**DEPARTMENT OF HEALTH AND HUMAN SERVICES**
FOOD AND DRUG ADMINISTRATION

| DISTRICT OFFICE ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| ATTN: Mr. Concepcion (Coki) Cruz<br>10903 New Hampshire Avenue, WO51 RM 4316<br>Silver Spring, MD 20993<br>Phone: (301)-796-3254 Fax: (301)-847-8738 Email: CDEROSIAB@fda.hhs.gov<br>Industry Information: www.fda.gov/oc/industry | 01/16-19/2017 |
| | FEI NUMBER<br>3007719313 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Lin Jian Qiu, President

| FIRM NAME | STREET ADDRESS |
|---|---|
| Zhejiang Hisun Pharmaceutical Co., Ltd. | 46 Waisha Road, Jiaojiang District |
| CITY, STATE AND ZIP CODE | TYPE OF ESTABLISHMENT INSPECTED |
| Taizhou City, Zhejiang, CHINA | Active Pharmaceutical Ingredient 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

Quality Control laboratory control procedures are not followed.

Specifically, your firm received a Warning Letter from the FDA dated 12/31/15 regarding breaches in the integrity of analytical data generated in support of the registration, batch release, and stability of your API products. As part of your firm's response, you committed to and submitted the results of a "full-scale investigation" of historical data collected during the period 01/01/13 to 03/01/15 to determine if there are "any similar data integrity issues", as outlined on page 2 of your "Evaluation Report for HPLC Analytical Data in QC Lab" dated 01/24/16.

Your conclusion submitted to the Agency found "no data related with product failures were identified during the full-scale investigation". However, our limited review of the electronic data and associated metadata for during this same time period during this current inspection identified numerous examples of data integrity issues that were not identified and investigated as part of your "full-scale investigation". Examples identified included the same categories as outlined in the previous FDA 483 dated 03/07/15; namely:

1. deletion and overwriting of data, and
2. running analyses without the audit trail enabled.

Our limited spot-check review identified approximately 23 such instances, only 3 of which were included in your "full-scale investigation" report submitted to the Agency. Representative examples identified during this inspection and not submitted in your Evaluation Report are outlined below:

A) (b) (4) (unknown batch number)

- An analyst (unknown) performed an analysis of (b) (4) on 03/20/2104 with the audit trail function disabled.

| SEE REVERSE OF THIS PAGE | EMPLOYEE(S) SIGNATURE | EMPLOYEE(S) NAME AND TITLE (*Print or Type*) | DATE ISSUED |
|---|---|---|---|
| | Lindsey M. Schwierjohann | Lindsey M. Schwierjohann, Investigator<br>Peter E. Baker, Investigator | 01/19/2017 |

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- Your analyst (b) (6) performed processing of these chromatograms on 03/21/2014 starting at 8:21 with the audit trail enabled.

B) (b) (4) 24 month stability batch # (b) (4) Impurities by HPLC

- During the running sample set on 03/12/14, your analyst (b) (6) deleted/overwrote a total of 5 sample injections related to these stability sample aliquots:

- (b) (4) injected 11:36 (this injection result was deleted)
- injected 12:26 (this injection result was reported)

- (b) (4) injected 13:15 (this injection result was deleted)
- injected 13:37 (this injection result was deleted)
- injected 15:05 (this injection result was reported)

- (b) (4) injected 14:02 (this injection result was deleted)
- injected 15:29 (this injection result was reported)

- (b) (4) injected 14:26 (this injection result was deleted)
- injected 15:53 (this injection result was reported)

C) (b) (4) API batch # (b) (4) degradation study by HPLC

- During the running sample set on 06/10/14, your analyst (b) (6) stopped the running chromatogram after approximately 8 minutes at 16:36
- The sample was re-injected at (b) (4) and the original result was deleted/overwritten

OBSERVATION 2

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| | Lindsey M. Schwierjohann | Lindsey M. Schwierjohann, Investigator<br>Peter E. Baker, Investigator | 01/19/2017 |

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Labeled storage conditions are not justified by stability studies.

Specifically, an OOS result for impurities by HPLC was confirmed for (b) (4) stability (12 months at (b) (4) C) batch # (b) (4) during the investigation OOS-FLUD-1501. The labeled expiration date and conditions for this batch are (b) (4) at NMT (b) (4) C. There is currently no stability data to support these label claims.

Notably, following this confirmed stability failure your firm transferred samples of this batch from the retain samples storage ((b) (4) C) to the (b) (4) C stability chamber in order to support the label claim of NMT (b) (4) C. However, storage at (b) (4) C is not representative of the worst case label conditions.

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