DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	06/01/2015 - 06/12/2015
	FEI NUMBER 3011564121

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: James H. Cook, Regional Manager

FIRM NAME	STREET ADDRESS
Lincare, Inc.	1527 S Bowman Rd Ste D
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Little Rock, AR 72211-4200	Producer of Sterile 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

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

Specifically,

1. On June 1, 2015, we observed the ISO 8 Ante Room was out of certification as of 4-9-2015. Furthermore, the pressure differential between the non-classified area and the ISO 8 Ante Room pressure gauge was observed to read at 0.015 inches of water [acceptable range= (b) (4) water column per firm's SOP].

   Your firm produced approximately (b) (4) sterile products in the ISO 7 Buffer Rooms at ISO 5 Hoods without a certified ISO 8 Ante Room between 4-9-15 and 5-29-15. For example,

Production Date	Product	Quantity	Distribution Date
5/28/15	Deferoxamine Mesylate 3gm/ NS 240mL	(b) (4)	5/28/15
5/28/15	Meropenem 2gm/NS 100mL		5/28/15
5/26/15	Fluorouracil 2000mg/D5W 290mL		5/26/15
5/21/15	Hydromorphone 1000mg/500mL		5/21/15
5/20/15	Vancomycin 1500mg/D5W 300mL		5/20/15
4/22/15	Fluorouracil 5760mg/NS 265mL		4/22/15

2. On June 1, 2015, we observed the pressure differential between the ISO 7 Buffer Room (b) and the ISO 7 Hazard Room reading was at 0. As stated by your firm, the pressure between the rooms should read at a minimum of -(b) (4) inches of water prior to production. Record review of ISO 7 Hazard Room pressure differentials shows pressure recording of "-0" from January 2, 2014 through May 29, 2015. Your firm produced sterile drug products in the ISO 5 (b) (4) Hood, serial number (b) (4) in your ISO 7 Hazard Room without the appropriate

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pressure differential January 2, 2014 to May 29, 2015 . For example,

Production Date	Product	Quantity	Distribution Date
5/26/15	Fluorouracil 200mg/D5W 290mL	(b) (4)	5/26/15
5/18/15	5-Fluorouracil 4000mg/NS 2800mL		5/18/15
3/9/15	Fluorouracil 4800mg/ NS 246mL		3/9/15

3. Review of pressure differential logs from 2014 and 2015 revealed out of range results as followed:

NON-CLASSIFIED AREA TO ISO 8 ANTE ROOM	
Actual Reading [inches of water]	**Dates Out of Range**
0.01	12-11-14 through 5-29-15
0	1-2-14 through 6-30-14
ISO 8 ANTE ROOM to ISO 7 BUFFER ROOM (b)	
.01	5-29-15
0	11-1-14 through 12-9-14
0	9-29-14 through 10-27-14
0	7-1-14 through 9-25-14
.005	1-2-14 through 6-30-14
ISO 7 BUFFER ROOM (b)	
no documentation*	no documentation*
ISO 7 Hazard Room	
0	1-2-15 through 5-29-15

*The firm has never recorded the pressure differentials for this room, but used the room to produce sterile drug products. In addition, your firm does not have acceptable ranges listed in SOPs.

4. Your firm used a contractor to perform the certification and re-certification of the cleanrooms and hoods. Reports dated May 15, 2014, October 1, 2014 and April 9, 2015 showed the following failed readings:

Date	Report #	Area	Findings	Date of re-cert	Use of Area in Failed Status
4-9-15	40798-5	ISO 8 Ante Room*	1. Failed segregation with a room pressure of 0.01" w.c.	Currently Uncertified	Yes (Approximately

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			2. HEPA Filter Leak testing was not performed**	As of 6/8/15	(b) (4) drug products from 4/9/15 to 5/29/15)
4-9-15	30798-2	(b) (4) Hood (serial# (b) (4)) Located in ISO 7 Buffer Room(b)	1. Failed Velocity Test for low airflow due to blower not being operational	5/5/15	Unknown
10-1-14	30568-6	ISO 7 Buffer Room(b) (4	1. Failed segregation with a room pressure of 0.0004"w.c. 2. HEPA Filter Leak testing was not performed**	4/9/15	Yes (Approximately (b) (4) drug products from 4/9/15 to 5/29/15)
5-15-14	30401-7	ISO 7 Buffer Room(b)	1. failed segregation with a room pressure of 0.01" w.c 2. HEPA Filter Leak testing was not performed**	10/1/14	Yes (Approximately (b) (4) drug products from 4/9/15 to 5/29/15)
5-15-14	30401-6	ISO 8 Ante Room*	1. failed segregation with a room pressure of 0.002 2. HEPA Filter Leak testing was not performed**	10/1/14	Yes (Approximately (b) (4) drug products from 4/9/15 to 5/29/15)

* recurring pattern for ISO 8 Ante Room
**recurring pattern for HEPA Filter Leak testing; firm management stated HEPA filters have not been changed since acquiring the building in December 2011.

5. Your firm does not calibrate the pressure gauges used to monitor the measurement of the pressure differential between the ISO 7 Buffer Room(b) and the ISO 7 Buffer Room (b) (4 between the ISO 7 Buffer Room(b) and the ISO 7 Hazard Room, ISO 7 Buffer Room(b) and ISO 8 Ante Room and between the ISO 8 Ante Room and the non-classified area.

6. Your firm does not calibrate or monitor the temperature of the (b) (4) Incubator, (b) (4), Serial #(b) (4), used to incubate your environmental monitoring samples in your ISO 8 Ante Room.

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7. There is a chair located in ISO 7 Buffer Room (b) which appears to be difficult to clean due to construction design and material; chair shows signs of damage and the chair padding shows deterioration. The chair is located directly in front of a laminar airflow hood where sterile products are produced.

8. The ISO 5 (b) (4) Hood, serial number (b) (4), is located on top of a wooden table in your ISO 7 Buffer Room (b)(

9. ISO 5 hoods have visible corrosian on appear to have build-up that is difficult to clean.

10. Your firm sanitizes the area prior to surface sampling.

OBSERVATION 2

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

Specifically, your SOP subject titled "Clean/Buffer Area Activity" section 04-08-01, date 2-21-08 located in your infusion manual on 6-5-15 states "***Proper garbing procedure: shoe covers, hair covers, face mask, (b) (4) hand washing, gown enter buffer area, use (b) (4) hand gel, and then don sterile powder-free gloves. All personnel are required to scrub hands with an antimicrobial soap solution and dry with lint free towel before doning nonshedding knee-length gown and sterile gloves***"

On June 1, 2015 we observed your 2 technicians cleaning the ISO 8 ante room, (b) (4 ISO 7 buffer rooms and (b)-ISO 5 hoods donning non-sterile isolation gowns, non-sterile gloves, non-sterile hair nets, and non-sterile face masks. Both employees had facial hair and did not don sterile beard covers. The gowning requirements leave skin around the eyes, forehead, neck and wrists exposed to areas required to be free of microbial contamination. Furthermore, on June 1, 2015, we observed the entire upper body of both technicians inside of the ISO 5 hoods when cleaning.

OBSERVATION 3

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

Specificically, on June 1, 2015 we observed the following:

1. Two Technicians cleaning the ISO 5 hoods touched the liner of the garbage can then placed their hands back into the ISO 5 areas without sanitizing or changing their gloves.

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2. Technicians cleaning the ISO 5 hoods, ISO 7 buffer rooms, ISO 7 hazard room and ISO 8 ante room did not frequently sanitize or change their gloves throughout the cleaning process. We observed 1 Technician change (b) (6) gloves while continuously touching the outside of the gloves without first cleaning or sanitizing (b) hands.

3. Spray bottles of sterile (b) (4) a packet of (b) (4) tablets, isolations gowns, a biohazard bin used as a mop bucket and a box of gloves were brought from the non-classified into the ISO 8 area without first being sanitized.

4. A reusable mop and reusable multi-layer adhesive rolling broom stored between the refrigerator and wall of the ISO 8 ante room was moved to the ISO 7 buffer room without first being sanitized

Furthermore, on June 5, 2015 we observed 5 insect-like pests in the ISO 8 area:

1. A live worm-like pest was observed on the sticky mat adjacent to the double doors between the ISO 8 Ante Room and ISO 7 Buffer Room (b) (4) An approximately 1/4" gap was observed between the double doors.

2. A live spider approximately the size of a quarter was observed adjacent to the sink and medication storage area approximately 8 feet from the door between the ISO 8 Ante Room and ISO 7 Buffer Room (b) (4)

3. A dead housefly-like pest was observed inside of the refrigerator inside of a yellow plastic bin holding (b) (4) ; a dead moth-like pest and a dead beetle-like pest were both observed on the bottom shelf of the refrigerator. This refrigerator is used to hold drug components and finished sterile products. For example,

   a. TPN 2:1 600mL, produced 6/2/15, QTY (b), discard date 6/11/15.
   b. Immune Globulin Infusion (Human) 10%, (b) (4)

OBSERVATION 4

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

Specifically, your firm does not have any documentation supporting that smoke studies were perfomed in dynamic conditions in the ISO 5 and other clean areas.

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OBSERVATION 5

The building lacks adequate space for the orderly placement of equipment and materials to prevent mix-ups between different components, drug product containers, closures, and drug products and to prevent contamination.

Specifically, we observed the following during the current inspection:

1. An approximately 1/4" gap between the double doors separating the ISO 8 Ante Room from the ISO 7 Buffer Room; approximately 1" gap at the base of the door between ISO 7 Buffer Room (b) and ISO 7 Buffer Room (b)(4)
2. The door between ISO 7 Buffer Room (b) and ISO 7 Hazard Room does not remain closed when manually pushed to the closed position; the door remains ajar approximately 5".
3. Floors in the ISO 7 Buffer Rooms and ISO 8 Ante Room are made of a material that reacts to cleaning agents and were observed with purple stains on the floors throughout the cleanrooms.
4. The floor in the ISO 8 Ante Room near the wheels of the rolling shelves used to hold components are stained.
5. The front double doors of the facility have an approximately 1/4" gap between the two doors. The double doors are approximately (b)(4) feet from the door separating the entry area and the ISO 8 Ante Room. The door between the entry area and the hallway area of the ISO 8 Ante room has an approximately 1/4" gap at the base of the door. On June 5, 2015 we observed pests in your ISO 8 Ante Room.
6. A ceiling tile in the ISO 7 Hazard Room is not sealed and moved up and down during cleaning on June 1, 2015.
7. An approximately ½" gap around the HEPA filter in the ceiling of ISO 7 Buffer Room (b)(4)

Furthermore, On June 5, 2015, we observed expired materials comingled with unexpired materials in your warehouse area.

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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 judgement, 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."