WARNING LETTER

Vida International, Inc.

MARCS-CMS 573082 — MAY 29, 2019

Product:

Drugs

Recipient:

Mr. Ching Wen (Kevin) Wu

Plant Manager

Vida International, Inc.

Number 8, Lane 281
Lung Chiang Road
Taipei City 10491
Taiwan

Issuing Office:

Center for Drug Evaluation and Research

10903 New Hampshire Avenue
Silver Spring, MD 20993
United States

Via UPS **Warning Letter** 320-19-23

Return Receipt Requested

May 29, 2019

Mr. Ching Wen (Kevin) Wu
Plant Manager
Vida International, Inc.
Number 8, Lane 281
Lung Chiang Road
Taipei, Taiwan 10491

Dear Mr. Wu:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility Vida International, Inc. at Number 263-2 Zhongshan North Road, Dayuan District, Taoyuan City, 33759, Taiwan, from December 10 to 13, 2018.

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 product is 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 December 21, 2018, response in detail.

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

1. Your firm failed to perform, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release, and conduct appropriate laboratory testing for each batch of drug product required to be free of objectionable microorganisms (21 CFR 211.165(a) and (b)).

You released an over-the-counter (OTC) drug product, **(b)(4)**, to the U.S. supply chain without testing the identity, strength, purity, and quality of the active ingredient. In addition, you did not adequately test for critical microbial attributes (e.g., absence of objectionable microorganisms, total count) before release.

2. Your firm failed to conduct at least one test to verify the identity of each component of a drug product. Your firm also failed to test each component for conformity with all written specifications for purity, strength, and quality (21 CFR 211.84(d)(1) and (2)).

Your firm lacked testing of incoming raw materials, used in the manufacturing of your drug product, including active pharmaceutical ingredients and other components to verify their identities before using them. Furthermore, you failed to determine whether each component conformed with all appropriate written specifications for purity, strength, and quality before using them. For example, your firm accepted and used raw materials, including a drum purportedly containing **(b)(4)**, in the manufacture of **(b)(4)**, lot **(b)(4)**, without testing identity, strength, and other quality attributes and without Certificate of Analysis information.

3. Your firm failed to establish an adequate 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 (21 CFR 211.22(a)).

Your firm lacks an adequate quality control unit. You failed to establish adequate written procedures for numerous quality functions, including but not limited to, the release of drug product batches and the oversight for a drug stability program. In addition, your firm drafted forms to document activities such as raw material receipt, change control, deviations, complaints, recalls, equipment cleaning, and employee training. However, you had not yet implemented these forms or established written procedures to describe the activities therein.

4. 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).

The batch production record for lot **(b)(4)** of **(b)(4)** is deficient because it does not represent the formula and ingredients that the product purports on its label. Specifically, the batch record does not list all inactive ingredients included on the product label. The batch record also lacked the actual amounts of each active and inactive ingredient used during manufacturing, a calculation of theoretical or actual yields, documentation of the equipment used, and critical manufacturing parameters such as **(b)(4)** speeds and **(b)(4)** times.

Inadequate Response and Drug Distribution Ceased

In your response of December 13, 2018, you acknowledged significant violations of CGMP regulations and stated you would no longer ship drug products to the United States. Your response to the CGMP violations observed did not provide a timeline or sufficient information that your firm will remediate your operations to ensure compliance with CGMP. It also did not address the quality of drug products that you have distributed to the U.S. market. In response to this letter, provide the following:

- Your plan for testing retain samples of all batches of drug product distributed to the U.S. market for identity and strength of active ingredients and microbial quality, including total count and objectionable microorganisms. If any unexpired batch is found to be out-of-specification, indicate the corrective actions you will take, such as customer notifications and product recalls.

- A risk assessment of all drug product batches distributed to the U.S. market within expiry, to determine the effect of your failure to test components (e.g., **(b)(4)** active ingredient) and the lack of adequate stability testing to support your expiration dates.

In response to this letter, also clarify whether you intend to resume manufacturing drugs for the U.S. market at this facility in the future. If you plan to resume manufacturing drugs for the U.S. market, notify this office prior to resuming your operations and provide the following additional information:

- The test methods and specifications you use to analyze each batch of drug product before release, including both chemical and microbial quality attributes. Include a summary of all test results obtained from testing all batches of drug products intended for the U.S. market within expiry. Include your procedures that will ensure you test each batch of finished drug product, before release, according to batch release specifications.
- Batch release specifications for all incoming components including the **(b)(4)** active ingredient. Include your procedures for analyzing each batch of incoming components and the procedure that requires testing of components before release and use.
- A comprehensive assessment and corrective action and preventive action (CAPA) plan, with timelines, to implement an adequate stability program. Your remediated program should include, but not be limited to:
    - Stability indicating methods
    - Stability studies for each drug product in its marketed container-closure system before distribution is permitted
    - An ongoing program in which representative batches of each product are added each year to the program to determine if the shelf-life claim remains valid
    - Detailed definition of the specific attributes to be tested at each station (time point)
    - All procedures that describe these and other elements of your remediated stability program
- Revised batch production records and product labeling for **(b)(4)**.
- Your CAPA plan for establishing an effective quality control unit with the appropriate authority and sufficient resources to carry out its responsibilities and consistently ensure drug quality. Include newly established and updated procedures.

Quality Systems

Your firm's quality systems are inadequate. See FDA's guidance document *Quality Systems Approach to Pharmaceutical CGMP Regulations* for help implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR, parts 210 and 211 at https://www.fda.gov/media/71023/download (https://www.fda.gov/media/71023/download).

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.

Conclusion

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

FDA placed your firm on Import Alert 66-40 on March 11, 2019.

Until you correct all violations completely and we confirm your compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as a drug manufacturer.

Failure to correct these violations may also result in FDA continuing to refuse admission of articles manufactured at Vida International Inc., Number 263-2 Zhongshan North Rd., Dayuan District, Taoyuan City into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Under the same authority, articles may be subject to refusal of admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B).

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.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov (mailto:CDER-OC-OMQ-Communications@fda.hhs.gov) or mail your reply to:

Carrie Ann Plucinski

Compliance Officer

U.S. Food and Drug Administration

White Oak Building 51, Room 4359

10903 New Hampshire Avenue

Silver Spring, MD 20993

USA

Please identify your response with FEI 3003220372.

Sincerely,

/S/

Francis Godwin

Director

Office of Manufacturing Quality

Office of Compliance

Center for Drug Evaluation and Research

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