U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
OFFICE OF PHARMACEUTICAL QUALITY OPERATIONS

DATE: May 19, 2022

Case #: 630202

VIA Electronic Mail
Return Confirmation Requested

Kristopher Fishman, President & CEO
Wells Pharmacy Network, LLC
3420 Fairlane Farms Road, Suite 300
Wellington, FL 33414

Dear Mr. Fishman:

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 June 7, 2016, and most recently on November 10, 2021.

From December 1, 2020, to January 28, 2021, FDA investigators inspected your facility, Wells Pharmacy, Inc., located at 450 US Highway 51 BYP N Dyersburg, TN 38024. During the inspection, the investigators collected evidence indicating 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 products intended or expected to be sterile, which put patients at risk.

FDA issued a Form FDA 483 to your facility on January 28, 2021. FDA acknowledges receipt of your facility's response provided on February 18, 2021. 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

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

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 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, it must be compounded in an outsourcing facility that is in compliance with the requirement to submit adverse event reports to FDA "in accordance with the content and format requirements established through guidance or regulation under section 310.305 of title 21, Code of Federal Regulations (or any successor regulations)" (section 503B(a)(1) and (b)(5) of the FDCA [21 U.S.C. §353b(a)(1) and (b)(5)]).

B. Failure to Meet the Conditions of Section 503B

During the inspection, the FDA investigators collected evidence indicating that drug products produced by your facility failed to meet the conditions of section 503B. More specifically, your facility did not submit adverse event reports to FDA in accordance with the content and format requirements established through guidance or regulation under section 310.305 of title 21, Code of Federal Regulations (or any successor regulations)[3]. For example, your documented procedures for reporting adverse events do not define what constitutes an "unexpected" adverse event[4] and do not include a timeline for investigating or providing a follow-up report of an adverse event[5].

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

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[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.
[3] For more information, see, FDA's guidance, "Adverse Event Reporting for Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act," which can be found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM434188.pdf.
[4] 21 CFR 310.305(b).
[5] 21 CFR 310.305(c)(2).

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 in the ISO 7 (b) (4) rooms: gaps around the perimeter of ceiling HEPA filter screens; excess caulking on the ceiling that was not smooth or easily cleanable; and light fixtures that were not smooth or easily cleanable.

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 have buildings used in the manufacture, processing, packing, or holding of a drug product of a suitable size, construction, and location to facilitate cleaning, maintenance, and proper operations (21 CFR 211.42(a)).
2. Your firm failed to clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).
3. Your firm failed to ensure that each person responsible for supervising the manufacture, processing, packing, and holding of a drug product has the education, training, or experience, or any combination thereof, to perform assigned functions in such a manner as to provide assurance the drug product has the safety, identity, strength, quality, and purity that it purports or is represented to possess (21 CFR 211.25(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 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.[6] 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. 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 use causing them to be misbranded under section 502(f)(1) of the FDCA.[7] 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 provided on February 18, 2021.

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[6] 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.

[7] 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).

We are unable to fully evaluate some of your corrective actions due to lack of adequate supporting documentation:

1. Regarding the observed condition of the face plate of the (b) (4) pellet press (b) (4) in the ISO 7-(b) (4) (b) (4) Room, your corrective action cannot be verified based on the work order documentation provided. The work order record, dated February 10, 2021, documents service conducted on more than one pellet press. The work order record identifies the pellet presses by model number, not equipment number, and it is not clear which piece of equipment on which pellet press may have been serviced.

You did not address certain observations:

1. Regarding the cracks, ridges, and residue observed in the light shield within your ISO 7 (b) (4) rooms, your response did not address repairing the damage to the cracked light shield or residue accumulated inside of the light shield.

2. Regarding the documentation of CGMP training by your firm's management, it is unclear whether your firm will require all supervising managers to be trained in CGMPs and whether such training will be documented.

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 issues related to the conditions of section 503B of the FDCA, we have reviewed the Standard Operating Procedure (SOP) you submitted, which "describes the procedures associated with the receipt of safety information related to pharmaceuticals compounded by [Well Pharmacy, Inc.]." We note that this SOP does not appear to adequately address adverse event reporting.[8] For example:

[8] We note that Section 3 of your SOP ("References") refers to certain FDA guidance documents that were issued prior to the enactment of the DQSA. As you make corrective actions, you should consult the guidance that FDA issued after enactment of the DQSA to address adverse event reporting by outsourcing facilities under section 503B(b)(5). See FDA's Guidance for Industry, "*Adverse Event Reporting for Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*," which can be found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM434188.pdf.

1) Your SOP does not define what constitutes an "unexpected" serious adverse event;

2) Your SOP makes reference to MedWatch reporting instead of the required adverse event submission process utilizing the Safety Reporting Portal (SRP) or Electronic Submission Gateway (ESG); and
3) Your SOP does not include information regarding follow-up reports or investigation procedures, and there is no timeline for investigating or providing a follow-up report of an adverse event.

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 that 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.

Your written notification should refer to case # **630202**.

Please electronically submit your reply, on company letterhead, to Rebecca Asente, Compliance Officer, at ORAPHARM2_RESPONSES@fda.hhs.gov. In addition, please submit a signed copy of your response to Rebecca.asente@fda.hhs.gov and orapharm2actingdcb@fda.hhs.gov .

If you have questions regarding the contents of this letter, you may contact Rebecca Asente, Compliance Officer, via (504) 846-6104 or Rebecca.asente@fda.hhs.gov.

Sincerely,

Jose R. Lopez Martinez -S

Digitally signed by Jose R. Lopez Martinez -S
Date: 2022.05.19 14:36:20 -04'00'

Jose R. Lopez
Acting Director, Compliance Branch
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