DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave - White Oak (Bldg. 51 Rm. 4225) Silver Spring, MD 20993 Phone: 301-796-3334 email: CDEROSIAB@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	08/07-11/2017 FEI NUMBER 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, Zhejiang, 318000. CHINA	API/Finished Drug Product Manufacturer

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

OBSERVATION 1

Laboratory records do not always include relevant metadata in order ensure established procedures are followed.

Specifically, during our review of historical (2012-2014) original chromatography (HPLC) data collected in support of (b) (4) API DMF (b) (4) and (b) (4) API DMF (b) (4), we found that the integrity of data collected and reported could not be fully verified:

For example (this list is not exhaustive):

A) For (b) (4) API

a) The audit trail for stability data collected at the 12 month timepoint for batch (b) (4) was not available for review. According to your analyst, the audit trail was not archived and cannot be retrieved.
b) Data for the 0 and 24 month stability timepoints for batch (b) (4) were collected using stand-alone Agilent HPLC systems with no system audit trail or other controls enabled to ensure data integrity.

B) For (b) (4) API

a) Data for the 0 month stability timepoint for batch (b) (4) was collected using stand-alone Agilent HPLC system with no system audit trail or other control enabled to ensure data integrity.

OBSERVATION 2

Written procedures are deficient regarding the cleaning and maintenance of equipment.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
		Peter E Baker, Investigator Parul Patel, Investigator	08/11/2017

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Specifically,

A) During our review of your cleaning validation study performed for the (b) (4) tablet press to be used in the manufacture of (b) (4) tablets, we found that there is no scientific rationale (e.g. risk assessment) justifying the (b) (4) sampling points.

Additionally, there are no specific instructions (e.g. diagrams, pictures) available to define where the swabbing was to take place. For example, your validation report states that the "(b) (4) inner surface" was sampled; however, there is no evidence available to define the sampling location in order to ensure that the worst-case location was sampled.

B) Your firm uses purified water as the solvent during routine cleaning of the (b) (4) tablet press following the manufacture of (b) (4) tablets, however, there has been no scientific evaluation to justify the use of purified water and evaluate its effectiveness considering the API and excipients used during manufacturing.

C) Your cleaning procedure document H5-SOP-5204 for cleaning of the (b) (4) tablet press lacks specific instructions regarding how to disassemble/reassemble the equipment, the temperature of purified water to be used, and the cleaning tools (e.g. brush) and actions to be used.

OBSERVATION 3

Storage conditions for samples retained for testing are not monitored appropriately.

Specifically, your firm's stability chambers' routine monitoring is performed at the locations found to be the highest temperature and humidity during the qualification studies. These locations do not represent the worst-case locations (coldest/lowest humidity) within the chambers.

OBSERVATION 4

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Records are not completed contemporaneously.

Specifically, during my inspection of your microbiology laboratory on 08/08/17, I observed your microbiologist preparing to load the purified water and (b) (4) plates into the incubator for samples collected and prepared earlier that day. However, the sample preparation worksheets for these samples were either partially completed or blank.

OBSERVATION 5

Laboratory records do not include complete data derived from microbial limit testing to ensure established procedures are followed.

Specifically,

1. During our review of the microbial limits test method validation for (b) (4) Tablets (b) (4) mg, we noted the following discrepancies:

a) The weight of product sample used is not documented.
b) The initials and/or signature and date of the analyst are not documented on microbial test record sheets.
c) There is no documentation to demonstrate when and who performed the (b) (4) and (b) (4) transfer between incubators.

2. Our review of historical stability data for (b) (4) Tablets (b) (4) mg, we noted the following discrepancies:

a) The initials and/or signature and date of the analyst are not documented on the microbial test records sheet.
b) There is no documentation to demonstrate when and who performed the (b) (4) and (b) (4) transfer between incubators for batch #'s (b) (4) (b) (4) (b) (4) and (b) (4).

OBSERVATION 6

PEB 8/11/2017

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SEE REVERSE OF THIS PAGE	PEB PP	Peter E. Baker, Investigator Parul Patel, Investigator	08/11/2017

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Changes to manufacturing processes are not fully documented.

Specifically, your firm performed two "major" changes to the (b) (4) API manufacturing process in 2016 documented under VC-(b) (4) -1602 and VC-(b) (4) -1603. There was no risk assessment or other scientific evaluation documented to justify the actions taken to monitor the acceptability/effectiveness of these process changes.

OBSERVATION 7

Process validation studies do not contain a history of all relevant data.

Specifically, during our review of your in-process control (b) (4) data collected during the process validation study for (b) (4) API performed in 2010, we found the following deficiencies:

A) Original in-process electronic data is not available for review.

B) During our review of the printed (b) (4) for in-process (b) (4) of (b) (4) we identified what appears to be an (b) (4) peak in the standard (b) (4) peak summary table at ~(b) (4) However, your printed (b) (4) traces are only available up to (b) (4) The presence of this (b) (4) peak in the remaining (b) (4) (e.g. samples) could not be determined.

OBSERVATION 8

The final API storage areas are not maintained in a good state of repair.

Specifically, on August 9, 2017 during my walk-through of the finished API storage areas, I observed what appeared to be water leakage in room #'s 102, 104 and 105.

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(b) (4) API was stored in room 102, (b) (4) API was stored in room 104 and (b) (4) API was stored in room 105.

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