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

| DISTRICT ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| 6000 Metro Drive, Suite 101<br>Baltimore, MD 21215<br>(410) 779-5455 Fax:(410) 779-5707<br>Industry Information: www.fda.gov/oc/industry | 01/24/2014 - 02/21/2014*<br>FEI NUMBER<br>3008723337 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

**TO:** Christopher K. Currin, RPh., Co-Owner

| FIRM NAME | STREET ADDRESS |
|---|---|
| RX South LLC DBA RX3 Pharmacy | 12230 Iron Bridge Rd<br>Ste. C |
| CITY, STATE, ZIP CODE, COUNTRY | TYPE ESTABLISHMENT INSPECTED |
| Chester, VA 23831-1534 | 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 I OBSERVED:**

PRODUCTION SYSTEM

**OBSERVATION 1**

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

Specifically,

A. The [redacted (b) (4)] used to sterilize injectable drug products such as Prostaglandin E-1 (UD) 500mcg/mL Injectable and Triple-Mix (UD) 10mcg/30mg/1mg/mL solution both of which are produced from non-sterile components have not been validated. Additionally, no [redacted (b) (4)] have been established in order to ensure that [redacted (b) (4)] (REPEAT OBERVATION)

B. The [redacted (b) (4)] for the sterilization of Hydroxyprogesterone Caproate (Sesame) 250mg/mL Solution have not been validated, the depyrogenation of process equipment has not been validated, and there are no established [redacted (b) (4)]. Additionally, steps 3.3.3 and 3.3.3.1 of SOP 2.290 entitled [redacted (b) (4)]" approved 6/15/13 and Step 3.2.3.3 of SOP 4.30 entitled "Sterile Preparations" approved 6/15/13 are not being followed in that a [redacted (b) (4)] is not being used in each [redacted (b) (4)] "to verify effectiveness of sterilization [redacted (b) (4)]".

C. The [redacted (b) (4)] for sterilization of drug products, such as Estradiol Pellets 22mg, and Testosterone Pellets 200mg, used in the production of sterile drug products have not been validated, and there are no established [redacted (b) (4)]. Furthermore, the results of the [redacted (b) (4)] which are used in each [redacted (b) (4)] are not documented in the logbook, and there is no procedure governing their use. (REPEAT OBSERVATION)

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|---|---|---|
| | Brooke K. Higgins, Investigator | 02/21/2014 |

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D. The [redacted (b) (4)], used for sterilization of drug products and process equipment, is supplied with [redacted (b) (4)] which is not tested for endotoxins or sterility.

E. No results are listed on the [redacted (b) (4)] Log" for the [redacted (b) (4)] used in the sterilization [redacted (b) (4)] of "Pellets" on 12/10/13 and 1/6/14.

**OBSERVATION 2**

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

Specifically, the environmental monitoring program is inadequate as follows:

A. Microbiological monitoring of the surfaces of the ISO 5 filling hoods is only performed [redacted (b) (4)] and not each day filling activities take place. (REPEAT OBERVATION)

B. No non-viable particulate air monitoring is performed in the ISO 5 filling hoods each day sterile drug products are produced. The current monitoring program only evaluates the classified areas for non-viable particulates [redacted (b) (4)] during the HEPA requalifications. (REPEAT OBERVATION)

C. No active or passive microbial air monitoring is performed in the ISO 5 filling hoods each daysterile drug products are produced. The current monitoring program only evaluates the classified areas using an active air sampler [redacted (b) (4)] during the HEPA requalifications. (REPEAT OBERVATION)

D. The gloves of the technician performing aseptic manipulations are not monitored each day that a batch of sterile drug product is produced. Gloves are only monitored [redacted (b) (4)] following gowning prior to the media fill simulation. (REPEAT OBERVATION)

**OBSERVATION 3**

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically, the production processes have not been adequately validated to assure that drug products have the identity, strength, quality, and purity they purport or are represented to possess. For example,

the specific mixing times required for uniform distribution of components have not been determined through controlled studies for the following products: Hydroxyprogesterone Caproate (Sesame) 250mg/mL Solution, Estradiol Pellets 22mg, and Testosterone Pellets 200mg. (REPEAT OBSERVATION)

**OBSERVATION 4**

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

Specifically, the gown, booties, and facemask worn in the clean room are not sterile. Gowning does not provide complete coverage of the skin on the face and neck. Furthermore, during sterile processing operations of Suby's Solution lot 01310214:03 on 1/31/14, Sterile Compounding Technician (b) (6) was observed to be wearing his hair net in a manner such that approximately one to two inches of hair was exposed.

**OBSERVATION 5**

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

Specifically, materials, such a syringes and (b) (4), are not always wiped down with sterile disinfectant prior to being brought from the unclassified pharmacy areas into the ISO 6 IV Cleanroom and transferred into the ISO 5 hood. (REPEAT OBSERVATION)

FACILITIES AND EQUIPMENT SYSTEM

**OBSERVATION 6**

Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.

Specifically,

A. Airflow studies (smoke studies) performed in the ISO 5 chemo hood have not been performed to evaluate laminarity of the airflow.

B. There is a lack of documentation of the conditions evaluated during the dynamic airflow studies (smoke studies) performed in the ISO 5 filling hood in the IV Cleanroom. It is unclear if personnel were simulating filling activities.

C. There is no continuous monitoring of air pressure differentials from the classified cleanrooms and ante room to the surrounding non-classified prep area.

**OBSERVATION 7**

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

Specifically,

A. The suitability and efficacy of disinfecting agents and procedures has not been assessed to ensure potential contaminants are adequately removed from surfaces in the classified areas.

B. Not all disinfecting agents used in the clean rooms and filling hoods are sterile. For example, a [redacted] (b) (4) is used to clean the surfaces of the ISO 5 laminar flow hoods where injectable drug products are filled.

**OBSERVATION 8**

Routine inspection of equipment is not performed according to a written program designed to assure proper performance.

Specifically, there is no assurance incubator temperatures remain within acceptable limits at all times. The temperatures are only required to be verified [redacted] (b) (4) per SOP 2.200 entitled "Incubator" effective 6/15/13. The incubators are used to incubate biological indicators, environmental monitoring media, and media used for the media fills.

QUALITY SYSTEM

**OBSERVATION 9**

The quality control unit lacks responsibility for approving or rejecting drug products manufactured and processed under contract by another company.

Specifically, an audit has not been conducted to evaluate the suitability of the contract testing laboratory

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used to perform release testing, including sterility, endotoxin, and potency testing.

LABORATORY CONTROLS SYSTEM

**OBSERVATION 10**

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications prior to release.

Specifically, step 3.2.3 of SOP 4.50 entitled "Finished Preparation Check" approved 6/15/13 requires sterile drug products to be visually inspected; however, the results of the visual examinations are not always documented. For example, the Logged Formula Worksheets for Mitomycin Ophthalmic Solution 0.04% lot t12042013:92, Mitomycin Irrigation 20mg/20mL lot 01082014:47, and Hydroxyprogesterone Caproate (Sesame) 250mg/mL Solution lot 12052013:03 do not include results of the visual examinations for particulates.

MATERIALS SYSTEM

**OBSERVATION 11**

Containers and closures are not tested for conformance with all appropriate written procedures.

Specifically, vials, stoppers, and syringes used in the packaging of drug products are not examined for conformance to specifications. (REPEAT OBSERVATION)

*** DATES OF INSPECTION:**
01/24/2014(Fri), 01/31/2014(Fri), 02/05/2014(Wed), 02/12/2014(Wed), 02/21/2014(Fri)

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| | Brooke K. Higgins, Investigator | 02/21/2014 |