DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	8/7/2023-8/18/2023*
	FEI NUMBER 3003995556

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
LV Liang, CEO and Chairman

FIRM NAME	STREET ADDRESS
Hangzhou Zhongmei Huadong Pharmaceutical Co., Ltd	866 Moganshanlu
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Hangzhou, Zhejiang, 310011 China	Sterile Drug, Non-sterile Capsule, and Non-sterile API 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 OBSERVED:

OBSERVATION 1

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

Specifically,

The following discrepancies were observed on 09 August 2023, during the aseptic filling of (b) (4) Injection, (b) (4) mg per vial, batch number (b) (4) (non-US batch) in Workshop (b) (4).

-The Operator in the Grade B supporting room opened the (b) (4) restricted access barrier (b) (4) RABS) (b) (4) adjacent to the filling machine and proceeded to reach into the (b) (4) RABS with their arm, shoulder, and part of their head while placing a settle plate and an active air plate. The Grade A inside of the (b) (4) RABS (b) (4) the Operator's gloves, and the media plates were not disinfected immediately prior to, during, or after this process.

-Your firm does not disinfect the (b) (4) hanging around the (b) (4) LAF area adjacent to the (b) (4) stopper (b) (4) section of the (b) (4) RABS during set up and filling activities. For example, during set up activities, employees placed their gloved hands and arms through the (b) (4) while moving wrapped tools and bags of (b) (4) stoppers through the (b) (4) in order to place them into the (b) (4) RABS. The (b) (4) were not disinfected prior to, during, or after these processes. In addition, you do not perform environmental monitoring during set up and filling operations inside the

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FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS

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(b) (4) LAF area.

Your cleaning procedure for Workshop (b) (4) number (b) (4) SOP-B052-08, only requires disinfecting the (b) (4) RABS (b) (4) once the (b) (4) stopper (b) (4) has been installed and during filling operations. The SOP does not mention disinfecting the (b) (4) or media plates before or during filling operations. Your environmental monitoring SOP, number (b) (4) SOP-A071-12, does not require any settle plates, contact plates, active air samples, or non-viable particle samples in the (b) (4) LAF area during dynamic conditions. Workshop (b) (4) contains (b) (4) aseptic filling line, which is used for manufacturing (b) (4) Injection and the (b) (4) injection drug product as part of (b) (4).

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic process.

Specifically,

Your employee visual inspection qualification program does not include qualifying employees on detecting Type B (major) and Type C (minor) defects in liquid filled, (b) (4) vials. Your employees have only been qualified on Type B and Type C defects using (b) (4) vials with (b) (4) product. Type B defects include, but are not limited to, vial cracks and low fill vials. Type C defects include, but are not limited to, (b) (4) stopper defects and vial (b) (4) defects. Your employees performed visual inspection activities on (b) (4) process validation batches (batch numbers (b) (4)) of the (b) (4) injection drug product as part of (b) (4) in August 2022. In addition, your firm did not have an effective SOP for visual inspection qualification of liquid filled (b) (4) vials until 15 August 2023. The new SOP, number (b) (4) RSOP-L006, only focuses on Type A defects ((b) (4) chips, (b) (4) chips, and fibers) in liquid filled (b) (4) vials and refers to the visual inspection qualification results from (b) (4) in (b) (4) vials for Type B and Type C defects.

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OBSERVATION 3

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

Your (b) (4) visual inspection program for (b) (4) drug product vials is inadequate as evidenced by employees inspecting the vials at a speed of approximately (b) (4) vials per (b) (4) (approximately (b) (4) vials per (b) (4) during visual inspection of (b) (4) Injection, batch number (b) (4) on 11 August 2023. Your visual inspection procedure for (b) (4) for Injection, number (b) (4) SOP-D084-14, states the light inspection (visual inspection) process must be performed at no more than (b) (4) vials per (b) (4) and does not have a recommended speed. Your procedure for manufacturing (b) (4) Injection, number (b) (4) SMP-U001-03, states employees must examine each vial for "broken bottles, foreign matters, abnormal filling volume, empty vials, (b) (4) that cannot be stripped off easily in stoppers, vial defects, stopper defect, (b) (4) cap defect, unqualified (b) (4) appearance, unqualified (b) (4) appearance". During visual inspection activities of (b) (4) Injection, batch number (b) (4) the (b) (4) speed fluctuated between approximately (b) (4) and (b) (4) vials per (b) (4) This speed did not allow for adequate inspection of each vial for the criteria listed in your procedure.

OBSERVATION 4

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically,

Your laboratory computers used to control your bacterial endotoxin testing (BET) machine (Building (b) (4)) and your HPLCs (Building (b) (4)) do not contain adequate security controls to prevent deletion and modification of files related to the analytical software (Pyros EQS and OpenLab CDS) used on these

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computers by Analysts. The Pyros EQS software is used for BET for the (b) (4) injection drug product as part of (b) (4) The HPLCs in Building (b) are used for testing (b) (4) (b) (4) Injection.

***DATES OF INSPECTION**

8/07/2023(Mon), 8/08/2023(Tue), 8/09/2023(Wed), 8/10/2023(Thu), 8/11/2023(Fri), 8/14/2023(Mon), 8/15/2023(Tue), 8/16/2023(Wed), 8/17/2023(Thu), 8/18/2023(Fri)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."