DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
11155 Dolfield Boulevard, Suite 117 Owings Mills, MD 21117 (410)779-5455 Fax:(410)779-5707 ORAPHARM1_RESPONSES@fda.hhs.gov	12/5/2022-12/16/2022* FEI NUMBER 3011627411

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Paul A.. Gaden, Regional President

FIRM NAME	STREET ADDRESS
Sentara Infusion Services	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:

OBSERVATION 1

Disinfecting agents and cleaning wipes used in the ISO 5 classified aseptic processing areas were not sterile.

Specifically,

A. The (b) (4) used inside the ISO 5 classified laminar airflow hoods are not sterile. The non-sterile wipes were observed being used as a disposable work surface (upon which items such as, but not limited to syringes, connectors, and IV bags with exposed ports were placed) and during cleaning operations. We observed: on December 5 and 7, 2022, Technician (b) (6), (b) (7)(C) used the non-sterile wipers as a disposable work surface on the ISO 5 work surface (for example, in the production of Rx (b) (6), (b) (7)(C)); on December 7, 2022, Technician (b) (6), (b) (7)(C) used the non-sterile wipers to clean a ISO 5 classified work surface; and on December 8, 2022, Technician (b) (6), (b) (7)(C) wiped the interior of the ISO 5 classified hood with the non-sterile wipers.

B. The disinfectant contact time (also known as "dwell time") and coverage of items being disinfected were insufficient to achieve adequate levels of disinfection. On December 8 and 9, 2022, we observed Technician (b) (6), (b) (7)(C) performing the (b) (4) cleaning of the ISO 5 classified laminar airflow hoods and ISO 7 classified buffer room. The technician sprayed (b) (4) onto the stainless-steel working tables and the (b) (4) interior surfaces of the laminar airflow hoods, and all surfaces air-dried within no more than three minutes. The manufacturer's direction for use as a disinfectant is a (b) (4) contact time.

OBSERVATION 2

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Sena G Dissmeyer, Investigator Brandy N Lepage, Investigator Karen A Briggs, Investigator	X Sena G Dissmeyer Investigator Signed By: Sena G. Dissmeyer -S Date Signed: 12-19-2022 18:18: 9	12/16/2022

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You did not make adequate product evaluation and take remedial action where actionable microbial contamination was found to be present in an area adjacent to the ISO 5 classified aseptic processing area during aseptic production.

Specifically, your firm conducts air and surface environmental sampling of your ISO classified areas every (b) (4) . In each environmental monitoring sampling performed since November 2020, actionable microbial contamination was identified, for example, in your ISO 7 classified areas, which contain ISO 5 classified hoods where drugs intended to be sterile are produced, as follows:

November 2020

- Buffer Room: Fungal Air Sample (6 cfu/m^3)
  - *Penicillum* sp.
  - *Exserhilum* sp.
  - *Hormographiella* sp.
- Anteroom: Fungal Air Sample (4 cfu/m^3)
  - *Cladosporium* sp.
  - *Geotrichum* sp.
- (b) (4) : Bacterial Air Sample (3 cfu/m^3)
  - *Penicillum* sp.
  - Coagulase (-) *Staphlococcus* sp.
  - *Bacillus* sp.

April 2021

- Buffer Room: Fungal Air Sample (3 cfu/m^3)
  - *Trichoderma* sp.
  - *Aspergillus* sp.

October 2021

- Buffer Room: Bacterial Air Sample (3 cfu/m^3)
  - *Aspergillus* sp.
  - *Bacillus* sp.
  - Coagulase (-) *Staphylococcus* sp.

- Buffer Room: Fungal Air Sample (5 cfu/m^3)
  Trichoderma sp.
  Arthrographis sp.
  Penicillium sp.
  Chrysosporium sp.
  Acremonium sp.
- (b) (4) Room: Bacterial Air Sample (27 cfu/m^3)
  Microbacterium sp.
  Coagulase (-) *Staphylococcus*
  Micrococcus sp.
- Anteroom: Fungal Air Sample (2 cfu/m^3)
  Verticillium sp.

April 2022

- Buffer Room: Bacterial Air Sample (4 cfu/m^3)
  Chrysosporium sp.
  Micrococcus sp.
- Buffer Room: Fungal Air Sample (9 cfu/m^3)
  Trichoderma sp.
  Phialemonium sp.
  Aspergillus sp.
  Chrysosporium sp.
- (b) (4) Room: Fungal Air Sample (1 cfu/m^3)
  Aspergillus sp.
- Anteroom: Fungal Air Sample (1 cfu/m^3)
  Chrysosporium sp.

October 2022

- Buffer Room: Fungal Air Sample (6 cfu/m^3)
  Fusarium sp.
- (b) (4) Room: Fungal Air Sample (21 cfu/m^3)
  Penicillium sp.

Scopulariopsis sp.

- (b) (4) Room: Bacterial Air Sample (20 cfu/m^3)
  Coagulase (-) *Staphylococcus* sp.
  Acremonium sp.
- Anteroom: Fungal Air Sample (8 cfu/m^3)
  Penicillium sp.
- Anteroom: Bacterial Air Sample (7 cfu/m^3)
  Cornebacterium sp.
  Acremonium sp.

There were no assessments conducted to evaluate whether sterile drug products produced during the respective timeframes were negatively impacted.

OBSERVATION 3

You produced beta-lactam drugs without providing adequate cleaning of work surfaces to prevent cross-contamination.

Specifically, on December 7, 2022, we observed the production of the non-beta lactam drug product Caspofungin (Rx(b) (6), (b) (7)(C)), after the production of Cefazolin Sodium 2000mg IV (Rx(b) (6), (b) (7)(C)); Ertapenem (Intvanz) Sodium 1GM NS (Rx(b) (6), (b) (7)(C)); and Meropenem 500mg IN VS 125 mL (Rx(b) (6), (b) (7)(C)). During the production of these beta-lactam drug products there was spillage on the ISO 5 classified work surface that was not deactivated during the technician's cleaning between products. The technician cleaned the beta-lactam products' spillage by wiping the exposed ISO 5 classified work surface of the laminar flow hood with a non-sterile wipe and sterile(b) (4). You do not have a specific process to deactivate and remove any beta-lactam product spillage during your handling, processing, and filling operations.

OBSERVATION 4

Personnel engaged in aseptic processing were observed with exposed wrists and exposed hair.

Specifically,

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A. On December 7, 2022, we observed Technician (b) (6), (b) (7)(C) producing drug products intended to be sterile in the ISO 5 classified (b) (4) laminar airflow hood with exposed wrists, such as while producing Rx (b) (6), (b) (7)(C), Cefazolin 3gm in NS 150mL Homepump.

B. On December 12, 2022, we observed Technician (b) (6), (b) (7)(C) working in the ISO 5 classified (b) (4) laminar airflow hood with exposed hair, for example, during the production of Rx (b) (6), (b) (7)(C), Milrinone Lactate 52mg in 0.45% NS 65mL.

OBSERVATION 5

Materials or supplies were not disinfected prior to entering the aseptic processing areas.

Specifically, on December 5, 6, 7, and 8, 2022, during the production of drug products intended to be sterile, for example, but not limited to, Rx (b) (6), (b) (7)(C), Rx (b) (6), (b) (7)(C) Rx (b) (6), (b) (7)(C), Rx (b) (6), (b) (7)(C) and Rx (b) (6), (b) (7)(C)

Technicians brought materials, such as component vials, syringe pouches, and IV bags, from the ISO 7 classified buffer room into the ISO 5 classified laminar flow hoods, without disinfecting the outer surfaces of the materials. We observed technicians (b) (6), (b) (7)(C), and (b) (6), (b) (7)(C) use these materials without sanitizing their outer surfaces. Furthermore, these materials and plastic totes were not disinfected when placed in the (b) (4) when introducing materials from the unclassified (b) (4) room into the ISO 7 classified buffer room. Similarly, the (b) (4) automated compounding device (ACD) hand-held barcode scanner was introduced into the ISO 5 classified laminar flow hood after resting on the stock cart adjacent to the hood in the ISO 7 classified buffer room, without sanitizing the outer surface and the cord of the barcode scanner.

OBSERVATION 6

Personnel conducted aseptic manipulations and placed equipment/supplies in an area that blocked the movement of first pass air around an open unit, either before or after it was filled with sterile product.

Specifically,

A. On December 6, 2022, in the ISO 5 classified (b) (4) laminar flow hood, we observed purportedly

sterile connections being made to setup the automatic compounding device and replace empty component product vials, in front of other component materials and the metal vial rack, blocking first pass air. Furthermore, we observed the connection to the finished product bag being made in front of hanging IV component bags, blocking first pass air.

B. On December 12, 2022, in the ISO 5 classified (b) (4) laminar flow hood, Technician (b) (6), (b) (7)(C) punctured the septum of components while blocking first pass air with a gloved hand during the production of Ampicillin/Sulbactam 12gm in NS 600mL (Rx (b) (6), (b) (7)(C)

C. On December 5, 2022, we observed Technician (b) (6), (b) (7)(C) move rapidly in the vicinity of sterile components, such as connectors, as well as and vigorously striking filled IV bags with the plunger of a large, empty syringe (for example, in the production of Rx (b) (6), (b) (7)(C), which may disrupt the airflow and increase the risk of bringing lesser quality air into the ISO 5 classified aseptic processing area.

OBSERVATION 7

The ISO 5 classified aseptic processing areas had difficult to clean and visibly dirty equipment or surface.

Specifically,

A. On December 5, 6, 7, 8, and 9, 2022, we observed dark, orange-colored (rust-like) spots on the (b) (4) vial rack in ISO 5 classified (b) (4) laminar airflow hood ((b) (4) , used in the production of all total parenteral nutrition (TPN) products. The vial rack is situated in the path of first-pass air, between the rear HEPA diffuser screen and where we observed connections were made to component vials, hanging IV bags, and the finished product bag. The dark, orange-colored (rust-like) spots were not removed before or in between production of all TPN products, such as, but not limited to Rx (b) (6), (b) (7)(C) and Rx (b) (6), (b) (7)(C).

B. On December 7 and 12, 2022, we observed (b) (4) (b) (4) laminar airflow hoods ((b) (4) (b) (4)), had cracked and difficult to clean surfaces between the left (b) (4) stainless-steel panel and the hood worksurface. Drug products intended to be sterile were produced in

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these ISO 5 classified (b) (4) laminar airflow hoods, including but not limited to Rx (b) (6), (b) (7)(C), Cefazolin Sodium 2000mg IV, and Rx (b) (6), (b) (7)(C), Milrinone Lactate 52mg in 0.45% NS 65mL.

OBSERVATION 8

Personnel touched equipment or other surfaces located outside of the ISO 5 classified aseptic processing area with gloved hands and then engaged in aseptic processing without changing or sanitizing gloves.

Specifically,

A. On December 5, 6, and 7, 2022, technicians repeatedly reached back and forth between the ISO 5 classified laminar airflow hoods and items in the ISO 7 classified buffer room, without cleaning or sanitizing gloved hands, and resuming purportedly sterile production operations. Items in the ISO 7 classified buffer room included trash cans, wrapped syringes and connectors, pens, markers, calculators, bins, chairs, a phone, production log papers (non-autoclavable), and a barcode scanner. Furthermore, items were obtained from the stock carts located outside the ISO 5 classified laminar flow hoods and brought into the hoods without disinfecting the outer surfaces of those items.

B. On December 5, 6, and 7, 2022, technicians touched non-sterile gowning, such as bouffant caps, frocks, and disposable face masks, with gloved hands and engaged in sterile production without changing or sanitizing their gloves.

C. On December 5, 2022, Technician (b) (6), (b) (7)(C) reached into a trash receptacle and pushed down trash with a gloved hand and forearm, within the ISO 7 classified buffer room and then returned to sterile production (for example, in the production of Rx (b) (6), (b) (7)(C)) in the ISO 5 classified laminar airflow hood without changing or sanitizing gloves or frocks.

D. On December 5, 2022, Technician (b) (6), (b) (7)(C) was observed resting her arm on the product bag surface of Rx (b) (6), (b) (7)(C) with a non-sterile gown inside the ISO 5 classified laminar airflow hood.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Sena G Dissmeyer, Investigator Brandy N Lepage, Investigator Karen A Briggs, Investigator	X Sena G Dissmeyer Investiga or Signed By: Sena G. Dissmeyer -S Date Signed: 12-16-2022 18:18: 9	12/16/2022

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OBSERVATION 9

Media fills were not performed that closely simulate aseptic production operations incorporating, as appropriate, worst-case activities and conditions that provide a challenge to aseptic operations.

Specifically,

A. For example, the media fills were not representative of container-closure types (for example, syringes, elastomeric pumps, large IV bags), the quantity and volume of finished drug products per order, and equipment (for example, (b) (4) automated compounding device, repeater pump).

B. The plates and media used in environmental monitoring sample testing performed in November 2022 were incubated for (b) (4) prior to reading. The (b) (4) (b) (4) plates used in fingertip sampling and the media-filled bag samples have a procedurally required incubation time of (b) (4) and (b) (4), respectively.

OBSERVATION 10

ISO-5 classified areas were not certified under dynamic conditions.

Specifically, unidirectional airflow was not verified under dynamic operational conditions representative of your typical aseptic processing practices. Air visualization studies ("smoke studies") conducted in October 2021, April 2022, and October 2022 in your ISO 5 classified laminar airflow hoods did not demonstrate the movement of first pass air around equipment, supplies, or operator manipulations as observed during sterile production operations.

A. In one hood (b) (4) which is designated for use in the production of all total parenteral nutrition (TPN) products, we observed hanging IV bags and component vials mounted on the metal vial rack of the (b) (4) ® automatic compounding device (ACD). The metal vial rack consists of approximately (b) (4) poles, and with the ACD, occupies approximately (b) (4) of the width of the respective hood. Additionally, component bags are hung on the bar within the hood. Your smoke studies do not provide assurance that first pass air is maintained for purportedly sterile connections made in front of other component materials, the number of items observed during typical TPN production, nor airflow originating from behind the equipment.

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B. The smoke studies did not demonstrate unidirectional airflow, for example, in (b) (4) hoods which each contain a repeater pump and large graduated cylinder. A single stream of smoke was used to visualize the flow of air around one or two items in the ISO 5 classified laminar flow hoods. Furthermore, production in those hoods include multiple hanging IV bags, multiple component vials, elastomeric pumps, and syringes. The smoke studies were conducted with tubing connections made to one vial, one IV bag, and manipulation on the hood deck with one syringe. Your smoke studies do not provide assurance that first pass air is maintained for purportedly sterile connections made in front of other component materials nor the number of items observed during typical production in these laminar flow hoods.

C. Insufficient "smoke" was used to visualize airflow in ISO 5 classified laminar flow hoods. A single stream of smoke was utilized. At times, the smoke stream was not placed close enough to dynamic aseptic manipulations to observe the airflow.

***DATES OF INSPECTION**

12/05/2022(Mon), 12/06/2022(Tue), 12/07/2022(Wed), 12/08/2022(Thu), 12/09/2022(Fri), 12/12/2022(Mon), 12/14/2022(Wed), 12/16/2022(Fri)

X Brandy N Lepage
Investigator
Signed By: Brandy N. Lepage -S
Date Signed: 12-16-2022 18:19:19

X Karen A Briggs
Investigator
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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."