檔　　號：
保存年限：

正本

衛生福利部食品藥物管理署　函

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受文者：中華民國西藥代理商業同業公會

發文日期：中華民國106年7月25日
發文字號：FDA風字第1061104621號
速別：
密等及解密條件或保密期限：
附件：美國FDA Warning Letter 320-17-39影本1份

主旨：美國FDA發布中國原料藥委託檢驗單位「Shandong Analysis and Test Center」（地址：19 Keyuan RoadJinan, Shandong, China）Warning Letter乙案，詳如說明段，請轉知所屬會員知照。

說明：美國衛生主管機關US Food and Drug Administration（FDA）查核旨揭原料藥委託檢驗單位，判定違反CGMP，並於106年6月22日正式發布Warning Letter（詳如附件），請轉知所屬會員檢視並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：

署長吳秀梅

Shandong Analysis and Test Center 6/22/17

U.S. FOOD & DRUG
ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS

Warning Letter 320-17-39

June 22, 2017

Mr. Liu Jian Hua
Professor and Director
Shandong Analysis and Test Center
19 Keyuan Road
Jinan, Shandong, China 250014

Dear Mr. Liu Jian Hua:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Shandong Analysis and Test Center at 19 Keyuan Road, Jinan, Shandong, from January 16–18, 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 February 20, 2017 response in detail.

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

1. Failure to ensure that test procedures are scientifically sound and appropriate to ensure that your API conform to established standards of quality and/or purity.

Your site is a contract testing lab that analyzes samples of heparin and heparin-related drugs for the presence of over-sulfated chondroitin sulfate (OSCS) using Nuclear Magnetic Resonance (NMR) spectroscopy.

You failed to routinely establish system suitability when testing samples for OSCS.

Furthermore, on December 26, 2014, you conducted a system suitability test that failed. You did not investigate why your equipment failed system suitability for detection of OSCS, or determine the reliability of other OSCS tests conducted prior to the date of the system suitability failure.

In your response, you acknowledge that your laboratory performed system suitability infrequently, noting that "the heparin standards (USP) and OSCS were detected at least **(b)(4)**." You committed to routinely establish system suitability before analyzing batch samples in the future.

Your response is inadequate because you did not investigate the validity of all test results for OSCS in heparin or heparin-related drugs during the period in which you failed to conduct system suitability in coordination with sample analyses.

System suitability testing determines whether requirements for precision are satisfied and ensures the NMR spectrometer is fit for the intended testing before analyzing samples. It is critical that your system be demonstrated as suitable for detecting OSCS contamination in heparin to avoid the possibility of samples erroneously passing when an instrument is not working properly.

For further reference regarding heparin, see the guidance for industry *Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality* at **http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291390.pdf (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291390.pdf)**.

2. Failure to prevent unauthorized access or changes to data, and to provide adequate controls to prevent manipulation and omission of data.

Your quality control unit did not have basic controls to prevent changes to your electronically-stored laboratory data. During our inspection, we requested that you display original electronic data for analysis of heparin and heparin-related drug samples. Your analyst was unable to retrieve requested data, and explained that he deletes older data to make space for newly acquired data.

In your response, you committed to revise procedures regarding analyst computer permission levels, but did not address the data that was deleted.

Access to information during inspection

During the inspection, you provided a document listing the names of **(b)(4)** customers for which you performed testing. However, you only provided additional requested information, such as sample information and test results, regarding **(b)(4)** of these customers. You stated that you would not provide data related to testing performed for other customers until you obtained their prior consent.

For example, you failed to provide information pertaining to samples analyzed for **(b)(4)**, a firm that produces heparin and heparin-related drugs for the U.S. supply chain.

When an owner, operator, or agent delays, denies, limits, or refuses an inspection, the drugs manufactured, processed, packed, or held in the facility may be deemed adulterated under section 501(j) of the FD&C Act. See FDA's guidance document, *Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection*, at **https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm360484.pdf (https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm360484.pdf)** .

Conclusion

The deviations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating the 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 Shandong Analysis and Test Center at 19 Keyuan Road, Jinan, Shandong, 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:

Rokhsana Safaai-Jazi
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 3011060456.

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)