Polaroisin International Co., Ltd. 1/25/18

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS

Warning Letter 320-18-27

January 25, 2018

Mr. Li Chung Lung
President
Polaroisin International Co., Ltd.
Xinzhuang District, NO 173, 10F, Siyuan Road
New Taipei City, 24250
Taiwan

Dear Mr. Li Chung Lung:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Polaroisin International Co., Ltd. at Xinzhuang District, NO 173, 10F, Siyuan Road, New Taipei City, from September 11 to 15, 2017.

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 reviewed your response, received on October 6, 2017, in detail.

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

1. Your firm does not have, 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 (21 CFR 211.165(a)).

Your firm released your finished over-the-counter (OTC) drug product, **(b)(4)**, without testing for the identity and strength of the active ingredient, **(b)(4)**. Without this testing, you do not have scientific evidence that your drug product conformed to specifications prior to release.

Your response does not specify how you will conduct assay analysis to verify the strength and identity of your **(b)(4)** OTC drug product prior to release. You also stated in your response that you will follow the “cosmetics production standard” to manufacture your **(b)(4)** OTC drug product.

If you market your **(b)(4)** OTC drug product in the United States, this drug product must be manufactured in accordance with CGMP standards for drugs, not cosmetics.

In response to this letter, provide test specifications and validated methods for testing your **(b)(4)** OTC drug product for identity and strength. Also, test retain samples for all batches of products shipped to the United States that are within expiry to ensure they meet final specifications.

2. Your firm failed to ensure the identity of components, including your active ingredients and excipients from various suppliers (21 CFR 211.84(d)(1) and (2)).

Your firm failed to test incoming active pharmaceutical ingredients and other components you use in manufacturing your **(b)(4)** OTC drug product to ensure that each component met specifications, including identity. You also do not have a supplier qualification program. While you source components from various suppliers, you have not performed any testing to validate the reliability of each supplier's certificate of analysis (COA).

Your response included your revised SOP for incoming material inspection. However, it is unclear how you will analyze your incoming raw material batches for identity, or how you will verify the reliability of your suppliers' COA.

In your response, summarize test results obtained from full testing of all your incoming components to ensure the reliability of your suppliers' COA. Also, commit to testing each incoming lot of raw materials (i.e., drug product ingredients) for identity.

3. Your firm failed to ensure that its drug product bore an expiration date that was supported by appropriate stability testing (21 CFR 211.137(a)).

You did not have stability data demonstrating that your **(b)(4)** OTC drug product met all established specifications, such as active ingredient content, throughout its labelled shelf life.

In your response, you stated that you are discussing a stability program with your contract laboratory, but you require additional time to complete this corrective action.

In your response, provide an update on your stability protocol and a timeline for implementation.

4. Your firm failed to establish written procedures for production and process control designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess (21 CFR 211.100(a)).

You did not perform process performance qualification studies for your **(b)(4)** OTC drug product, and you lack an ongoing process control monitoring program to ensure stable manufacturing operations and consistent drug quality.

In your response, you stated that you need additional time to develop training for your employees. Your response is inadequate as you failed to address your lack of process validation prior to distribution of drugs and your lack of a plan to validate your manufacturing process.

See FDA's guidance document, *Process Validation: General Principles and Practices*, for general principles and elements of process validation at: **http://www.fda.gov/downloads/Drugs/.../Guidances/UCM070336.pdf. (http://www.fda.gov/downloads/Drugs/.../Guidances/UCM070336.pdf.%20)**

In response to this letter, provide a timeline for implementing process validation to ensure that your manufacturing process results in consistent drug quality.

Over-the-Counter Monograph for (b)(4) Drug Products

During the inspection, FDA investigators collected three products intended for sale in the United States. Two of the labels include **(b)(4)** OTC drug products. As a manufacturer of OTC drug products, it is the responsibility of firms to comply with all requirements of federal law and FDA regulations, and to ensure that its products are safe and effective and do not violate the provisions of the Federal Food, Drug and Cosmetic Act.

Products that are marketed and indicated for use as **(b)(4)**, such as **(b)(4)** and **(b)(4)**, are subject to the Final Rule for **(b)(4)** Drug Products for Over-the-Counter Human Use **(b)(4)**. OTC **(b)(4)** drug products may be marketed under the OTC Drug Review if they meet the conditions set forth in **(b)(4)**. Otherwise, the product may only be legally marketed under an FDA-approved new drug application. Specifically, **(b)(4)** drug products marketed under the **(b)(4)** Final Rule are only permitted to contain **(b)(4)** as an active ingredient within the specified concentrations and in the established dosage form **(b)(4)**. In addition, OTC drugs marketed in the United States. must include a Drug Facts panel which identifies, among other things, the indications for use, the active and inactive ingredients, applicable warnings, and directions for use (21 CFR 201.66).

Consultant Recommended

Based upon the nature of 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 drug CGMP requirements.

Your use of a consultant does not relieve your firm's obligation to comply with drug CGMP. Your firm's executive management remains responsible for fully resolving all deficiencies and ensuring ongoing drug 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 January 8, 2018.

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 Polaroisin International Co., Ltd., Xinzhuang District, NO 173, 10F, Siyuan Road, New Taipei 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:

Ms. Carla Norris
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 3008004582.

Sincerely,
/S/
Francis Godwin
Acting Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

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