

檔 號：
保存年限：

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受文者：中華民國西藥代理商業同業公會

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密等及解密條件或保密期限：
附件：美國FDA Warning Letter 320-17-24影本1份(A21020000I106110150301-1.pdf)

主旨：美國FDA發布中國原料藥廠「Chongqing Pharma Research Institute Co., Ltd.」（廠址：No. 565 Tushan Road, Nanan District, Chongqing 400061 China）Warning Letter乙案，詳如說明段，請轉知所屬會員知照。

說明：

- 一、美國衛生主管機關US Food and Drug Administration (FDA) 查核旨揭原料藥廠，判定違反CGMP，並於106年2月14日正式發布Warning Letter（詳如附件）。
- 二、鑑於旨揭原料藥之製造品質恐無法符合GMP之要求，導致對藥品製造品質帶來影響與危害，請轉知所屬會員釐清相關輸台製劑產品是否使用旨揭原料藥廠所生產原料藥，並應依風險管理原則辦理相關後續處置。

正本：中華民國西藥商業同業公會全國聯合會、中華民國西藥代理商業同業公會、台北市西藥代理商業同業公會、中華民國開發性製藥研究協會、中華民國藥品行銷暨管理協會

副本：

Chongqing Pharma Research Institute Co., Ltd. 2/14/17



**U.S. FOOD & DRUG
ADMINISTRATION**

10903 New Hampshire Avenue
Silver Spring, MD 20993

**Via UPS
Return Receipt Requested**

Warning Letter 320-17-24

February 14, 2017

Mr. Jie Deng
General Manager
Chongqing Pharma Research Institute Co., Ltd.
No. 565 Tushan Rd., Nanan District
Chongqing 400061
China

Dear Mr. Deng:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Chongqing Pharma Research Institute Co., Ltd. at No. 565 Tushan Road, Nanan District, Chongqing, from May 16–19, 2016.

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 June 7, 2016 response in detail and acknowledge receipt of your subsequent correspondence.

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

Failure to maintain complete data derived from all laboratory tests conducted to ensure compliance with established specifications and standards.

Our investigators reviewed audit trails from various stand-alone pieces of laboratory equipment you used to perform high performance liquid chromatography (HPLC) and gas chromatography (GC) analyses. Our investigators found that you had deleted entire chromatographic sequences and individual injections from your stand-alone computers.

For example, your written system suitability procedure for (b)(4) requires only six injections. However, your records showed that on January 5, 2016, you injected seven system suitability standards when performing system suitability for batch #(b)(4). The audit trail showed that the final standard injection was permanently deleted from the instrument's computer. Your analyst told our investigator that it is laboratory practice to perform more injections than are required by the procedure, and then delete any undesirable result to ensure passing system suitability results.

Without providing scientific justification, you repeated analyses until you obtained acceptable results. You failed to investigate original out-of-specification or otherwise undesirable test results, and you only documented passing test results in logbooks and preparation notebooks. You relied on these manipulated test results and incomplete records to support batch release decisions.

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. We strongly recommend that you retain a qualified consultant to assist in your remediation.

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 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 analyses of 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

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.

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 refusing admission of articles manufactured at Chongqing Pharma Research Institute Co., Ltd. at No. 565 Tushan Road, Nanan District, Chongqing 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:

Joseph Lambert, Pharm.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 3001204127.

Sincerely,
/S/
Thomas J. Cosgrove, J.D.
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

More in 2017
</ICECI/EnforcementActions/WarningLetters/2017/default.htm>