DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407) 475-4700 Fax:(407) 475-4768 Industry Information: www.fda.gov/oc/industry	03/04/2014 - 03/17/2014
	FEI NUMBER 3006412304

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Mr. Riccardo D. Roscetti, President and CEO

FIRM NAME	STREET ADDRESS
KRS Global Biotechnology, Inc	791 Park Of Commerce Blvd Suite 600
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Boca Raton, FL 33487-3633	Drug Outsourcing Facility

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 do not include adequate validation of the sterilization process.

Specifically,

A. Your written procedures *07-31.01 Sterilization and Depyrogenation of Vials and Glassware* and *03-42.01* (b) (4) have not been fully validated for all surfaces that come into contact with drug product after (b) (4).

1. For example, these procedures do not include (b) (4) for the auto dispenser transfer tubing with fittings, glassware, vials, and stoppers for the (b) (4) and the (b) (4) have not been validated using an appropriate (b) (4).

2. For example, the depyrogenation of the auto dispenser transfer tubing with fittings, glassware, finished product vials, and stoppers by (b) (4) was not validated using a known amount of endotoxin standard to demonstrate that the process achieves a three-log reduction.

B. You do not perform and your processing procedures do not require a (b) (4) to determine if the (b) (4) functions properly. This (b) (4) is used to sterilize drug products produced from nonsterile components such as Bimix #10 (Papaverine/Phentolamine 30mg/4mg/ml), Droperidol 2.5 mg/ml, Human Chorionic Gonadotropin 10,000 IU lyophilized, and Cyanocobalamin 1 mg/ml. On 3/5/2014, I observed that the (b) (4) used to sterilize Cyanocobalamin 1 mg/ml for injection lot # 03052014@2 was (b) (4) without performing a (b) (4) to determine if the (b) (4) functioned properly.

C. (b) (4) sterilization process (b) (4) used to (b) (4) sterilize drug products such as Carnitine (L) 500 mg/ml for injection and Methionine/Inositol/Choline 25mg/50mg/50mg/ml for injection have not been validated and there are no established (b) (4).

D. On 3/5/2014, I observed that an (b) (4) holding septa and a tray holding sterilized vials were placed in front of the unidirectional air flow over the ISO 5 work space in the laminar flow hood during the processing of Cyanocobalamin 1mg/ml for injection lot # 03052014@2 and that the operator stoppered vials with gloved fingers.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Joanne E. King, Investigator — Joanne E. King, Investigator	03/17/2014

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OBSERVATION 2

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

Specifically, on 3/15/2014 I observed that sterile gloves that were used to manipulate nonsterile equipment were (b) (4) (b) (4) but were not changed before re-entering the sterile ISO 5 work area and used to press the septa into the vials.

OBSERVATION 3

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

Specifically, you were unable to determine if there was a loss in positive pressure in the clean room during the compounding of Cyanocobalamine (Vitamin B12) 1mg/ml for injection in 10 ml vial lot # 03052014@2 on 3/5/2014 since the clean room gauge was not operational. According to your Sterile Pressure Differential Log the pressure differential check is conducted only (b) (4) rather than continuously or periodically during production to ensure positive pressure.

OBSERVATION 4

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

Specifically,

Given the observed inadequate aseptic processes at your firm, testing is deficient in that:

A. You are not testing some of your sterile drug products for pyrogens if they interfere with the endotoxin test. Specifically, you did not test Cyanocobalamin (Vitamin B12) 1mg/ml for injection lot # 03052014@2, Bimix#10 (Papaverine/Phentolamine 30 mg/4mg/ml for injection lot # 01152014@4, and your preservative free Mitomycin 0.05 % solution for veterinary use.

B. You have not evaluated a need to neutralize preservatives that are part of some of your product formulations prior to sterility test inoculations such as (b) (4) which is used in products such as Cyanocobalamin 1mg/ml for injection lot # 03052014@2.

OBSERVATION 5

The accuracy, sensitivity, specificity, and reproducibility of test methods have not been established and documented.

Specifically, you have not performed tests to determine the preservative content in your sterile drug products and their

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effectiveness. As an example, your finished product analysis performed on Cyanocobalamin (Vitamin B12) 1 mg/ml lot # 03052014@2 does not include a test to determine (b) (4) content.

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	Joanne E. King, Investigator Joanne E. King, Investigator	03/17/2014