Kelley-Ross & Associates, Inc. dba Kelley-Ross Compounding Pharmacy 7/30/18

Division of Pharmaceutical Quality
Operations IV
19701 Fairchild Rd., Irvine, CA
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WARNING LETTER

VIA SIGNATURE CONFIRMED DELIVERY

July 30, 2018

Ryan D. Oftebro, PharmD, FACA, Principal/CEO
Kelley-Ross & Associates, Inc.
dba Kelley-Ross Compounding
805 Madison Street #702
Seattle, WA 98104-1172

Dear Dr. Oftebro:

From July 17, 2017, to August 1, 2017, U.S. Food and Drug Administration (FDA) investigators inspected your facility, Kelley-Ross & Associates, Inc., dba Kelley-Ross Compounding, located at 805 Madison Street #702, Seattle, WA 98104-1172. 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. Additionally, the investigators noted serious deficiencies in your practices for producing sterile drug products, which put patients at risk.

FDA issued a Form FDA 483 to your firm on August 1, 2017. FDA acknowledges receipt of your facility's response, dated August 21, 2017. 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.

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.

Therefore, you compounded drug products that do not meet the conditions of section 503A and are not eligible for the exemptions in that section from 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. Your firm did not disinfect materials prior to their placement in an ISO 5 classified area.

2. Your firm has classified areas with difficult to clean, particle-generating, or visibly dirty equipment. Specifically, our investigators observed residue on equipment located in ISO 7 classified areas, including **(b)(4)** HEPA filter screens and a balance used for **(b)(4)**. Additionally, cracks were noted in a glass window separating **(b)(4)** ISO 7 classified rooms.

3. 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. Furthermore, sterile drug products were produced in your ISO 5 classified work stations in **(b)(4)**, although their certifications expired in **(b)(4)**.

4. Your firm did not conduct adequate routine environmental monitoring. Specifically, you acknowledged that you could not provide documentation of personnel sampling performed on an operator who handled sterile drugs from **(b)(4)**.

5. Your firm does not properly use a sporicidal agent as part of your cleaning and disinfection program of the aseptic processing areas.

6. Non-microbial contamination, such as white residue, was found on various pieces of equipment used 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 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. Your firm does not have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient (21 CFR 211.165(a)).

2. Your firm failed to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products and to use results of such stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).

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.

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 response to the Form FDA 483. Regarding the insanitary condition observations in the Form FDA 483, some of your corrective actions appear to be adequate. However, we are unable to fully evaluate the following corrective actions due to a lack of adequate supporting documentation:

1. In your response to the ISO areas with difficult to clean, particle-generating, or visibly dirty equipment, you stated you cleaned the residue from the **(b)(4)** HEPA filter screens.

Although you provided photographs as evidence of the cleaning performed, the quality of the photographs is poor. Consequently, we cannot verify the adequacy of the cleaning performed.

2. In your response to the ISO 5 hood certification, you stated the ISO 5 hoods were scheduled for certification; however, you did not include supporting documentation to verify the hoods were tested and successfully certified. Furthermore, we remain concerned that multiple batches of sterile drug products were produced during a period in which the hoods were not certified. You did not provide a risk assessment to determine if the environment was suitable for sterile drug production and ensure the quality of sterile drug products.

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, you have not adequately addressed the compounding and distribution of drug products for office stock. As explained above, receipt of valid prescriptions for individually-identified patients is a condition of section 503A that your firm failed to meet for a portion of the drug products you produced.

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]

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)].

FDA strongly recommends that your management undertake a comprehensive assessment of operations, including facility design, procedures, personnel, processes, maintenance, materials, and systems. This review should assess your aseptic processing operations. A third-party consultant with relevant sterile drug manufacturing expertise should assist you in conducting this comprehensive evaluation.

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.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction.

Within fifteen (15) 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. 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 action within fifteen (15) working days, state the reason for the delay and the time within which you will complete the correction.

Your written notification should refer to the Warning Letter Number above (560795). Please address 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

If you have questions regarding the contents of this letter, please contact Lance De Souza, Compliance Officer via email at lance.desouza@fda.hhs.gov or by phone at 510-337-6873 and reference unique identifier **560795.**

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

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