

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

Food and Drug Administration OIA/OP20/HQ
12420 Parklawn, Room 2032
Rockville, MD 20857

DATE(S) OF INSPECTION

07/24 - 07/28/2023
07/31 - 08/01/2023

FBI NUMBER

3003663281

Industry Information: www.fda.gov/oc/industry

ORAPHARM INTERNATIONAL@FDA.HHS.gov

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: YU Bin, General Manager and The chairman of The Board

FIRM NAME

Zhejiang Jinhua Conba Bio-Pharm Co. Ltd

STREET ADDRESS

288 Jinqv Road

CITY, STATE AND ZIP CODE

Jinhua, Zhejiang, P.R. China, 321016

TYPE OF ESTABLISHMENT INSPECTED

Finished Drug Product Manufacturer

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

OBSERVATION 1

Your firm failed to perform operations related to the Manufacture, processing and packing of (b) (4) in facilities separate from those used for other drug products for human use.

You manufacture drug products and drug substances in (b) (4) buildings/workshops spread in an area of approximately (b) (4) square meters within the same facility. In addition to US products, domestic (b) (4) including (b) (4)

(b) (4)

API are manufactured in the following (b) (4) workshops within your facility.

(b) (4)

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EMPLOYEE(S) SIGNATURE

P. H. Robles

EMPLOYEE(S) NAME AND TITLE (Print or Type)

RAFEEQ A. HABEER
INVESTIGATOR

DATE ISSUED

08/01/2023

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TO: YU Bin, General Manager and The Chairman of The Board

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Zhejiang Jinhua Conba Bio-Pharm Co. Ltd 288 Jingu Road

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

You manufacture drug products (b) (4) Tablets and (b) (4) Solution for us market in FDF workshops (b) (4) respectively. Your study QAL3000SR4 "Risk Assessment of (b) (4) Manufacturing on Environmental Impact" is inadequate as it does not identify all the potential risks of manufacturing of (b) (4) on (b) (4) products.

A. Risk of (b) (4) CROSS CONTAMINATION

- 1) Employees from all manufacturing buildings including employees working in FDF workshops NO (b) (4) can access one common Cafeteria within the premise of the facility for breaks and meals. These common areas are non monitored for any of the (b) (4) products and were not part of your risk assessment study.
- 2) The exhaust air from the (b) (4) FDF workshop NO (b) (4) is passed through a (b) (4) micron filter followed by a H13 (HEPA) filter before releasing directly into the outside. The air is not passed through a (b) (4) (b) (4) The H13 filter is changed (b) (4) and the integrity and function of the filter

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Zhejiang, Jinhua Conba Bio-Pharm Co. Ltd	288 Jingu Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Jinhua, Zhejiang, P.R. China, 321016	Finished drug Product Manufacturer

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

is not monitored. The location of the (b) (4) (b) (4) FOF workshop no. (b) (4) is around (b) (4) from the (b) (4) of (b) (4) FOF workshop no. (b) (4)

3) (b) (4) from (b) (4) used for (b) (4) products in FOF workshop no. (b) (4) is released into the (b) (4) of the building. The (b) (4) is not passed through any filter or (b) (4) and is not monitored for (b) (4) residues.

4) In FOF workshop no. (b) (4) the exhaust air from API (b) (4) production area of production line (b) (4) and (b) (4) growing area, shower room, and container preparation areas of both line (b) (4) and (b) (4) is released after passing through a HEPA filter H13 and is not passed through a (b) (4). The exhaust air from both these (b) (4) is not monitored for residues at regular intervals.

INADEQUATE MONITORING OF (b) (4) AREAS AND PRODUCTS
You do not monitor for (b) (4) residues in (b) (4) areas of your facility including FOF workshops (b) (4)

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288 Jinpu Road

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Jinhua, Zhejiang, P.R China, 321016

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

Except for one finished product (b) (4) API, you have not tested any other finished product including (b) (4) Tablets and (b) (4) solution for (b) (4) residues.

C. INADEQUATE MONITORING OF (b) (4) AREAS

Your monitoring of (b) (4) FDF workshops (b) (4) is not at regular frequency. You have monitored for (b) (4) residues in FDF workshop (b) (4) and (b) (4) residues in workshop (b) (4) and the last date of monitoring for each of these residues is as follows

- 1) (b) (4) - 2021, March
- 2) (b) (4) - 2021, June
- 3) (b) (4) - 2020, May

You have not monitored for (b) (4) and (b) (4) residues in workshops (b) (4)

D. VALIDATION OF (b) (4) DECONTAMINATION METHOD

Your firm used (b) (4) to decontaminate exhaust air from few locations and also to decontaminate tools and parts. You have

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RABEEA A. HABEER
INVESTIGATOR

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not done an effectiveness check/validation study to show that your decontamination solution used to clean the (b) (4) residues is effective.

E. (b) (4) ASSAY METHOD

Your method for detecting (b) (4) residues is not sufficiently sensitive to detect low levels of contamination. The limit of detection for your method is not capable of detecting levels in parts per billion. The limit of detection (LOD) for your method was reported as follows:

(b) (4) (b) (4) ppm

(b) (4) ppm

(b) (4) ppm

(b) (4) (b) (4) ppm

Furthermore you have not established a detection limit for (b) (4)

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RACEED A. HABEEB
INVESTIGATOR

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FIRM NAME Zhejiang Jinhua Conba Bio-Pharm. Co., Ltd.	STREET ADDRESS 288 Jinpu Road
CITY, STATE AND ZIP CODE Jinhua Zhejiang, P.R. China, 321016	TYPE OF ESTABLISHMENT INSPECTED Finished drug Product Manufacturer

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

OBSERVATION 2

Employees engaged in the manufacture and processing of a drug product lack the training required to perform their assigned function.

Specifically, the employees engaged in the 100% visual inspection of (b) (4) sterile solution are not adequately trained to do visual inspection within the specified time. Your validation batch records for (b) (4) solution show that employees took (b) (4) trial to complete visual inspection. However your training records for employees performing visual inspection show that employees were allowed to take up to (b) (4) to complete inspection of each vial. Furthermore you did not perform visual inspection using a white background. You did visual inspection using only a (b) (4) background during both the training and inspection of all (b) (4) validation batches.

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ORA PHARM INTERNATIONAL
FDA #HS-50V

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

OBSERVATION 3

Laboratory Controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that components and drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically,

You do not perform growth promotion testing on all lots of prepared media. You prepare the following media for testing of incoming raw materials, (b) (4) finished product, and environmental samples.

- 1) (b) (4) media - Testing of (b) (4)
- 2) (b) (4) media - Mold and yeast testing of raw materials and finished products
- 3) (b) (4) media - Testing of finished products for E. coli, and sterility testing of finished product for mold and yeast
- 4) (b) (4) media - Specific microbial testing of E. coli in finished products (in media)
- 5) (b) (4) media - Specific microbial testing of E. coli in finished products (b) (4) plate)
- 6) (b) (4) media - Finished product testing for both aerobic and anaerobic microorganisms

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RAFEED A HABEER
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OBSERVATION 4

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established.

Specifically,

A) You do not test the integrity of the (b) (4) before each batch during the manufacturing of the sterile product (b) (4) solution. You test (b) (4) integrity only (b) (4) (b) (4) or between two different products.

B) You dilute (b) (4) and filter it through a (b) (4) micron filter to produce (b) (4) for use in cleaning of your RABS and the surrounding areas. You do not record the concentration of (b) (4) produced.

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INVESTIGATOR

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