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

VIA EMAIL CONFIRMED DELIVERY

August 26, 2022

Dana Madievsky
Owner and Pharmacist-in-Charge
Expert Compounding Pharmacy Inc.
6744 Balboa Boulevard
Lake Balboa, CA 91406
dana@expertpharmacy.org

Dear Dr. Madievsky:

From February 23 to March 4, 2022, a U.S. Food and Drug Administration investigator inspected your facility, Expert Compounding Pharmacy Inc., located at 6744 Balboa Boulevard, Lake Balboa, CA 91406. During the inspection, the investigator noted that drug products you produced failed to meet the conditions of section 503A of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353a] for exemption from certain provisions of the FDCA. In addition, the investigator noted deficiencies in your practices for producing drug products, which put patients at risk.

The FDA issued a Form FDA 483 to your firm on March 4, 2022. The FDA acknowledges receipt of your facility's response, dated March 20, 2022. Based on this inspection, it appears that you produced drug products that violate the FDCA.

A. Compounded Drug Products Under the FDCA

Section 503A of the FDCA describes the conditions under which human drug products compounded by a licensed pharmacist in a state licensed pharmacy or a Federal facility, or a licensed physician, qualify for exemptions from three sections of the FDCA: compliance with current good manufacturing practice (CGMP) (section 501(a)(2)(B)); labeling with adequate directions for use (section 502(f)(1)); and FDA approval prior to marketing (section 505) [21 U.S.C. §§ 351(a)(2)(B), 352(f)(1) and 355(a)].[1] Receipt of valid prescriptions for individually-identified patients is one of the conditions for the exemptions under section 503A.

[1] 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 503A of the FDCA.

Division of Pharmaceutical Quality Operations IV
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B. Failure to Meet the Conditions of Section 503A

During the inspection, the FDA investigator noted that drug products produced by your firm failed to meet the conditions of section 503A. For example, the investigator noted that your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced, such as your Lidocaine/Tetracaine (b) (4) Ointment.

Therefore, you compounded drug products that do not meet the conditions of section 503A and are not eligible for the exemptions in that section, including the FDA approval requirement of section 505 of the FDCA, the requirement under section 502(f)(1) of the FDCA that labeling bear adequate directions for use, and the requirement of compliance with CGMP under section 501(a)(2)(B) of the FDCA. In the remainder of this letter, we refer to your drug products that do not qualify for exemptions under section 503A as the "ineligible drug products."

Specific violations are described below.

C. Violations of the FDCA

Adulterated Drug Products

The FDA investigator noted that 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, the investigator observed that

1. You produced hazardous drugs without providing adequate cleaning of utensils to prevent cross-contamination.

2. Non-microbial contamination was observed in your production area.

Furthermore, the manufacture of the ineligible drug products is subject to the FDA's CGMP regulations, Title 21, Code of Federal Regulations (CFR), parts 210 and 211. The FDA investigator observed significant CGMP violations at your facility, causing the ineligible drug products to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA. The violations included, for example:

1. Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications and identity and strength of each active ingredient prior to release. (21 CFR 211.165(a)).

2. Laboratory controls do not include determination of conformance to appropriate written specifications for the acceptance of each lot within each shipment of components used in the manufacture, processing, packing, or holding of drug products. (21 CFR 211.160(b)).

3. The batch production and control records are deficient in that they do not include documentation of the accomplishment of each significant step in manufacturing and processing. (21 CFR 211.188(b)).

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 the ineligible drug products that you compounded.[2] 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

The ineligible drug products you compounded 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.[3] Accordingly, these ineligible drug products are misbranded under section 502(f)(1) of the FDCA. The introduction or delivery for introduction into interstate commerce of these products therefore violates section 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 and results in the drug being misbranded.

D. Corrective Actions

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

Regarding your response related to the insanitary conditions, some of your corrective actions appear adequate; however, we cannot fully evaluate the adequacy of the following corrective actions described in your response because you did not include sufficient information or supporting documentation:

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[2] 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) [21 U.S.C. 321(p)] of the FDCA because they are not generally recognized as safe and effective for their labeled uses.

[3] Your ineligible 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).

1. We acknowledge your statement "We have adopted the use of (b) (4) to deactivate contaminants," but you did not provide a retrospective review of lots already released to determine cross contamination risks.

2. We acknowledge your statement that you are implementing (b) (4) cleaning and replacing the porous boards and replacing the tiles (b) (4). However, you did not provide supporting documentation such as photos of cleaned surfaces, timelines for completion, or a description of cleaning methods and frequency of changeover. You did not provide a risk evaluation of products already released.

Please be aware that section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether drug products you compound meet the conditions of section 503A, including receipt of valid prescriptions for individually-identified patients.

In addition, regarding issues related to the conditions of section 503A of the FDCA, your corrective actions appear deficient. You did not address whether you plan to cease producing drug products without first receiving a patient-specific prescription.

Should you continue to compound and distribute drug products that do not meet the conditions of section 503A, the compounding and distribution of such drugs would be subject to the new drug approval requirement, the requirement to label drug products with adequate directions for use, and the drug CGMP regulations. Before doing so, you must comply with the requirements of section 505 and 502(f)(1) and fully implement corrections that meet the minimum requirements of the CGMP regulations.[4]

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)].

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 the FDA regulations.

[4] In this letter we do not address whether your proposed corrective actions would resolve the CGMP violations noted above.

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 in which you will do so.

Please identify your notification with unique identifier: **CMS # 640647.**

Send your electronic response to ORAPHARM4_Responses@FDA.HHS.GOV with ATTN: CDR Steven E. Porter, Jr. or mail your written response to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
U.S. Food & Drug Administration
19701 Fairchild Road
Irvine, CA 92612-2506

If you have questions regarding the contents of this letter, please contact LCDR Rumany Penn, Compliance Officer, at (949) 608-4409 or Rumany.Penn@fda.hhs.gov.

Sincerely,

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

SP:rp

cc: Anne Sodergren
Executive Officer
California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833