provided.

2. Your firm committed to performing disinfectant efficacy studies in December 2023, with expected results in January 2024, but we have not received these studies. It is important to note that the agency does not object to an outsourcing

[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).

facility relying on published literature and supplier certificates of analysis when initially determining the effectiveness of agents used to clean and disinfect. Beyond initial operations, the suitability and efficacy of cleaning agents and cleaning methods should be evaluated, and the cleaning agent's compatibility with applicable work surfaces should be assessed.

3. Your firm conveyed commitment to enhancing your visual inspection training program with the obtainment of additional qualification sets and the implementation of a more rigorous detection limit when qualifying personnel performing visual inspections. However, supporting documents were not provided, such as photos of the new test kits, purchase orders, and possible changes made to your library of defects. Additionally, wording in your SOP 9.180 Visual Inspection Qualification Version 2.0 requires further clarification. Currently, Section 9.4.7 reads, "In the event of a failing (b) (4) result, operators may repeat the test. Production should evaluate performing additional training prior to re-testing." This could be interpreted as not requiring the operators who fail the test to always repeat the test.

Some of your corrective actions appear deficient:

1. Your firm inadequately requalified your (b) (4), Equipment ID# E-0832-W. A (b) (4) tolerance for failing (b) (4) temperature and/or calibration does not ensure a state of control and does not allow for detection of potential (b) (4) in the (b) (4). Additionally, a thorough investigation of (b) (4) was lacking and processing continued despite the failure. It is important to note that the average temperature reading for a (b) (4) during a specific cycle does not represent the actual temperature measured throughout the entire sterilization cycle as was concluded in Deviation Report 23DR0059. Furthermore, your firm mentioned plans to revalidate the (b) (4) with various run cycles by mid-December 2023. However, the supporting documents have not been provided.

2. Your smoke studies do not demonstrate adequate airflow throughout the entire production process, from introduction of materials into the hood through completion of compounding. All activities, interventions, and movements performed should be done deliberately such that they do not disturb unidirectional airflow. Additionally, the dynamic conditions of one hood do not provide assurance of adequate unidirectional airflow of the other hoods, therefore, each hood needs to be independently assessed. Furthermore, your firm stated smoke studies of your entire process would be performed by mid-January 2024 for each hood; however, we have not received these studies.

3. We acknowledge receipt of your new SOP 9.200 Version 1.0 Acceptable Quality Limit (AQL) for Visual Inspection of Sterile Products. However, staff training records were not provided. Additionally, your firm did not provide an assessment of all previously distributed batches within expiry that failed to undergo an AQL for visual inspection.

4. We acknowledge your firm re-evaluating the retains of the lots associated with the complaints as well as retraining your staff on SOP 5.031 Version 5.0 Customer Complaints. However, your SOP lacks a clear definition of what comprises a "quality related event." It is unclear why your Quality team would consider particulates and discoloration in your products, which were commonly noted in the complaint reports, as "not a quality related event."

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. 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, your corrective action appears adequate: you acknowledged that "the complete company name was missing on the label" and provided a copy of the updated label.

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.

Please send your electronic reply to ORAPHARM4_Responses@FDA.HHS.GOV or mail your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV

U.S. Food & Drug Administration
19701 Fairchild Road
Irvine, California 92612-2506

Please identify your responses with the unique identifier: **CMS 679675**

If you have questions regarding the contents of this letter, please contact Andrew Haack, compliance officer by telephone at 206-340-8212 or email at Andrew.Haack@fda.hhs.gov.

Sincerely,

Lance De Souza

Lance M. De Souza
Acting Director, Division of Pharmaceutical Quality Operations IV

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