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

VIA ELECTRONIC MAIL

January 08, 2021

Joseph Tawil
President & CEO
Metro Drugs 3rd Ave. Corp.
931 Lexington Avenue
New York, NY 10065-5771

Dear Mr. Tawil:

From March 14, 2019, to April 5, 2019, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, Metro Drugs 3rd Ave. Corp. located at 931 Lexington Avenue, New York, NY 10065-5771. During the inspection, the investigator noted deficiencies in your practices for producing sterile drug products, which put patients at risk.

FDA issued a Form FDA 483 to your firm on April 5, 2019. FDA acknowledges receipt of your facility's responses dated April 26, 2019 and November 1, 2019. Based on this inspection, it appears that you produced drug products that violate the Federal Food, Drug, and Cosmetic Act (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.

Specific violations are described below.

[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.

B. 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. For example, the investigator observed that:

1. Wipes used in the ISO 5 aseptic processing areas were not sterile.

2. Your firm failed to perform adequate smoke studies under dynamic conditions to demonstrate unidirectional airflow within the ISO 5 areas. Therefore, your products that are intended to be sterile are produced in an environment that may not provide adequate protection against the risk of contamination.

3. There was a failure to maintain an adequate pressure cascade between areas of higher air quality and areas of lower air quality. Corrective actions were not implemented in response to out-of-specification pressure readings.

4. Your media fills were not performed under the most challenging or stressful conditions. An operator who had consecutively failed media fills continued to prepare drug products that were intended or expected to be sterile. Therefore, there is a lack of assurance that your firm can aseptically produce drug products within your facility.

5. Your firm had no assurance that (b) (4), used to sterilize drug products, was performed according to the specifications of the (b) (4) manufacturer.

In addition, your firm released and distributed drug products in which the strength differs from the label claim. For example, your firm released and distributed Tri-Mix Quad (Alprostadil 10mcg/Papaverine 12mg/Phentolamine 1mg/Atropine 0.15mg/mL), which was determined to have 134.5% the Atropine Sulfate Monohydrate listed on the label. Under section 501(c) of the FDCA [21 U.S.C. § 351(c)], a drug is adulterated if it is unrecognized in an official compendium and its strength differs from, or its quality or purity falls below, that which it purports or is represented to possess. The strength of your Tri-Mix Quad differed from and exceeded the labeled amount of Atropine Sulfate Monohydrate the product was purported to possess, causing it to be adulterated under section 501(c) of the FDCA.

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

Under section 502(a) of the FDCA [21 U.S.C. § 352(a)], a drug product is misbranded if its labeling is false or misleading in any particular. As noted above, analyses showed that your Tri-Mix Quad drug product contained 134.5% of the labeled concentration of Atropine Sulfate Monohydrate. Because the labeling of this drug product was false, it was misbranded under section 502(a) of the FDCA.

The introduction or delivery for introduction into interstate commerce of these products therefore violates section 301(a) of the FDCA [21 U.S.C. § 331(a)]. It is also a prohibited act under section 301(k) [21 U.S.C. § 331(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 adulterated.

C. Corrective Actions

We have reviewed your firm's responses dated April 26, 2019 and November 1, 2019. Regarding your responses related to the insanitary conditions, some of your proposed corrective actions appear adequate. However, we cannot fully evaluate the following corrective actions described in your responses because you did not include sufficient information or supporting documentation:

1. Your response to the Form FDA 483 stated that differential pressures are monitored (b) (4) as reflected in the updated SOP 3.060, Temperature, Pressure, and Humidity Monitoring. However, no supporting documentation was provided to demonstrate that an adequate pressure cascade is being maintained between areas of higher air quality and areas of lower air quality.

2. In some instances, excessive humidity levels were recorded for the cleanrooms.

3. Part of the media fill performed on May 4, 2019, had to be redone on May 20, 2019. No explanation was provided for why a portion of the media fill had to be repeated.

4. It is unclear why (b) (4) filled units were not incubated from the media fills performed on July 17, 2019, and August 22, 2019.

5. It is also unclear why the (b) (4) were recorded as (b) (4) for the media fills performed on August 7, 2019, and August 22, 2019. Failure of the (b) (4) to support microbial growth would invalidate the result of the media fill.

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.

D. 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. 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 thirty (30) working days, state the reason for the delay and the time within which you will complete the correction.

Please send your electronic response to orapharm1_responses@fda.hhs.gov. Please also identify your response with FEI #3011795133.

If you have any questions, contact Compliance Officer Juan Jimenez at juan.jimenez@fda.hhs.gov or call 1-518-453-2314 ext.1014.

Craig W. Swanson -S

Digitally signed by Craig W. Swanson -S
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for Diana Amador-Toro
Program Division Director/District Director
U.S. Food and Drug Administration
OPQO Division I / New Jersey District