WARNING LETTER

Hunan Norchem Pharmaceutical Co. Ltd.

MARCS-CMS 538815 — JAN 09, 2018

Recipient:

Mr. Xirong Liu

Hunan Norchem Pharmaceutical Co. Ltd.

No. 186, Guyuan Road, Hi-tech Park
Room 601, Unit 1, West Building
Changsha, Hunan 410001
China

Issuing Office:

Center for Drug Evaluation and Research

United States

U.S. FOOD & DRUG ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS
Return Receipt Requested

Warning Letter 320-18-24

January 9, 2018

Mr. Xirong Liu
President
Hunan Norchem Pharmaceutical Co. Ltd.
Room 601, Unit 1, West Building
Hu Da Technical Park
No. 186, Guyuan Road, Hi-tech Park
Changsha, Hunan, 410001
China

Dear Mr. Liu:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Hunan Norchem Pharmaceutical Co. Ltd. at No. 20 Mengjiangnv Avenue, Economic Development Zone, Jinshi, Hunan, from July 24 to 28, 2017.

This warning letter summarizes significant deviations from current good manufacturing practice (CGMP) for active pharmaceutical ingredients (API).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your API 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 August 18, 2017, response in detail. In your response, you stated that you discontinued the manufacturing of **(b)(4)** base intended for the U.S. market. You did not provide sufficient evidence to support that your proposed corrective actions will bring your operations into compliance with CGMP. You also stated that you have transferred the manufacturing of **(b)(4)** base to **(b)(4)**.

During our inspection, our investigators observed specific deviations including, but not limited to, the following.

1. Failure to prepare and use production and control records for each intermediate and API batch.

Your Quality Unit failed to retain and locate 20 of **(b)(4)** of your **(b)(4)** base batch records, including but not limited to records for batches **(b)(4)** and **(b)(4)**. In your response, you stated the batch records "are not missing" and are "archived properly." Your response is inadequate because you did not provide evidence, such as copies of the executed batch records.

Additionally, your Quality Assurance department approved batch record 0220151203 and batch record 0220151204 despite the inaccuracy of the weight of raw materials added. In your response, you stated the operator "did not follow the procedure" and did not recognize this as a deviation. You also stated personnel had "inadequate awareness of deviations." It is your responsibility to ensure the accuracy and completeness of your batch records in order to establish that your manufacturing process was followed and is reproducible.

2. Failure to maintain complete data derived from all laboratory tests conducted to ensure your API and intermediates comply with established specifications and standards.

Your firm failed to retain and locate the analytical raw data for batches **(b)(4)** and **(b)(4)** of **(b)(4)** base which you shipped to the United States in 2014. In your response, you stated the "analytical data was not backed up." You also said that you transferred the instrument that generated the data to your **(b)(4)** branch in 2015 and that the staff there deleted the data. It is essential to retain raw data to ensure the ability to reconstruct CGMP activities and review raw data, as necessary, for deviations and investigations.

Our findings demonstrate that you lack understanding of the basic elements of a compliant manufacturing operation, such as adequate documentation, trained personnel, and written procedures.

Additional API CGMP guidance

FDA considers the expectations outlined in ICH Q7 in determining whether API are manufactured in conformance with CGMP. See FDA's guidance document, *Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients,* for guidance regarding CGMP for the manufacture of API, at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073497.pdf (/media/71518/download).

Conclusion

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

FDA placed your firm on Import Alert 66-40 on October 18, 2017.

Until you correct all deviations 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 deviations may also result in FDA continuing to refuse admission of articles manufactured at Hunan Norchem Pharmaceutical Co. Ltd., at No. 20 Mengjiangnv Avenue, Economic Development Zone, Jinshi, Hunan, 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 deviations 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:

Lynnsey Renn, Ph.D.
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 3010784755.

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

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