Shanghai Weierya Daily Chemicals Factory 2/7/18

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS
Return Receipt Requested

Warning Letter 320-18-31

February 7, 2018

Mr. Zhifang Ma
General Manager
Shanghai Weierya Daily Chemicals Factory
1072 Dongsheng Road
Heqing Industrial Park
Shanghai, 201201, P.R. China

Dear Mr. Ma:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Shanghai Weierya Daily Chemicals Factory at No. 1072 Dongsheng Road, Shanghai, from April 10 to 14, 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 7, 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 does not have, for each batch of drug product, appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable organisms (21 CFR 211.165(b)).

Your firm released your finished over-the-counter (OTC) drug product, **(b)(4)** CT, without adequate testing for total count and objectionable microorganisms. You did not test each batch prior to release and distribution (e.g., batch **(b)(4)**). Your procedures permitted you to test one lot every six months. Without testing each batch, you do not have scientific evidence that all drug product batches conformed to specifications prior to release.

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)).

Your firm failed to adequately test incoming components, including excipients, you use in manufacturing your OTC drug product to determine their identity prior to use in manufacturing. You stated in your response that you only tested a subset of lots of incoming active pharmaceutical ingredients. You must test all lots of incoming components for identity prior to release by the quality unit.

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 quality unit was not effectively exercising its responsibilities. For example, your quality control unit failed to approve raw materials, including active pharmaceutical ingredients and packaging and labeling materials, to ensure their suitability prior to use in manufacturing your OTC drug products. In addition, your quality unit failed to review records, such as batch production records and **(b)(4)** records, prior to release of finished OTC drug products.

Inadequate Response

Your May 7, 2017, response to FDA's inspectional observations was inadequate. You did not provide sufficient evidence that you are taking corrective actions to bring your operations into full compliance with CGMP.

In response to this letter, provide the following:

- Your firm's plan for ensuring all OTC drug product batches released to the U.S. market are tested for microorganisms, including total count and objectional microorganisms.
- Your firm's plan to promptly test all batches within expiry in U.S. distribution to determine if they are free from objectionable microbiological contamination.
- A detailed sampling and testing plan for all incoming components.
- A detailed summary of your firm's quality unit procedures.
- Your firm's plan for reviewing all records for previously released batches that are still within expiry.
- A thorough assessment of your adherence to all CGMP requirements, and a corrective action and preventive action plan to assure full remediation.

Comprehensively address each of these items in your written response.

Quality Unit Authority

Significant findings in this letter indicate that your quality unit is not able to fully exercise its responsibilities. Your firm must provide the quality unit with the appropriate authority, sufficient resources, and staff to carry out its

responsibilities and consistently ensure drug quality.

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 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/guidances/ucm353925.pdf (https://www.fda.gov/downloads/drugs/guidances/ucm353925.pdf)**.

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. 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 ensuring ongoing CGMP compliance.

Cosmetic Product Concerns

Furthermore, the conditions found in your facility may also cause your cosmetic products to be adulterated under section 601(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 USC 361(c).

Conclusion

Violations cited in this letter are not intended as an all-inclusive list. It is FDA's understanding that you intend to **(b) (4)**. 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 September 14, 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 Shanghai Weierya Daily Chemicals Factory, No. 1072 Dongsheng Road, Shanghai, 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:

Karen E. D'Orazio
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 3010166363.

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

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

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