WARNING LETTER

Swabplus, L.P.

MARCS-CMS 584803 — OCTOBER 31, 2019

Delivery Method:

VIA SIGNATURE CONFIRMED DELIVE

Product:

Drugs

Recipient:

Mr. Andy M. Ku

Chief Operating Officer/General Partner

Swabplus, L.P.

9669 Hermosa Avenue
Rancho Cucamonga, CA 91730
United States

Issuing Office:

Division of Pharmaceutical Quality Operations IV

19701 Fairchild Road
Irvine, CA 92612-2506
United States

WARNING LETTER

October 31, 2019

Dear Mr. Ku:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Swabplus L.P, FEI 3003053677 at 9669 Hermosa Avenue, Rancho Cucamonga, from March 19, 2019 to April 11, 2019.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See 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 received your response to our Form FDA 483 on April 24, 2019. We reviewed it in detail and acknowledge receipt of your subsequent correspondence. Your response is inadequate because it did not provide sufficient detail or evidence of corrective actions to bring your operations into compliance with CGMP.

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

1. Your firm failed to test samples of each component for identity and conformity with all appropriate written specifications for purity, strength, and quality. Your firm also failed to validate and establish the reliability of your component supplier's test analyses at appropriate intervals (21 CFR 211.84(d)(1) and (2)).

Inadequate Component Testing

Your firm contract manufactures over-the-counter (OTC) drug products (e.g., topical swabs) with labeled indications for application to sores and open wounds. Your firm failed to test incoming components, including the active ingredient benzalkonium chloride, for their identity, purity, strength, and other appropriate quality attributes. Instead, you relied on the suppliers' certificates of analysis (COA) from unqualified vendors, including for identity. FDA requires identity testing for each component lot used in drug product manufacturing, and you can only rely on a COA for other component attributes by validating the supplier's test results at appropriate intervals.

We note that during the June 2016 FDA inspection, we found that you were not periodically verifying the reliability of your suppliers' COA. Your response to the previous inspectional finding was to revise your incoming raw material procedure. However, the current inspection found you were not following this procedure.

In your response to this letter provide the following:

• The chemical and microbiological quality control specifications you use to test and release each incoming lot of component for use in manufacturing.

• A description of how you will test each component lot for conformity with all appropriate specifications for identity, strength, quality, and purity. If you intend to accept any results from your supplier's COA instead of testing each component lot for strength, quality, and purity, specify how you will robustly establish the reliability of your suppliers' results through initial validation as well as periodic re-validation. In addition, include a commitment to always conduct at least one specific identity test for each incoming component lot.

Inadequate Water System Monitoring

Your firm failed to routinely monitor your water system for all required quality attributes. Water from this system is used as a component in your OTC drug products labeled for application to sores and open wounds. Your standard operating procedure required **(b)(4)**.

This infrequent monitoring of your water system is inadequate. In addition, your firm failed to adhere to these minimal schedules as described in your procedures. Without routine water monitoring, you lack assurance that your water meets minimum microbiological and chemical standards suitable for the manufacture of your drug products.

In your response to this letter provide the following:

• A procedure for your water system monitoring that specifies routine microbial testing of water to ensure its acceptability for use in each batch of drug products produced by your firm.

• The current action/alert limits for total counts and objectionable organisms used for your purified water system.

• A procedure governing your program for ongoing control, maintenance, and monitoring that ensures the remediated system consistently produces water meeting Purified Water, USP monograph specifications and appropriate microbial limits.

• A validation report for the water system obtained after an appropriately designed system has been installed. Include the system validation protocol, the complete test results, and the final validation report.

• A list of all products you manufacture, the water content of each formulation, and the intended use of the products. Specify if the products are human or veterinary drugs.

2. Your firm failed to conduct, for each batch of drug product, appropriate laboratory testing, as necessary, required to be free of objectionable microorganisms and your firm failed to establish the accuracy, sensitivity, specificity, and reproducibility of its test methods (21 CFR 211.165(b) and (e)).

Unsuitable Microbial Test Methods

Your firm lacked adequate testing for microbial attributes. Specifically, your firm stated to our investigator that you do not perform growth promotion on each lot of prepared media to ensure your plates are suitable for use in microbial testing of incoming components, finished drug products, and your water system. You also failed to neutralize the anti-microbial preservatives in your drug products during finished product microbial testing. Without appropriate testing of media and neutralization of preservative activity, you cannot ensure your drug products are free of objectionable microorganisms and meet appropriate microbial limits.

Inadequate Method Validation

Your firm lacked appropriate validation of your analytical test methods. For example, you stated you utilized a non-compendial method to determine assay for the active ingredient benzalkonium chloride in your drug product before release and distribution. You also stated that you have not validated this method prior to use. Analytical methods must be validated to show they are suitable for their intended use, and equivalent or better than applicable USP compendial methods. Verifying the accuracy, sensitivity, specificity, and reproducibility of your test methods is essential to determine if the drug products you manufacture meet established specifications for chemical and microbial attributes.

In response to this letter provide the following:

• A list of chemical and microbial specifications, including test methods, used to analyze each lot of your drug products before a lot disposition decision. Also include method validation and/or method verification data and reports that evaluate these test methods.

• An action plan and timelines for conducting full chemical and microbiological testing of retain samples to determine the quality of all batches of drug product distributed to the United States within expiry as of the date of this letter. Summarize all results obtained from testing retain samples from each batch. If such testing reveals substandard quality drug products, take rapid corrective actions, such as notifying customers and product recalls.

• A comprehensive, independent assessment of your laboratory practices, procedures, methods, equipment, documentation, and analyst competencies. Based on this review, provide a detailed plan to remediate and evaluate the effectiveness of your laboratory system.

3. Your firm failed to establish a quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products, including drug products manufactured, processed, packed or held under contract by another company. Your firm also failed to establish adequate written responsibilities and procedures applicable to the quality control unit (21 CFR 211.22(a) and (d)).

You lacked an adequate quality unit (QU). Specifically, your firm lacked an appropriate change management procedure applicable to the QU. Additionally, your QU did not open a timely investigation into an ultraviolet (UV) light failure in your water system which occurred in February 2019 and continued for several weeks. The

role of the UV component in the water system is to reduce bioburden. You continued to use water from this system without assessing the impact on the quality of the water. Your QU and operations managers failed to assure that appropriate facilities, and manufacturing and quality standards, were met when producing each batch of your drug products.

Your response to this observation stated that the investigation into the failed UV light is ongoing and you are working on repairing the system. Your response is inadequate. You did not address the need for monitoring your water system (i.e., microbiological tests, total organic carbon conductivity) to determine if your water system is suitable for its intended use and maintains reliability throughout its lifecycle. Extensive monitoring of your system during validation followed by routine vigilant monitoring is necessary to determine if the water system is reliable, maintained, and operating in a state of control.

Your response also did not adequately describe what you are doing in the interim to ensure the quality of the water. This is especially concerning as you infrequently test the quality of the water produced by your water system.

In response to this letter provide the following:

• A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:
  o A determination of whether procedures used by your firm are robust and appropriate.
  o Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices.
  o A complete and final review of each batch and its related information before the QU disposition decision.
  o Oversight and approval of investigations and discharging of all other QU duties to ensure identity, strength, quality, and purity of all products.

• A comprehensive, independent assessment of your water system design, control, and maintenance.

• A thorough remediation plan to install and operate a suitable water system. Include a robust ongoing control, maintenance, and monitoring program to ensure the remediated system design consistently produces water adhering to Purified Water, USP monograph specifications and appropriate microbial limits.

• A procedure to ensure that your total microbial count limit for water is appropriate in view of the intended use of the products produced by your firm.

• A detailed risk assessment addressing the potential effects of the observed water system failures on the quality of all drug product lots currently within expiry. Specify actions that you will take in response to the risk assessment, such as customer notifications and product recalls.

• A summary of all water test results from 2018 to present, including any retest results. For results that exceed established limits, provide detailed laboratory results. including raw data and the associated investigations.

4. Your firm failed to exercise appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records, or other records (21 CFR 211.68(b)).

Your firm failed to have adequate controls in place for your High-Performance Liquid Chromatography (HPLC) and Fourier Transform Infrared Spectrometer (FTIR) systems. For example, you did not establish unique user names for each analyst. Additionally, you did not properly maintain backup copies of your original data from your laboratory equipment.

In your response, you stated that your systems were “legacy equipment” incapable of an appropriate backup. Your response is inadequate because your firm lacked a comprehensive assessment and retrospective review of all data generated from all computerized laboratory systems used in CGMP operations.

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. See FDA's guidance document Data Integrity and Compliance with Drug CGMP for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/media/119267/download (https://www.fda.gov/media/119267/download).

We strongly recommend that you retain a qualified consultant to assist in your remediation. In response to this letter, provide the following:

• A comprehensive, independent assessment and corrective action and preventive action (CAPA) plan for computer system security and integrity. Include:
o An assessment of vulnerabilities in your systems to data manipulation in infrastructure, configuration, and network requirements (e.g., segregation of duties including administrator rights).
o A report that identifies vulnerabilities in the design and controls for each of your laboratory and manufacturing computer systems. Include specific remediations.
o Provisions for oversight from QU managers, executives, and internal auditors with adequate information technology expertise.

• A complete assessment of documentation systems used throughout your manufacturing and laboratory 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.

• A comprehensive investigation into the extent of the inaccuracies in data records and reporting including results of the data review for drugs distributed to the United States. Describe the scope and root causes of your data integrity lapses in detail. Also include a current risk assessment of the potential effects of the observed failures on the quality of your drugs. Analyze the risks to patients caused by the release of drugs affected by a lapse of data integrity and the risks posed by ongoing operations.

Responsibilities as a Contractor

Drugs must be manufactured in conformance with CGMP. FDA is aware that many drug manufacturers use independent contractors, such as production facilities, testing laboratories, packagers, and labelers. FDA regards contractors as extensions of the manufacturer.

You are responsible for the quality of drugs you produce as a contract facility, regardless of agreements in place with product owners. You are required to ensure that drugs are made in accordance with section 501(a)(2)(B) of the FD&C Act for safety, identity, strength, quality, and purity. See FDA's guidance document, Contract Manufacturing Arrangements for Drugs: Quality Agreements, at https://www.fda.gov/downloads/drugs/guidances/ucm353925.pdf (https://www.fda.gov/downloads/drugs/guidances/ucm353925.pdf).

Conclusion

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

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 schedule for completion.

Your response should refer to unique identifier CMS 584803 and be sent electronically to ORAPHARM4_Responses@fda.hhs.gov or mailed to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
U.S. Food and Drug Administration
19701 Farichild Road
Irvine, CA 92612

If you have any questions regarding this letter, please contact William V. Millar, Compliance Officer, at (503) 671-9711 Ext. 30, or by email at william.millar@fda.hhs.gov.

Sincerely,
/S/

CDR Steven E. Porter, Jr
Director, Division of Pharmaceutical Quality Operations IV

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