WARNING LETTER

Auro Pharmacies, Inc., dba Central Drugs Compounding Pharmacy

MARCS-CMS 608369 — JUNE 03, 2020

Delivery Method:

VIA UPS

Product:

Drugs

Recipient:

Nayan Patel, Pharm.D.

President

Auro Pharmacies, Inc., dba Central Drugs Compounding Pharmacy

520 W. La Habra Blvd.
La Habra, CA 90631-5308
United States

Issuing Office:

Division of Pharmaceutical Quality Operations IV

United States

WARNING LETTER

June 3, 2020

Dear Dr. Patel:

From July 9, 2018, to August 2, 2018, U.S. Food and Drug Administration (FDA) investigators inspected your facility, Auro Pharmacies, Inc., dba Central Drugs Compounding Pharmacy, located at 520 W. La Habra Blvd., La Habra, CA 90631. 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. 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 2, 2018, and an amended Form FDA 483 on August 15, 2018. FDA acknowledges receipt of your facility's response, dated August 16, 2018. FDA acknowledges that on August 16, 2018, your firm voluntarily ceased sterile production and on August 21, 2018, voluntarily recalled

all drug products intended to be sterile within expiry. 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, FDA investigators noted that drug products produced by your firm failed to meet the conditions of section 503A. For example, investigators noted your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced. For example, your firm did not receive valid prescriptions for individually-identified patients for the following non-sterile drug products: Lidocaine/Tetracaine TE (Plasticized) 23%/7% Gel, Lidocaine/Prilocaine/Phenylephrine TL 10/10/1% Gel and BLT 20/6/4% TL Gel (w/DMSO).

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:

1. The FDA investigators observed vermin in your production areas. Specifically, ants were observed on the floor in your pre-gown room where non-sterile hairnets and masks are donned prior to entering the ISO 8 classified gowning room. In addition, an ant was observed on the outer surface of an FDA investigator’s sterile hood cover in the ISO 8 classified gowning room after he exited the ISO 7 classified aseptic production room. Vermin are a source of microbial contamination. Therefore, your products intended to be sterile were produced in an environment that may not provide adequate protection against the risk of contamination.

2. Your ISO 5 classified aseptic processing areas had visibly dirty equipment and surfaces. Specifically, an apparent white and brown residue was observed on the **(b)(4)** within an ISO 5 classified hood that was used in sterile drug production. In addition, an apparent brown residue was observed on the HEPA filter within an

ISO 5 classified hood that was used in sterile drug production. Residues or stains on filters generally indicate contact with a liquid. Wet HEPA filters are a suitable environment for microbial growth. When wet HEPA filters dry out they become brittle and weak, which may negatively impact their performance.

3. 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.

4. 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 provide adequate protection against the risk of contamination.

5. Your personnel conducted aseptic manipulations in an area that blocked the movement of first pass air around an open unit that was being filled with a drug product intended to be sterile. If unidirectional air over the critical surface is blocked by personnel conducting aseptic manipulations, contamination on personnel could be introduced into the critical area.

6. During viable air monitoring sampling, your firm identified microbial contamination within the ISO 5 aseptic processing area for three consecutive months. Your firm continued sterile production without implementing appropriate corrective and preventive actions.

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 conduct microbiological testing before use of each lot of a component with potential for objectionable microbiological contamination in light of its intended use (21 CFR 211.84(d)(6)).
2. Your firm failed to establish and follow a written testing program designed to assess the stability characteristics of drug products and to use results of stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).
3. 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).

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 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. We acknowledge that your firm voluntarily ceased sterile production on August 16, 2018. We also acknowledge your firm recalled all lots of drug products intended to be sterile that were within expiry due to a lack of sterility assurance on August 21, 2018. Furthermore, we acknowledge that your sterile compounding pharmacy license with the California State Board of Pharmacy expired on December 18, 2018.

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.

You did not address certain issues related to the conditions of section 503A of the FDCA. For example, you have not addressed the compounding of 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.[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)].

FDA strongly recommends that if you decide to resume production of sterile drugs, your management first undertake a comprehensive assessment of operations, including facility design, procedures, personnel, processes, maintenance, materials, and systems. In particular, 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.

If you decide to resume sterile operations, 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 if you have taken any specific steps to correct the violations cited in this letter, or you may inform us that you do not intend to resume production of sterile drugs. If you intend to resume production of sterile drugs in the future, 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 violated the FDCA, include your reasoning and any supporting information for our consideration. In addition to taking appropriate corrective actions, you should notify this office fifteen (15) days prior to resuming production of any sterile drugs in the future.

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
Irvine, California 92612-2506

Please identify your response with the unique identifier: CMS 608369

If you have questions regarding the contents of this letter, please contact Mariza Jafary, Compliance Officer at 949-608-2977 or email at Mariza.Jafary@fda.hhs.gov.

Sincerely,
/S/

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

---

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 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).

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

More Warning Letters (/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters)