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	11/17/2022-11/25/2022*
	FEI NUMBER 3008538640

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Takuya Moto, Division Director, Production Division

FIRM NAME	STREET ADDRESS
Fuji Yakuhin Co., Ltd.	682, Itakura, Fuchu-Machi
CITY, STATE, ZIP CODE, COUNTRY Toyama-Shi, Toyama, 939-2721 Japan	TYPE ESTABLISHMENT INSPECTED Sterile Drug 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,

A. Operators' actions working within the aseptic manufacturing (Building (b) (4) Line (b) (4) during a simulation run (b) (4) Run) were insufficient. For example, on November 17, 2022 I observed the following:

- Two aseptic operators' movements were not slow and deliberate.
- Aseptic operator was not sanitizing the interior of the (b) (4) each time it was opened.
- Two aseptic operators' hands were hanging below their waist throughout the filling operation.
- Aseptic operator did not fully remove settle plate cover during operations.
- Aseptic operator had sprayed (b) (4) on his hands and sleeves just prior to conducting personnel monitoring.
- Aseptic operator's finger sampling was insufficient in that the operator press down fingers straight down on monitor plate without rolling to include the full surface of fingers.
- Aseptic operator had sampled his upper arms instead of (b) (4) as required.
- Aseptic operator had crawled under the conveyer belt located within the RABs (Grade A)

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	Robert J Martin, Investigator X Robert J Martin Investigator Signed By: Robert J. Martin -S Date Signed: 11-25-2022 15:46:59	11/25/2022

to setup EM monitoring in the corner of the room.

- Aseptic operator noted carrying the batch record around filling room within a plastic binder.
- Aseptic Operator noted leaning upper body within the RABs to make an intervention on the transfer conveyer belt.

B. Microbiologist action while performing sterility test simulation for (b) (4) Injection (b) (4) (b) (4) within the Aseptic Testing Room was insufficient. For example, on November 21, 2022, I observed:

- Microbiologist had sprayed hands with (b) (4) just prior to plating fingertips.

C. Operators' actions working within the aseptic manufacturing (Buildin (b) (4) Lin (b) (4) during the manufacturing of (b) (4) Injection Lot Number (b) (4) were insufficient. For example, on November 25, 2022 I observed the following from the room security camera footage:

- Aseptic Operator was noted placing half of his body within the stopper assembly section of the RABs.
- Aseptic Operator was noted swing back and forth will standing in from of the control panel.
- Aseptic Operator was noted touch his face several times during the filling operation.
- Aseptic Operator had opened the (b) (4) to the Stopper Assembly Unit rapidly and place half of his body within the RABs over the vial conveyor blocking the first pass air as part of an intervention of the Stopper Assembly.
- Aseptic operator's hands were hanging below their waist throughout the filling operation.
- Aseptic operator had crawled under the conveyer belt located within the RABs (Grade A) to setup EM monitoring in the (b) (4)

Filling Line (b) (4) n Building (b) (4) s used to manufacture (b) (4) Injection, (b) (4)

D. The firm has failed to demonstrate unidirectional airflow over Grade A production equipment used in the manufacturing of sterile drug product. For example, the firm has failed to conduct airflow pattern studies (smoke studies) demonstrating that setup processes within the Stopper (b) (4) and Sterile Fill Line (Fill Line (b) (4) Building (b) (4) affect the unidirectional airflow within the RABs and (b) (4) This filling line is used to manufacture (b) (4) Injection, (b) (4)

OBSERVATION 2

Routine calibration of automatic, mechanical and electronic equipment is not performed according to a written program designed to assure proper performance.

Specifically,

- The firm failed to complete Operational Qualification on newly installed Stability Chamber in that the firm did not conduct recovery test ("open door") and power loss test. For example, in April 2020 the firm had qualified Stability Chamber (T377, 2-8°C); however, the qualification did not contain recovery test ("open door") and power loss study. The qualification was approved on 6/19/2020. This stability chamber is used for long term stability for (b) (4) Injection, (b) (4)

- The firm has failed to conduct (b) (4) studies within Parts (b) (4) (C2-Instrument (b) (4) 2) and (b) (4) (C2 Vial Sterilization (b) (4) 2) since their initial qualification. For example, the Parts (b) (4) was installed on April 7, 2004 and the (b) (4) was installed on March 24, 2004; however, neither have undergone (b) (4) (b) (4) studies (empty chamber (b) (4) since. The (b) (4) and

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(b) (4) are used in the sterile manufacturing process for (b) (4) Injection, (b) (4)

OBSERVATION 3

A sample which is representative of each lot in each shipment of each active ingredient is not retained.

Specifically,

The firm failed to retained samples of (b) (4) Drug Substances received for the manufacturing of (b) (4) Injection. For example, the firm received (b) (4) of batches of (b) (4) Drug Substance; however, they did not retain samples of these batches as part of their retention program.

***DATES OF INSPECTION**

11/17/2022(Thu), 11/18/2022(Fri), 11/21/2022(Mon), 11/22/2022(Tue), 11/23/2022(Wed), 11/24/2022(Thu), 11/25/2022(Fri)

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