U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Xian Libang Pharmaceutical Co., Ltd.

Department of Health and Human Services

Public Health Service
Food and Drug Administration
CENTER FOR DRUG EVALUATION AND RESEARCH
Division of Manufacturing and Product Quality
International Compliance Branch
White Oak, Building 51
10903 New Hampshire Avenue
Silver Spring, MD 20993

Warning Letter

VIA FEDERAL EXPRESS MAIL

WL: 320-10-0

January 28, 2010

Mr. Tao Chen
General Manager
XiAn Libang Pharmaceutical Co., Ltd.
No. 18 Gaoxin 2nd Road
Xian Hi-Tech Zone
Shaanxi, China

Dear Mr. Chen:

This is regarding our July 27-30, 2009 inspection of your active pharmaceutical ingredient (API) manufacturing facility, Xian Libang Pharmaceutical Co., Ltd. located at ShanXi, China.. The inspection identified significant deviations from the Current Good Manufacturing Practice (CGMP) for the manufacture of APIs. These deviations cause your API(s) to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 351(a)(2)(B)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered i conformity with CGMP.

We have reviewed your firm's response of September 2, 2009, and note that it lacks sufficient corrective actions.

Specific deviations observed during the inspection include, but are not limited, to:

1. Failure of your quality unit to ensure that materials are appropriately tested and the results are reported.

For example, your firm used the infrared spectra for the raw material **(b)(4)**, lot # Y584-090301, tested on March 5, 2009, to support the release of two subsequent incoming lots of **(b)(4)** # Y584-090401 and # Y584-090701.

Your firm used the IR spectra for one lot to approve and release two subsequent incoming lots. This practice is unacceptable and raises serious concerns regarding the integrity and reliability of the laboratory analyses

conducted by your firm. It is essential that at least one test be conducted to verify the identity of each lot of incoming material. In addition, the laboratory control records should include complete documentation of all raw data generated during each test, including graphs, charts and spectra from laboratory instrumentation. These records should be properly identified to demonstrate that each raw material batch was tested and met the release specification before its use in production.

Your response of September 2, 2009 is inadequate because you did not perform a comprehensive investigation. A cursory review of records is not sufficient to ensure that other personnel did not manipulate or inaccurately report test data.

2. Failure of your quality unit to exercise its responsibility to ensure the APIs manufactured at your facility are in compliance with CGMP, and meet established specifications for quality and purity.

For example, your quality control unit failed to detect that IR spectra were being substituted by a laboratory employee and therefore, misrepresenting the actual results of the tested incoming material. Your response is inadequate in that it does not address the ability of your quality unit to control and detect the manipulation or alteration of laboratory documents.

In your response of September 2, 2009, you indicated that you "fired the chemist who was responsible for falsifying the data." You indicated that your firm has removed both the previous quality control manager and quality manager from Libang's quality management team. You also indicate that you found another incident of data manipulation involving the IR Spectra for **(b)(4)**, lot # Y535-090601. Your response is incomplete because you have not provided a more comprehensive plan to ensure the integrity of all data used to assess the quality and purity of APIs manufactured at your facility.

3. Failure to have adequate controls to prevent manipulation of raw data during routine analytical testing.

For example, your firm's laboratory analyst had modified printed raw data related to the IR Spectra test of **(b)(4)** and **(b)(4)**. We are concerned that the lack of security or system controls allows for this practice.

Your response is inadequate because it fails to completely address how your firm will ensure the integrity of raw analytical data. Your response stated that a computer server will be purchased and installed to save and print the IR spectra by September 30th, 2009.

Provide describe the new configuration of the system involved, the associated new or revised procedures, and your planned approach to qualify this system.

You are responsible not only for having controls to prevent omissions in data, but also for recording any change made to existing data, which should include the date of change, identity of person who made the change, and a explanation or reason for the change. Your response should address your laboratory equipment and any other process-related equipment that may be affected by the lack of adequate controls to prevent data manipulation. All changes to existing data should be made in accordance with an established procedure.

Please provide your Corrective Action Plan that describes your commitment, procedures, actions, and controls to ensure data integrity. This plan should include the corrective actions implemented to ensure that all managers, supervisors, and quality unit personnel are properly trained in detecting data integrity and manipulation. The investigation should provide detailed descriptions of other incidents where your quality unit failed to ensure proper testing of materials and include a retrospective review of all test results generated by your laboratory personnel. If other instances of non-existent, inaccurate or unreliable tests results are found, your investigation should assess the impact of these discrepancies on the quality of the APIs manufactured at your facility. Provide the documentation of specific training offered to all employees regarding the importance of following CGMP and ensuring that all required tests are performed.

We highly recommend that you hire a third party auditor, with experience in detecting data integrity problems, to assist you with this evaluation and assist with your overall compliance with CGMP. It is your responsibility to ensure that data generated during operations is accurate and that the results reported are a true representation of the quality of your APIs. Provide a list of all the lots of APIs shipped to the US. where release relied upon non existent, inaccurate or unreliable test data.

In addition to evaluating and correcting these data integrity concerns, we recommend that you conduct a complete and extensive evaluation of your overall quality and manufacturing controls to ensure that APIs manufactured at your facility meet the quality and purity characteristics that they purport to possess.

The deviations cited in this letter are not intended to be an all-inclusive statement of deviations that exist at your facility. You are responsible for investigating and determining the causes of the deviations identified above and for preventing the recurrence of these deviations and the occurrence of other deviations. If you wish to continue to ship APIs to the United States, it is the responsibility of your firm to ensure compliance with all US. standards for CGMP and all applicable US. laws and regulations.

Until all corrections have been completed and FDA has confirmed corrections of the deviations and your firm's compliance with CGMP, this office will recommend withholding approval of any new applications or supplements

listing your firm as the API manufacturer. In addition, failure to correct these deviations may result in FDA denying entry of articles manufactured at Xian Libang Pharmaceutical Co., Ltd., ShanXi, China into the United States. The articles could be subject to refusal of admission pursuant to section 801(a)(3) of the Act [21 U.S.C. 381(a)(3)], in that, the methods and controls used in their manufacture do not appear to conform to current good manufacturing practice within the meaning of section 501(a)(2)(B) of the Act [21 U.S.C. 351(a)(2)(B)].

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct deviations. Include an explanation of each step being taken to prevent the recurrence of deviations and copies of supporting documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will have completed the correction. Additionally, your response should state if you no longer manufacture or distribute Ropivacaine HCL, Metolazone, Ibutilide Fumarate and Succinylcholine Chloride, and provide the date(s) and reason(s) you ceased production. Please identify your response with FEI # 3003657863.

If you have questions or concerns regarding this letter, contact Maan Abduldayem, Compliance Officer, at the below address and telephone number.

U.S. Food and Drug Administration
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Sincerely,

/S/
Richard L. Friedman
Director
Division of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research

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