DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US Customhouse Rm900 2nd & Chestnut St Philadelphia, PA 19106 (215)597-4390 Ext:4200 Fax:(215)597-0875	4/18/2016-4/22/2016
	FEI NUMBER 3012124170

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Francis H. Ranier , Owner

FIRM NAME	STREET ADDRESS
Ranier's Compounding Laboratory	1107 Lowry Ave Ste A
CITY, STATE, ZIP CODE, COUNTRY Jeannette, PA 15644-3030	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 I OBSERVED:

OBSERVATION 1

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

Specifically,

1. Technicians were observed not practicing good aseptic technique while performing aseptic manipulations in the ISO 5 critical area. For example,

   a. On multiple occasions technicians were observed donning sterile gloves inside the ISO 5 hood immediately prior to prior to beginning aseptic processing.

   b. On 4/18/16, during the production of Amphotericin B Liposome 25mg /6ml Inhalation Solution the technician was observed vigorously shaking product after addition of a (b) (4) to aid in dissolution of lyophilized powder with the gloved index finger covering the stopper. This process was (b) (4) (b) (4) of finished product. No additional sterilization method was observed or documented. Additionally, components were staged in manner requiring the technician to extend arms and upper torso over the stoppered vials.

   c. Technicians were observed introducing nonsterile components and equipment into the ISO 5 critical zone without disinfecting. Additionally, several components were observed placed in such a manner potentially disrupting the (b) (4) flow of first air. For example, a clear plastic bag used for collected trash was placed up against the face panel providing HEPA filtered air.

   d. Technicians did not sanitize hands with sterile (b) (4) after touching non-sterile components

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equipment and materials prior to beginning aseptic processing.

e. On 4/18/16, during the production of Cyclosporin 1% Ophthalmic Drops the technician was observed removing two opened and exposed syringes (one containing (b) (4) and the other Cyclosporine (b) (4) from the ISO 5 hood and held up in the surrounding environment for pharmacist's verification of the fill volume. The final product is subsequently to sterile (b) (4) (b) (4) .

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process.

Specifically,

1. (b) (4) are not used to verify the (b) (4) sterilization (b) (4) to sterilize Medroxyprogesterone Ophthalmic Suspension 1%.

2. The effectiveness of the (b) (4) sterilization (b) (4) sterilize glassware (b) (4) for use in sterile operations has not been verified through the performance of an endotoxin challenge.

3. (b) (4) is not performed on (b) (4) used in the sterile (b) (4) of drug product.

4. There is no evidence that media fills are performed under the most stressful or challenging conditions. The Media-Fill Test Procedure for CSPs Sterilized by (b) (4) provided lacks sufficient detail with respect to technician instruction and materials, components and equipment used

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in the process.

OBSERVATION 3

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

Specifically,

1. Environmental monitoring of surfaces for microbial contamination is not performed on a daily basis after the completion of sterile operations in the ISO 5 area. Your firm only performs such monitoring on a (b) (4) basis. Additionally, it was reported that the ISO 5 critical area is wiped with sterile (b) (4) (b) (4) (b) (4)

2. Technician's gloves are not monitored for microbial contamination after the completion of sterile operations. Glove tips are monitored on a (b) (4) basis. Additionally, it was reported by that the (b) (4) is only sampled.

3. Environmental monitoring for non-viable particulates and viable air counts is not performed on a daily basis during routine sterile operations. Such monitoring is performed on a (b) (4) basis (b) (4).

4. Pressure gauges in the ISO 5 Hood and the ISO 7 Ante Room are not continuously monitored for air pressure differential. Instead personnel perform a (b) (4) of the pressure reading and make a record on the Pressure Gauge Log. Additionally, there is no pressure gauge to monitor the pressure differential between the ISO 7 Ante Room and the outside uncontrolled environment.

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OBSERVATION 4

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

Specifically,

1. The firm does not use a sporicidal agent to disinfect the clean room including the ISO 5 area. (b) (4) cleaning of the ISO 5 critical areas consists of Sterile (b) (4) .

2. On 4/17/16, a spray bottle labeled (b) (4) was observed on a cart in the clean room. The firm reported that the spray bottle contains (b) (4) used during sterile operations in the ISO 5 area. The spray bottle is non-sterile but sanitized using sterile (b) (4) (b) (4) prior to the addition of (b) (4) On 4/20/16, the spray bottle was observed inside the ISO 5 critical area being used by the technician to wet a non-sterile towel to wipe residue from the pH meter during the compounding of Lipoic Acid 25mg/ml INJ Solution (batch 41915-2CR).

4. Non-sterile lint free wipes are used by the firm to clean and disinfect the ISO 5 hood.

3. White spotty residue was observed on the ISO 5 aseptic hood (b) (4)

OBSERVATION 5

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

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Specifically,

Gowns/coveralls, facemasks and bouffant hair nets worn by operators working inside ISO 5 zones are not sterile. Additionally, the technician's face and neck are not fully covered allowing exposed facial skin and hair over the ISO 5 critical area.

OBSERVATION 6

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Specifically,

Finished product is not tested for sterility and/or endotoxin. According to the firm, sterility and/or endotoxin testing is only performed (b) (4) [redacted]. For example,

1. Lipoic Acid 25mg/ml INJ Solution (batch # 041916-2CR) beyond use date of 5/19/16 (30 days) was dispensed without sterility and/or endotoxin testing.

2. Hydrochloric Acid 2.0mg/ml preservative free INJ Solution (batch # 030915-6CR) beyond use date of 4/18/16 (30 days) was dispensed without sterility and/or endotoxin testing.

OBSERVATION 7

There is no written testing program designed to assess the stability characteristics of drug products.

Specifically,

No studies have been conducted to evaluate the characteristics of drug product for the beyond use dates assigned. For example,

1. Lipoic Acid 25mg/ml INJ Solution (batch # 041916-2CR) beyond use date of 5/19/16 (30 days).

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2. Hydrochloric Acid 2.0mg/ml preservative free INJ Solution (batch # 030915-6CR) beyond use date of 4/18/16 (30 days)

3. Thiamine HCl 100mg/ml Injectable (batch # 032916-4CR)) beyond use date of 6/27/16 (90 days).

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