

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER One Montvale Avenue Stoneham, MA 02180 (781)587-7500 Fax: (781)587-7556	DATE(S) OF INSPECTION 7/22/2019-8/14/2019*
	FEI NUMBER 3013662663

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Susan C. Benfeito, Vice President of Quality, Risk and Performance Management

FIRM NAME Roger Williams Medical Center	STREET ADDRESS 50 Maude St, Oncology Pharmacy Clinic
CITY, STATE, ZIP CODE, COUNTRY Providence, RI 02908-4325	TYPE ESTABLISHMENT INSPECTED Producer of Sterile Drugs

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

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, you failed to present any documentation that the pharmacy has adequately investigated or taken remedial action to control objectionable organisms found in the ISO 7 Clean rooms.

- A. Routine environmental monitoring done during production on 5/13/2019, resulted in an airborne viable recovery of 2 CFU/m³ of "Irpex (mold)" in the Chemo Room. You received the May 2019 environmental monitoring report on 5/21/2019 and you did not respond to the excursion until a (b) (4) of the Chemo Room was performed on 5/24/2019. You continued to produce in the ISO 5 hoods from 5/21/2019 to 5/23/2019 before performing (b) (4) of the Chemo Room. For example, you produced the chemotherapy treatments Carboplatin 623 MG in NS 250 MLS and Irinotecan 300 MG IV D5W500 on 5/21/2019 and Oxaliplatin 160 MG in D5W 250 MLS on 5/22/2019. You did not investigate the root cause of the excursion and assess the potential impact on drug products produced during that period.

- B. Routine environmental monitoring done during production on 7/23/2019, resulted in an airborne viable recovery of 3 CFU/m³ of "Irpex (mold)" fungal growth in the Center of the Chemo Room. During the environmental monitoring you produced the drug Palonosetron 25MG/5ML IV. You received the July 2019 environmental monitoring report on 07/30/2019 and you failed to investigate the root cause of the microbial contamination, implement corrective actions, or assess the potential impact on drug products produced during that period.

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C. Routine environmental monitoring done on 8/08/2018, resulted in an airborne viable recovery of 1 CFU/m³ of "Aspergillus fumigatus (mold)" in the center of the Chemo Room and a surface viable recovery of 2 CFU/25cm² of gram-negative rod bacteria "Methylobacterium (bact, GNR)" in the wash sink counter of the Ante Room. You received the environmental monitoring report on 8/15/2018 and the next (b) (4) of the Chemo Room was performed 9 days later on 8/24/2018. You failed to investigate the root cause of the microbial contamination and implement corrective actions. In addition, you failed to present any assurance objectionable organisms present in the ISO 7 Ante Room are not transferred to the (b) (4) ISO 7 Chemo Room from personnel movement between the two rooms.

OBSERVATION 2

Your facility design allowed the influx of poor quality air into a higher classified area.

Specifically,

- A. There is an (b) (4) the unclassified pharmacy area and the ISO 7 classified Clean Room (b) (4) the unclassified pharmacy area and the ISO 7 classified Chemo Room. Components used in production are (b) (4) (b) (4) were observed to be cluttered with papers, supplies and equipment. You do not have information or data to provide assurance that the unclassified air from the pharmacy area is not entering the ISO 7 classified Clean Room and Chemo Room though the (b) (4) during production.
- B. You do not monitor the pressure differential between the ISO 7 Ante Room and the ISO 7 Chemo Room. On 07/22/2019, it was observed that the differential pressure gauge between the two rooms was not operating properly, and the needle on the pressure gauge was resting on the

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pin below the pressure gauge's minimum scale reading of 0.0 inches of water (b) (4) (b) (4). You have also been documenting a reading of -0.01 inches of water as the pressure reading between the ISO 7 Chemo Room and ISO 7 Ante Room on your (b) (4) "Temperature, Humidity, and Pressure Log," which is a reading below the capability of your differential pressure gauge. The documented pressure reading does not indicate the actual daily pressure differential between the ISO 7 Ante Room and the ISO 7 Chemo Room. Instead, -0.01 inches of water pressure is documented, which was the differential pressure between the two rooms when the pressure between the rooms was last balanced approximately one year ago.

C. You failed to appropriately monitor the pressure differential between the ISO 7 Clean Room and the ISO 7 Chemo Room. You document 0.01 inches of water as the pressure reading between the ISO 7 Clean Room and ISO 7 Chemo Room on your (b) (4) "Temperature, Humidity, and Pressure Log," when there is no pressure differential gauge installed between the ISO 7 Clean Room and the ISO 7 Chemo Room. You document a 0.01 inches of water pressure reading, which was the differential pressure between the two rooms when the pressure between the rooms was last balanced approximately one year ago.

D. On 08/05/2019, the pharmacy replaced the pressure differential gauge between the ISO 7 Ante Room and the ISO 7 Chemo Room. On 08/05/2019, it was observed that the pressure gauge between the two rooms indicated an Ante Room pressure of 0.025 inches of water (b) (4) (b) (4). (b) (4) was opened, the needle on the pressure gauge was resting on the pin below the pressure gauge's minimum scale reading of 0.0 inches of water pressure. The minimum acceptance criteria for the pressure differential between the two rooms are (b) (4) (b) (4) indicates (b) (4) the (b) (4) is lost (b) (4).

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OBSERVATION 3

Your facility was designed and/or operated in a way that permits poor flow of personnel.

Specifically, the design of your facility requires personnel to (b) (4) Room, where (b) (4) are produced, into the (b) (4) Room (b) (4) are produced. Production personnel were observed during the inspection producing hazardous drug products in one of the (b) (4) BSCs located in the (b) (4) Room, and then moving into the (b) (4) Room to produce non-hazardous drug products in the LFH without changing all of their gowning materials. The design of the facility creates the potential for cross contamination of non-hazardous materials and hazardous materials when personnel (b) (4) Room.

OBSERVATION 4

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

Specifically, you use non-sterile, low lint pads to wipe down all drug component containers, packaging materials and production equipment with sterile, (b) (4) prior to placing these items into the (b) (4) ISO 5 Biological Safety Cabinets (BSCs) and the ISO 5 Laminar Flow Hood (LFH). You also use non-sterile, low lint pads when you perform a "Surface Safe" cleaning of each BSC, which includes applying (b) (4) disinfectant cleaner to the interior of each BSC. In addition, you use non-sterile, low lint pads when you perform a "Surface Safe" cleaning of the LFH, which includes applying non-sterile (b) (4) disinfectant to the interior of the LFH.

OBSERVATION 5

The use of sporicidal agents in the cleanrooms and ISO 5 classified aseptic processing area was inadequate.

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Specifically, you have not defined a required contact time for each of the disinfectant solutions used to disinfect the (b) (4) ISO 5 BSCs, ISO 5 LFH and ISO 7 areas of the production areas. Pharmacy personnel who perform cleaning and disinfectant operations did not follow the disinfectant manufacturer's recommended contact time for (b) (4). In addition, pharmacy personnel do not document the disinfectant contact time when they perform cleaning and disinfecting operations.

OBSERVATION 6

The ISO 7 classified areas have difficult to clean, particle-generating equipment or surfaces.

Specifically, you installed (b) (4) Systems" in your production area, (b) (4) ISO 7 (b) (4) and (b) (4) (b) (4) personnel do not have access to clean and disinfect the interior of the units during routine cleaning and disinfecting operations of the ISO 7 classified rooms. In addition, you have failed to demonstrate that each of the (b) (4) units can be properly cleaned and disinfected and failed to demonstrate that each unit does not generate particulates in the ISO 7 classified areas.

OBSERVATION 7

ISO 5 Areas are not certified under dynamic conditions.

Specifically, you did not demonstrate laminar, uni-directional airflow over critical zones under dynamic conditions meant to simulate aseptic manipulations during smoke pattern testing of the (b) (4) ISO 5 Biological Safety Cabinets (BSCs), (b) (4) and the ISO 5

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Laminar Flow Hood (LFH), (b) (4) . For example, reports of smoke pattern testing conducted on 06/12/2019, 12/12/2018 and 06/13/2018 failed to describe the equipment set up within each hood and the specific operations to be performed during smoke pattern testing and failed to determine if all critical and worse case operations were performed and captured. In addition, there is no evidence indicating the certification reports were reviewed, evaluated and accepted by pharmacy personnel.

***DATES OF INSPECTION**
7/22/2019(Mon), 7/23/2019(Tue), 7/24/2019(Wed), 7/25/2019(Thu), 7/26/2019(Fri), 8/01/2019(Thu), 8/06/2019(Tue), 8/14/2019(Wed)

X Jonah S Ufferfilge
Investigator
Signed By: Jonah Ufferfilge -S
Date Signed: 08-14-2019 14:18:54

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