WARNING LETTER

KVK-Tech, Inc.

MARCS-CMS 608236 — OCTOBER 08, 2020

Delivery Method:

Via Email

Product:

Drugs

Recipient:

Mr. Anthony Tabasso

President and CEO

KVK-Tech, Inc.

110 Terry Drive
Newtown, PA 18940
United States

Issuing Office:

Division of Pharmaceutical Quality Operations I

United States

Warning Letter CMS # 608236

October 8, 2020

Dear Mr. Tabasso:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, KVK-Tech, Inc., FEI 301367632, at 100 Campus Drive, Newtown, Pennsylvania, from February 4 to March 13, 2020.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products 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 April 4, 2020, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

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

1. Your firm failed to establish and follow adequate written procedures for cleaning and maintenance of equipment (21 CFR 211.67(b)).

You performed packaging operations for approximately **(b)(4)** solid oral dosage form drug products at this facility. You did not validate the processes used to clean your non-dedicated packaging equipment such as your slat counter prior to use, as required by your cleaning validation standard operating procedure SOP-0030.

Inadequate removal of residues from product contact surfaces of non-dedicated manufacturing (e.g., packaging) equipment can lead to cross-contamination of drug products subsequently manufactured on that equipment.

Your response stated that you did not perform cleaning validation on the slat counter because you believed the slat counter was constructed of materials similar to the **(b)(4)** tablet counters used at your second facility in Newtown, Pennsylvania.

We acknowledge that you are now initiating cleaning validation of your slat counter, and tested swab samples for residues of **(b)(4)** of your drug products (**(b)(4)**). You also committed to performing cleaning validation for the remaining **(b)(4)** drug products. In addition, you stated that the cleaning validation procedure will be revised to specify that an assessment will be performed whenever modifications impacting equipment or cleaning procedures are made.

Your response is inadequate. Both the design and most difficult to clean surfaces of your **(b)(4)** tablet counter significantly differ from your slat counter. You did not establish the worst-case scenario for cross-contamination in your new cleaning validation studies because you lacked swab sites within the slat cavities, which can be one of the most difficult-to-clean locations and a potential site of carryover. Furthermore, your response failed to explain why you did not document your rationale to deviate from your cleaning validation SOP or specify how you would improve your overall change management system to prevent recurrence.

In response to this letter provide:

• Appropriate improvements to your cleaning validation program, with special emphasis on incorporating conditions identified as worst-case in your drug manufacturing operation. This should include but not be limited to identification and evaluation of all worst-case:
o drugs with higher toxicities
o drugs with higher drug potencies
o drugs of lower solubility in the cleaning solvents specified in your procedures
o drugs with characteristics that make them difficult to clean, (e.g., uncoated tablets)
o swabbing locations for areas most difficult to clean, including but not limited to slat cavities
o maximum hold times before cleaning

In addition, describe the steps that must be taken in your change management system before you introduce new manufacturing equipment or a new product.

A summary of updated SOPs that ensure an appropriate program is in place for verification and validation of cleaning procedures for products, processes, and equipment.

2. Your firm failed to prepare batch production and control records with complete information relating to the production and control of each batch of drug product produced. (21 CFR 211.188)

During packaging of one lot of hydroxyzine HCl tablets, USP 50 mg, our investigator observed that the air pressure gauge reading was outside the acceptable range for your capper, although a conforming value was recorded in the batch record. In addition, our investigator observed readings on other gauges that were lower than your validated parameters.

Our investigator also noted that in the batch record for promethazine HCl tablets, USP 25 mg, your employees failed to record actual readings for the air pressure for several pieces of packaging equipment, including your slat counter, capper, and **(b)(4)**.

In your response, you explained that during the packaging of the hydroxyzine HCl tablets your mechanic observed that the caps were not feeding into the capper properly, and he adjusted the air pressure of the capper machine below qualified limits. However, the deviation was not documented. You also stated that you found that some equipment gauges were malfunctioning and replaced them. In addition, you retrained your personnel to document the actual values in batch records.

Your response is inadequate because you did not conduct a comprehensive review to determine the scope and impact of inaccurate data recording in production records, and did not provide a plan for improving management oversight of operations.

In your response to this letter, provide the following:

• A complete assessment of documentation systems used throughout your manufacturing and laboratory operations to determine where documentation practices are insufficient. Include a detailed corrective action and preventive action (CAPA) plan that comprehensively remediates your firm's documentation practices to ensure you retain attributable, legible, complete, original, accurate, and contemporaneous records throughout your operation.
• Your CAPA plan to implement routine, vigilant operations management oversight of facilities and equipment. This plan should ensure, among other things, prompt detection of equipment/facility performance issues, effective execution of repairs, adherence to appropriate preventive maintenance schedules, timely technological upgrades to the equipment/facility infrastructure, and improved systems for ongoing management review.

Your plan should also ensure that appropriate actions are taken throughout the company network.

• A comprehensive, independent assessment of your change management system. This assessment should include, but not be limited to, your procedure(s) to ensure changes are justified, reviewed, and approved by your quality unit. Your change management program should also include provisions for determining change effectiveness.

Other Observations

During this inspection, we found that the cleaning validation sample for oxybutynin chloride tablets, USP 5 mg lot 15749, was documented in the incoming sample logbook as received on September 24, 2019, at 10:50 PM. The chromatographic analysis for this sample was completed at approximately 5:50 PM on September 24, about five hours before the sample was received, according to your logbook.

A review of the building access card reader record showed that the analyst who logged in the sample was not in the building at approximately 10:50 PM that day. Your analyst gave conflicting accounts for this discrepancy but eventually admitted to putting incorrect information in the logbook.

Repeat Violations at Multiple Sites

FDA cited similar CGMP violations at other facilities in your company's network. Your 110 Terry Drive site received an FDA warning letter dated February 11, 2020. These repeated failures at multiple sites demonstrate that management oversight and control over the manufacture of drugs is inadequate.

Your executive management remains responsible for fully resolving all deficiencies and ensuring ongoing CGMP compliance. You should immediately and comprehensively assess your company's global manufacturing operations to ensure that systems, processes, and the products manufactured conform to FDA requirements.

CGMP Consultant Recommended

Based upon the nature of the violations we identified at your firm, we strongly recommend engaging a consultant qualified as set forth in 21 CFR 211.34 to assist your firm in meeting CGMP requirements if your firm intends to resume manufacturing drugs for the U.S. market. We also recommend that the qualified consultant perform a comprehensive audit of your entire operation for CGMP compliance and that the consultant evaluates the completion and efficacy of your corrective actions and preventive actions before you pursue resolution of your firm's compliance status with FDA.

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 Production Suspended

We acknowledge your commitment to suspend manufacture of drugs at the **(b)(4)** facility. In response to this letter, clarify whether you intend to resume manufacturing any drugs at this facility in the future. If you plan to resume manufacturing drugs, notify this office before resuming your operations.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility in connection with your products. You are responsible for investigating and determining the causes of these violations and for preventing their recurrence or the occurrence of other violations.

If you are considering an action that is likely to lead to a disruption in the supply of drugs produced at your facility, FDA requests that you contact CDER's Drug Shortages Staff immediately, at drugshortages@fda.hhs.gov, so that FDA can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you

may have to report discontinuances or interruptions in your drug manufacture under 21 U.S.C. 356C(b). This also allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products.

Correct the violations cited in this letter promptly. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction. Unresolved violations in this warning letter may also prevent other Federal agencies from awarding contracts.

FDA may also withhold approval of requests for export certificates and approval of pending new drug applications or supplements listing your facility as a supplier or manufacturer until the above violations are corrected. We may re-inspect to verify that you have completed your corrective actions.

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your violations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your provide your schedule for completion.

If you believe that your products are not in violation of the FD&C Act (or you have complied with FDA regulations), include your reasoning and any supporting information for our consideration.

Send your electronic reply and response to ORAPHARM1_RESPONSES@fda.hhs.gov and copy lisa.orr@fda.hhs.gov.

Please identify your written response with FEI 3013676321 and Warning Letter CMS 608236.

If you have any questions, contact Compliance Officer Lisa Orr at lisa.orr@fda.hhs.gov.

Sincerely,
/S/

Diana Amador-Toro
Program Division Director/District Director
U.S. Food and Drug Administration
OPQO Division I/New Jersey District

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