Bicooya Cosmetics Limited 8/11/17

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS
Return Receipt Requested

Warning Letter 320-17-47

August 11, 2017

Mr. Tao Yang, General Manager
Bicooya Cosmetics Limited
No. 17, Yan Hu Road
Shangxi Town
Yiwu Zhejiang 322006
China

Dear Mr. Yang:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Bicooya Cosmetics Limited at No. 17, Yan Hu Road, Shangxi Town, Zhejiang, from May 22–25, 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 May 31, 2017, response in detail and acknowledge receipt of your subsequent correspondence. Your cursory response did not provide adequate corrective actions for any of the observations made during the inspection.

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

1. Your firm failed to keep the buildings used in the manufacture, processing, packing, or holding of a drug product free of infestation by rodents, birds, insects, and other vermin (21 CFR 211.56(a)).

Our investigator observed rodent feces throughout your facility:

- in direct proximity to the filling machine where you manufacture OTC drug products
- in direct proximity to the **(b)(4)** system, which produces **(b)(4)** incorporated in your drug products
- throughout the warehouse, around both raw materials and finished drug products

Your over-the-counter (OTC) drug products include **(b)(4)** ointments and **(b)(4)**.

2. Your firm failed to clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).

For example, our investigator observed residue build-up in the **(b)(4)** tanks you use to manufacture OTC drug products, and damaged transfer hoses held together with plastic wrap. When an employee attempted to open a **(b)(4)** tank lid during the inspection, a hinge broke.

3. 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 did not test all lots of your drug products for active ingredient content prior to release. You also failed to conduct microbial testing (i.e., total count, objectionable microorganisms) for each batch of drug product you release.Your firm stated that your customer only requires microbiological tests to be performed **(b)(4)**. Because you lack microbiological testing, there is insufficient assurance that the products you distribute are safe and sanitary.

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).

Our investigator requested batch records for OTC drug product lots distributed to the United States, including **(b)(4)** Ointment and **(b)(4)**. You were unable to provide batch records.

In addition, analytical testing records were missing data, dates, and signatures. Our investigator observed your staff altering information in analytical test reports during the inspection. For example, you significantly altered the analytical testing report for **(b)(4)** Ointment lot **(b)(4)**, although this lot had already been distributed to the U.S. market.

CGMP consultant recommended

Based upon the nature of the violations we identified at your firm, we strongly recommend engaging consultants qualified as set forth in 21 CFR 211.34, to assist your firm in meeting CGMP requirements. Your use of consultants does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for fully resolving all deficiencies and ensuring ongoing CGMP compliance.

Data Integrity Remediation

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.

In response to this letter, provide the following.

A. A comprehensive investigation into the extent of the inaccuracies in data records and reporting. Your investigation should include:

- A detailed investigation protocol and methodology; a summary of all laboratories, manufacturing operations, and systems to be covered by the assessment; and a justification for any part of your operation that you propose to exclude.
- Interviews of current and former employees to identify the nature, scope, and root cause of data inaccuracies. We recommend that these interviews be conducted by a qualified third party.
- An assessment of the extent of data integrity deficiencies at your facility. Identify omissions, alterations, deletions, record destruction, non-contemporaneous record completion, and other deficiencies. Describe all parts of your facility's operations in which you discovered data integrity lapses.
- A comprehensive retrospective evaluation of the nature of the testing and manufacturing data integrity deficiencies. We recommend that a qualified third party with specific expertise in the area where potential breaches were identified should evaluate all data integrity lapses.

B. A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analysesof the risks to patients caused by the release of drugs affected by a lapse of data integrity, and risks posed by ongoing operations.

C. A management strategy for your firm that includes the details of your global corrective action and preventive action plan. Your strategy should include:

- A detailed corrective action plan that describes how you intend to ensure the reliability and completeness of all of the data you generate, including analytical data, manufacturing records, and all data submitted to FDA.
- A comprehensive description of the root causes of your data integrity lapses, including evidence that the scope and depth of the current action plan is commensurate with the findings of the investigation and risk assessment. Indicate whether individuals responsible for data integrity lapses remain able to influence CGMP-related or drug application data at your firm.
- Interim measures describing the actions you have taken or will take to protect patients and to ensure the quality of your drugs, such as notifying your customers, recalling

product, conducting additional testing, adding lots to your stability programs to assure stability, drug application actions, and enhanced complaint monitoring.
- Long-term measures describing any remediation efforts and enhancements to procedures, processes, methods, controls, systems, management oversight, and human resources (e.g., training, staffing improvements) designed to ensure the integrity of your company's data.
- A status report for any of the above activities already underway or completed.

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 all your facilities.

FDA placed your firm on Import Alert 66-40 on June 29, 2017.

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 Bicooya Cosmetics Limited at No. 17, Yan Hu Road, Shangxi Town, Zhejiang, 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 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 3010671652.

Sincerely,
/S/
Thomas J. Cosgrove
Director

Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

cc: **(b)(4)**