DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2037 Rockville, MD 20857 ORAPHARMInternationalresponses@fda.hhs.gov	09/17/2024-09/27/2024
	FEI NUMBER 3011248248

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Dr. Rhonda Duffy, Ph.D., Executive Vice President and Chief Operations Officer

FIRM NAME	STREET ADDRESS
Biocon Sdn Bhd	No.1, Jalan Bioteknologi 1, Kawasan Perindustrian SiLC
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Iskandar Puteri, Johor, Malaysia, 79200	Sterile 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

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

A. Poor aseptic behavior was observed during the review of videos for the aseptic filling of (b) (4) (b) (4) Injection (b) (4) IU/mL intended for the US market and smoke studies conducted for the same line (line (b) (4) For example:

1. At least three instances were observed of operators sanitizing their hands prior to being finger dabbed after setup operations for the Grade A line for batch # (b) (4)
2. One operator was observed sanitizing his hands prior to being finger dabbed after performing set up of the Grade A (b) (4) stopper station for batch # (b) (4)
3. An operator was observed blocking first pass air while removing fallen (b) (4) at the (b) (4) area for batch # (b) (4)
4. An operator was observed sanitizing their hands prior to being finger dabbed during filling operations for batch # (b) (4)
5. Operators were observed using the (b) (4) gloves instead of sterile tools/forceps during the execution of the (b) (4) stopper track adjustment intervention during the filling of batch (b) (4)

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SEE REVERSE OF THIS PAGE	Jeffrey P. Raimondi -S Digitally signed by Jeffrey P. Raimondi -S Date: 2024.09.27 05:27:25 -05'00' Sandra A. Boyd -S Digitally signed by Sandra A. Boyd -S Date: 2024.09.27 05:15:43 -05'00' Paranthaman Senthamarai Kannan -S Digitally signed by Paranthaman Senthamarai Kannan -S Date: 2024.09.27 05:41:31 -05'00'	Jeffrey P. Raimondi, Consumer Safety Officer Sandra A. Boyd, Drug National Expert Paranthaman Senthamarai Kannan, Investigator	09/27/2024

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6. An operator was observed touching the inside top cover of the settle plate during the (b) (4) smoke study for environmental monitoring of (b) (4) air).

7. An operator was observed sanitizing his hands at the conclusion of environmental monitoring intervention which required finger dabbing during the (b) (4) smoke study performed for the environmental monitoring of (b) (4) (settle plate) and (b) (4) air).

8. Operators were observed leaning on equipment, sitting with their arms on their legs, propping their knee on a stool, touching the wall, gesturing, and talking during the filling of (b) (4) Injection, batch (b) (4) This occurred in the Grade B / extended LAF Grade B area.

9. The operators inside Grade B aseptic filling area sanitizing the gloves with (b) (4) before performing personnel monitoring during setup operations of (b) (4) batch (b) (4)

10. Personnel monitoring performed by the operators includes finger dab sampling of (b) (4) (b) (4) on one plate. However, there is no scientific rationale or study to assure that the microorganisms dabbed from the first impression are not lifted off by the subsequent impressions.

11. The microbiology QC analyst performing self-monitoring inside the Grade B aseptic area touched (b) (4) bottle after performing finger dab testing to sanitize the gloves, for (b) (4) (b) (4) batch # (b) (4) Further, the same analyst without changing the gloves touched the pen, paper and the cart prior to wheeling the cart out of room to change the gloves. And there is no assurance that these surfaces were cleaned by the operator before he returned these items to the Grade B area.

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B. During the review of the [redacted] Injection [redacted] IU/mL batch records, videos, [redacted] Injection (containing [redacted] IU/mL batch record along with BM/PDP/SOP/139 Handing of Interventions during Aseptic Filling Operation procedure, the following discrepancies were noted:

1. There is no intervention for removal of broken glass separate from broken glass removal when a fallen vial is removed.
2. The number of times the [redacted] conveyer belt, located in the Grade A area, is shifted to gain access to the back side of the line is not tracked or trended.
3. Operators are not documenting all interventions taking place during aseptic filling. Review of filling batch records determined operators documenting interventions in the Machine Down Time Record for Filling instead of the intervention list. This results in the number of interventions not being accurately tracked or trended. This includes the two new interventions which occurred 4 times in [redacted]

Batch	Date	Intervention	Occurred
[redacted] Injection [redacted] IU/mL	11 JUL 23	Stuck [redacted] at [redacted]	1X
		[redacted] station [redacted] alarm (Overload at [redacted]	2X
		Broken glass not doc in intervention	3X
		Cap stuck in track	1X
[redacted] Injection [redacted] IU/mL	18 AUG 24	Capping [redacted] station adjustment	5X
		[redacted] stopper issue	1X
[redacted] Injection [redacted] IU/mL	21 AUG 24	Remove stuck [redacted]	3X*
	22 AUG 24	Removal of broken glass	1X *
[redacted] Injection (containing [redacted] IU/mL	06 JAN 24	Fallen vial at [redacted]	1X

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*New intervention

4. Interventions are documented under the incorrect category. During the review of (b) (4) (b) (4) Injection videos for the aseptic filling of lot (b) (4) management confirmed that intervention 6 (minimum accumulation on track position (b) (4) was incorrectly documented as intervention 5 (b) (4) stopper track and bowl adjustment or stopper position lock at position (b) (4) seven times.

5. Intervention procedure does not require the documentation of the specific intervention performed by the operator. Instead, the operator specifies when he executes one of several interventions listed within that group. For example,
   - Capping (b) (4) station adjustment or cap stuck in track (consecutive cap missing) and cap chute
   - Fallen (b) (4) vials at (b) (4) – this intervention also discusses how to remove glass particles if noted during picking up the fallen (b) (4) vial. Whether or not glass was removed during removal of a fallen (b) (4) vial or otherwise is not tracked or trended.
   - (b) (4) stopper & (b) (4) stopper track and bowl adjustment or stopper position lock at position (b) (4)

   The location and amount of activity the separate interventions require within a group can vary. For example for the last bullet point listed above, the (b) (4) stopper track adjustment might require the removal of a (b) (4) and taking several minutes which the stopper position lock at position (b) (4) requires a removal of a stuck (b) (4) which might take a couple seconds.

C. BM-QA/FOR/001-02 Trending of Microbiological Monitoring Data states finger dabs or gown samples which exceed <(b) (4)% recovery rates should be handled through an investigation. During

review of the Trending Report for Environmental Monitoring in DP Area (b) (4) Trending Report for (b) (4) I noted the following personnel exceeded a <(b) (4)% recovery rate in the Grade B area associated with the filling of (b) (4) Injection:

- QC Microbiology (QCM) - 2 people (b) (4)%, (b) (4)%)
- Production Drug Product (PDP) – 2 people (b) (4)%, (b) (4)%)
- QA – 2 people (b) (4)%, (b) (4)%)
- EM – 2 people (b) (4)%, (b) (4)%)

No investigations have been initiated. The Head of Microbiology – Manager stated they only use recovery rates to determine the qualification of their personnel. Aseptic personnel exceeding the recovery rate of (b) (4)%, (b) (4) times within a (b) (4) period would be disqualified from working in the aseptic filling area.

D. The visual inspection kits used in the qualification of visual inspectors and the challenge kit used to verify the equipment (b) (4) use for the (b) (4) does not adequately challenge the ability to detect defects in that:

1. The (b) (4) ml vial (b) (4) solution challenge kits do not assure visual inspections can see glass particles smaller than (b) (4) µm. Each kit contains (b) (4) glass particles with the following sizes: vial kit (b) (4) (b) (4)
2. The (b) (4) vial challenge kits do not address white particles, black particles, and fibers of a known size.
3. The (b) (4) sample kit verification performed to identify discoloration or changes in physical appearance which may differ from the determined type of defect, required by BM/PDP/SOP/159 Qualification of Visual Inspector procedure, is not documented.
4. The challenge kit used for (b) (4) challenge verification of (b) (4) (b) (4) does not contain particles (glass, black, and white) and fibers of

known size. Additionally, a specification or criteria has not been established for these (b) (4) (b) (4) challenge verification runs for false rejects.

This is a repeat observation.

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. The smoke studies performed on aseptic fill line (b) (4) does not pass the acceptance criteria of smoke being uniformly supplied with the airflow patterns being unidirectional and covering the entire cascade from filter to working area without evidence of turbulence as listed in SOP 193 Procedure for Air Flow Visualization Testing Smoke studies.
    1. The firm uses a smoke generator using (b) (4) for evaluating the airflow during the smoke studies. There is no evidence that the smoke generated is neutrally buoyant.
    2. Ceiling lights are located between the overhead HEPA filters in the Grade A (b) (4) RABs resulting in a gap between the HEPA filters of approximately 80mm. The impact on the airflow resulting from these gaps have not been evaluated.
    3. Turbulence was noted during the review of the following the (b) (4) smoke study videos filmed to demonstrate air flow visualization for the installation of (b) (4) (b) (4) air samplers, (b) (4) at (b) (4) conveyor, event based smoke study and new corrective interventions performed during batch activities. For example,

(b) (4)

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[redacted] (b) (4)

a. Smoke studies have not been performed for the following activities:
   - Removal of broken glass
   - Stopper track adjustment
   - Stopper track adjustment including removal of screw
   - Stopper track adjustment including removal of [redacted] (b) (4)
   - [redacted] (b) (4) removal
   - Personnel monitoring
   - The firm did not evaluate whether smoke could potentially be ingressing from the Grade C to the Grade A area.

b. The firm uses a [redacted] (b) (4) background film for better smoke perception and air flow visualization. The use of the film during smoke studies is not reflective of routine production and/or could alter the flow of air which is being evaluated.

c. The source of the smoke is not held perpendicular from the direction of the air being evaluated and instead it held pointing upwards, directly into the source of the air. This results in the air reversing direction and immediately hitting the [redacted] (b) (4) diameter pipe supplying the smoke. This creates unnecessary turbulence, making it more difficult to evaluate the direction of air within the aseptic area.

B. The design of the aseptic area does not promote unidirectional air flow. The air intake vents which supply the Grade A LAF [redacted] (b) (4) RABs) unit are located near the overhead Grade B HEPA filters. This results in the air in the Grade B area being sucked into the air intake vents instead of flowing unidirectionally downward from the Grade B HEPA filters.

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C. Media Fills are not representative of routine production. Media fills currently do not represent interventions such as (b) (4) stopper track adjustment (with and without (b) (4) removal) or fallen vial (with broken glass removal). These interventions are listed as corrective interventions in your BM/PDP/SOP/139 Handing of Interventions during Aseptic Filling Operation. Additionally, due to interventions not being documented on the intervention form, categorized as the wrong intervention, or inadequate tracking of individual interventions, there is no assurance the media fills represent the number of interventions which take place during routine production.

D. The (b) (4) rejection of vials on filling line (b) (4) when the (b) (4) (b) (4) into the Grade A (b) (4) RABs area, has not been validated. Filling line (b) (4) is used in the aseptic filling of (b) (4) Injection (b) (4) IU/mL and (b) (4) Injection (containing (b) (4) IU/mL

OBSERVATION 3
The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed. Specifically,

A. Plate reading records do not accurately document results. Environmental monitoring and personnel monitoring plates were read for (b) (4) Injection (b) (4) IU/mL batch # (b) (4) on 16-September-2024 at approximately (b) (4) placed in a biohazard bag and transfer from DP to the microbiology laboratory for future disposal. Prior to destruction, on 17-September-2024 at approximately 10:18 am, the FDA investigator opened the biohazard bag and reviewed plates whose covers were still intact. The following discrepancies were observed:

1. Personnel monitoring for a production operator at (b) (4) documented (b) (4) cfu for the left-hand finger dab, however, (b) (4) cfu was identified on the plate. The specification for this specific sample is (b) (4) because it was a Grade A specification finger dab.

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2. Personnel monitoring for a production operator at (b) (4) documented (b) (4) cfu for the left-hand finger dab, however, (b) (4) cfu was identified on the plate. This is a Grade B plate with a specification of less than (b) (4) cfu for finger dab.

3. Personnel monitoring for a Quality Control Microbiologist at 15:54 documented (b) (4) cfu for left-hand finger dab, however, at least (b) (4) cfu of what appeared to be mold, was identified on the plate. This is a Grade B plate with a specification for mold of (b) (4)

B. The Quality Unit does not ensure that CAPAs are closed in a timely manner. For example:

1. CAPA 156430 was initiated on 03-Nov-2023 in response to Deviation 156131 to perform a protocol-based evaluation to further assess the different vibration levels the (b) (4) stopper machine has on the non-viable particle excursions. The study has not been executed and at least three Due Date Extension requests have been approved. The most recent reason for the due date extension request states in part: "…priority was given for batch manufacturing to full fill the market demand and business continuity". The current tentative closure date is in Nov 2024.

2. CAPA 166665 was initiated on 27-Dec-2023 to assess and identify the potential areas and reasons for glass breakages of the (b) (4) and vials within the Grade A aseptic filling line during the filling process. This CAPA has not been closed and at least three due date extension requests have been approved. The current proposed due date is 15-Nov-2024.

3. CAPA 133344 was initiated on 06-July-2023 to review and perform the current disinfectant efficacy study across all materials of construction present (not previously performed) within your aseptic processing area. Three extension requests have been approved and the study is not completed.

C. The Quality Unit did not ensure the equipment under maintenance activities are not withheld from use. (b) (4) 03-01- (b) (4) -02 was under maintenance beginning 27-June-2024 and was not approved for use by the Quality Unit until 22-Sept-2024. The equipment usage e-log indicates this equipment was used on 06-Sept-2024 and again 08-Sept-2024 in both the Grade D (b) (4) area and the Grade A aseptic processing filling line, respectively.

D. The personnel who review the media fill (b) (4) vials upon completion of the incubation period are only trained to inspect for uniform turbidity.

E. The Quality Unit does not ensure (b) (4) replacements for the (b) (4) used in the aseptic processing area is performed by its due date. The (b) (4) for (b) (4) 03-01 (b) (4) -01, which is used within the aseptic filling room, is required to be changed (b) (4) replacement records show the (b) (4) was due for replacement on 29-May-2023 but was not performed until 06-July-2023. Between these dates, the (b) (4) was used in the aseptic processing area as part of post batch cleaning operations for three batches.

F. Written specification was not established for the (b) (4) glove used in the aseptic filling of the drug product (b) (4) and further the (b) (4) glove suppliers were not qualified.

OBSERVATION 4
There is a failure to review any unexplained discrepancy whether or not the batch has been already distributed. Specifically,

A. The criteria in which to initiate an investigation into non-viable particle excursions, which is monitored in cubic feet, exceeding action limits within the aseptic processing area is not justified. Procedure: BM/PDP/EOP/050, Operation of (b) (4) Non-Viable Particle Monitoring System, Version No: 009 states a deviation will be raised if there are more than (b) (4) of continuous alarms and if the cumulative counts for the (b) (4) the alarm

exceed the limit for (b) (4) µ of (b) (4) particles. However, (b) (4) particle counters are not programed to record any value higher than (b) (4) particles (b) (4) so there is no assurance that any value recorded at (b) (4) particles is the true result. For example:

An investigation into the various non-viable particle excursions occurring throughout aseptic filling of (b) (4) Injection (b) (4) IU/mL, batch # (b) (4) occurring at particle counter station (b) (4) stopper station where (b) (4) get stoppered (b) (4) was opened under Deviation 153440 and subsequently cancelled because the batch did not exceed (b) (4) particles based on the cumulative counts for the (b) (4) alarm. No investigation was performed to determine product impact, the cause of the excursions, or if a CAPA should be implemented to prevent recurrence.

Additionally, the (b) (4) consecutive excursion criteria is not adequately justified as the document CPN/PDP/010-01, titled: Approach to Determine Excursion Limit for (b) (4) Non-Viable Particle Counter, Approved: 08-Feb-2020, does not take into account the equipment is programmed to only records values up to (b) (4) particles (for (b) (4) µ size) for (b) (4)

B. Deviation PR 156131 investigation for non-viable particle excursions during filling of (b) (4) (b) (4) IU/mL, batch # (b) (4) recorded a "breakage observed at the (b) (4) station" at (b) (4) on 10-September-2023. Although the batch production record identifies an (b) (4) station intervention occurring during this time, there is no reference to any breakage or removal of units as would be required by procedure: BM/PDP/SOP/139, Handling of Interventions During Aseptic Filling Operation, when a breakage occurs. When questioned where the "breakage observed" came from, the author of this deviation verbally stated the breakage is "probable" during this specific intervention.

C. Deviation PRID 213215, dated 22 Aug 2024, was initiated to investigate why the color indicator on the (b) (4) bag of the (b) (4) glove for (b) (4) did not fully change colour. This was observed during the (b) (4) of the (b) (4) glove on 20 Aug 2024. The deviation did not

address the delay in initiation of the deviation or why the operator continued to [(b) (4)] use the glove for the aseptic filling of [(b) (4)] Injection [(b) (4)] IU/mL batch [(b) (4)] without the approval from Quality. When the FDA Investigator asked why the operator did not [(b) (4)] glove whose tape did adequately change colour, she was told there were no other [(b) (4)] gloves ready for use. As part of your investigation, you documented an interview with the operator which stated, "after checked multiple times, it is confirmed that only [(b) (4)] wrapped [(b) (4)] bag changed color from [(b) (4)] to [(b) (4)] and the color indicator of the [(b) (4)] wrapped remain intact" and not fully change colour as stated repeated in your investigation. [(b) (4)] was released on [(b) (4)]

D. The Trending Report for Environmental Monitoring in DP Area [(b) (4)] Trending report is compiled to evaluate and draw conclusions from EM and PM results. During the trending report for [(b) (4)] your report identified *Bacillus cereus* group as a recurring organism for environmental monitoring for [(b) (4)] The report states the [(b) (4)] of [(b) (4)] had 2 occurrences, with 13 occurrences documented from [(b) (4)] The report also identified *Bacillus cereus* group as occurring 31 times during [(b) (4)] during personnel monitoring of the Grade B area. The trends report does not identify this as an adverse trend and no investigation was initiated as no alert limits have been reached.

E. During visual inspection, results which exceed the alert limit are handled through a Communication Memo for Exceeding Alert Limit instead of the Out of Limit procedure. This results in the excursions to the visual inspection alert limits not being tracked or trended.

On 17 JUL 2023, the critical alert limit of [(b) (4)]% was obtained for glass pieces in [(b) (4)] [(b) (4)] lot [(b) (4)] (alert limit for glass pieces [(b) (4)]%). This form reviews the manufacturing process including [(b) (4)] equipment's breakdown, sealing [(b) (4)] process, and line interventions. This document identified three instances where broken glass was

identified in the Machine Down Time Record for Filling table for this batch. Your investigation did not evaluate in which [(b) (4)] (time manufactured) the glass was identified during visual inspection and whether those times correlated to the times broken [(b) (4)] at the stopper station were identified in the Machine Down Time Record. The communication memo did not identify that the 3 broken glass comments in the Machine Down Time Record were not documented as interventions in the Interventions Details section of the MBR.

F. The deviations related to post-integrity glove test failures for the following aseptic batches of [(b) (4)] were not thoroughly investigated to identify the root cause and implement corrective action and preventative action (CAPA).

1. Batch # [(b) (4)] - The root cause identified for the deviation investigation (DEV-212552) as inconsistent handling of the [(b) (4)] glove during integrity testing however the operator clearly mentioned during the interview that glass particle was stuck between [(b) (4)] glove and [(b) (4)] The root cause analysis of the report (PR No. 212552) did not include the glass particle noted by the operator.

2. Batch # [(b) (4)] - During BMR review QA identified that post-integrity test report for glove number [(b) (4)] was missing. According to Sterile Glove Leak Test procedure (Document No.: BM/PDP/SOP/069), the post-integrity test report requires production (PDP) review, however the report was neither verified nor reviewed by production. This was not included in the root cause analysis of the investigation (PR No. 212553).

3. Batch #BS24002659 - According to the procedure "Sterile Glove Leak Test" (Document No.: BM/PDP/SOP/069), post-integrity test failure of the [(b) (4)] glove at critical location [(b) (4)] in the aseptic filling line requires [(b) (4)] testing under the supervision of QA. However, the operator repeated [(b) (4)] followed by [(b) (4)] [(b) (4)] testing for glove # [(b) (4)] in the absence of Quality. The root cause analysis (PR No.

210267) did not include the fact that the repeat testing was not performed under the supervision of quality.

G. Deviation investigation did not include the interview of the operator who failed to perform confirmatory post-integrity (b) (4) glove testing for a media fill batch (b) (4)

H. Missing documentation of interventions performed by the operators was not included in the root cause analysis of a post-integrity test failure investigation (PR No. 154245, batch no. BS23005286).

I. Deviation was not initiated by the production department when the operator collected (b) (4) filling sample from incorrect location that resulted in OOS (64 CFU/mL, NMT (b) (4) CFU/mL; PRID-183777). Further, QA did not initiate deviation when the OOS investigation identified that the correct end of filling sample was not collected for the (b) (4) batch (b) (4)

This is a repeat observation.

OBSERVATION 5
Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions. Specifically,

A. The cleaning procedure SOP 039 Operation, Cleaning and Changeover of (b) (4) Filling Machine requires the operator to spray (b) (4) directly on the entire machine and to ensure the wetness of all the sprayed surfaces. Just spraying of (b) (4) without wiping does not ensure the (b) (4) reaches all surfaces.

Although documented as being done, during the review of the cleaning videos performed after the manufacturing of (b) (4) Injection (b) (4) IU/mL batch (b) (4) we

observed the operator spraying (b) (4) in only half of the Grade A area. For some of the areas sprayed, the operator stopped opening the (b) (4) and only sprayed into the (b) (4)

B. The cleaning procedure SOP 023 Cleaning and Disinfection of Clean Room requires the cleaning of the LAF (b) (4) to be cleaned (b) (4) of a batch. Although documented as being cleaned, review of the cleaning videos for (b) (4) batches of (b) (4) Injection (b) (4) IU/mL shows the LAF (b) (4) were never cleaned.

C. Disinfectant Efficacy study was not performed on all surfaces within the aseptic processing room in which these disinfectants are used. These surfaces include, in part, (b) (4) and (b) (4) cover.

D. Cleaning with use of (b) (4) and (b) (4) on the (b) (4) used within the aseptic processing room to remove broken glass on the Grade A filling line is not documented. The (b) (4) and cleaning from a lower classified areas to higher classified area is not documented. (b) (4) usage log for 03-01-(b) (4)-02 shows this (b) (4) was used within the Grade D (b) (4) area on 06-September-2024 and then used in the Grade A/B filling room on 08-September-2024.

E. There is no data to support a dirty hold time exceeding (b) (4) During review of the batch record and videos associated with (b) (4) Injection (b) (4) IU/mL, batch (b) (4) the time between end of batch (b) (4) and dismantling started (b) (4) (b) (4) was (b) (4)

F. Cleaning activities for the Grade A filling line and surrounding Grade B area do not include the specific operator who performs each activity. The times in which each specific activity is performed, such as dismantling, or execution of specific steps.

OBERVATION 6

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2037 Rockville, MD 20857 ORAPHARMInternationalresponses@fda.hhs.gov	09/17/2024-09/27/2024
	FEI NUMBER 3011248248

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Dr. Rhonda Duffy, Ph.D., Executive Vice President and Chief Operations Officer

FIRM NAME	STREET ADDRESS
Biocon Sdn Bhd	No.1, Jalan Bioteknologi 1, Kawasan Perindustrian SiLC
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Iskandar Puteri, Johor, Malaysia, 79200	Sterile Drug Product Manufacturer

Your firm failed to establish adequate written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess. Specifically,

A. Sterile glove leak test procedure (Document No.: BM/PDP/SOP/069) is inadequately written to provide clear instructions to employees to perform post-integrity (b) (4) glove testing. According to the SOP, (b) (4) post-integrity (b) (4) glove testing requires QA or production verification, however upon review it was noted that the reports were not reviewed by Quality.

B. The operators are neither trained nor provided instructions in the SOP 'Operation of (b) (4) (b) (4) for filling machine, Document No.: BM/PDP/SOP/082' to collect in-process samples during end filling operations of (b) (4) batch (b) (4)

OBSERVATION 7

The batch production and control records are deficient in that they do not include documentation of the accomplishment of each significant step in manufacturing, processing, and packing. Specifically,

Start and stop times of each step of set-up activities for filling operations, such as, but not limited to: set-up of (b) (4) stopper station, (b) (4) Vessel and Manifold, is not documented. There is no system to link finger dab results to these activities in the case of the need of an investigation. For example, a production operator was involved in set-up activities for (b) (4) station, (b) (4) vessel and manifold, and subsequently had three separate finger dabs. The finger dab taken at (b) (4) resulted in (b) (4) cfu which is outside the specification for Grade A of (b) (4) There is no system to routinely identify which activity this finger dab is linked to. Without a system to link finger dab results to specific operations during set-up activities, data needed to perform potential investigations would not available.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Jeffrey P. Raimondi -S Digitally signed by Jeffrey P. Raimondi -S Date: 2024.09.27 05:39:20 -05'00' Sandra A. Boyd -S Digitally signed by Sandra A. Boyd -S Date: 2024.09.27 05:24:28 -05'00' Paranthaman Senthamarai Kannan -S Digitally signed by Paranthaman Senthamarai Kannan -S Date: 2024.09.27 05:59:15 -05'00'	Jeffrey P. Raimondi, Consumer Safety Officer Sandra A. Boyd, Drug National Expert Paranthaman Senthamarai Kannan, Investigator	09/27/2024

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2037 Rockville, MD 20857 ORAPHARMInternationalresponses@fda.hhs.gov	09/17/2024-09/27/2024
	FEI NUMBER 3011248248

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Dr. Rhonda Duffy, Ph.D., Executive Vice President and Chief Operations Officer

FIRM NAME	STREET ADDRESS
Biocon Sdn Bhd	No.1, Jalan Bioteknologi 1, Kawasan Perindustrian SiLC
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Iskandar Puteri, Johor, Malaysia, 79200	Sterile Drug Product Manufacturer

OBSERVATION 8

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

A. General Format documents not controlled or reconciled. These forms can be used in part for DEV/CAPA investigations, assessment/evaluation of CAPAs, and as a form for attaching data printouts.

B. Changes made by engineers during filling operators to PLC parameters are not attributable. The engineers have a general log in (bosch service). This was observed during the review of the MLD audit trail.

C. Analytical balance XP205 (b)(4) units), Micro balance XP26 (b)(4) unit), precision balance SP802S (b)(4) unit), and high-capacity microbalance MSA36S (b)(4) unit), used in the analytical laboratory have general sign in feature. This results in weight sheets not being attributable to a specific analyst.

Sandra A. Boyd -S
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Date: 2024.09.27 05:25:41 -05'00'

Paranthaman Senthamarai Kannan -S
Digitally signed by Paranthaman Senthamarai Kannan -S
Date: 2024.09.27 06:01:05 -05'00'

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	Jeffrey P. Raimondi -S Digitally signed by Jeffrey P. Raimondi -S Date: 2024.09.27 05:40:11 -05'00'	Jeffrey P. Raimondi, Consumer Safety Officer Sandra A. Boyd, Drug National Expert Paranthaman Senthamarai Kannan, Investigator	09/27/2024