DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 (973)331-4900 ORAPHARM1_RESPONSES@fda.hhs.gov	12/11/2023-12/22/2023* FEI NUMBER 3015534630

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Bijaygopal Chakrabarti, Senior Vice President

FIRM NAME	STREET ADDRESS
Eugia US Manufacturing LLC	203 Windsor Center Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
East Windsor, NJ 08520-1410	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

There is no quality control unit.

Specifically,

Your quality unit is not shown to be prepared to perform quality unit activities for control of GMP operations for commercial production at this site.

For example,

a. Your firm's quality unit failed to demonstrate ability to adequately investigate and close quality documentation in a reasonable timeline. Of the firm's 34 unplanned deviations opened in 2023, 16 remain open, 14 of which are beyond due date without extension requests. Additionally, the firm has 12 investigations opened in 2023 for out-of-specification, out-of-alert-level, and out-of-trend results that remain open, out of a total of 21. Additionally, the firm has opened 14 CAPAs in 2023, of which only 1 is closed. The remaining 13 are all open beyond due date.

b. Your firm lacks control over processes conducted by third-party vendors on behalf of the firm, including but not limited to: pest control; cleaning of controlled production corridors used to access your aseptic processing core; management of the NetSCADA software application (and affiliated computer workstation) used to operate (b) (4), used in production of (b) (4) and qualification and requalification of HVAC systems serving the production core.

c. Your quality unit lacks access control and knowledge of the NetSCADA software used to control

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	James R Birkenstamm, Investigator Daniel L Zheng, Investigator Ruben C Quintana, Investigator Yoriann M Cabrera Bartolomei, Investigator X James R Birkenstamm Investigator Signed By: James Birkenstamm - S Date Signed: 12-22-2023 16:19:01	12/22/2023

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(b) (4) used in production of (b) (4) Your quality unit was unable to provide information regarding equipment programming and the permissions for different user accounts.

d. Your quality unit failed to create, approve, and establish procedures specific to your firm's processes, including but not limited to: SOP-U3-QA-003 Planned Deviations, Unplanned Deviations and Non-conformances, SOP-U3-QA-004 Training Program, and SOP-U3-QA-021 Submission of Samples to Quality Control/Analytical/Microbiology Laboratory for Testing.

OBSERVATION 2

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

Specifically,

a. You failed to provide documentation supporting validation of cleaning, sanitization and disinfection procedures used for cleaning of product contact surfaces in your aseptic processing area, which is used for production of (b) (4) and (b) (4) (b) (4). Also, you failed to assess if the cleaning agents are safe and effective for use in processing surfaces and equipment.
b. You failed to provide documentation supporting the adequacy and reliability of the cleaning agents used in the aseptic processing rooms used for production of (b) (4) and (b) (4)

OBSERVATION 3

Buildings used in the manufacture, processing, packing, or holding of a drug product do not have the suitable size and construction to facilitate cleaning, maintenance, and proper operations.

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a. On 12/20/2023, it was observed that your quality unit documentation failed to demonstrate control over differential pressure in your production core to maintain aseptic conditions. For example:

i. During qualification activities taking place on 9/12/2023, total pressure for (b) (4) rooms in your aseptic processing core were out of specification, including Grade D (b) (4) Room (b) at 56.25 Pa (specification >(b) (4)), Grade C Corridor (b) (4) at 22.23 Pa ((b) (4) <), and Grade C (b) (4) Room (b) (4) at 17.52 Pa (>(b) (4) <). Additionally, your firm requires positive pressure from Grade C (b) (4) Filling Room to Grade C Corridor (b) (4) However, during qualification activities taking place on 9/12/2023, your firm recorded a total pressure of 21.83 Pa in the (b) (4) Filling Room and 22.23 Pa in Corridor (b) (4) Your quality unit did not identify these failures and approved the HVAC pressure system as meeting specifications and qualified on 11/16/2023. Your firm uses (b) (4) Room (b) Corridor (b) and (b) (4) Room (b) (4) during production of (b) (4)

ii. During qualification activities for your HVAC pressure system in the aseptic processing core taking place on 7/8/2022, your firm reported acceptance criteria for differential pressure as (b) (4) (b) (4) During the inspection, your quality unit was unable to provide the specification contemporaneous to the 2022 qualification for the designed room pressure (b) (4) (b) (4) in the aseptic processing area.

Additionally, in your 2022 qualification, your firm had no documentation or data to demonstrate that the rooms in your aseptic processing area, including Grade C areas, met your firm's specifications for each room's ambient pressure with respect to the surrounding non-classified production corridor.

Examples of Grade C areas for which your firm lacked qualification data include (b) (4) Filling Room (b) (4) (b) (4) and Corridor (b) Your firm used the aseptic processing core, including these three Grade C rooms, for production of (b) (4) exhibit batches (b) (4) (manufactured 10/2/2022), (b) (4) (manufactured 10/9/2022), and (b) (4) (manufactured 10/14/2022), as well as for production of (b) (4) (b) (4) exhibit batch (b) (4) (manufactured 2/16/2023). You lack data to demonstrate that your aseptic processing core room pressures were qualified as of production of your exhibit batches for (b) (4) and (b) (4)

iii. Your specifications for periodic monitoring of differential pressure of your aseptic processing core are not scientifically justified. During the inspection, the Quality Unit was unable to provide documentation, for whether the aseptic processing core pressure monitors record differential pressure (b) (4) rooms or between each room and the non-classified production corridor outside the aseptic processing core. Logbook MF078-201-23 Daily Room Differential Pressure Monitoring Logbook reports the specification as "area difference pressure should be minimum of (b) (4) inches of (b) (4) (≥ (b) (4) pa) with respect to (b) (4) " This logbooks do not contain sufficient data to demonstrate that the rooms meet this specification, including: no data for pressure readings for (b) (4) rooms; no details on if pressure data are differential (b) (4) spaces or betwee m and the non-classified corridor; and on 12/20/2023, it was observed the operator signing off room pressures in the above logbook as meeting specifications based on recorded room data being greater than (b) (4) inches of (b) (4) without determining pressure differential with respect to adjacent spaces. You do not have sufficient data to demonstrate that your rooms are meeting specifications. The aseptic processing core serves production of (b) (4) and (b) (4) .

b. During walkthroughs of your facility on 12/12/2023 and 12/13/2023, the following facility

deficiencies were observed:

i. What appeared to be (b) (4) damage on the HVAC mezzanine physically located (b) (4) rooms in the classified aseptic processing core associated with Line (b) which your firm uses for production of (b) (4) and (b) (4) It was also observed what appeared to be (b) (4) damage due to ceiling leaks in the controlled production corridors and (b) (4) equipment room, which are located immediately adjacent to the aseptic process

ii. A loose panel exposing the Grade C room (b) (4) Filling Room (b), which hosts Filling Line (b) to the non-controlled and unclassified (b) (4) equipment room, which your firm uses for operation of (b) (4) Additionally, it was observed a hole approximately 2 cm in diameter in the ceiling of the (b) (4) equipment room leading to the non-controlled and unclassified HVAC mezzanine located immediately (b) (4) the aseptic processing core. Your firm uses Filling Line (b) in Vial Filling Room (b) (4) for production of (b) (4) (b) (4) and (b) (4) . Additionally, your firm uses (b) (4) (b) (4) for production of (b) (4)

c. On 12/11/2023, during the walkthrough of the facility, construction activities were observed in the following areas - product warehouse, which the firm currently uses for storage of all components and materials other than product vials, including raw materials, finished product, retain samples, consumable equipment (tubing, filters, etc.), rejected exhibit batch units, and spare gowning; stability chamber room, located across (b) (4) and approximately (b) (4) feet away from the firm's microbiology laboratory; and the future expansion area, located adjacent to the sterile core supporting Lines (b) (4) and exposed to the material flow pathway for incoming shipments transiting from delivery to the product warehouse. Additionally, your firm lacks quality documentation, including change control documents, to govern control of contamination

due to construction activities in the future expansion area. Your firm lacks adequate controls to prevent contamination of production areas due to ongoing construction. These areas are all used to support production of (b) (4) and (b) (4)

d. Your firm lacks adequate space and control of environmental conditions for storage of retain samples, including for products (b) (4) and (b) (4) Additionally, stored retain samples are at risk of cross-contamination with ongoing construction activities currently observed at the firm.

e. Your quality unit failed to assure an adequate qualification supported with documentation for Incubation Room (b) (4) with regards to (b) (4) mapping, and there is a lacks documentation to demonstrate that Incubation Room (b) (4) and Incubation Room (b) (4) were in calibration during media fills supporting aseptic production processes for all (b) (4) (b) (4) (b) (4) mg/vial (b) (4) (b) (4) exhibit batches and the (b) (4) (b) (4) (b) (4) mg (b) (4) mL (b) (4) exhibit batch. Additionally, your quality unit failed to establish procedures governing cleaning of your incubation rooms, and cleaning of your incubation rooms.

OBSERVATION 4

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

Specifically,

1. Your firm shares your Empower data server with a different pharmaceutical company with a separate FEI number that has administrator-level access and the ability to alter testing data and audit trails to which you don't have direct access to.
2. Your firm's NetSCADA software used to operate (b) (4) all users have access to a non-specific administrator-level account. For example, operators log into NetSCADA

system with their own username and password, operate the (b) (4) cycles during production or other test cycles and log into the shared admin account when specific system securities need to be addressed by admin permissions. Your firm uses (b) (4) for production of (b) (4)

3. Your firm uses a any to manage your computer systems, including IT, workstations, and servers, as well as laboratory software such as Empower and inventory software such as Oracle ERP. Your quality unit lacks any documentation establishing controls over information technology systems and personnel, including quality agreements or contracts.

OBSERVATION 5

Input to and output from the computer and records or data are not checked for accuracy.

Specifically,

On 12/15/2023, upon review of the NetSCADA computer application, used to operate (b) (4) cycle runs associated to (b) (4) exhibit batches (b) (4) as well as (b) (4) associated to (b) (4) exhibit batches (b) (4) re not available on the NetSCADA system upon query. However, on 12/19/2023, data for the (b) (4) and stoppering cycle runs for (b) (4) exhibit batches (b) (4) he same location previously reviewed/queried. As of 12/22/2023, it is unclear how this data were acquired in this system and whether or not there are controls in place to avoid the addition or deletion of data.

OBSERVATION 6

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

Specifically,

a. You failed to provide documentation of initial, operational, and performance qualification (IQ, OQ, PQ), of equipment used for production of (b) (4) and (b) (4) including but not limited to Grade A (b) (4) used for the production of (b) (4).

b. You failed to install and qualify (IQ, OQ, PQ) the necessary equipment intended to label and package (b) (4) mg/vial (b) (4) and (b) (4) mg/ml (b) (4). Additionally, the procedures for labeling and packaging for these drug products have not been written and or established.

OBSERVATION 7

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

Specifically,

Upon review of batch production records for (b) (4) exhibit batches (b) (4) environmental monitoring settling plates located inside Grade A (b) (4) before production was complete. Your firm uses (b) (4) for production of both (b) (4) and (b) (4)

OBSERVATION 8

Evidence of reserve drug product sample deterioration was not investigated.

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On 12/19/2023, it was observed multiple instances of retain samples for product (b) (4) (b) (4) mg/vial (b) (4) exhibit batches (b) (4) that demonstrated deterioration of (b) (4) formation as well as product spread throughout the vial and near the cap. Your firm does not have any documentation of investigation into these discrepancies. These (b) (4) exhibit batches were produced in October of 2022.

OBSERVATION 9

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

Specifically,

a. During exhibit batch production of (b) (4) Injection (b) (4) mg/vial (b) (4) your firm collects (b) (4) vials as samples for bacterial endotoxin testing as per your exhibit batch sampling protocol. This procedure does not require sample vials to be pulled from specific time points during batch production. Additionally, of the (b) (4) pulled samples, your firm's procedures only require bacterial endotoxin testing to be completed on (b) (4) vial, which is randomly pulled from the above (b) (4) During production of exhibit batches for (b) (4) your firm produced (b) (4) ials for batch (b) (4) vials for batch (b) (4) and (b) (4) vials for batch (b) (4) Your firm lacks scientific rational to demonstrate that your sampling method of testing (b) (4) vial out of approximately (b) (4) total units is representative of the batch. Additionally, your firm lacks scientific rationale to justify that your bacterial endotoxin testing process can detect bacterial endotoxin throughout the batch.

b. You failed to conduct performed method verifications covering laboratory methods for testing bioburden, bacterial endotoxin, and sterility of in-process samples taken during production of (b) (4) exhibit batches (b) (4)

(b) (4)

c. Your quality unit failed to document and to demonstrate adherence to sterility test methods. For example, during sterility testing procedure EU-MB-GEN-007.00 for your product (b) (4) (b) (4) requires a (b) (4) wait period during (b) (4) of the sample to ensure product dissolution. There is no documentation of time records and therefore lacks assurance of completion for this (b) (4) wait time. In addition, the sterility testing is completed on (b) (4) vial samples, (b) (4) consisting of a mix of vials taken from the beginning, middle, and end of a batch. However, the firm lacks processes governing or the documentation to demonstrate how many vials from the beginning, middle, and end of the batch were (b) (4)

d. Your quality unit failed to document and to demonstrate that in-process and finished product samples are pulled in accordance with your sampling plan and in a manner that is representative of the production batch. Examples include but are not limited to batch production records for (b) (4) (b) (4) require collection of (b) (4) finished product units for sterility release testing to be taken from "initial, middle & end." You lack documentation recordings that the samples were actually pulled from the beginning, middle and end of the production batch. Other methods lacking such documentation of specific sampling include but are not limited to sampling for bacterial endotoxin testing, assay, and impurity testing.

OBSERVATION 10

Written procedures are lacking which describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval and rejection of components, drug product containers and closures.

Specifically,

You failed to follow procedure SOP-U3MB033.03 "Sampling of Raw Materials" which requires fully recording Material Receipt Reports for all Components, Drug Product Containers and closures received. Also there is a failure to document Sample Login # and the quantity of samples withdrawn for chemical

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analysis, microbiological analysis and retention samples for (b) (4) USP API used in the production of (b) (4) Injection (b) (4) g/(b) (4) ml exhibit batch (b) (4) for (b) (4) and (b) (4) API used in the production of (b) (4) Injection (b) (4) mg/vial exhibit batches (b) (4) (b) (4)

Furthermore, (b) (4) lot #'s (b) (4) received on 08/10/2022 and (b) (4) received on 08/10/2022 state Product Code (b) (4) which does not match Item code number (b) (4) of (b) (4) used in the manufacture of the aforementioned exhibit batches for (b) (4)

***DATES OF INSPECTION**
12/11/2023(Mon), 12/12/2023(Tue), 12/13/2023(Wed), 12/15/2023(Fri), 12/19/2023(Tue), 12/20/2023(Wed), 12/21/2023(Thu), 12/22/2023(Fri)

X Daniel L Zheng
Investigator
Signed By: Daniel L. Zheng -S
Date Signed: 12-22-2023 16:20:00

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	James R Birkenstamm, Investigator Daniel L Zheng, Investigator Ruben C Quintana, Investigator Yoriann M Cabrera Bartolomei, Investigator X James R Birkenstamm Investigator Signed By: James Birkenstamm -S Date Signed: 12-22-2023 16:19:01	12/22/2023