DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6000 Metro Drive, Suite 101 Baltimore, MD 21215 (410) 779-5455 Fax:(410) 779-5707 Industry Information: www.fda.gov/oc/industry	07/13/2015 - 07/23/2015* FEI NUMBER 3011627411

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Mr. James R. Schwamburger, Director of Pharmacy

FIRM NAME	STREET ADDRESS
Sentara Enterprises	535 Independence Pkwy Ste 300
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Chesapeake, VA 23320-5176	Producer of Sterile Drug Products

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:

Production

OBSERVATION 1

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

Specifically,

On 07/13/2015, the following aseptic techniques were observed in the cleanroom:

A) An operator was observed placing tube tips (used for puncturing vials and bags containing sterile material) on the bench top inside a Biological Safety Cabinet (BSC) before it was disinfected during a set-up for sterile drug production.

B) A gowned operator was observed leaving the BSC/ hood in the middle of an operation (filling of sterile drug product into elastomeric infusion devices) to grab supplies from the gowning area (outside the Cleanroom). When she returned she continued with the operation without disinfecting her gloves. There is no procedure in place that prevents operators from exiting the cleanroom area to grab supplies from non-classified areas (gowning room and hall way) fully gowned.

C) An operator was observed placing a syringe (used for transferring diluents or drugs from vials to multiple elastomeric infusion device or aka home-pump) on the bench top inside the BSC; the syringe is not disinfected in between filling or transferring diluents or drugs into other elastomeric infusion devices.

D) Multiple operators were observed introducing material (i.e. diluents or components) to be used for sterile drug manufacturing, into the BSC/hood without disinfecting the outside cover.

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OBSERVATION 2

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

Specifically,

A) Sterile drug products produced from non-sterile components are sterile filtered through a 0.2 micron filter. However, the firm does not perform any filter integrity testing after producing drug products purported to be sterile. Currently, products such as Hydromorphone, Morphine, Fentanyl, Bupivacaine and Clonidine are sterile filtred for intrathecal administration.

B) Currently media-fills are conducted to monitor operators' aseptic technique. However, no media fill study was conducted to simulate the production of sterile drug products produced from non-sterile components Examples of these sterile drug products include Hydromorphone, Morphine, Fentanyl, Bupivacaine and Clonidine.

OBSERVATION 3

Clothing of personnel engaged in the manufacturing and processing of drug products is not appropriate for the duties they perform.

Specifically,

During the inspection of your firm, the operators we observed performing aseptic operations in the ISO 5 hoods were wearing non-sterile gowns. Specifically, the laboratory coat, face mask and pants are not sterile. Additionally, the face mask does not fully cover operator's face.

Facilities and Equipment

OBSERVATION 4

Buildings used in the manufacture, processing, packing or holding of drug products are not maintained in a clean and sanitary condition.

Specifically,

Biological Safety Cabinets (BSC)/Hoods #2 & #4, which are ISO 5, are located in a clean room classified as ISO 7. BSC # 2

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is used for Total Parenteral Nutrition (TPN) bag production only and BSC #4 is used for producing products such as, Meropenem (10ml syringe) and large volume parenterals such as Vancomycin HCl and Daptomycin. The following deficiencies were observed in the above listed BSCs/Hoods:

A) Stained ceiling near the entrance of the gowning area to the clean room. Various types of materials such as vitamins and sterile water are kept under this ceiling.

B) Rusted vents were observed on Hood # 2 (used for preparing TPNs).

C) Rust was observed in the HEPA filter grills inside Hood #2.

D) A black substance was observed above the HEPA filter grills (Hood #2)

E) Minor rusting was observed on the HEPA grills inside Hood # 4.

F) Rust and foreign black substance was observed above the HEPA filters inside Hood #4

G) Stains on the inside roof and exposed light bulb were observed inside Hood # 4

H) Rust and chipped paint was observed on the vents of Hood #4

OBSERVATION 5

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

Specifically,

A) Personnel monitoring is conducted on a monthly basis, whereby only the finger-tips of the operators are monitored. Environmental sampling is conducted for bench tops (BSCs), counters, and sinks on a monthly basis. The sampling medium ("paddle") used for finger-tips and surface sampling is currently not tested for growth promotion. The "Paddle" is also used for air sampling (passive) in the BSC on a monthly basis.

B) No settle plates, active air and non-viable air is monitored in the BSC during aseptic operations.

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OBSERVATION 6

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

Specifically,

A) The following disinfectants are used for sanitizing the BSCs and the surrounding areas: 70% IPA, "Peridox RTU" (label claims it's fungicidal, sporicidal and virucidal), "Accel TB" (label claims it's bactericidal & virucidal), and pre-soaked wipes "Prostat Sterile". No efficacy study was performed to determine if these disinfectants are capable of reducing the microbial load to an acceptable levels in the BSCs and other surfaces (i.e. benchtops, walls and floor) in the cleanroom (ISO 7) where aseptic operations take place.

B) Cleaning procedure, P-304.2 entitled "CLEANING AND DISINFECTING OF THE COMPOUNDING AREA" does not clearly indicate the type of disinfectants to be used. Specifically, there is no mention of the various disinfecting agents used in the ISO 5 (BSC/Hood) area currently. Additionally, 70% IPA and the sporicidal disinfectant ("Peridox RTU") are not being used in the cleanroom or the Hoods in alternating fashion.

OBSERVATION 7

Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.

Specifically,

The last qualification of the Biological Safety Cabinets/ISO 5 Hood was conducted in June, 2015 and it did not challenge all the BSCs during the smoke study under dynamic conditions.

Laboratory Controls

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OBSERVATION 8

Each batch of drug product purporting to be sterile is not laboratory tested to determine conformance to such requirements.

Specifically,

No sterility and endotoxin testing has been conducted for sterile drug products produced from non-sterile components since November, 2014. Additionally, TPNs are tested for sterility on a weekly basis and other sterile drug products are tested periodically (up to every 6 months) for sterility. The sterility samples (on a TSB Medium) for the TPNs were incubated at a temperature ranging from 33-35 °C for 14 days. However, the direction for the sampling unit, Quick Test™ System, instructs the user to incubate at 20 to 25°C. Furthermore, the firm did not evaluate the sterility samples using media intended to support anaerobic microbes.

OBSERVATION 9

Drug products do not bear an expiration date determined by appropriate stability data to assure they meet applicable standards of identity, strength, quality and purity at the time of use.

Specifically,

No stability or potency testing has been conducted for sterile drug products produced from non-sterile components since November, 2014. Examples of non-sterile powders include Hydromorphone, Morphine, Fentanyl, Bupivacaine and Clonidine.

OBSERVATION 10

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

Specifically,

The environmental monitoring records from 05-01/2014 to 05/30/2015 contain positive results that were obtained for personnel's' finger-tips. No investigation was conducted to determine the source of the contamination and impact on product quality and safety. Furthermore, the microbes were not quantified and identified, and no alert or action limit is established for environmental monitoring. The observed growth was for the following "finger-tip testing":

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- Testing date 05/09/2014: Left-hand
- Testing date 05/16/2014: Left-hand
- Testing date 05/27/2014: Left-hand and second operator had growth on his right-hand
- Testing date 05/30/2014: Left-hand
- Testing date 11/26/2014: Left-hand
- Testing date 05/28/2015: Left-hand

Additionally, no trending is performed for monitoring environmental conditions.

OBSERVATION 11

Procedures describing the calibration of instruments, apparatus, gauges and recording devices are not written or followed.

Specifically,

There are no calibration and qualification records for incubator, Boekal Industries, Model 133000. This incubator is used for incubating enviromental samples from the cleanroom and ISO 5 Hoods, and for TPN sterility samples.

*** DATES OF INSPECTION:**
07/13/2015(Mon), 07/14/2015(Tue), 07/15/2015(Wed), 07/20/2015(Mon), 07/22/2015(Wed), 07/23/2015(Thu)

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