DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 12420 Parklawn Drive Room 2032 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	August 7-10 and 13-15, 2023
	FEI NUMBER 3013501887

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Fadi Al-Atrash, General Manager

FIRM NAME	STREET ADDRESS
Amman Pharmaceutical Industries	Building 108, Street A3, King Abdullah II Industrial City
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Amman, Jordan 11152	(b) (4) Drug Manufacturer

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

OBSERVATION #1

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

During the set-up, filling, and transfer of equipment and components into the aseptic filling room, poor aseptic processing behavior was observed on the aseptic filling lines used to manufacture US market product, including the aseptic fill lines identified as (b) (4) For example:

A. During set-up and aseptic filling on (b) (4) batch (b) (4) on (b) (4) (b) (4) the following was observed:

1. The operators performing line set-up and manual interventions during the filling operations were not wearing goggles, resulting in exposed skin in the Grade A areas of the aseptic filling line.

2. During the filling from approximately (b) (4) until approximately (b) (4) there were approximately 376 times when an operator (b) (4) a (b) (4) or entered the (b) (4) at the (b) (4) to perform a manual intervention. During these manual interventions, the operators had their heads and torso inside the Grade A areas and leaned over open sterile bottles, sterile (b) (4) sterile (b) (4) and the (b) (4) (b) (4) Sterile primary packaging components are not cleared following manual interventions.

3. Prior to performing manual interventions inside of the filling barrier, the operators routinely touched their face and then subsequently performed the manual intervention without disinfecting their hands. Procedure SOPPE003 "Behavior Inside Sterile Area" instructs the use of forceps for picking things up. However, throughout the batch none of the operators used forceps and they directly contacted sterile components that were not subsequently removed or surfaces that were not subsequently disinfected.

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4. The operators were observed repeatedly performing a manual intervention to inspect bottles for defects caused by the bottle sorting equipment. The operators would handle the open, sterile bottle with their hands. If there was no defect, the bottle would be placed back on the line to be filled.

5. During set-up, the sterilized tube used to transfer sterile filtered product into the (b) (4) sterile receiving tanks was handled by the operator unprotected in the Grade B area multiple times. The operator touched the exterior surface of the tubing that was then placed inside the sterilized (b) (4) tanks.

6. During set-up an operator placed their forearm on the filling machine and pressed down on the exposed (b) (4) (b) (4)

7. The (b) (4) of the (b) (4) (b) (4) dropper stations, and open bottles were unnecessarily left open for extended periods of time while the operator performed activities in other areas of the room.

8. The panels below the filling machine were removed multiple times during the filling to make adjustments to the machine. The operators knelt while making adjustments and then touched surfaces inside the Grade A area without sanitizing their hands.

9. The operators were observed to remove bags of sterile components from a (b) (4) without first sanitizing them. The bags were carried through the Grade B area and placed on the floor in the Grade B area until they were needed. Bags of bottles were picked up off the floor, and without disinfecting, brought into the Grade A area and poured into the (b) (4).

10. Employees were observed crawling under the machine on their hands and knees, kneeling on the floor, and sitting while leaning against the wall and the (b) (4) product tanks. The operators did not change their gown after these activities.

11. Operators were observed to pick rejected bottles, disinfectant bottles, and empty component bags up from the floor. They did not change gloves or disinfect their hands after this occurred.

12. An operator was observed to bring a cell phone into the aseptic filling room.

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B. During aseptic filling on the (b) (4) filling line for (b) (4) batch (b) (4) (b) (4) the following was observed:

1. An operator had exposed skin on their nose while they had their head and torso inside the Grade A area while loading sterile (b) (4) into the tube box. While loading the sterile tubes, the operator repeatedly leaned and reached over open sterile tubes and the tube box. The tube box contacts the open sterile tubes.

2. A second operator entered the aseptic filling room during ongoing operations without wearing any goggles, resulting in exposed skin on their face. The operator walked through a Grade A area to talk to the filling operator.

3. Following a line stoppage due to a (b) (4) non-viable particle count excursion, the (b) (4) in the filling line had (b) (4) and could not be filled into tubes without build-up on the outside of the tube and (b) (4) b) (4) . The operator was observed to repeatedly wipe the excess product off the (b) (4) b) (4) , which is a direct product contact surface for the sterile product. The operator used a wipe wetted with (b) (4) on the (b) (4) but the wipe was previously used on non-product contact surfaces before use on the (b) (4) b) (4) . Additionally, the operators gloved hands touched the product contact surface of the (b) (4) b) (4) multiple times during this intervention.

4. During multiple interventions to clear a jammed tube, the operator only removed the jammed tube, but left other tubes that the operator touched or reached over while removing the jammed tube. The operator did not use forceps as directed by SOPPE003.

5. The operators carried boxes of the sterile tubes through the Grade B area and then placed them directly into the Grade A area for loading into the machine without any additional disinfection steps.

C. During set-up of the (b) (4) filling line for (b) (4) batch (b) (4) on August 9, 2023, the following was observed:

1. The open end of the tube used to transfer sterile (b) (4) from the bulk tank to the filling line (b) (4) was observed to protrude into the Grade B area and rest on the floor. Previously, the open end of this tube touched the (b) (4) and protruded into the Grade B area during handling and aseptic connections to extend the length of

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the tube. After the aseptic connections are made, this tube is used for the sterile transfer of (b) (4) to the product (b) (4)

2. The sterile product (b) (4) is not covered to protect its product contact surfaces when it is removed from the (b) (4) (b) (4). It is transferred through a Grade B area with exposed product contact surfaces.

3. The operator's arms, head, and part of the torso was observed leaning over the open sterile product (b) (4) during (b) (4) installation. Additionally, while installing the (b) (4) the operator needed to stand on the base of the filling machine.

D. During aseptic filling on (b) (4) Line (b) (4) for (b) (4) batch (b) (4) on August 8, 2023, the following was observed:

1. During an intervention to remove a jammed (b) (4) near the (b) (4) station an operator was observed to bend down and make a weight adjustment by turning a knob near to the floor. Without sanitizing their hands, the operator picked up forceps and reached their arm over the (b) (4) and exposed (b) (4) to reach the jammed (b) (4)

2. The operator moved the forceps used to contact sterile (b) (4) packaging components in and out of the Grade A area. The forceps were not sanitized.

E. During aseptic filling on (b) (4) Line (b) (4) for (b) (4) batch (b) (4) on August 7, 2023, the following was observed:

1. The operator cleared jammed (b) (4) and (b) (4) with their hands. During these interventions, the operator reached over other sterile components and the contact surfaces of the (b) (4) and (b) (4) b) (4) In multiple instances, the jammed component the operator cleared with their hand was put back into the (b) (4) to be used. The operator did not have forceps available to perform these interventions.

2. During addition of sterile (b) (4) to the (b) (4) (b) (4) the operator reached over the (b) (4) and allowed the external surface of the (b) (4) bag to contact (b) (4) that were already in the (b) (4) The (b) (4) bag is

transferred through Grade B and not disinfected before transfer into Grade A for (b) (4) (b) (4).

3. Disinfectant bottles were stored on the floor.

OBSERVATION #2

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

A. Smoke studies have not been performed under dynamic conditions. They do not include the entire filling line, do not evaluate line set-up, do not evaluate the filling line in operation, and do not evaluate interventions. The limited static studies that were performed do not allow for thorough evaluation of the air flow patterns and they demonstrate air turbulence in the Grade A filling areas.

B. Media fills are not designed to ensure they provide a representative challenge to the aseptic filling process. The protocols do not establish the number of interventions that must occur. Routine batch records did not include documentation of interventions. Documentation during the media fill did not specifically include all interventions performed. For example:

1. For the (b) (4) media fill (b) (4) there was no documentation that interventions for jammed tubes or cleaning of the (b) (4) occurred. These open (b) (4) manual interventions are not documented in the routine or media fill batch records, but were observed to occur multiple times on August 7, 2023, during aseptic filling of (b) (4) batch (b) (4)

2. For the sterile (b) (4) line (b) (4) media fill (b) (4) there was no documentation that interventions for jammed (b) (4) near the (b) (4) jammed (b) (4) on the track near the (b) (4) station, and jams of the (b) (4) occurred. These (b) (4) manual interventions are not documented in the routine or media fill batch records, but were observed to occur multiple times on August 7, 2023 during aseptic filling of (b) (4) batch (b) (4)

3. For the sterile (b) (4) line (b) (4) media fill (b) (4) there was no documentation that the intervention for jammed (b) (4) near the (b) (4) station occurred. This (b) (4) manual intervention is not documented in the

routine or media fill batch records, but was observed to occur on August 8, 2023 during aseptic filling of (b) (4) (b) (4) batch (b) (4)

C. Sealed, integral units are rejected during media fills and not incubated. There is no documented justification for not incubating these units. For example:

1. 200 rejected sealed bottles were not incubated during media fill (b) (4)

2. 67 rejected sealed tubes were not incubated during media fill (b) (4)

3. 17 rejected sealed bottles were not incubated during media fill (b) (4)

D. Contact surfaces of the sterile (b) (4) components are not sterilized. For example:

1. On the Sterile (b) (4) filling lines (b) (4) the (b) (4) (b) (4) contact sterile (b) (4) packaging components. These pieces of equipment are left in place between batches and disinfected, but not sterilized.

2. On the Sterile (b) (4) filling line, the tube box that contacts the open, sterile tubes, the equipment that orients the tube contacting the open end of the tube, and the tube sensor that contacts the open end of the tube are disinfected between batches, but not sterilized.

OBSERVATION #3

Laboratory records do not include complete data derived from all tests, examinations and assay necessary to assure compliance with established specifications and standards.

A. Laboratory records document results for samples that were not collected:

1. Review of contemporaneous recordings of (b) (4) batch (b) (4) on July 13-14, 2023, showed there were no settle plates or active air monitoring samples collected on the (b) (4) . Operators confirmed no samples were collected because microbial media was not available. However, the batch record

documents that all samples were collected and the microbiology laboratory reported no growth for these samples.

2. The (b) (4) operators performing filling activities and interventions during (b) (4) batch (b) (4) are documented in the batch record to have had personnel monitoring performed upon exit. Review of contemporaneous recordings showed no samples were collected. Operators confirmed no personnel monitoring was conducted because no microbial media was available. The laboratory reported no growth for these samples.

3. During the (b) (4) of (b) (4) batch (b) (4) the operator was observed in the contemporaneous video recording to collect the (b) (4) active air samples from the same location (b) (4) even though the records indicate they were collected from different locations. The operator confirmed the samples were taken from the same location because the operator was too busy to collect the samples from the locations specified in the procedure.

The active air samples and settle plates collected during (b) (4) were documented to be received by the microbiology laboratory and placed in the incubator at 2:10pm on July 13, 2023. However, contemporaneous video recordings show the samples did not leave the filling room until approximately (b) (4) on July 13, 2023.

4. During (b) (4) decontamination of Sterile (b) (4) Line (b) (4) with (b) (4) on July 14, 2023, biological indicators were documented to have been placed in (b) (4) different locations. Review of contemporaneous video recordings showed no biological indicators were placed during (b) (4) The microbiology laboratory reported results for all (b) (4) samples indicating they were negative for growth.

5. The microbiology laboratory reported results for (b) (4) batch (b) (4) for (b) (4) different (b) (4) of filling. The batch record and sampling records show filling and sampling was only documented to occur over (b) (4) (b) (4)

B. Counting of colonies on microbial plates is not accurate.

1. Active air sample (b) (4) from the Grade A area (limit < (b) CFU) collected on August 8, 2023, associated with batch (b) (4) of (b) (4) (b) (4) had a reported result of < (b) CFU, but approximately (b) (4) (b) (4) after the plate was read, the plate was observed to have (b) CFU, an action level result.

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2. Active air sample (b) (4) from the Grade A area (limit < (b) CFU) collected on August 8, 2023, associated with batch (b) (4) of (b) (4) (b) (4) had a reported result of < (b) CFU, but approximately (b) (4) (b) (4) after the plate was read, the plate was observed to have (b) CFU, an action level result.

C. Records are not made when plates are counted. On August 13, 2023, plates were observed in the waste area that were reportedly read on August 12, 2023, or August 13, 2023, but there were no corresponding records for all samples. For example:

1. Complete records were not made for environmental monitoring on Sterile (b) (4) Line # (b) associated with aseptically filled batch (b) (4) batch (b) (4) on August 7, 2023. With the exception of 3 Grade A excursions, no counts were reported for any other Grade A, B, or C samples observed in the waste area. Review of plates still available in the waste area identified (b) (4) Grade A samples containing microbial growth, (b) (4) Grade B samples with microbial growth, and (b) (4) Grade C samples with microbial growth. Included in the discarded samples with no recorded results were:

a. Settle plate sample (b) (4) (b) (4) from the Grade B area (action limit (b) CFU). When the plate was viewed on August 10, 2023, before the end of incubation, (b) CFU was observed, an action level result.

b. Settle plate sample (b) (4) (b) (4) from the Grade B area (action limit (b) CFU). When the plate was viewed on August 10, 2023, before the end of incubation, (b) (4) CFU was observed, an alert level result.

2. Complete records were not made for environmental monitoring on (b) (4) associated with aseptically filled batch (b) (4) batch (b) (4) on (b) (4) . With the exception of (b) Grade A excursions, no counts were reported for any other Grade A, B, or C samples observed in the waste area. Review of plates still available in the waste area identified (b) additional Grade A samples containing microbial growth and (b) (4) Grade C samples with microbial growth. Included in the discarded samples with no recorded results were:

a. Settle plate sample (b) (4) from the Grade A area (limit < (b) CFU), (b) (4) When the plate was viewed on August 10, 2023, before the end of incubation, (b) (4) CFU was observed, an action level result. When it was viewed in the waste area on August 13, 2023, there were (b) (4) CFU.

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b. Settle plate sample (b) (4) from the Grade A area (limit < (b) CFU), (b) (4) When the plate was viewed on August 10, 2023, before the end of incubation, (b) (4) CFU was observed, an action level result.

3. Samples not scheduled to be removed from the incubator or read until August 14, 2023, associated with (b) (4) lot (b) (4) were observed in the waste area on August 13, 2023. There were no records for the counts on these plates. Included in these samples were:

a. (b) (4) settle plate sample (b) (4) and active air sample (b) (4) (b) (4) which all had visible microbial growth. These were collected from Grade A areas that would have resulted in an OOS result.

b. (b) (4) settle plate (b) (4) (35 CFU) and (b) (4) (29 CFU). These samples were from a Grade B area with an action limit of (b) (4) CFU.

D. The microbiology laboratory reported no OOS result for any microbial test for the two years prior to the inspection, including no alert or action level results for environmental monitoring, personnel monitoring, or (b) (4) monitoring. For samples collected from (b) (4) the microbiology laboratory opened seven OOS investigations that are related to 56 excursions in the aseptic manufacturing lines, including 27 Grade A excursions, 14 Grade B action level excursions, 10 Grade B alert level excursions, and 5 Grade C action level excursions.

OBSERVATION #4

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

A. Risk assessment 026-RMR/2021 justifies the environmental monitoring locations and frequencies that already existed at the time of the assessment in October of 2021. It did not assess risks or consider other points that could be monitored. For example:

1. There is no surface monitoring of locations in the Grade A areas of the aseptic filling lines used for US market product (b) (4) associated with (b) (4) batch. Samples are only collected on a (b) (4) basis.

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2. (b) (4) line (b) (4) has no air monitoring (settle plates or active air) inside the barrier where bottles are filled, where the (b) (4) is inserted, and the bottle is capped. The non-viable monitoring (b) (4) in this area is above the working height and is approximately (b) (4) above from where bottles are filled.

B. Personnel monitoring is only conducted (b) (4) There is no personnel monitoring associated with aseptic operations including aseptic connections and complex manual interventions.

C. On August 9, 2023, operators in the Grade A area of the (b) (4) filling line and the Grade C area of the (b) (4) preparation room were observed spraying disinfectant directly above and towards exposed settle plates. Additionally, microbial media used for environmental monitoring does not contain any inactivating agents.

D. Completed environmental monitoring and personnel monitoring microbial plates exit the filling room through (b) (4) with (b) (4) No evaluation has been done to determine whether the (b) (4) can impact the recovery of microbial contamination. On August 7, 2023, personnel monitoring plates collected during filling of (b) (4) batch (b) (4) were observed to be left in a (b) (4) with a (b) (4) for approximately 30 minutes.

E (b) (4) plates used for environmental monitoring are prepared in-house and some plates appeared to be thin, drying out, and cracked.

F. Microorganisms isolated during environmental monitoring have not been identified to establish the microbial flora of the aseptic manufacturing facility. Only (b) (4) microorganism is chosen per (b) (4) and only three of the organisms chosen since procedure SOPQC068 "Microbe Identification Procedure" was implemented November 2, 2022, were from samples in the production facility. Identification only included colony morphology and Gram staining.

OBSERVATION #5

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

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A. Following the filling of batch (b) (4) of (b) (4) the batch record and filling machine use and cleaning log documents machine cleaning occurred. However, review of contemporaneous video recording showed no machine cleaning was performed. Bottles were left on the filling line and in the (b) (4) following this batch and were still present at the start of the next batch, (b) (4) of (b) (4) Following batch (b) (4) no machine cleaning was observed in the contemporaneous video recordings before the next batch, (b) (4) (b) (4).

B. Disinfectant efficacy studies have not evaluated the effectiveness of disinfectants including (b) (4) (b) (4) used on machine surfaces inside the Grade A aseptic filling areas including (b) (4) format parts, or protective covers over the (b) (4) Additionally, the effectiveness of (b) (4) was not evaluated on the (b) (4) gloves worn by operators or the bags containing the (b) (4) packaging materials.

OBSERVATION #6

Batch production and control records do not include complete information relating to the production and control of each batch.

A. Manual interventions requiring personnel to enter into the Grade A filling area are not recorded in the batch record. Prior to August 1, 2023, there was no requirement to record interventions in the batch record, including all batches that have been distributed to the US market.

Form MMSQA002/F-01.00 was implemented on August 1, 2023, to record interventions. However, it does not capture all manual interventions. For example, on August 7, 2023, during the filling of (b) (4) batch (b) (4) from approximately (b) (4), the operator entered the Grade A area 15 times to perform various manual interventions, but none were recorded on Form MMSQA002/F-01.00.

B. Personnel working in the aseptic filling room are not permitted to have records available for recording during the filling operations. Information related to the production of the batch including weight checks, changes to filling machine settings, interventions, and other information cannot be recorded contemporaneously by the responsible personnel.

1. Review of contemporaneous video recordings of (b) (4) batch (b) (4) showed the times recorded in

the batch records for steps including filling, cleaning, and environmental monitoring did not reflect the entries in the batch record.

2. On August 7, 2023, during filling of (b) (4) batch (b) (4) the batch record showed settle plates were opened at (b) (4) and had recorded that the plates were closed at (b) (4) but the plates were not closed until (b) (4) It was reported a person in Grade C area made the entries on behalf of the operator in the filling room.

OBSERVATION #7
Established test procedures are not followed.

Procedures related to integration of chromatographic peaks and the review of chromatographic data are inadequate. For example:

A. During the review of the assay results related to the 18-month stability time point for (b) (4) (b) (4) Lot (b) (4) the integration parameters applied to the sequence were timed integration events, which forced the integration of all chromatographic peaks from (b) (4) There was no justification for the use of these timed integration events and was not proper integration according to SOPQC242, "HPLC Analysis, Control of Chromatograms, and Documentation". In addition, integration parameters are not provided as part of the test method, and the integration performed during the method validation are not consistent with the chromatograms reviewed.

On August 15, 2023, the chromatographic data for the 18-month stability assay of (b) (4) Lot (b) (4) was (b) (4) using correct integration events per SOPQC242. The (b) (4) data with correct integration applied resulted in an OOS for (b) (4) (b) (4) (b) (4)

B. The peer review performed by the supervisor does not require review of chromatograms within the electronic system unless manual integration is applied, and only those chromatograms printed within the test package are reviewed. According to SOPQC234, "Data Integrity and Electronic Audit Trail of the HPLC Analytical Data", the audit trail is required to be printed and reviewed; however your QC supervisor stated that only manual integration is reviewed electronically within the ChromNav system and not related information for the chromatographic run,

including unreported samples, aborted runs, and adequate integration. In addition, SOPQC234 and SOPRD068, "Operation of (b) (4) HPLC System", does not explain how to specifically review the audit trails within the chromatography system.

C. The chromatography data previously processed within the ChromNav system is not retained or reviewed. The data processed is overwritten when changes are saved by the analyst within the system, and only the (b) (4) processed result is available and reviewed as part of data review. During the review of the assay results related to the18-month stability time point for (b) (4) Lot (b) (4) manual integration of the chromatogram for the (b) (4) sample was conducted. This chromatogram could not be retrieved within the chromatography system and was not available as part of the test package.

OBSERVATION #8
There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

A. Investigations into unexplained discrepancies during the manufacture of a batch are not initiated or are inadequate. For example,

1. Non-viable particulate (NVP) count alarms obtained by the continuous particle monitoring system during filling operations require the initiation of SOPVA067/F-01. During the manufacture of (b) (4) Lot (b) (4) on (b) (4) (b) (4) (b) (4) NVP out of limit excursions occurred, which required the filling line to be stopped, additional sample collected, and recleaning, when applicable. The investigation into the NVP out of limit did not adequately assess the impact of the batch being filled as the (b) (4) that contains the sterile drug product is exposed to the Class A environment where the excursion occurred due to openings in the lid design. There was no assessment conducted on this solution within the (b) (4) to ensure the drug product was not impacted by the NVP excursions. In addition, there was no documentation for the recleaning conducted during the NVP excursion from (b) (4) (b) (4) as stated on the out of limit form. These out of limit forms are also not controlled by the Quality Unit.

2. During the manufacture of (b) (4) Lot (b) (4) on March 14, 2023, unplanned deviation (b) (4) was initiated due to an outage of the NVP (b) (4) The batch resumed using a (b) (4) particle counter as outlined in SOPPE010, "Operating of Air Particle Counter and Air Sampler". However, during

the filling operation, NVP out of limits were obtained on March 14, 2023 from (b) (4) within the Class A area. A note was added to the record indicating to remove the product filled during this time, however there was no investigation or NVP out of limit form initiated for the excursion. Furthermore, there is no procedure that provides instructions on the required documentation in the event of a NVP excursion using the (b) (4) particle counter.

B. Investigations initiated for drug products do not extend to other batches regardless if they had been distributed. For example, (b) (4) was initiated on October 6, 2022 due to an out of specification on appearance for (b) (4) Lot (b) (4) containing foreign particles during in-process testing. The root cause was attributable to not verifying the (b) (4) of the (b) (4) during (b) (4) There was no documented assessment conducted to confirm if this root cause impacted any other batches manufactured, as this process is consistent for all batches manufactured. Furthermore, procedure SOPQA076, "Deviation Handling Procedure", does not require an impact assessment be performed on batches previously manufactured.

OBSERVATION #9

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

The HPLC method for the Assay of (b) (4) is not scientifically sound to ensure that the method is robust or stability indicating. According to the validation report and your R&D personnel, no forced degradation studies have been performed to ensure the method utilized can adequately determine the assay concentration during stability, as required per SOPRD012, "HPLC Method Validation for Degradation Products". In addition, robustness testing was not performed during this method validation, which is required for non-official methods per SOPRD017, "HPLC Method Validation".

OBSERVATION #10

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

A. The (b) (4) and (b) (4) installed on sterile (b) (4) ine (b) (4) extends beyond the coverage of the laminar flow.

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 12420 Parklawn Drive Room 2032 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	August 7-10 and 13-15, 2023 FEI NUMBER 3013501887

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Fadi Al-Atrash, General Manager

FIRM NAME	STREET ADDRESS
Amman Pharmaceutical Industries	Building 108, Street A3, King Abdullah II Industrial City
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Amman, Jordan 11152	(b) (4) Drug Manufacturer

B. The (b) (4) and (b) (4) on sterile (b) (4) line (b) (4) have exposed threaded bolts and nuts that contact sterile (b) (4) packaging materials. They are not designed to facilitate appropriate cleaning and disinfection.

OBSERVATION #11

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

A. The qualification of suppliers is inadequate and does not follow SOPQA074, "Supplier Approval and Evaluation". For example:

1. The qualification documents provided for active pharmaceutical ingredient (API) suppliers, including (b) (4) (b) (4) (supplier for (b) (4) API used in (b) (4) and (b) (4) (supplier for (b) (4) API used for (b) (4) (b) (4) have not been reviewed and suppliers approved for API use in drug products. According to these qualification documents, the suppliers provide bulk raw materials for pharmaceuticals and not APIs, and these suppliers did not complete Section 12 indicated for API suppliers to complete a (b) (4) risk assessment.

2. The supplier questionnaire and qualification documents do not ensure that the materials supplied are manufactured in accordance with the applicable Good Manufacturing Practices. The questionnaire and certificate provided for (b) (4) (supplier for (b) (4) API used in (b) (4) (b) (4) stated that the products manufactured do not have GMP certifications for pharmaceutical applications.

3. The qualification documents for (b) (4) (supplier for (b) (4) API used in (b) (4) (b) (4) have not been completed as per SOPQA074, including the submission and review of a supplier questionnaire.

Furthermore, the qualification questionnaire used for API suppliers does not include information relevant for API suppliers for products intended for the US market. For example, the questionnaire does not request or confirm that the firm is registered with FDA, including for those suppliers providing an API.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
	Justin A. Boyd Joseph A. Piechocki	Justin A. Boyd, Investigator Joseph A. Piechocki, Investigator	08/15/2023

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B. The Quality Control examination of incoming raw material labeling according to SOPQC060, "Receiving and Sampling of Packaging Materials and Non-Sterile Raw Materials", is not adequate. Per SOPQC060, the QC analyst examines the containers fully for appropriate labeling content and container damage. During the walkthrough of the warehouse on August 13, 2023, containers of (b) (4) Lot (b) (4) (b) (4) Lot (b) (4) (b) (4) Lot (b) (4) and (b) (4) Lot (b) (4) supplied by (b) (4) contained additional labeling which read "Samples not for human use". Procedure SOPQC060 does not provide sufficient information regarding what is appropriate labeling, and there was no conclusion regarding the adequacy of this labeling and the use of the product for drug product manufacturing. In addition, the (b) (4) for (b) (4) Relief Lot (b) (4) was cracked, and the physical status of this material had not been recorded.

JWB 8/15/23

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	Justin A. Boyd Joseph A. Piechocki	Justin A. Boyd, Investigator Joseph A. Piechocki, Investigator	08/15/2023