Millers of Wyckoff, Inc. 6/7/16

Department of Health and Human Services

Public Health Service
Food and Drug Administration
New Jersey District Office
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone: (973) 331-4900
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VIA UNITED PARCEL SERVICE

WARNING LETTER

June 07, 2016

16-NWJ-09

David M. Miller, R.Ph., Owner/President
Millers of Wyckoff, Inc.
678 Wyckoff Ave.
Wyckoff, NJ 07481-1430

Dear Mr. Miller:

From June 29, 2015, to July 16, 2015, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Millers of Wyckoff, Inc., located at 678 Wyckoff Ave., Wyckoff, New Jersey 07481-1430.

During the inspection, the FDA investigators noted that you were not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. In addition, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigators observed an operator that failed to disinfect materials prior to introducing them into the ISO 5 area and an operator that re-used a laboratory coat

that fell on the floor. Your firm's anteroom was noted to have a sink sourced with **(b)(4)**, located adjacent to the **(b)(4)**, which is used **(b)(4)**. Moreover, review of your **(b)(4)** previous certification reports noted that the pressure differential from your anteroom to the unclassified area was inadequate as it failed to meet minimum pressure differential requirements. Furthermore, your firm failed to demonstrate through appropriate studies that your aseptic processing areas are able to provide adequate protection of the ISO 5 areas in which sterile products are processed. Therefore, your products may have been produced in an environment that poses a significant contamination risk.

FDA issued a Form FDA 483 to your firm on July 16, 2015. FDA acknowledges receipt of your firm's response to the Form FDA 483, dated July 27, 2015.

Based on this inspection, it appears that you are producing drugs that violate the Federal Food, Drug, and Cosmetic Act (FDCA).

A. Compounded Drugs Under the FDCA

Section 503A of the FDCA [21 U.S.C. § 353a] describes the conditions under which certain compounded human drug products may qualify for exemptions from three sections of the FDCA: compliance with current good manufacturing practice (CGMP) requirements, section 501(a)(2)(B) of the FDCA [21 U.S.C. § 351(a)(2)(B)]; labeling with adequate directions for use, section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)]; and FDA approval prior to marketing, section 505 of the FDCA [21 U.S.C. § 355]. Receipt of valid prescriptions for individually identified patients is one of the conditions for the exemptions under section 503A of the FDCA.

During the FDA inspection, the investigators observed that your firm does not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce. Accordingly, the drugs you compound without valid prescriptions for individually identified patients are not entitled to the exemptions in section 503A of the FDCA.

In addition, we remind you that there are other conditions that must be satisfied to qualify for the exemptions in section 503A of the FDCA.***1***

B. Violations of the FDCA

As discussed below, the drug products that you manufacture and distribute without valid prescriptions for individually-identified patients are misbranded drugs in violation of section 502(f)(1) of the FDCA.

In addition, drug products that are intended or expected to be sterile were prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth, or whereby they may have been rendered injurious to health, causing them to be adulterated within the meaning of section 501(a)(2)(A) of the FDCA [21 U.S.C. § 351(a)(2)(A)]. Furthermore, because you manufacture and distribute a portion of your drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs is subject to FDA's CGMP regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (CFR), Parts 210

and 211. FDA investigators observed significant CGMP violations at your facility, causing your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA.

Misbranded Drug Products

You compound drug products, for which you have not obtained valid prescriptions for individually-identified patients, that are intended for conditions that are not amenable to selfdiagnosis 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, causing them to be misbranded under section 502(f)(1) of the FDCA, and they are not exempt from the requirements of section 502(f)(1) of the FDCA (see, e.g., 21 CFR § 201.115). Therefore, these drug products are misbranded under section 502(f)(1) of the FDCA.

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 misbranded.

Adulterated Drug Products

Additionally, FDA investigators noted that drug products in your facility that were 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, FDA investigators noted that:

1. An operator failed to disinfect materials prior to introducing them into the ISO 5 area and an operator re-used a laboratory coat that fell on the floor.

2. Your firm's anteroom has a sink sourced with **(b)(4)**, located adjacent to the **(b)(4)**, which is **(b)(4)**. **(b)(4)** faucets and sink drains are known sources of microbial contamination.

3. Your **(b)(4)** previous certification reports noted that the pressure differential from your anteroom to the unclassified area was inadequate as it failed to meet minimum pressure differentials requirements in the certified clean room.

4. Your firm failed to demonstrate through appropriate studies that your aseptic processing areas are able to provide adequate protection of the ISO 5 areas in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

The FDA investigators also noted CGMP violations at your facility, causing the drug products for which you have not obtained valid prescriptions for individually-identified patients to be adulterated under section 501(a)(2)(B) of the FDCA; The violations include, for example:

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

2. Your firm failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).

3. 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)).

4. Your firm failed to adequately design the facility with adequate separation or defined areas or such other control systems necessary to prevent contamination or mix-ups (21 CFR 211.42(b)).

5. Your firm failed to establish an adequate air supply **(b)(4)** through high-efficiency particulate air filters under positive pressure in the aseptic processing areas (21 CFR 211.42(c)(10)(iii)).

6. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

7. Your firm does not have, for each batch of drug product purporting to be sterile and/or pyrogen-free, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product (21 CFR 211.167(a)).

8. 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)).

9. Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed (21 CFR 211.192).

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 adulterated.

C. Corrective Actions

We acknowledge your response to the FDA Form 483 inspectional observations, dated July 27, 2015. Although several of your proposed corrective actions appear adequate, others are deficient. For example, in your response to our observation of a sink located adjacent to the **(b)(4)**, which is **(b)(4)**, you indicated that you have added additional sampling sites to your **(b)(4)** sampling routine to monitor this area. However, your corrective actions are inadequate as you have not addressed how components and other items entering the **(b)(4)** will be protected from potential **(b)(4)** contamination.

In your response to our observation of **(b)(4)** to produce finished drug products without a **(b)(4)**, you indicated that, "We shall be preparing **(b)(4)**, and in the event that this is not possible, **(b)(4)** be sent to a qualified third party testing laboratory for stability, sterility, and potency characteristics...." We acknowledge your updated policy provided in your response. However, your response does not indicate how you will ensure the sterility of the finished product **(b)(4)**. Specifically, it is not clear if **(b)(4)** will be sterilized (e.g., sterile **(b)(4)**) **(b)(4)** drug product container closure.

In your response to our observation regarding inadequate contact time for sporicidal disinfection, you indicated that, "We purchase and utilize the agents for their intended use and we use them consistent with their labeling." We acknowledge the disinfection information sheets provided in your response. However, it is not clear from your response what the concentration of the sporicidal agent will be and how long the contact time will be to achieve sporicidal disinfection.

FDA strongly recommends that your management immediately undertake a comprehensive assessment of your operations, including facility design, procedures, personnel, processes, materials, and systems. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation.

Please be aware that section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether the drugs are compounded and distributed after receipt of a prescription for an identified individual patient.

In addition, should you continue to manufacture and distribute drug products without valid prescriptions for individually-identified patients, the manufacture of such drugs would be subject to FDA's drug CGMP regulations (21 CFR Parts 210 and 211), among other requirements described above, and, before doing so, you should fully implement corrections that meet the minimum requirements of 21 CFR Part 211 in order to provide assurance that the drug products produced by your firm conform to the basic quality standards regarding safety, identity, strength, quality, and purity. As indicated above, such drug products would also be subject to the requirement to be labeled with adequate directions for use in section 502(f)(1), among other requirements of the FDCA.

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.

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 the corrective actions cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be completed. Your written notification should be addressed to:

Stephanie Durso, Compliance Officer
FDA New Jersey District Office
U.S. Food and Drug Administration
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

If you have questions regarding any issues in this letter, please contact Ms. Durso via email at Stephanie.Durso@fda.hhs.gov or by phone at 973-331-4911.

Sincerely,
/S/
Craig Swanson
Acting District Director
New Jersey District

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1 For example, section 503A also addresses anticipatory compounding, which includes compounding (not distribution) before receipt of a valid prescription order for an individual patient. We are not addressing anticipatory compounding here.