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 ORAPHARMInternational483responses@fda.hhs.gov	11/11/2024-11/19/2024
	FEI NUMBER 3012637764

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

John Yi, General Manager

FIRM NAME	STREET ADDRESS
Janssen Vaccines Corporation	23 Harmony-ro 303 Beon-gil, Yeonsu-gu
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Incheon 22014, Korea, Republic of (South)	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 WE OBSERVED:

OBSERVATION 1

Responsibilities and procedures for quality units are not in writing and/or followed to ensure the FARS (BPDR) are submitted for the distributed products that are implicated with product quality issues.

Specifically,

You failed to follow your procedure, TV-WI-21853 Version 29.0 Product Quality Complaint Investigation (Effective date 5/25/2024) Section 7.11.1.2 that sets the requirement for FAR (BPDR) as, "***Two or more complaints with the same confirmed defect with same root cause for the same finished good lot or a root cause related to a common component lot in more than one finished good lot, with or without signal***". Your procedure, TV-SOP-31402 Version 6.0 Advisory Notices, US FDA Form 3911 (Drug Notification and Health Authority (HA) Communication – Reportable Events Procedure (Effective date 7/17/2024) sets the timeline for reporting BPDR as, "***as soon as possible, but no more than (b) (4) from the date the information is acquired***.

Between 11/13/2023 and 11/8/2024, you recorded at least 25 market complaints for (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S Date: 2024.11.19 14:26:28 +09'00'	Rajiv R Srivastava, CSO	11/19/2024

stopper (b) (4) for you (b) (4) Vial (b) (4) mg (b) (4) ml. Two and more complaints were received for the same lot. E.g., Two (2) complaints of (b) (4) were received for each of the Lot No's. (b) (4) (Mfg. date 6/20/2023, Expiry date (b) (4) (Mfg. date 7/5/2023, Expiry date (b) (4) (Mfg. date 8/8/2023, Expiry date (b) (4) (Mfg. date 8/10/2023, Expiry date (b) (4) (Mfg. date 12/12/2023, Expiry date (b) (4) (Mfg. date 2/16/2024, Expiry date (b) (4) Three (3) complaints of (b) (4) were received for each of the Lot No's (b) (4) (Mfg. date 7/21/2023, Expiry date (b) (4) (Mfg. date 11/11/2023, Expiry date (b) (4) In addition, a complaint for four (4) (b) (4) vials was received for Lot No. (b) (4) (Mfg. date 2/2/2024, Expiry date (b) (4)

Your Senior Director Business Director, Compliance (ET) stated that the investigation concluded the (b) (4) was not related to manufacturing process and hence the defect was not confirmed and no CAPA was implemented. Your Site Quality Head (SO) stated that the quality issue is related to end user and not with the drug product manufacturing.

OBSERVATION 2

Procedure designed to prevent microbiological contamination of drug products purporting to be sterile are not established or followed.

A. On 11/13/2024, your vial filling operation recorded multiple interventions during the filling of (b) (4) Injection (b) (4) mg (b) (4) mL vial Batch No. (b) (4) During the filling, the vials got stuck simultaneously in IPC (b) (4) stoppering stations, and the vial (b) (4) (b) (4) The interventions took > (b) (4) that necessitated running IPC before the line was restarted.

During the intervention, multiple adjustments were made, e.g., loosening and wiggling the (b) (4) (b) (4) bolts for IPC (b) (4) loosening and wiggling (b) (4) transferring a pair of extralong hemostat tweezers from one of the (b) (4) doors # 5.

Transferring of a hemostat from (b) (4) door # 5, and use of a hemostat for removing the jammed vials are not part of an established/regular intervention, ID # (b) (4) Removal of Jammed and Broken Vial from (b) (4) According to your procedure, TV-WI-32841 Intervention in Aseptic Process (Effective date 9/12/2024), intervention ID # (b) (4) is done using (b) (4) gloves (b) (4) (b) (4) using tweezers stored in the (b) (4) The intervention ID # (b) (4) is simulated in your media fill for (b) (4) You used gloves (b) (4) and a hemostat. In addition, the intervention that required the use of gloves (b) (4) and a hemostat, took almost (b) (4) for much longer duration than you simulated in your media fill for (b) (4) Your QC Site Head (SO) initially insisted that this intervention was considered a regular intervention, ID # (b) (4) where a hemostat was used just like the one the firm uses for intervention, ID # (b) (4) Removal of Jammed (b) (4) Stoppers in (b) (4) A review of your smoke study for intervention ID # (b) (4) confirmed that the hemostat for (b) (4) used a (b) (4) like device at the tip of the hemostat to help with removing the (b) (4) stoppers. You finally decided to open a non-conformance.

B. On 11/13/2024, at around (b) (4) during the filling of (b) (4) Injection (b) (4) mg Batch No. (b) (4) water condensation was seen on the inside of the goggle of one of production operator (BS) in the aseptic area. Your procedure, SOP No. TV-WI-15914 Version 18.0 Behavior in Aseptic Room and RABS (Effective date 8/8/2023), Section 7.1.14 states, "*** When goggles get damp, operators should temporarily stop movement to minimize such damp or, if necessary, operators should change goggles***".

C. On 11/13/2024, at around (b) (4) during the filling of (b) (4) Injection (b) (4) mg Batch No. (b) (4) your operators in the aseptic area were seen fully inserting the tweezers (b) (4) and hemostat by its tips inside the jammed vials and forcefully wiggling it to remove the jammed vials. Your operator was also seen placing the tweezer into the holders by rubbing against the body of the tweezer holder. Your procedure, SOP No. TV-WI-15914 Version 18.0 Behavior in

Aseptic Room and RABS (Effective date 8/8/2023), Section 7.1.14 states, "*** Be cautious not to let the tweezer tip touch the tweezer holder nor the tweezer body to rub against the holder when putting the tweezer into the tweezer holder***".

OBSERVATION 3

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically,

A. Aseptic filling processing of finished drug product i.e. from (b) (4) vials to aseptic filling and to glass vial sealing processing steps, are performed within a Grade A (ISO 5) environment. The following observation was made regarding your non-viable particle (NVP) monitoring:

   You manufacture (b) (4) Injection (b) (4) mg on you Vial Filler ID # B1-2018 that consists of (b) (4) You monitor airborne particles in the RABS with (b) (4) non-viable particle (NVP) counters ID's; (b) (4) (b) (4) (b) (4) of the NVP counters, (b) (4) are meant to monitor the (b) (4) (b) (4) and the NVP counter in the center of a (b) (4) of (b) (4) monitors the NVP on the (b) (4) vials. These (b) (4) NVP counters do not provide adequate coverage to assure that Grade A is maintained around and over the (b) (4) and (b) (4) vials.

B. Your procedure, TV-SOP-40940 Version 18.0 Validation of Unidirectional Airflow (Laminar) Device (Effective date 11/6/2024) Section 5.3.7.5.1 specifies the acceptance criteria for smoke study as, "***Airflow should be linear and uniform without turbulence, eddies, or reflux in both At rest (static conditions) and In operation (dynamic condition) status.

The following table lists several instances where the unidirectional airflow patterns could not be determined and/or observed. Note: the summary provided in the table is not intended to be an all-inclusive and/or exhaustive list of concerns, for example;

Approximate time stamp	RABS Setup: Transfer and Installation of (b) (4) Set, Chute, and (b) (4)
(b) (4)	Not enough smoke over left hand to observe unidirectional airflow (UDA)
	Not enough smoke over left hand to observe UDA
	Attaching the (b) (4) to filling line, not enough smoke to verify UDA
	Attaching the (b) (4) to filling line, right hand is blocked by left hand
	Tightening the (b) (4) assembly, not enough smoke to verify UDA
	(b) (4) Calibration
(b) (4)	Adjusting the IPC (b) (4) not adequate smoke to verify UDA
	Adjusting the (b) (4) with both hands: not enough smoke to UDA
	(b) (4) Sample Bag Replacement and (b) (4)
(b) (4)	Removing the sample bag, not enough smoke to verify UDA
	Replacing the sample bag, not enough smoke to verify UDA
	Removing the sample bag, not enough smoke to verify UDA

OBSERVATION 4

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,

Your (b) (4) stoper transfer pipe was seen to have a small hook (~1.5 cm) like structure welded on the top of the pipe. The welding was rough and consisted of a crack at the

welding site. On the inside of the pipe right beneath the welded hook, the surface was not smooth, appeared to be (b) (4) in color, and shedding the surface particle. You have recorded a complaint # 90000338418 for Uncharacteristic Color. This complaint was received for (b) (4) Vial (b) (4) mg (b) (4) mL Batch No. (b) (4) Mfg. date 2/7/2024, Expiry date (b) (4) for the drug product being (b) (4) color. No root cause was determined.

OBSERVATION 5

Equipment used in the manufacture, processing, packing, or holding of drug products is not of appropriate design to facilitate operations for its intended use.

Specifically,

Your firm's (b) (4) integrity test (b) (4) machines are not adequately qualified such that the (b) (4), and operating ranges (b) (4) associated with your drug products manufacturing are not adequately qualified. You carried out Operation Qualification in two parts; Parts 1 and 2. The OQ Part 1 is general functional testing of critical parameters, e.g., data entry, error messages, test on accuracy of pass/fail analysis, and running tests for test functions such as (b) (4) The Part 2 test is designed to verify the functionality of the instrument.

You did not carry out OQ Part 1 test for your (b) (4) machines on site and used the vendor provided data (from a different (b) (4) machine) to supplement the OQ Part 1. The OQ Part 2 is merely a single point verification of the (b) (4) machines. E.g., the (b) (4) ID # B1-2755 is verified for (b) (4) at (b) (4) at (b) (4) You ensure (b) (4) integrity during (b) (4) of the drug product via measuring the specified (b) (4) at a specific (b) (4) You use (b) (4) product (b) (4) None of your (b) (4) machines (ID's (b) (4) are qualified for any of the (b) (4)

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You used (b) (4) ID # B1-2370 to manufacture (b) (4) Injection (b) (4) mg Batch No's (b) (4) and (b) (4) Both baches recorded failed (b) (4) results for the (b) (4) (b) (4) closest to the filling line); Batch No. (b) (4) recorded (b) (4) failed (b) (4) test, Batch No. (b) (4) recorded (b) (4) failed (b) (4) test result. Your procedure allows (b) (4) failed (b) (4) results before a nonconference/deviation will be initiated.

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SEE REVERSE OF THIS PAGE	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S Date: 2024.11.19 14:29:51 +09'00'	Rajiv R Srivastava, CSO	11/19/2024