DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
300 River Place, Suite 5900 Detroit, MI 48207 (313) 393-8100 Fax:(313) 393-8139 Industry Information: www.fda.gov/oc/industry	10/29/2014 - 11/13/2014* FEI NUMBER 3011130315

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Bradley J. McCloskey, Pharmacist in Charge

FIRM NAME	STREET ADDRESS
Diversified Pharmacy Inc dba University Compounding Pharmacy	2520 Livernois Road
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Troy, MI 48083	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:

OBSERVATION 1

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

Specifically,

i. Adequate validation of aseptic processing operations, specifically, process simulations (media fills), have not been performed under representative worst case aseptic processing conditions to assure the sterility of drug products. Currently, SOP 1.60, *Orientation and Training*, requires use of a syringe for the filling of two 10ml vials through a 0.22 micron filter. This process does not include, for example, worst case lot sizes, vial sizes, and equipment used in normal aseptic operations such as repeater pumps. For example, media fill simulations are not representative of:

- -Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66, filled with a repeater pump, vial size of 30ml and lot size of (b) (4) vials
- -Methylcobalamin 1,000mcg/ml Injectable lot 09292014@63, vial sizes of 4ml, 10ml, 12ml, and 30ml, and lot size of (b) (4) vials
- -Testosterone Cypionate (PF) Olive Oil 200mg/ml Injectable, vial size of 3ml, lot size of (b) (4) vials

ii. Non-sterile disposable wipes are used to wipe "ISO 5" laminar flow hoods with sterile (b) (4) For example, such wipes were used for cleaning "ISO 5" laminar flow hood #1 prior to the aseptic processing of Selenium 40mcg/ml Injectable lot 10302014@16 on 10/30/2014.

iii. The bioburden of non-sterile drug components is not evaluated, and bioburden limits have not been established, for non-sterile bulk formulated products to ensure the sterilizing process is adequate to remove the microbiological load. For example, non-sterile drug components used in the processing of Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66.

iv. In situ air pattern analysis has not been performed in the "ISO 5" laminar flow hoods, where sterile drug products are processed and filled, to demonstrate unidirectional airflow over the product during static or dynamic conditions. For example, the "ISO 5" laminar flow hood in which Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66 was processed on 9/5/2014. Additionally, such analysis has not been performed in areas classified "ISO 7".

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	Sarah M. Napier, Investigator Emily J. Orban, Investigator	11/13/2014

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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,

Gowning of operators performing aseptic operations in the "ISO 5" laminar flow hoods is inadequate in that protective gowns, face masks, and hair nets worn during aseptic processing are not sterile. Additionally, the current gowning method leaves facial skin exposed, including eyes and forehead. For example, gowning worn as observed during the aseptic processing of Selenium 40mcg/ml Injectable lot 10302014@16 on 10/30/2014.

OBSERVATION 3

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

Specifically,

i. Environmental monitoring is not performed at least daily during drug production in the critical areas, to evaluate the quality of the aseptic processing environment and assess whether aseptic conditions are maintained.

a. Non-viable particulate monitoring is performed in the aseptic processing room once every six months
b. Viable air monitoring is performed in each laminar flow hood once every six months
c. Viable surface monitoring is performed in each laminar flow hood once per month
d. Personnel fingertip monitoring is performed for one operator once every two weeks

ii. No data was provided to support that the incubator used to incubate environmental monitoring surface and fingertip samples is qualified for its intended use. EnviroTest Media Paddles Directions for Use states, "Incubate at an elevated temperature (USP <797>) 30-35°C for 48 to 72 hours". The temperature of the incubator is checked only daily on business days, and no documentation was provided to support calibration of the unit's temperature probe.

The above apply to aseptic processing areas used to process and fill all sterile drug products, for example, Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66 and Selenium 40mcg/ml Injectable lot 10302014@16 on 10/30/2014.

OBSERVATION 4

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically,

The monitoring frequency of pressure differentials between the aseptic processing areas and surrounding areas of lower air

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quality is not justified. Currently, such pressure differentials are checked and documented by operators once per day on each day of use according to SOP 1.40, *Compounding Area Requirements (Sterile)*. Assurance was not provided to support that a temporary loss in differential pressure during filling operations would be detected and appropriately handled. For example, the aseptic processing areas in which all sterile drug products are processed and filled, including but not limited to Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66 and Selenium 40mcg/ml Injectable lot 10302014@16 on 10/30/2014.

OBSERVATION 5

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

Specifically,

i. Beyond use dates assigned to sterile drug products are not always supported by sterility testing over the labeled shelf life in representative container closure systems, for example:
- -Methylcobalamin 1,000mcg/ml Injectable lot 09292014@63, beyond use date of 180 days
- -Testosterone Cypionate (PF) Olive Oil 200mg/ml Injectable, beyond use date of 90 days
- -Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66, beyond use date of 90 days

ii. For drug products containing a preservative, testing has not been performed to support that the preservative system retains antimicrobial effectiveness over the labeled shelf life of the drug product. For example, Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66.

OBSERVATION 6

Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.

Specifically,

Adequate container closure integrity testing has not been performed for any sterile product container closure systems. Specifically, vials are filled through insertion of a needle through the rubber vial closure, and data was not provided to support that this closure will prevent the ingress of microbial contamination post puncture. For example, the container closure system used to package Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66.

OBSERVATION 7

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

Specifically,

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Aseptically filled sterile injectable drug products are released and distributed prior to receiving final laboratory results for sterility and endotoxins. For example, Hydroxocobalamin 1,200mcg/ml Injectable lot 09052014@66 was made on 9/5/2014 and distributed on 9/10/2014. On 9/18/2014, investigations into a suspected sterility failure commenced at the firm and contract laboratory, resulting in the recall of this drug.

OBSERVATION 8

The responsibilities and procedures applicable to the quality control unit are not in writing.

Specifically,

A 100% visual inspection for contamination is not performed on each lot of sterile drug products prior to release and distribution. Currently, one or two vials from each finished lot of sterile drug product are examined visually for contamination; such examinations are not documented. For example, Dimercaptopropane Sulphonate 50mg/ml Injectable lot 10302014@6.

OBSERVATION 9

The operations relating to the processing of penicillin are not performed in facilities separate from those used for other drug products for human use.

Specifically,

Procedures have not been established for the separation of tasks and segregation of personnel handling beta-lactam drug products from those for all other human drug products. For example, Amoxicillin/Clavulonic Acid (4.5 capsules = 500mg-125mg) lot 10302014@43 was processed in a containment hood in the non-sterile laboratory area on 10/30/2014, and subsequently, Estradiol 1.2mg/gm HRT Cream lot 10302014@69 and Progesterone Slow Release 50mg Veggie Capsule lot 10302014@62 were compounded in the same laboratory area on that same day.

*** DATES OF INSPECTION:**
10/29/2014(Wed), 10/30/2014(Thu), 11/03/2014(Mon), 11/04/2014(Tue), 11/05/2014(Wed), 11/13/2014(Thu)

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