WARNING LETTER

Spectrum Laboratory Products

MARCS-CMS 573311 — 04/06/2019

Delivery Method:

VIA SIGNATURE CONFIRMED DELIVE

Product:

Drugs

Recipient:

Mr. Randy Burg

President/CEO

Spectrum Laboratory Products

14422 S. San Pedro Street
Gardena, CA 90248
United States

Issuing Office:

Division of Pharmaceutical Quality Operations IV

19701 Fairchild
Irvine, CA 92612-2506
United States

WARNING LETTER

VIA UPS SIGNATURE CONFIRMED DELIVERY

June 4, 2019

Mr. Randy Burg
President/CEO
Spectrum Laboratory Products, Inc.
14422 S. San Pedro Street
Gardena, CA 90248

Dear Mr. Burg:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Spectrum Laboratory Products, Inc. (Spectrum), FEI 2020632, at 14422 South San Pedro Street, Gardena, California, from November 8 to 16, 2018.

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 drugs 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).

In addition, your firm commercially distributes acetylcysteine, doxylamine, pyrimethamine, tamoxifen, and trichlormethiazide. A review of FDA's drug listing database confirms that these drugs are currently not listed with FDA as required by section 510 of the FD&C Act, 21 U.S.C. 360(j), which is prohibited under section 301(p) of the FD&C Act, 21 U.S.C. 331(p). Failure to properly list a drug with the FDA will also render it misbranded under section 502(o) of the FD&C Act, 21 U.S.C. 352(o).

In addition, your fentanyl citrate, hydrocodone bitartrate, buprenorphine hydrochloride, hydromorphone hydrochloride, morphine sulfate, and nalbuphine hydrochloride API are misbranded under sections 502(a) of the FD&C Act, 21 U.S.C. 352(a).

We reviewed your December 10, 2018, response in detail and acknowledge receipt of your subsequent correspondence.

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

CGMP Charges

1. Failure to transfer all quality or regulatory information received from the API manufacturer to your customers.

You omitted the names and addresses of the original manufacturers of your repackaged API on certificates of analysis (COA) you issued to your customers. For example, you omitted the manufacturer information on your COA or your label for opioid API fentanyl citrate, USP and morphine sulfate, USP. You distributed these opioid API with incomplete information to your customers, including compounding pharmacies.

In your response, you asserted that your current practice is sufficient. Your response is inadequate in that you do not commit to ensure that your COA contain information about the original manufacturer.

Customers and regulators rely on COA for information about the quality and source of drugs and their components. Omitting information from the COA compromises supply chain accountability and traceability, and may put consumers at risk.

See Guidance for Industry: Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients and Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients—Questions and Answers for more information on how API, from original manufacturers as well as API repackagers and relabelers, should be labeled and should clearly identify the original API manufacturer as the API moves through the supply chain. The guidance can be found at: https://www.fda.gov/media/71518/download (https://www.fda.gov/media/71518/download) and https://www.fda.gov/media/112426/download (https://www.fda.gov/media/112426/download).

In response to this letter, provide the following:
 a remediated program for generating COA, including systems and procedures to assure that COA issued by your firm include necessary original manufacturer information;
 a retrospective review to determine how your failure to provide required information may have affected drug quality, and indicate any actions you have taken or will take, such as notifying customers, or invalidating previously issued COA for any drugs still within their labeled retest dates; and
 examples of recently-issued COA that include specific information regarding the original manufacturer, including a copy of their original batch certificate.

2. Failure of your quality unit to ensure that critical deviations are investigated and resolved.

You failed to perform and document adequate investigations to determine root cause and identify a corrective action. For example, you failed to thoroughly investigate a cracked bottle of repackaged Buprenorphine HCl (Lot #1HH0338). During the inspection, your employee stated the Hazardous Material Incident Report, which did not include a root cause determination and corrective action, was the only document available for this deviation.

In your response, you stated that you investigated the container defect, including other drugs that may be impacted by this issue. However, you failed to provide copies of documents to support your conclusion. For example, you did not provide a copy of the batch record for the 2-dram bottle Item **(b)(4)** Lot **(b)(4)** which you stated contained the full investigation.

In addition, while you noted your Hazardous Material Incident Report form was revised to include a "notes field," you did not include a copy of the form with your response or explain how this revision will ensure adequate investigations into product quality issues going forward.

You also failed to thoroughly investigate customer complaints. For example, you failed to identify a root cause for a customer complaint that noted batch variation and potential quality defects for fluconazole, USP. Your Complaint Report for complaint #PC58672 lacked a comprehensive investigation into the root cause for this batch and a proposed corrective action. Also, you did not extend your investigation to other batches that may have been associated with this specific deviation.

In your response, you stated the root cause analysis and corrective action are available in the full complaint records. However, you failed to provide copies of the records to support your response.

In response to this letter, provide the following:
 the full reports for the root cause investigations performed; and
 a comprehensive assessment of your system for investigating deviations, atypical events, and complaints.
Your corrective action and preventive action (CAPA) plan should include, but not be limited to, improvements in investigations, root cause analysis, written procedures, and quality unit oversight.

Concerns Regarding Glycerin

Your product list collected during the inspection, which is also available on your website, included the drug glycerin. The use of glycerin contaminated with diethylene glycol (DEG) has resulted in various lethal poisoning incidents in humans worldwide. See FDA's guidance document, Testing of Glycerin for Diethylene Glycol, to help you meet CGMP requirements when distributing glycerin for use in drug products, including testing for DEG and recommendations for supply chain integrity, at https://www.fda.gov/media/71029/download (https://www.fda.gov/media/71029/download).

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 Listing Violation

According to the sales record obtained at the time of inspection, Spectrum Laboratory Products Inc. (FEI 2020632) manufactures drugs for commercial distribution in the United States, of which some have not been listed with FDA as required by the law. These drugs include acetylcysteine, doxylamine, pyrimethamine, tamoxifen, and trichlormethiazide. Under section 510 of the FD&C Act, as amended, and 21 CFR, all drugs

manufactured, prepared, propagated, compounded, or processed for U.S. commercial distribution must be listed with FDA. See 21 U.S.C. 360(j)(1); see also 21 CFR 207.17 and 207.41. Failure to properly list a drug product is prohibited and will render the drug misbranded. See 21 U.S.C. 331(p) and 352(o).

Misbranding Violations

The fentanyl citrate, hydrocodone bitartrate, buprenorphine hydrochloride, hydromorphone hydrochloride, morphine sulfate, and nalbuphine hydrochloride API labels identify Spectrum but do not designate the firm's role. Since these API labels bear only Spectrum's name without further qualifications, the labels falsely represent that Spectrum is the sole drug manufacturer. (See 21 CFR 201.1(h)(2)). Therefore, the API are misbranded under section 502(a) of the FD&C Act because the labels are false and misleading.

Conclusion

Deviations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating these deviations, for determining the causes, for preventing their recurrence, and for preventing other deviations.

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

Until these deviations are corrected, we may withhold approval of pending drug applications listing your facility. 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 deviations 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.

Please send your electronic reply to ORAPHARM4_Responses@FDA.HHS.GOV (mailto:ORAPHARM4_Responses@FDA.HHS.GOV) or mail your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
U.S. Food & Drug Administration
19701 Fairchild Road
Irvine, California 92612-2506

Please identify your responses with the unique identifier: **CMS 573311**.

If you have questions regarding the contents of this letter, please contact Mariza Jafary, Compliance Officer via email at Mariza.Jafary@fda.hhs.gov (mailto:Mariza.Jafary@fda.hhs.gov) or by telephone at 949-608-2977.

Sincerely,
/S/

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

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