WARNING LETTER

MD Pharmaceutical Supply, LLC

MARCS-CMS 637815 — NOVEMBER 22, 2022

Delivery Method:

Email

Product:

Drugs

Recipient:

Mr. Richard J. Romeo

Owner and President

MD Pharmaceutical Supply, LLC

P.O. Box 244
Hanover, PA 17331-2921
United States

Issuing Office:

Division of Pharmaceutical Quality Operations I

United States

Warning Letter

November 22, 2022

Dear Mr. Romeo:

The U.S. Food and Drug Administration (FDA) inspected your drug repackaging and relabeling facility, MD Pharmaceutical Supply, LLC at 210 Poplar Street, Suite B, Hanover, PA from April 25 to May 9, 2022.

This warning letter summarizes significant deviations from current good manufacturing practice (CGMP) for active pharmaceutical ingredients (API).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your API are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

We reviewed your May 25, 2022, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigators observed specific deviations including, but not limited to, the following.

1. Failure to adequately investigate and document complaints or any unexplained discrepancies with the original API manufacturer.

Your firm did not adequately investigate customer complaints for returned API. For example, you were made aware by **(b)(4)** that phentolamine mesylate API lot# **(b)(4)** was returned to your facility for "quality issues." Nonetheless, you redistributed the same lot of API to a different customer without performing an adequate investigation to assess drug quality. Additionally, records collected during the inspection indicated that 19 days after the redistribution of the same API lot, your supplier, **(b)(4)**, instructed you to destroy the remainder of the API lot that remained in your inventory.

In addition, FDA investigators observed a certificate of analysis (COA) for aminocaproic acid API lot# **(b)(4)** with an expiration date of April 19, 2024, that **(b)(4)** provided you for distribution. At the request of FDA investigators, you contacted **(b)(4)** for a copy of the COA for aminocaproic acid API lot# **(b)(4)** you distributed. **(b)(4)** provided you with a COA with a different expiration date of April 19, 2023. You received COAs with disparate expiration dates for aminocaproic acid API lot# **(b)(4)**. However, you did not initiate an investigation to assess whether the change in the expiration date was accurate and appropriate and whether the API lot you distributed with a year longer expiration date was scientifically justified.

In your response, you stated that you have established a procedure, *SOP MD#3-Returned goods*, for handling returned goods.

Your response is inadequate. You did not provide a retrospective review of your distribution operations, including product quality issues identified by your supplier to assess if other API are impacted. Your newly established procedure does not include storage condition verification for API that is returned to your inventory and redistributed. It is your responsibility to ensure that API returned to your inventory and redistributed has the identity, strength, quality, and purity that it is purported to have.

In response to this letter, provide:

- A comprehensive assessment of your overall system for investigating deviations, discrepancies, complaints, OOS results, and failures. Provide a detailed action plan to remediate this system. Your action plan should include, but not be limited to, significant improvements in investigation competencies, scope determination, root cause evaluation, corrective actions and preventive actions (CAPA) effectiveness, quality unit oversight, and written procedures. Address how your firm will ensure all phases of investigations are appropriately conducted.
- Your action plan to address any product quality or patient safety risks for API you placed in U.S. distribution, including complaints, customer notifications, returns, recalls, and market withdraws.

2. Failure to perform holding of API under appropriate CGMP to avoid loss of API identity or purity.

You did not adequately monitor your API storage conditions. For example, the temperature probes you used to monitor your controlled substances storage area and refrigerator were not operational at the time of FDA inspection. In addition, you did not monitor your storage areas for humidity. You were unable to provide records for temperature and humidity monitoring to demonstrate that your facility held API under appropriate storage conditions that comply with manufacturers' temperature and humidity storage requirements.

In your response, you stated that you have established a procedure, *SOP MD#5-Temperature and Humidity Controls*, for temperature and humidity monitoring.

Your response is inadequate. You did not provide information on how the probe locations you select to monitor temperature and humidly are representative of the worst-case environmental conditions of your storage areas. In addition, your procedure does not identify those responsible for performing the storage condition monitoring, and how the data will be controlled, maintained, and reviewed.

In response to this letter, provide:

- A comprehensive assessment of your storage, holding, and environmental monitoring controls. Include all CAPA to be implemented, including but not limited to procedures and equipment maintenance.
- A complete assessment of documentation systems used throughout your repackaging and relabeling operations to determine where documentation practices are insufficient. Include a detailed CAPA plan that comprehensively remediates your firm's documentation practices to ensure you retain attributable, legible, complete, original, accurate, contemporaneous records throughout your operation.

3. Failure to perform repackaging and relabeling of API under appropriate CGMP to avoid mix-ups and potential cross-contamination.

Your firm performed repacking and relabeling operations of API in an uncontrolled and open environment without adequate controls to prevent mix-ups and cross-contamination. For example, you relabeled Dasatinib monohydrate API and repackaged sirolimus API without label issuance, line clearance procedures, and documentation such as a batch record. Dasatinib monohydrate API is classified as highly potent and a toxic antineoplastic agent and sirolimus API is classified as an immunosuppressive agent. Both require appropriate handling and controls to prevent cross-contamination into other drugs. The drugs distributed by your firm were at risk for contamination and other hazards to drug safety because you failed to appropriately design your facility, establish effective procedures, maintain records of your activities, and implement robust controls.

In your response, you stated that you will no longer perform repacking and relabeling operations.

Your response is inadequate. You did not provide a retrospective assessment to ensure that no API distribution mix-ups or cross-contamination occurred.

In response to this letter, provide:

- A comprehensive assessment of your distribution operation (e.g., shipping documents, emails correspondence with suppliers), including but not limited to reconciliation of all API received with API distributed to identify occurrence of label mix-ups.
- Your action plan to address API mix-up occurrences or potential cross-contamination identified during your retrospective review, including supplier and customer notifications and recalls. Include all associated procedures and dates for corrective actions.

CGMP Consultant Recommended

Based upon the nature of the deviations we identified at your firm, we strongly recommend engaging a consultant, qualified to evaluate your operations to assist your firm in meeting CGMP requirements. Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance

Drug Repackaging/Relabeling Cease

We acknowledge your commitment to cease repackaging and relabeling of drugs at this facility. In response to this letter, clarify whether you intend to resume repackaging and relabeling operations of drugs at this facility in the future. If you plan to resume repackaging and relabeling operations of drugs, notify this office prior to resuming these activities.

In addition, if you decide to transfer your ownership, contract out any processes, or move to a new location, notify this office prior to resuming your operations.

Conclusion

The deviations cited in this letter are not intended as an all-inclusive list of deviations. You are responsible for investigating and determining the causes of any deviations and for preventing their recurrence or the occurrence of other deviations.

Correct any deviations promptly. Failure to address this matter promptly and adequately may result in regulatory or legal action without further notice including, without limitation, seizure and injunction. Unresolved deviations may also prevent other Federal agencies from awarding contracts.

Failure to address deviations may also cause FDA to withhold issuance of Export Certificates. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any deviations are completely addressed and we confirm your compliance with CGMP. We may re-inspect to verify that you have completed corrective actions to address any and deviations.

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 15 working days (i.e. 12/15/2022). Specify what you have done to address any deviations and to prevent their recurrence. In response to this letter, you may provide additional information for our consideration as we continue to assess your activities and practices. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic response to orapharm1_responses@fda.hhs.gov. Please identify your response and electronic correspondence with: **MD Pharmaceuticals Supply FEI # 3012369470, Case# 637815**.

If you have any questions, contact Compliance Officer, Juan Jimenez, at juan.jimenez@fda.hhs.gov; 973-832-9409.

Sincerely,
/S/
Nerizza Guerin
Acting Program Division Director/District Director
U.S. Food and Drug Administration
OPQO Division I / New Jersey District

Cc:**(b)(4)**

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