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	2/19/2024-2/29/2024*
	FEI NUMBER 3011905047

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Yugandhar Puvvala, CEO & Executive Director

FIRM NAME	STREET ADDRESS
Eugia SEZ Private Limited	Plot No:S-5/B, S-6 & S-7, Survey 408-412, 418-435, 437-445, 452-459 Sez, Tsiic, Polepally (Village), Jadcherla Mandal
CITY, STATE, ZIP CODE, COUNTRY Mahabubnagar District, Telangana, 509302 India	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 WE OBSERVED:

OBSERVATION 1

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

Specifically,

A. Your firm failed to follow EP4-PR-SOP-042, "Guidelines for Working in Aseptic Area" and EP4-MB-SOP-028, "Viable Monitoring Program". The following are examples but are not intended to be a list of all times the procedures were not followed.

1. Interventions into critical areas during aseptic manufacturing are not replicated during Aseptic Process Simulations, to assess risk and validate the performance of the interventions. For example:

- Removal of stuck vials through (b) (4) No. (b) (4) at (b) (4) during manufacture of (b) (4) Injection USP (b) (4) g, Batch No. (b) (4) the operator was observed reaching his whole arm, including the (b) (4) portion of his arm and the fabric cleanroom gown, into the Grade A filling area to remove vials and stoppers. Aseptic Process Simulation Batch No. (b) (4) replicated intervention, occurring between 3:33 PM and 3:35 PM, did not include the operator reaching to the same depth into the Grade A area, nor was the

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2/29/2024

intensity of movement and duration of the intervention accurately replicated.

2. The written procedure, EP4-MB-SOP-028, mandates that operators perform personnel monitoring after interventions into critical areas (Grade A/ISO 5, while under Grade A air supply, prior to sanitization of hands. Examples of inadequate personnel monitoring, post (b) (4) interventions during filling operations of (b) (4) Injection USP (b) (4) g, Batch No. (b) (4) on 02/19-20/2024, on (b) (4) Line-(b) (4) include:

- Removal of vials through (b) (4) No. (b) (4) at (b) (4) on 02/19/2024. The operator was observed reaching his whole arm, including the (b) (4) portion of his arm and the fabric cleanroom gown, into the Grade A filling area to remove vials and stoppers from the (b) (4) (b) (4) area. No personnel monitoring was performed.

3. During aseptic filling of (b) (4) Injection USP (b) (4) g, batch (b) (4) February 17, 2024 on (b) (4) the following interventions were observed:

- At (b) (4) one operator passed a (b) (4) spray bottle underneath the (b) (4) conveyer to another operator on the other side without either operator first sanitizing their hands or the spray bottle. At (b) (4) the same operator left the RABS (b) (4) and returned to the (b) (4) conveyer where another operator passed a (b) (4) box of wipes underneath the (b) (4) conveyer without either operator first sanitizing their hands or the box of wipes. At this time there was (b) (4) drug product crossing the conveyer.

- From 2:57PM - 3:07PM, one operator was performing aseptic corrective interventions while placing his entire arm inside the Grade A area and did not clear the vials located directly at the (b) (4) conveyer near (b) (4) The operator did not sanitize the area after performing

the interventions and did not perform personnel monitoring on his (b) (4) as required per EB4-MB-SOP-028-02 Viable Monitoring Program. The operator did not use slow and deliberate movements while performing the interventions. The operator used quick motion to wipe the (b) (4) and (b) (4) the RABS (b) (4) much quicker than the technique used during aseptic process simulations.

4. During aseptic filling of (b) (4) Injection (b) (4) g, Batch (b) (4) February 16, 2024, on (b) (4) the following interventions were observed:

- From (b) (4) an operator was performing an aseptic corrective intervention near the (b) (4) He was leaning into the Grade A area over (b) (4) vials and touched multiple surfaces with his (b) (4) hands. After the manipulations there was no finger plating and one (b) (4) vial where manipulations were performed was not cleared from the line.

- From (b) (4) an operator (b) (4) to perform an aseptic corrective intervention of clearing fallen/stuck vials from the filling conveyer. He was leaning into the Grade A area over the filling line while performing the intervention. The operator touched the filling line tubing with his (b) (4) sleeve several times during this intervention. He also adjusted the conveyer with his (b) (4) hands and did not sanitize the same areas that were touched. The operator did not perform personnel monitoring on his (b) (4) as required per EB4-MB-SOP-028-02 Viable Monitoring Program.

B. Your firm failed to follow SOP HO-CQA-SOP-072, Enumeration of Microbial Colonies. On February 19, 2024, while reviewing the personnel monitoring plates, one plate for employee number (b) (6) for Finger Dab Right Hand, was observed to have one colony. The action level

for this sample is (b) (4) CFU. This plate had been read by both the analyst and a reviewer and documented as "Nil" on the "Personal Monitoring Data Sheet For: (b) (4) Q1-24 -Feb 13, 2024".

OBSERVATION 2

Written records are not always made of investigations into unexplained discrepancies.

Specifically,

A. During finished product testing for (b) (4) injection USP (b) (4) g, batch (b) (4) your firm received OOS results for bacterial endotoxin testing. Your investigation initiated on September 26, 2023, determined the source of the endotoxin was attributed to the (b) (4) API used to manufacture these batches.

The investigation at the API manufacturer did not identify a definitive root cause but determined the probable cause of the OOS was "operating person might have missed to apply the (b) (4) (b) (4) to release the (b) (4) present inside the (b) (4) and this might have resulted in hold up of (b) (4) in (b) (4) in the stated batches. Considering the scope of proliferation on storage and stagnation of (b) (4) in any given system, there is a scope for the microbial proliferation, which in turn might have probably contributed for the development of endotoxins in the (b) (4) which would have forwarded with the further manufacturing process pertaining to subject batches." This probable cause was not confirmed to be the source of endotoxin and this probable cause is also not limited specifically to the (b) (4) API batches (b) (4) used to manufacture the OOS finished product batches.

Furthermore, on December 2, 2023, your raw material testing for (b) (4) API confirmed three batches tested positive for endotoxin. The API manufacturer investigation again did not identify a definitive root cause but identified additional probable causes. These causes were not specific to these three batches but were identified as "no specific cleaning procedure (b) (4) (b) (4) cleaning procedure) after usage of (b) (4) dedicated for (b) (4) % (b) (4) solution, (b) (4) As a preventive action, your firm rejected the confirmed OOS finished product and API batches, and tested all remaining API batches/containers in stock for bacterial endotoxin. All batches that tested negative were released for production.

Your firm utilized approximately (b) (4) other (b) (4) API batches after the initial OOS that were manufactured by this supplier before the supplier made any corrections to their manufacturing processes that resulted from their investigation.

B. While reviewing the test result for (b) (4) sampling point (b) (4) from February 5, 2024, a (b) (4) result of (b) (4) was observed, which is above the action limit of (b) (4) According to your SOP EP4-QC-SOP-005-00, "Sampling procedure for (b) (4) Samples", when the test exceeds the action limit, a process non-conformance has to be initiated. Your firm failed to initiate a non-conformance to investigate this out of limit result.

OBSERVATION 3

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

Specifically,

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Your firm's No. 04 Continuous Nonviable Particle Counter (NVPC), located near the (b)(4) conveyor area of (b)(4) Line (b)(4) is not located in the position depicted in (b)(4) Filling Machine Lay-out NVPC", Document No. APL-XVI-PR-EQP-002-02. It is actually located inside the Grade A area, near the (b)(4) accessible through (b)(4) No. (b)(4) of the (b)(4) RABS, which is separated from the conveyor area by an (b)(4) As such, there is no NVPC data to represent conditions during (b)(4) interventions that require movement of (b)(4) conveyor, or of any interventions performed through (b)(4) RABS (b)(4) No (b)(4)

OBSERVATION 4

Control procedures are not established which validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

Specifically,

Your firm has not validated your (b)(4) inspection Machine, Equipment No. PR-(b)(4)-001, to detect 316 (b)(4) particulates, smaller than (b)(4) Your firm was unable to provide any scientific justification or rationale for not including particulates on the lower end of the visual range (smaller than (b)(4) in the qualification of the (b)(4) Inspection system. Additionally, the (b)(4) inspection process has not been qualified and cannot detect particulates potentially generated from the (b)(4) stopper material (b)(4) in (b)(4) of (b)(4) mL and (b)(4) mL (b)(4) vials. (b)(4) inspection is the singular and primary mechanism for detection of objectionable foreign particulate matter within (b)(4) as visual inspection is limited to detection of surface level particulate contamination.

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OBSERVATION 5

Failure to maintain a backup file of data entered into the computer or related system.

Specifically,

(b) (4) Nonviable Particle Counters, Model Number, 3423, Equipment ID No. PR-NVPCP-001, PR-NVPCP-002, PR-NVPCP-004, lack the functionality to save data internally and/or via backup, by which to verify printed non-viable particle counts in the Grade B (ISO 7) aseptic processing areas during set-up of (b) (4) and during set-up and manufacture of (b) (4) drug product. Additionally, NVPCs used in support of production operations, lack audit trail functionality, for example: electronic records of configuration of user accounts, passwords, and system date/time. These records are managed using manual logs that could not be verified electronically during the inspection. Deficiencies regarding accuracy of data and subsequent particle count calculations were also noted during qualification of the NVPCs.

OBSERVATION 6

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

Specifically,

A. There is no disinfectant efficacy study performed for (b) (4) tubing used for drug product transfer during vial filling on (b) (4) Line (b) (4) The exterior of the (b) (4) tubing is not sterilized prior to

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installation in the filling assembly, located in the Grade A filling area, directly above (b) (4) and open vials during production operations.

B. Your firm has no written procedure detailing the cleaning of (b) (4) step ladders, (b) (4) and (b) (4) Laminar Airflow Cabinet (b) (4) the Grade A and B (ISO 5/7) aseptic processing areas of your (b) (4) Injection Line and your (b) (4) Drug Lines. Additionally, no routine monitoring is performed for the (b) (4) of the various (b) (4) step ladders, and (b) (4) Laminar Airflow Cabinets, that (b) (4) aseptic processing areas, before and during production operations. A (b) (4) plate sample collected of the (b) (4) of the (b) (4) step ladder in your firm's (b) (4) production area on 02/23/24, sampled at the request of investigators, was observed to have microbial growth. (b) (4) monitoring locations do not include areas where these (b) (4) within the aseptic processing suites.

OBSERVATION 7

Employees engaged in the manufacture and processing of a drug product lack the training required to perform their assigned functions.

Specifically,

The ability of visual inspectors to identify integrity defects during visual inspection of (b) (4) Restricted Access Barrier System (b) (4) RABS) (b) (4) has not been adequately assessed. Inspectors are provided a (b) (4) (b) (4) defect kit and trained on the defects within the training kit. Subsequently, on the (b) (4) inspectors are assessed on the ability to detect defects using (b) (4) of the (b) (4) numbered (b) (4) sourced from the same kit used for training. However, per FU16-MIS-VSP-0740, "Personnel Qualification Protocol for (b) (4) Inspection", step (b) (4) "The inspector shall inspect all the (b) (4) in the kit and record

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the details in the Annexure-III". Visual inspection is the primary defect detection method for (b) (4) RABS (b) (4) prior to, and post completion, of production activities. Mechanically assisted methods of (b) (4) integrity testing, are only performed (b) (4) on a (b) (4) basis.

***DATES OF INSPECTION**

2/19/2024(Mon), 2/20/2024(Tue), 2/21/2024(Wed), 2/22/2024(Thu), 2/23/2024(Fri), 2/26/2024(Mon), 2/27/2024(Tue), 2/28/2024(Wed), 2/29/2024(Thu)

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