WARNING LETTER

Chengdu Innovation Pharmaceutical Co., Ltd.

MARCS-CMS 698786 — FEBRUARY 05, 2025

Delivery Method:

VIA Electronic Mail

Reference #:

320-25-40

Product:

Drugs

Recipient:

Ren Zhongju

Chengdu Innovation Pharmaceutical Co., Ltd.

No.123, 1st Floor, No 91 Zhongheng Street
Jinniu Qu Chengdu Shi Sichuan Sheng, 610036
China

Issuing Office:

Center for Drug Evaluation and Research (CDER)

United States

Warning Letter 320-25-40

February 5, 2025

Dear Ren Zhongju:

Your facility was registered with the United States Food and Drug Administration (FDA) as a manufacturer of active pharmaceutical ingredients (APIs). FDA has reviewed the records you submitted in response to our April 29, 2024 request for records and other information pursuant to section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for your facility, Chengdu Innovation Pharmaceutical Co., Ltd., FEI 3027222600, No.123, 1st Floor, No 91 Zhongheng Street, Jinniu District, Chengdu, Sichuan, China.

This warning letter summarizes significant deviations from Current Good Manufacturing Practice (CGMP) for API.

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding of drugs as described in your response to our 704(a)(4) request do not conform to CGMP, your APIs 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).

Following review of records and other information provided pursuant to section 704(a)(4) of the FD&C Act, significant deviations were observed including, but not limited to, the following:

704(a)(4) Request for Records and Related CGMP Deviations

1. Failure to test the identity of each lot of incoming production material.

You manufacture APIs that were distributed to **(b)(4)** in the United States. Based on the records and information you provided, you have not demonstrated that you are adequately testing each shipment of each lot of incoming materials. Specifically in response to our request, you state that you do not perform identity testing on each shipment of each lot of incoming material before they are released for use in drug manufacturing.

Without adequate testing, you do not have scientific evidence that incoming materials conform to appropriate specifications prior to use in the manufacture of your drugs. As a manufacturer, you have a responsibility to sample, test, and examine incoming materials before use in production to assure adequate quality.

In response to this letter, provide:

- A description of how you will test each incoming material lot for conformity with all appropriate specifications for identity. If you intend to accept any results from your supplier's certificate of analysis (COA) instead of testing each incoming material lot for other tests, specify how you will ensure that you have adequate evidence to establish that the supplier consistently provides material meeting specifications. In addition, include a commitment to always conduct at least one specific identity test for each incoming material lot.
- A comprehensive, independent review of your material system to determine whether all suppliers of incoming materials are each qualified and the materials are assigned appropriate expiration or retest dates. The review should also determine whether incoming material controls are adequate to prevent use of unsuitable materials.
- A summary of your program for qualifying and overseeing contract facilities that test the drugs you manufacture.
- A summary of results obtained from testing all incoming materials to evaluate the reliability of the COA from each incoming materials manufacturer. Include your standard operating procedure that describes this COA validation program.

2. Failure of your quality unit to establish a system to release or reject raw materials, intermediates, packaging, and labeling materials.

The records and information you provided demonstrate that your quality unit (QU) did not effectively exercise its responsibilities to oversee the quality of your drug manufacturing operations. Specifically, your QU did not establish an appropriate system to approve or reject incoming materials.

Your QU is responsible for fully exercising its authority and responsibilities.

An adequate QU overseeing all elements of CGMP is necessary to consistently ensure drug quality. FDA considers the expectations outlined in ICH Q7 when determining whether API are manufactured in conformance with CGMP, including sections on quality oversight. See FDA's guidance document *Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* for guidance regarding CGMP for the manufacture of API at https://www.fda.gov/media/71518/download. (https://www.fda.gov/media/71518/download.)

In response to this letter, provide:

- A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:
  o A determination of whether procedures used by your firm are robust and appropriate.
  o Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices.
  o A complete and final review of each batch and its related information before the QU disposition decision.
  o Oversight and approval of investigations and discharging of all other QU duties to ensure identity, quality, and purity of all products.

CGMP Consultant Recommended

Based upon the nature of the deviations we identified at your firm, you should engage a consultant qualified to evaluate your operations and to assist your firm in meeting CGMP requirements. The qualified consultant should also perform a comprehensive six-system audit of your entire operation for CGMP compliance and evaluate the completion and efficacy of your corrective actions and preventive actions.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Conclusion

The deviations cited in this letter are not intended to be an all-inclusive list of deviations that exist at your facility. You are responsible for investigating and determining the causes of any deviations and for preventing their recurrence or the occurrence of other deviations.

FDA placed products offered for import into the United States from your firm on Import Alert 66-40 on January 17, 2025.

Correct any deviations promptly. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any deviations are completely addressed and we confirm your compliance with CGMP. We may inspect to verify that you have completed corrective actions to any deviations.

Failure to address deviations may also cause FDA to withhold issuance of Export Certificates. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any deviations are completely addressed and we confirm your compliance with CGMP. We may inspect your facility to verify that you have completed corrective actions to address any deviations.

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 30 working days. Specify what you have done to address any deviations and to prevent their recurrence. In response to this letter, you may provide additional information for our consideration as we continue to assess your activities and practices. 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. Identify your response with FEI 3027222600 and ATTN: William Yang.

Sincerely,
/S/

Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

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