DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue Stoneham, MA 02180 (781)587-7500 Fax:(781)587-7556	10/1/2018-10/19/2018* FEI NUMBER 3010955218

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Stuart E. Rosenberg, President

FIRM NAME	STREET ADDRESS
Johnson Memorial Cancer Center	142 Hazard Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Enfield, CT 06082-4520	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

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

Specifically, The firm produces chemotherapeutic drugs and other sterile prescription drug products for injection. The following actionable environmental excursions were reported recovered in the ISO 5 classified aseptic processing areas. The firm failed to adequately assess, investigate or perform corrective actions regarding these excursions.

Date Reported	Location	Recovery Type	Total number of colonies	Microbiological Identification
5/8/18	Biological Safety Cabinet (ISO 5)	Air	1	*Penicillium* spp.[1] (mold)
7/25/18	Laminar Air Flow Hood (ISO 5)	Air	1	*Cryptococcus* spp.[2] (mold)
8/30/18	Laminar Air Flow Hood (ISO 5)	Air	2	*Bacillus cereus*
8/30/18	Laminar Air Flow Hood (ISO 5)	Surface	3	1 *Bacillus cereus,* 2 Unidentified Gram + Sporeforming Rods

[1] The firm's contract laboratory identified these genera of fungi are known to have strains which may produce mycotoxins under the proper conditions.

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EMPLOYEE(S) SIGNATURE
John P Mistler, Investigator
Erik W Koester, Investigator

X John P Mistler
Investigator
Signed By John P. Mistler -S
Date Signed 10-19-2018 08 17 50

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[2] The firm's contract laboratory identified this microorganism as potentially highly pathogenic for immunocompromised patients.

OBSERVATION 2

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, The following actionable environmental excursions were reported recovered in the surrounding and supporting ISO 7 classified areas adjacent to the aseptic processing areas. The firm failed to adequately assess, investigate or perform corrective actions regarding these excursions.

Date Reported	Location	Recovery Type	Total number of colonies	Microbiological Identification
5/8/18	Anteroom (ISO 7)	Air	1	*Aspergillus fumigatus*[1] (mold)
6/27/18	Non-Hazardous Drug Buffer Room (ISO 7)	Air	1	*Cladosporium* spp.[1] (mold)
6/27/18	Non-Hazardous Drug Buffer Room (ISO 7)	Air	1	*Epicoccum* spp. (mold)
8/30/18	Non-Hazardous Drug Buffer Room (ISO 7)	Surface	6	4 *Bacillus cereus,* 2 Unidentified Gram + Sporeforming Rods
8/30/18	Anteroom (ISO 7)	Surface	2	1 *Bacillus cereus,* 1 Unidentified Gram + Sporeforming Rods
8/30/18	Anteroom Sink (ISO 7)	Surface	4	3 *Bacillus cereus,* 1 Unidentified Gram + Sporeforming Rods

[1] The firm's contract laboratory identified these genera of fungi are known to have strains which may produce mycotoxins under the proper conditions.

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The following actionable environmental excursions were reported recovered in the surrounding and supporting ISO 7 classified areas during the current inspection.

Date Reported	Location	Recovery Type	Total number of colonies	Microbiological Identification
10/3/18	Anteroom (ISO 7)	Air	1	*Cladosporium* spp.[1] (mold)
10/3/18	Anteroom (ISO 7)	Air	1	sterile hyaline mould (mold)
10/10/18	Anteroom (ISO 7)	Air	1	*Mucor* spp.[1, 3] (mold)
10/10/18	Anteroom (ISO 7)	Air	1	*Mucor* spp.[1, 3] (mold)

[1] The firm's contract laboratory identified these genera of fungi are known to have strains which may produce mycotoxins under the proper conditions.

[3] The firm's contract laboratory identified this microorganism can cause life-threatening disease in diabetics, burn patients, and immunocompromised patients.

Environmental excursions including mold recoveries in the ISO 7 classified areas were also noted during the 2014 FDA inspection.

OBSERVATION 3

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

Specifically,

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The firm failed to maintain proper room classification and environmental control of supporting areas in which ISO 5 classified aseptic processing equipment is located and sterile production occurs. The firm's air handling unit (AHU) was offline from 05/15/18 to 05/18/18, 6/01/18 to 6/04/18, and for approximately 10 hours on 06/06/18. This resulted in elevated temperatures and relative humidity levels, and loss of differential pressures for surrounding buffer and ante areas, for each of the offline time periods. Production activities were not always suspended during these offline timeframes. For example, on 6/01/18, the firm continued to produce (b) (4) chemotherapeutic drug products for injection, inside the ISO 5 Biological Safety Cabinet, even though there was a lack of adequate HEPA filtered airflow to the surrounding buffer and ante areas to maintain an adequate room cleanliness classification.

OBSERVATION 4

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

Specifically, The firm's cleaning of the ISO 5 Biological Safety Cabinet and ISO 5 Laminar Flow Hood are inadequate for the following reasons:

- The firm routinely utilizes non-sterile wipes (b) (4) (b) (4) to administer sterile (b) (4) (sporicidal disinfectant) and sterile (b) (4) (b) (4) to all interior surfaces of the ISO 5 hoods. In addition, the firm utilizes the non-sterile wipes to dry residual cleaning agents (b) (4) from the interior of the ISO 5 hoods. The firm has performed no risk assessments related to the use of non-sterile wipes in the ISO 5 classified areas where aseptic processing occurs.

- Firm personnel were observed cleaning the interior of the ISO 5 classified areas with their head and upper torso within the hood. The operator's gowning was observed coming into contact with the interior surfaces of the hood. The firm has performed no risk assessments related to the aforementioned cleaning activities.

- The firm's contact time for the use of the sporicidal disinfectant (b) (4) differed from the

manufacturer's recommendations. The firm's contact time was (b)(4) minutes vs. manufacturer recommended contact time (b) (4) minutes.

- An operator was observed exhibiting poor aseptic practice by cleaning the deck of the ISO 5 Laminar Flow Hood in an elliptical motion (not cleanest to dirtiest).

OBSERVATION 5

Personnel moved rapidly in the vicinity of open sterile units and instruments, which disrupted the airflow and increased the risk of bringing lesser quality air into the ISO 5 classified aseptic processing area.

Specifically, poor aseptic practice was observed during the production of sterile drug products while working within ISO 5 classified aseptic processing areas.

1) On 10/1/18, an operator was observed producing (b) (4) for injection in the firm's ISO 5 Laminar Flow Hood (LFH). The LFH is located in an ISO 7 Buffer room.

- The operator's hands exited and entered the LFH several times during operations to gather supplies and continue production. The operator did not sanitize their hands upon each entry to LFH.
- The operator failed to keep all production activities at least 6 inches inside the LFH.
- The operator's movements inside the LFH were quick, abrupt and had potential to disturb ISO 5 airflow.
- The operator was observed wearing eye makeup.

2) On 10/2/18, an operator was observed producing (b) (4) and (b) (4) for injection in the firm's ISO 5 Laminar Flow Hood (LFH). The LFH is located in an ISO 7 Buffer room.

- The operator's elbows were observed resting on the deck of the LFH, where sterile production occurs.
- The operator's movements inside the LFH were quick and abrupt and had potential to disturb ISO 5 airflow.
- The operator was observed wearing eye makeup.

3) On 10/2/18, an operator was observed producing several chemotherapeutic drugs for injection including, (b) (4) and (b) (4) n the firm's ISO 5 Biological Safety Cabinet (BSC). The BSC is located in an ISO 7 Buffer room.

- The operator placed a non-sterile (b) (4) on the deck of the BSC immediately prior to initiating sterile producing activities.
- The operator's movements inside the BSC were quick and abrupt and had the potential to disturb ISO-5 airflow.
- The operator was observed wearing eye makeup.

OBSERVATION 6

You had inadequate HEPA filter coverage and airflow over the area to which sterile product was exposed.

Specifically, The firm's air pattern analysis and media fills are deficient for the following reasons:

1) The firm conducted an air pattern analysis (smoke study) on 02/22/18 and 08/15/18 for the ISO 5

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Biological Safety Cabinet (BSC) utilized for the production of chemotherapeutic drug products and the ISO 5 Laminar Flow Hood (LFH) utilized for the production of non-hazardous drug products. The aforementioned smoke studies were inadequate as the studies did not include the transfer of starting components and materials into the ISO 5 classified areas. In addition, the firm's smoke studies for the BSC failed to simulate the most complex product to produce, which was identified as (b) (4)

2) The firm performs media fills on an (b) (4) basis. Media fills are not performed on site and do not represent actual production operations. The firm failed to evaluate and provide justification for this practice.

***DATES OF INSPECTION**
10/01/2018(Mon), 10/02/2018(Tue), 10/03/2018(Wed), 10/04/2018(Thu), 10/05/2018(Fri), 10/09/2018(Tue), 10/10/2018(Wed), 10/15/2018(Mon), 10/19/2018(Fri)

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EMPLOYEE(S) SIGNATURE
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