DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612 (949) 608-2900 Fax:(949) 608-4417 Industry Information: www.fda.gov/oc/industry	12/03/2013 - 01/09/2014* FEI NUMBER 3007200605

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Troy A. Albright, Owner / Pharmacist in Charge

FIRM NAME	STREET ADDRESS
Zions RX Formulations Services LLC dba RX Formuations Serv.	5949 E University Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Mesa, AZ 85205-7435	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:

PRODUCTION SYSTEM

OBSERVATION 1

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

Specifically,

Monitoring of the firm's ISO 5 Hood environments and ISO 7 Cleanroom Environment used to produce sterile drug products is not done during actual production, for example:

a) Lack of viable particulate air monitoring (ISO 5). There is no monitoring of the viable air particulates during aseptic processing of drug products in the ISO 5 environments. Air sampling is only conducted by an outside contractor during [redacted] (b) (4) certification.

b) Lack of viable particulate air monitoring (ISO 7). There is no monitoring of the viable air particulates during aseptic processing of drug products in the ISO 7 cleanroom environment. Air sampling is only conducted by an outside contractor during [redacted] (b) (4) certification.

c) Lack of active non-viable particulate air monitoring (ISO 5). There is no monitoring of the non-viable air particulates during aseptic processing of drug products in the ISO 5 environments. Particulate air analysis is only performed during certification by an outside contractor during [redacted] (b) (4) certification.

d) Lack of active non-viable particulate air monitoring (ISO 7). There is no monitoring of the non-viable air particulates during production of the drug products in the ISO 7 cleanroom. The ISO 5 Biosafety cabinets and Laminar air flow hoods are located within the ISO 7 cleanroom. Particulate air analysis is only performed during certification by an outside contractor during [redacted] (b) (4) certification.

e) Lack of active monitoring of differential pressures (ISO 7). There is no monitoring of the cleanroom pressure differentials during aseptic processing of drug products. There are no devices to read the pressure differential

between the ISO 7 cleanroom to the lesser clean areas. The firm's ISO 7 cleanroom is separated only by plastic strip curtains from the ante-room and non-sterile processing area. There is no further monitoring of the cleanroom pressure differential either manually or by electronic devices during production.

f) Lack of active monitoring of differential pressures (ISO 5). The ISO 5 environments are equipped with pressure differential gauges, however, the readings are not recorded nor are they routinely read. There is no further monitoring of the cleanroom pressure differential either manually or by electronic devices during production.

g) Lack of routine personnel monitoring for operators conducting compounding operations of aseptically processed drug products. Sampling of personnel gloves or arms is not conducted after every lot of aseptically processed drug products in the ISO 5 environment. Sampling of personnel gloves is conducted [redacted (b) (4)] for the purpose of gowning qualification of the firm's operators.

h) Insufficient frequency of environmental monitoring of the ISO 5 and ISO 7 environment surfaces. Surface sampling is not conducted after every lot of aseptically processed drug products. Surface sampling is conducted every [redacted (b) (4)]

OBSERVATION 2

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

Specifically,

a) The firm does not always conduct [redacted (b) (4)] testing of the [redacted (b) (4)] used as the sterilizing step for drug products produced such as Calcium Gluconate. The firm does not possess the equipment to conduct [redacted (b) (4)] of the [redacted (b) (4)] used in the sterile compounding of Calcium Gluconate. Calcium Gluconate is aseptically processed and there is no [redacted (b) (4)] of the finished drug product.

b) The firm prepares components in-house via moist heat sterilization utilizing the [redacted (b) (4)]; model [redacted (b) (4)] located in the non-sterile processing area. There is no written procedure outlining the use and maintenance of the equipment.

c) The [redacted (b) (4)] does not continuously monitor chamber temperature or pressure. In addition, the firm has not demonstrated through validation that the [redacted (b) (4)] is adequate for the sterilization of rubber stoppers for aseptically processed drug products.

d) Glass vials used for aseptically processed drug products are prepared by the firm via dry-heat depyrogenation utilizing [redacted (b) (4)]. There is no written procedure outlining the use and maintenance of the equipment.

e) The [redacted] (b) (4) do not continuously monitor temperature or time. In addition, the firm has not demonstrated through validation that the oven cycle is adequate for the depyrogenation of glass vials for aseptically processed drug products.

OBSERVATION 3

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 Sterility testing is not always conducted for aseptically processed drug products. For example, Calcium Gluconate 10% Injectable vials, Lot# 117433@15 produced on 11/07/13 was not sampled for USP sterility testing. In addition, an endotoxin analysis was not performed.

OBSERVATION 4

Protective apparel is not worn as necessary to protect drug products from contamination.

Specifically,

There is no provision for protection of exposed skin such as the areas of the face around the eyes and area around the neck within the cleanroom environment. The firm's written procedure for gowning for sterile operator's, SOP 9.050, "Required Garb for Buffer or Clean Area Access" revised 01/31/13, describes the use of non-sterile gowning within the cleanroom environment. The firm's uniform components for entry in the cleanroom includes: low particulate gowns, hair covers, shoe covers, face masks, and powder free gloves. It was explained that operators compounding aseptic drugs use sterile gloves; however, there are provisions in the SOP to allow for the use of non-sterile gloves during aseptic compounding.

FACILITIES AND EQUIPMENT SYSTEM

OBSERVATION 5

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

Specifically,

Certification conducted by an outside contractor for the firm's ISO 5 environments used to aseptically process drug products

includes performing smoke studies to demonstrate the air flow with the Biosafety Cabinet or Air Flow hood. There is no recording made of the smoke study to confirm that the airflow is smooth, laminar, and without turbulence. In addition, there have been no smoke studies conducted in the ISO 7 IV cleanroom.

OBSERVATION 6

Written procedures for cleaning and maintenance fail to include description in sufficient detail of methods, equipment and materials used and description in sufficient detail of the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance.

Specifically,

The firm's written procedures are deficient in that they do not include sufficient detail regarding the cleaning of the following:

a) Cleaning of the firm's autoclave for the sterilization of rubber stoppers used in sterile compounded drug products does not include inspection to assure that the equipment is visually clean. On 12/10/13, during a walkthrough of the facility, the [redacted] (b) (4), inner door, and top of the inner chamber were coated with a substance of black particles.

b) There are no written instructions provided to technicians that detail the cleaning of the [redacted] (b) (4) wall air conditioning unit. This air conditioning unit recirculates air within the ISO 7 cleanroom. This unit is located in the ISO 7 cleanroom which houses the ISO 5 environments (hoods and biosafety cabinets) used to aseptically compound drug products.

c) There are no written instructions provided to technicians regarding the cleaning of the firm's [redacted] (b) (4) portable dehumidifier unit. The dehumidifier is used within the ISO 7 cleanroom during times when humidity is high, i.e. during monsoon storms.

QUALITY SYSTEM

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OBSERVATION 7

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically,

During a [redacted] (b) (4) cleanroom certification conducted by a third party in July 2013, HEPA filter leaks in the firm's ISO 7 IV cleanroom were reported to the firm and a negative pressure condition of the rooms to the non-sterile areas was detected. The ISO 7 IV cleanroom houses the ISO 5 hood environments used to compound aseptic drug products. The firm replaced two HEPA filters in the cleanroom suite in response to the leaks, however, there was no investigation performed to determine the cause of the equipment failure and/or impact to compounded drug products produced under these conditions.

OBSERVATION 8

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

Specifically,

Beyond use dates and/or Expiration dates placed on drug products by the firm are not supported by stability studies of actual products.

For example, Calcium Gluconate is labeled by the firm with an expiration date of 30 days from the date of compounding. There is no stability study data to support this time period. It was explained that the 30 day time period was established based on a literature reference.

*** DATES OF INSPECTION:**
12/03/2013(Tue), 12/04/2013(Wed), 12/05/2013(Thu), 12/06/2013(Fri), 12/10/2013(Tue), 12/11/2013(Wed), 12/19/2013(Thu), 12/20/2013(Fri), 01/08/2014(Wed), 01/09/2014(Thu)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Joey V. Quitania, Investigator	Jquitania 01/09/14	
	Linda Thai, Investigator Timothy T. Kapsala, Investigator Marcus F. Yambot, Investigator	M. F. YA 01/09/14	01/09/2014