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

VIA SIGNATURE CONFIRMED DELIVERY

August 18, 2020

Tony E. Jones, Owner
Maple Rose Enterprises, Inc. dba Pencol Compounding Pharmacy
1325 S Colorado Boulevard, Suite B-024
Denver, Colorado 80222-3303

Dear Mr. Jones:

From February 11, 2019, to February 26, 2019, U.S. Food and Drug Administration (FDA) investigators inspected your facility, Maple Rose Enterprises, Inc., dba Pencol Compounding Pharmacy, located at 1325 S Colorado Boulevard, Suite B-024, Denver, Colorado 80222. During the inspection, the investigators 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.

FDA issued a Form FDA 483 to your firm on February 26, 2019. FDA acknowledges receipt of your facility's responses, dated May 17, 2019, August 20, 2019, and November 18, 2019. 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 investigators noted that drug products produced by your firm failed to meet the conditions of section 503A. For example, the investigators noted that your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced. The non-patient specific prescriptions included, for example, Moxifloxacin Intracameral 150mcg/0.1ml Solution, Riboflavin 0.1% Ophthalmic in BSS 0.1% Solution, and Methylcobalamin PF 25mg/ml Solution.

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 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. A dent was observed in the wall directly across from the ISO 5 biosafety cabinet workspace opening in Cleanroom (b) (4) The dent appeared to reveal white gypsum.

2. (b) (4) sprinkler heads were found in the ISO 7 buffer rooms and anteroom. The metal of the sprinkler heads appeared to be unclean.

3. The (b) (4) the anteroom and cleanroom was observed to have rust-like spots covering the handles and hinges of (b) (4) .

4. A non-sterile disinfecting agent was used to clean the ISO 5 areas.

5. (b) (4) testing was not effectively performed.

6. An operator was observed conducting aseptic manipulations in an area where the movement of "first air" in the ISO 5 area was blocked or disrupted.

7. 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 were produced in an environment that may not have provided adequate protection against the risk of contamination.

8. Your media fills were not performed under the most challenging or stressful conditions. Therefore, there is a lack of assurance that your firm can aseptically produce drug products within your facility.

9. Your firm failed to confirm that the quality of water was suitable for its intended use in the production of non-sterile drug products.

Furthermore, the manufacture of the ineligible drug products is subject to FDA's CGMP regulations, Title 21, Code of Federal Regulations (CFR), parts 210 and 211. The FDA investigators 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. Your firm failed to maintain buildings used in the manufacture, processing, packing or holding of drug products in a good state of repair (21 CFR 211.58).

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)).

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.

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.[2] Accordingly, these ineligible drug products are misbranded under section 502(f)(1) of the FDCA. 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 and results in the drug being misbranded.

D. Corrective Actions

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

[2] 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).

Regarding your responses related to the insanitary conditions, 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:

1. You stated that you painted over the dent "…to cover any possible gypsum exposure," however, you did not provide supporting documentation that the paint used was identified to be of adequate protection and coverage for the gypsum, and you did not provide photos of the repair and the work repair order.

2. You stated that the (b) (4) did not have rust on the handles and that a store-bought cleaner was used to remove the "tarnish," however, you did not provide supporting documentation, such as photos and cleaning logs.

3. You stated that your (b) (4) testing was adequate and did not make any changes; however, you did not demonstrate that the method used to conduct (b) (4) testing was properly performed and effective.

4. You stated that "Repeat training will be employed to ensure first-pass air is not interrupted during sterile operations," however, you did not provide supporting documentation such as revised procedures, training material, and training records.

5. Your submitted smoke studies did not include all equipment and supplies that are used in aseptic processing, maximum number of personnel allowed in the cleanroom, and simulation of all aseptic operations and manipulations.

You also did not address certain observations related to other insanitary conditions. For example, you have not addressed your firm's use of a non-sterile disinfecting agent to clean the ISO 5 areas. Supporting documentation such as updated procedures, replacement disinfectant utilized, training material, and training records were not submitted for review.

Regarding your response related to your media fills, your corrective actions appear deficient. For example, you stated that your "…media fill process exceeds USP <797> guidelines," however, you have not demonstrated that your media fill studies closely simulate aseptic production operations under the worst-case, most-challenging, and stressful conditions.

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 the condition on receipt of a prescription for an identified individual patient prior to compounding and distributing drug products.

Regarding issues related to the conditions of section 503A of the FDCA, some of your corrective actions appear adequate. We acknowledge your "promise to discontinue the

production of both sterile and non-sterile products for office-stock use" in the Form FDA 463a Affidavit dated February 26, 2019. We also acknowledge your written commitment in your firm's response to the Form FDA 483 to "stop office use sterile compounding," and that "as of April 1[, 2019] all prescribers who order from Pencol will have to provide patient names for sterile compounds." However, in your Form FDA 483 response you did not address the compounding of non-sterile drug products without valid prescriptions for individually-identified patients.

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.[3]

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 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, 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 correct violations. Please include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation and photographs if applicable. 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. If you cannot complete corrective actions within thirty (30) working days, state the reason for the delay and the time within which you will complete the corrections.

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
19701 Fairchild Road
Irvine, CA 92612-2506

Please identify your response with unique identifier 608378.

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

If you have questions regarding any issues in this letter, please contact CAPT Matthew R. Dionne, Compliance Officer via email at Matthew.Dionne@fda.hhs.gov or by phone at (303)-236-3064.

Sincerely,

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

SP: mrd