DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
U.S. Food and Drug Administration 4040 North Central Expressway, Suite 300 Dallas, Texas 75204 214-253-5200 FDA-483 Responses: ORAPHARMA2_RESPONSES@FDA.HHS.GOV	01/13-17/2020; 01/21-23/2020 FEI NUMBER 3013521045

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO:

FIRM NAME	
	TYPE ESTABLISHMENT INSPECTED 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.

OBSERVATION 1

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

Specifically,

A. On 13 January 2020, we observed your pharmacist use non-sterile (b) (4) during routine cleaning of the interior area of your biological safety cabinet (Classified ISO-5), located in the Hazardous Room of your "(b) (4) " mobile unit, where aseptic operations occur for sterile chemotherapeutic agents.

B. Your firm uses a non-sterile bactericidal (b) (4) cleaning solution during routine (b) (4) cleanings of your classified areas where aseptic operations are performed, for example, but not limited to, the interior surfaces of ISO-5 equipment:
   1. (b) (4) (2) ISO-5 Classified Biological Safety Cabinets (BSCs), located in your firm's "(b) (4) " Mobile Unit Hazardous Area;
   2. (b) (4) (2) ISO-5 Classified Laminar Air Flow Hoods (LAFHs), located in your firm's "(b) (4) " Mobile Unit Non-Hazardous Area;
   3. (b) (4) (2) ISO-5 Classified LAFHs, located in your firm's Segregated Compounding Area (SCA) on the ground floor of your in-patient pharmacy.

C. Your firm uses non-sterile (b) (4) Wipes (b) (4) as a fungicidal when transferring materials for use (from an unclassified area into a classified area) in aseptic operations in the Hazardous Room of your "(b) (4) mobile unit.

   According to your firm's 6-month prescription log, dated 07/08/2019-01/15/2020, your firm produces the following, but are not limited to the following routes of administration in your IV Sterile Area:

Route of Administration	Number of Rx Produced
Intravenous	(b) (4)
IV piggyback	
Subcutaneous	
Intravesical	
Intrahepatic	
IV push	
Intravenous or intramuscular	
Intra-pleural	
Epidural	
Intraperitoneal	
Miscellaneous	
Topical	
Intrathecal	
Intravitreal	
Grand Total	

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	June P. Page, Investigator Mina D. Ahmadi, Consumer Safety Officer June P. Page - S3	01/23/2020

DISTRICT ADDRESS AND PHONE NUMBER
U.S. Food and Drug Administration
4040 North Central Expressway, Suite 300
Dallas, Texas 75204
214-253-5200
FDA-483 Responses: ORAPHARMA2_RESPONSES@FDA.HHS.GOV

DATE(S) OF INSPECTION
01/13-17/2020; 01/21-23/2020

FEI NUMBER
3013521045

TYPE ESTABLISHMENT INSPECTED
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.

Your firm produces sterile hazardous drug products (e.g. chemotherapy agents, etc.) and non-hazardous drug products (e.g. fentanyl epidurals, etc.).

D. Disinfectant contact time (also known as "dwell time") and coverage of the item being disinfected were insufficient to achieve adequate levels of disinfection. Your Associate Chief of Pharmacy provided documentation that your firm uses (b) (4) disinfectant wipes during routine (b) (4) cleanings as your bactericidal agent in your ISO-5, ISO-7, and ISO-8 Classified Areas ("(b) (4) Mobile Unit and Ground Floor Inpatient Pharmacy) with a (b) (4) contact time.

However, the manufacturer's recommendations for this product states a contact time of [redacted] minutes is recommended to be effective when used as a bactericidal.

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, eleven (11) colony forming units (cfus) were identified in your firm's Hazardous Buffer Room (ISO-7 Classified) during viable air sampling conducted on 18 September 2019 at location "Trailer-(b)(4) Hazard Room". The firm's Sample Analysis Results, dated 23 September 2019, documents the colony identifications are: Gram-positive rods; micrococcus; staphylococcus colagulase (-); and other fungi. According to your firm's sampling plan and the firm's Sample Analysis Results report, your firm has not resampled in this location ("Trailer-[redacted]: Hazard Room") ensuring the area is acceptable to continue aseptic operations prior to this FDA inspection. In addition, your firm did not consider inadequate facility designs (Please refer to **OBSERVATION 4 & 8**); the condensation unit or water evaporation tray of the refrigerators located in the ISO-7 Classified areas (Please refer to **OBSERVATION 4, 7, & 8**); inadequate cleaning practices (Please refer to **OBSERVATIONS 1, 3, 6**); non-sterile gowning, and/or exposed skin (Please refer to **OBSERVATION 5**). In addition, your firm's inpatient pharmacy supervisor stated (b) (4) cleanings are routinely scheduled to occur prior to EM sampling.

Your firm continued aseptic operations in this room from 18 September 2019 – present, with the exception of the following closures:

- 15 – 30 October 2019
- 04 – 18 December 2019

Your firm's vendor, (b) (4) ., who performs Environmental Monitoring (EM) of your cleanrooms, has identified the following viable air sampling failures in 2019:

DISTRICT ADDRESS AND PHONE NUMBER
U.S. Food and Drug Administration
4040 North Central Expressway, Suite 300
Dallas, Texas 75204
214-253-5200
FDA-483 Responses: ORAPHARMA2_RESPONSES@FDA.HHS.GOV

DATE(S) OF INSPECTION
01/13-17/2020; 01/21-23/2020

FEI NUMBER
3013521045

NAME AND TITLE OF INDIVIDUAL(S) WHOM REPORT ISSUED

TO:

FIRM NAME

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.

Date	Location	Colony Forming Unit (cfu) Count	Colony Identification
07/08/2019	Trailer-(b)(4) Hazard Room (corner – between BSCs)	1	Other Fungi
09/18/2019	Trailer-(b)(4): Hazard Room (corner – between BSCs)	11	Gram-positive rods; Micrococcus; Staphylococcus Colagulase (-); and Other Fungi
09/18/2019	Trailer-(b)(4) Hazard AnteRoom (Shelf)	18	Gram-positive rods; Micrococcus; Staphylococcus Colagulase (-)
09/30/2019	Trailer-(b)(4) Hazard Room Near (b) (4)	4	Gram-negative rods; Staphylococcus Colagulase (-); and Other Fungi
10/08/2019	Trailer-(b)(4): Hazard Room Near (b) (4)	3	Gram-negative rods; Staphylococcus Colagulase (-)
11/26/2019	Trailer-(b)(4) Hazard Room Near (b) (4)	1	Other Fungi

According to your firm's 6-month prescription log, your firm compounded approximately (b) (4) units of sterile drug products in your firm's Hazardous Room.

OBSERVATION 3

Equipment was not disinfected prior to entering the aseptic processing areas.

Specifically, on 01/17/2020, your Environmental Management Service (EMS) Supervisor, who conducts periodic routine cleanings of your firm's cleanrooms, stated they do not disinfect the (b) (4) prior to entering your firm's cleanrooms (ISO-8 and ISO-7 Classified Areas). This cleaning equipment is stored in an unclassified area and are used on a (b) (4) basis.

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
June P. Page, Investigator
Mina D. Ahmadi, Consumer Safety Officer

June P. Page -S3

Digitally signed by June P. Page -S3
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=June P. Page -S3, 0.9.2342.19200300.100.1.1=2000497709
Date: 2020.01.23 07:42:49 -06'00'

DATE ISSUED
01/23/2020

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
U.S. Food and Drug Administration 4040 North Central Expressway, Suite 300 Dallas, Texas 75204 214-253-5200 FDA-483 Responses: ORAPHARMA2_RESPONSES@FDA.HHS.GOV	01/13-17/2020; 01/21-23/2020 FEI NUMBER 3013521045

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO:

TYPE ESTABLISHMENT INSPECTED

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.

OBSERVATION 4

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

Specifically,

A. On 1/13/2020, we observed two (2) flexible hoses which are connected to your "(b) (4) Mobile Unit and lead to a street water drain. The purpose of these hoses is to drain the (b) (4) from the sinks located in the "(b) (4) Mobile Unit (Hazardous Area: ISO-7 Classified Anteroom; and the Non-Hazardous: ISO-8 Classified Anteroom). The hoses are unprotected and exposed to the outside environment and appear to be cracked and discolored. Your firm has not provided any supporting documentation to prevent the ingress of vermin or outside unfiltered, less clean air.

B. On 01/22/2020, we observed your return air vents, located in your "(b) (4) Mobile Unit in the:
   1. Hazardous Buffer Room (ISO-7 Classified) where chemotherapeutic agents are aseptically processed were partially blocked by objects such as, but not limited to portable bins; stainless steel tables; and storage shelving;
   2. Non-Hazardous Buffer Room (ISO-7 Classified) where non-hazardous sterile drug products are processed were partially blocked by objects such as, but not limited to LAFH and a portable stainless-steel table.

C. On 01/22/2020, we observed what appears to be a particle-generating (b) (4) substances (black and off-white substances), located next to the condenser fan, on top of the refrigerator, in your firm's Hazardous Buffer Room (ISO-7 Classified) and Non-Hazardous Buffer Room (ISO-7 Classified). These (b) (4) substances are (b) (4) (b) (4) which aid in the prevention of condensation forming. The top of this refrigerator is open to the ISO-7 environment and the (b) (4) substances appear to be frayed and torn.

OBSERVATION 5

Personnel engaged in aseptic processing were observed with exposed face, neck, and ankles.

Specifically, on 01/13/2020 and 01/22/2020, we observed your pharmacy technician, who was engaged in aseptic operations of Carboplatin 520 mg and Doxorubicin 105 mg, respectively, with exposed face, neck, and ankles in the ISO-7 Classified Area of the "(b) (4) Mobile Unit Hazardous Compounding Area.

In addition, your pharmacy technicians don non-sterile gowns, bouffant, facemask, and booties.

OBSERVATION 6

Personnel did not disinfect and change gloves frequently enough to prevent contamination.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	June P. Page, Investigator Mina D. Ahmadi, Consumer Safety Officer	June P. Page -S3 (Digitally signed by June P. Page -S3 ... Date: 2020.01.23 07:43:34 -06'00')	01/23/2020

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
U.S. Food and Drug Administration 4040 North Central Expressway, Suite 300 Dallas, Texas 75204 214-253-5200 FDA-483 Responses: ORAPHARMA2_RESPONSES@FDA.HHS.GOV	01/13-17/2020; 01/21-23/2020 FEI NUMBER 3013521045

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO:

	STREET ADDRESS
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
	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.

Specifically, on 01/17/2020, your Environmental Management Service (EMS) Supervisor, who conducts periodic routine cleanings of your firm's cleanrooms, stated they do not sanitize their hands or change their gloves when moving from an area of cleaner air (ISO-7 Classified - Non-Hazardous Buffer) to an area of less cleaner air (ISO-8 Classified – Non-Hazardous Anteroom) and back to an area of cleaner air (ISO-7 Classified - Non-Hazardous Buffer) during routine (b) (4) cleanings of your firm's cleanrooms, where sterile drug products are produced.

OBSERVATION 7

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

Specifically, your firm's air flow patterns performed on 08 July 2019, by vendor, (b) (4), and as part of your firm's (b) (4) certifications are inadequate.

A. The smoke studies conducted under dynamic conditions did not generate smoke in all areas where aseptic operations were performed to verify unidirectional airflow, for example, but are not limited to: the movement of materials into the BSC (ISO-5 Classified); removing vials and syringes from outer packaging within the BSC (ISO-5 Classified); cleaning of vials with (b) (4). In addition, the smoke study did not capture your most challenging aseptic operation.
B. The smoke studies performed at the door from the Hazardous Anteroom (ISO-7 Classified), which is under positive pressure, into the Hazardous Buffer Room (ISO-7 Classified), which I under negative pressure, did not demonstrate the Hazardous Buffer Room (ISO-7 Classified) is maintained under negative pressure.
C. No smoke studies were performed to capture possible dust generating equipment, such as the refrigerator, located in the Hazardous Buffer Room (ISO-7 Classified) and Non-Hazardous Buffer Room (ISO-7 Classified). For example, the top of your refrigerator contains a condenser fan, which is open to the controlled environment.

OBSERVATION 8

The facility design of your cleanroom does not have a suitable construction to facilitate cleaning, maintenance, and proper operations.

Specifically,

A. Your firm ground floor inpatient pharmacy was observed to have two (2) wooden doors:

- Wooden door that separates the anteroom from the general pharmacy area; and a
- Wooden door that separates the anteroom from the buffer room.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
U.S. Food and Drug Administration 4040 North Central Expressway, Suite 300 Dallas, Texas 75204 214-253-5200 FDA-483 Responses: ORAPHARMA2_RESPONSES@FDA.HHS.GOV	01/13-17/2020; 01/21-23/2020 FEI NUMBER 3013521045

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO:

TYPE ESTABLISHMENT INSPECTED

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.

According to your most recent certification report, dated 11 November 2019, this compounding area is a segregated compounding area (SCA) and contains (b) (4) LAFH (ISO-5 Classified) in an unclassified area. Your firm's Chief of Pharmacy stated STAT (immediate use) for low-risk Compounded Sterile Product (CSP) orders are prepared in the LAFHs (ISO-5 Classified) of this area as a contingency compounding area. This area was converted to a SCA in September 2019.

B. Your firm utilizes (b) (4) Refrigerators to store drug products, located in your '(b) (4) Mobile Unit Hazardous and Non-Hazardous (ISO-7 Classified) Areas. According to the Service Manual provided by your firm's HVAC Supervisor for Engineering, preventative maintenance and routine cleanings are to be performed on this equipment. For example, but are not limited to: the condenser grill is to be cleaned (b) (4) the high and low temperature alarms are to be tested (b) (4) (b) (4) are to be examined and cleaned (or replaced) (b) (4) In addition, a condensation evaporation water tray is located on the backside of the refrigerators, which is (b) (4) (b) (4) . Pooling of water may occur if the (b) (4) is not working properly (i.e. (b) (4) (b) (4) alarms are to be tested (b) (4)

However, according to your firm's Chief of Pharmacy, preventative maintenance has not been performed since September 2018.