檔　　號：
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# 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105年9月19日
發文字號：FDA風字第1051105225號
速別：普通件
密等及解密條件或保密期限：
附件：原料藥廠違反GMP警訊乙份(A21020000I105110522501-1.pdf)

主旨：美國FDA發布中國原料藥廠「Xinxiang Tuoxin Biochemical Co.」2個廠區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）查核旨揭原料藥廠共2個廠區（如下列），判定嚴重違反cGMP，並於105年8月19日正式發布Warning Letter（詳如附件）。

（一）「Xinxiang Pharmaceutical Co., Ltd.」（No. 30 Jianshe West Road, Beigandao）。

（二）「Xinxiang Tuoxin Biochemical Co., Ltd.」（Muye and Deyuan Road cross street）。

二、鑒於旨揭原料藥之製造品質無法符合GMP之要求，可能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：電2015-09-20 交12:35:35章

**U.S. Food and Drug Administration**
Protecting and Promoting *Your* Health

# Xinxiang Tuoxin Biochemical Co. Ltd 8/19/16

**Department of Health and Human Services**

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

**Via UPS**
**Return Receipt Requested**

**Warning Letter 320-16-28**

August 19, 2016

Ms. Mona Ren
Xinxiang Tuoxin Biochemical Co., Ltd.
No. 23 Huagong East Road
Xinxiang Advanced Technology District
Xinxiang City, Henan 45300
China

Dear Ms. Ren:

The U.S. Food and Drug Administration (FDA) inspected the following drug manufacturing facilities in Xinxiang City, Henan:

- Xinxiang Pharmaceutical Co., Ltd., at No. 30 Jianshe West Road, Beigandao, on September 14 and 16, 2015 (FEI 3002773156).
- Xinxiang Tuoxin Biochemical Co., Ltd., at Muye and Deyuan Road cross street, on September 15, 17, and 18, 2015 (FEI 3008259785).

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 October 6, 2015, response in detail and acknowledge receipt of your subsequent correspondence.

During our inspections at both facilities, our investigator observed specific deviations including, but not limited to, the following.

**1. Failure to properly maintain equipment used in the manufacture of API and minimize the risk of contamination where open equipment is used.**

Our investigator observed non-dedicated drug manufacturing equipment in a state of disrepair. For example, product contact surfaces of your **(b)(4)** and reactors contained significant **(b)(4)**, product buildup, and chipped paint.

The documented state of disrepair demonstrates that you have not implemented an adequate preventive maintenance program. Although you have preventive maintenance schedules, our investigator found that for those preventative maintenance activities you state were conducted, you do not have records documenting their performance, and those records you did have lacked sufficient detail.

**2. Failure to properly maintain, repair, and keep clean buildings used in the manufacture of API in a manner that prevents contamination where open equipment is used.**

You utilized open equipment for the manufacture of API. Our investigator observed chipped paint on the ceiling directly above open **(b)(4)**, which could have fallen into your open equipment and contaminated your API. Our investigator also observed gaps around windows and doors, and holes in ceilings directly above open **(b)(4)**. Flying insects that were observed in clean rooms and on product transfer **(b)(4)** may have entered through these gaps and holes.

In your response, you stated that you would repair parts of your facility and replace some of your equipment. You did not provide details regarding your planned repairs and replacements, such as purchase orders and photographs of the renovations and replacements. As indicated above, at the time of our inspection, your facilities and equipment were in such a state of disrepair as to be unsalvageable; small or minor repairs will not adequately correct the problems and prevent their recurrence. In response to this letter, provide your written plans to renovate both facilities entirely, and submit photographic evidence of the completed renovations.

**CGMP consultant recommended**

Based upon the nature of the deviations we identified at your firm, we strongly recommend engaging a third-party consultant qualified to evaluate your operations to assist your firm in meeting CGMP requirements. Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for fully resolving all deficiencies and ensuring ongoing CGMP compliance.

**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 in all your facilities.

FDA placed both facilities on Import Alert 66-40 on April 6, 2016.

Until you completely correct all deviations and we confirm your compliance with CGMP, FDA may withhold approval of any new applications or supplements listing either of your facilities as a drug manufacturer.

Failure to correct these deviations may also result in FDA continuing to refuse admission of articles manufactured in Xinxiang City, Henan, at Xinxiang Pharmaceutical Co., Ltd., No. 30 Jianshe West Road, Beigandao, and Xinxiang Tuoxin Biochemical Co., Ltd., at Muye and Deyuan Road cross street, 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, you have 15 working days to respond to this office in writing. 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:

Towanda Terrell
Consumer Safety 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 3002773156 for Xinxiang Pharmaceutical Co., Ltd. and with FEI 3008259785 for Xinxiang Tuoxin Biochemical Co., Ltd.

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

**More in 2016 (/ICECI/EnforcementActions/WarningLetters/2016/default.htm)**