October 22, 2020

Case #: 600276

VIA ELECTRONIC MAIL

Victor Crawford, CEO
Cardinal Health
Pharmaceutical Segment
7000 Cardinal Place
Dublin, Ohio 43017
victor.crawford@cardinalhealth.com

Mr. Crawford:

From October 28, 2019 to November 7, 2019, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, Abilene Nuclear LLC dba National Central Pharmacy, located at 3402 South 14th St, Abilene, Texas 79605. 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 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 November 7, 2019. FDA acknowledges receipt of your facility's response, dated November 26, 2019. Additionally, FDA acknowledges your firm "has made the business decision to exit all sterile and non-sterile drug compounding activities, effective November 25, 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.

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 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 include, for example, cefuroxime 7.5mg/ml ophthalmic solution and tricaine 20-6-4% 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 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 [21 U.S.C. § 351(a)(2)(A)]. For example:

1) The face of your pharmacy manager was observed partially exposed in the LAF Hood during the production of sterile EPI-Shugarcaine Su/F Ophth 1 ml/vial, Rx (b) (6) .

2) Your pharmacy manager failed to adequately disinfect materials transferred from the ISO 7 Cleanroom into the LAF Hood (b) (4) used in the production of sterile EPI-Shugarcaine Su/F Ophth 1 ml/vial, Rx (b) (6) . Specifically, the pharmacy's manager failed to disinfect the tray containing ampules of Lidocaine prior to entering the ISO 5 LAF hood. In addition, the pharmacy's manager failed to

[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.

disinfect a plastic container used for the (b) (4) vials of finished sterile EPI-Shugarcaine Su/F Ophth 1 ml/vial, Rx (b) (6) .

3) Your pharmacy manager failed to disinfect their gloves prior to re-entry into the ISO 5 LAF Hood (b) (4) after collecting supplies in the ISO 7 Cleanroom during the production of sterile EPI-Shugarcaine Su/F Ophth 1 ml/vial, Rx (b) (6) . In addition, the pharmacy manager failed to change or disinfect their gloves after picking paper off the floor prior to re-entry into the ISO 5 area.

4) Your pharmacy manager placed supplies in an area, which inhibited first pass airflow within the Laminar Air Flow (LAF) Hood (b) (4), during aseptic processing of EPI-Shugarcaine Su/F Ophth 1 ml/vial, Rx (b) (6) . Specifically, they placed empty/filled vials and Lidocaine 4% Pres-Free 4.5 mls ampules arranged in a manner that created a disruption in first pass airflow within the ISO 5 LAF hood.

5) Your firm's facility has (b) (4) the ISO 7 Cleanroom and unclassified area where radio-pharmaceuticals are inspected, packaged, shipped, received, and cleaned. The inspection found there was airflow between the (b) (4) and there was no HEPA filter coverage to prevent poor quality air from entering the ISO 7 Cleanroom area.

6) Your firm uses non-sterile (b) (4) as a cleaning agent within the LAF Hood # 3.

7) Your media fills were not performed on products that closely simulate aseptic production operations.

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

[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).

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, dated November 26, 2019 and February 28, 2020, to the Form FDA 483. Regarding your response 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:

You state in your February 28, 2020 response that your third-party vendor performed clean room (ISO Class 8) and laminar flow hood (ISO Class 5) smoke studies which included the clean room and the (b) (4) . You report the testing of the clean room and (b) (4) included viable and non-viable environmental monitoring all of which had passing results. You also state that smoke testing was performed on the (b) (4) and demonstrated that air from the uncontrolled areas is not entering into the clean room and is not impacting the clean room in a negative manner. However, you did not provide the reports of the testing and smoke study videos.

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.

Regarding observations related to the conditions of section 503A of the FDCA your corrective actions appear adequate: your firm "has made the business decision to exit all sterile and non-sterile drug compounding activities, effective November 25, 2019."

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.

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 since your firm is still aseptically manipulating radiopharmaceuticals your management 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.

Within thirty (30) 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. If you intend to resume sterile or non-sterile compounding operations 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 thirty (30) working days prior to resuming sterile or non-sterile compounding operations in the future.

Please electronically submit your reply, on company letterhead, to Mark W. Rivero, Compliance Officer, at ORAPHARM2_RESPONSES@fda.hhs.gov. In addition, please submit a signed copy of your response to mark.rivero@fda.hhs.gov.

If you have questions regarding the contents of this letter, you may contact Mr. Rivero via phone at (504) 846-6103 or email at mark.rivero@fda.hhs.gov.

Sincerely,

Monica R Maxwell

Digitally signed by Monica R Maxwell -S
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Date: 2020.10.22 07:04:58 -05'00'

Monica R. Maxwell
Program Division Director
Office of Pharmaceutical Quality Operations,
Division II