Jalco Cosmetics Pty Ltd. 5/18/18

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov (http://www.fda.gov)

Warning Letter 320-18-54

Via UPS
Return Receipt Requested

May 18, 2018

Mr. Ian Martin
General Manager
Jalco Cosmetics Pty. Ltd.
Level 2 Unit 49
2 Slough Avenue
Silverwater, NSW 2128
Australia

Dear Mr. Martin:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Jalco Cosmetics Pty. Ltd. at Level 2 Unit 49, 2 Slough Avenue, Silverwater, NSW, from December 11 to 13, 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 December, 21, 2017, response in detail and acknowledge receipt of your subsequent correspondence.

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

1. Your firm failed to 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)).

You released **(b)(4)** Cream without testing the identity and strength of the active ingredients, **(b)(4)** and **(b)(4)**.

In your response, you stated: “Moving forward, all FDA drugs will be assayed for active ingredients if a test method is available.” You also stated that your customer, **(b)(4)**, “will discuss the possibility of assaying the two active ingredients in the finished product at release with a suitable external laboratory.”

Your response lacks a clear commitment to test each batch for all finished product attributes, including but not limited to identity and strength, prior to batch release. You must ensure each batch of your over-the-counter (OTC) drug products meet all chemical and microbiological specifications prior to release.

In response to this letter, provide the following:

- Appropriate specifications for each chemical and microbial attribute of your products.
- Protocols and timelines for the establishment and validation of all methods that you will use to test each batch of your U.S. drug products for identity, strength, quality and purity. Also include your test methods.
- Your procedure to assure that any future test methods contracted to a third-party laboratory are properly transferred and validated prior to use. Also include your procedures for assuring oversight of the adequacy of laboratory analyses performed on your behalf by a third-party laboratory, and any related investigations regarding these analyses.
- The actions you have taken to determine the quality of your U.S. drug products within expiry which were previously released without adequate testing, including identity and strength of active ingredients.

2. Your firm failed to test samples of each component for conformity with all appropriate written specifications for identity, purity, strength, and quality (21 CFR 211.84(d)(1) & (2)).

You failed to test incoming active pharmaceutical ingredients and other components you use in manufacturing **(b)(4)** Cream to ensure that each component met specifications. You relied on your suppliers’ certificates of analysis (COA) for the identity of each incoming component without performing identity testing.

In your response, you stated that a contract laboratory will test future component lots for identity prior to use in manufacturing drug products.

Your response is inadequate because you did not commit to establish the reliability of your suppliers’ COA.

In response to this letter, provide a detailed description of how you plan to test each component for conformance with all appropriate written specifications for identity, strength, quality and purity. If you plan to rely on your suppliers’ COA test results (with the exception of identity) in lieu of testing, describe in detail how you plan to establish the reliability of your suppliers’ test results prior to use of a supplier’s ingredient in production, as well as through periodic validation. Lastly, provide a risk assessment for all drugs within expiry and distributed within the United States that were manufactured from inadequately-tested and controlled components.

3. 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 have not validated the manufacturing process for **(b)(4)** Cream. Your firm distributed **(b)(4)** to the United States in 2016.

You also have not conducted equipment qualification for the R1 **(b)(4)** filling machine.

In your response, you stated that you will initiate process validation starting with the next production batch, and equipment qualification will be performed for the R1 **(b)(4)** filling machine.

Your response is inadequate because you failed to provide a detailed process performance qualification protocol and an overall program for assuring maintenance of a validated process.

Your firm lacks a process validation program. Process validation evaluates the soundness of design and state of control of a process throughout its lifecycle. Each significant stage of a manufacturing process must be designed to assure the quality of raw material inputs, in-process materials and finished drugs. Process qualification studies provide a determination whether an initial state of control has been established. Successful process qualification studies are necessary prior to commercial distribution. Thereafter, ongoing vigilant oversight of process performance and product quality is necessary to ensure you maintain a stable manufacturing operation throughout the product lifecycle.

See FDA's guidance document, *Process Validation: General Principles and Practices*, for general principles and approaches that FDA considers appropriate elements of process validation, at **https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070336.pdf (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070336.pdf)**.

In response to this letter, provide a detailed program for designing, validating, maintaining, controlling and monitoring each of your manufacturing processes that includes vigilant monitoring of intra-batch and inter-batch variation to ensure an ongoing state of control. Also, include your program for qualification of your equipment and facility.

4. Your firm failed to establish an adequate written testing program designed to assess the stability characteristics of drug products. (21 CFR 211.166(a)).

Your **(b)(4)**-month expiration date for **(b)(4)** Cream was based on stability test data from your customer's previous contract manufacturer. The formulation remained the same, but the manufacturing site, equipment, raw materials, and container-closures are different.

Furthermore, the stability study conducted by your customer's previous contract manufacturer contained out-of-specification (OOS) results including sub-potent **(b)(4)** content at 24 months, and low viscosity at 36 months.

Your response stated that you will initiate real-time stability studies for your next production batch.

Your response is inadequate because your stability test data does not support the **(b)(4)**-month expiration date on the drug product label. Without an adequate stability program, you cannot confirm your drug products continue to meet established specifications throughout their labeled shelf-life.

In response to this letter, provide analysis of retain samples for your drug products currently in U.S. distribution. Include your updated stability testing program. Describe stability-indicating methods and acceptance criteria for each chemical and microbiological test to support the labeled storage conditions and expiry dates for your drug products.

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 and your customer, **(b)(4)**, have a quality agreement regarding the manufacture of **(b)(4)** Cream. 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/GuidanceComplianceRegulatoryInformation/Guidances/UCM353925.pdf (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM353925.pdf)**.

Quality Unit Authority
Significant findings in this letter indicate that your quality unit is not fully exercising its authority and responsibilities. Your firm must provide the quality unit with the appropriate authority and sufficient resources to carry out its responsibilities and consistently ensure drug quality.

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. We also recommend that the qualified third party perform a comprehensive audit of your entire operation for CGMP compliance, including the quality assurance system, materials system, facility and equipment system, laboratory system, production system, and packaging and labeling system. Your CAPA should then be evaluated by the third party to help ensure systemic remediation before you pursue resolution of your firm's compliance status.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for fully resolving all deficiencies and for ensuring 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 in your facility

FDA placed your firm on Import Alert 66-40 on March 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 Jalco Cosmetics Pty. Ltd., Level 2 Unit 49, 2 Slough Avenue, Silverwater, 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 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:

Chelsea Sealey
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 3003906415.

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

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