DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 (973) 331-4900 Fax:(973) 331-4969 Industry Information: www.fda.gov/oc/industry	06/29/2015 - 07/16/2015* FEI NUMBER 3004600183

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: David M. Miller, R.Ph., Owner/President

FIRM NAME	STREET ADDRESS
Millers of Wyckoff, Inc.	678 Wyckoff Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Wyckoff, NJ 07481-1430	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 WE OBSERVED:

OBSERVATION 1

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

Specifically, the following poor aseptic techniques were observed during processing on 6/29/2015 and 6/30/2015:

- Materials such as syringes, wrapped sterile gloves, and vials were not wiped down with Sterile [redacted] prior to introduction into the [redacted]
- Incomplete sanitization of the stopper of each vial of drug product with sterile [redacted]
- Processing of product was performed on top of the sterile gloves wrapper, rather than the [redacted] worksurface.
- Gloves worn during processing in the [redacted] are not changed or sanitized with sterile [redacted] between production of different products and/or lots.
- Disposable, non-sterile laboratory coats used during processing of drug products were reused, even after falling on the floor.

OBSERVATION 2

Drug products do not bear an expiration date determined by appropriate stability data to assure they meet applicable standards of identity, strength, quality and purity at the time of use.

Specifically, there is a lack of potency and sterility assurance for preserved and non-preserved sterile preparations in that beyond use dates, up to 3 months, are assigned without stability data and the container closure integrity of the bottles has not been established. Examples of products include: Buprenorphine (multidose vial) 0.3mg/mL, Lot # 02172015@24; Procaine (Buffered) (PF) 1% injectable, Lot # 04212015@17; Magnesium Sulfate Lot # 05202015@11; and Methylcobalamin(P) 25mg/mL, Lot # 04302015@20; Cefazolin Ophthalmic (PF) 50mg/mL Solution, Lot # 04212015@26; and Methylprednisone (PF) eye drops, Lot # 05152015@1.

Additionally, there is a lack of test data to support that [redacted], which have been [redacted] sterilized when produced, can be [redacted] to ensure sterility remains.

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	Liatte Krueger, Investigator, ~~Investigator~~ LK 7/16/15 Liatte Krueger Susan M. Joseph, Investigator Susan M Joseph Zakaria I. Ganiyu, Investigator	07/16/2015

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OBSERVATION 3

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

Specifically,

A. There is no documented test method for sterility testing for all products, except for Trimix (various formulations). The executed method has not been defined to be a compendial method or a method, which has been shown to be as good or better than the compendial method. In addition, on 6/29/2015, Pharmacist (b) (6) failed to assure us that the executed sterility testing being performed was as per method suitability conducted by a contract testing laboratory. Furthermore, negative controls are not run for each sterility test performed.

B. Endotoxin testing is not performed on all finished lots of drug products. For example, (b) (4) x 10mL vials, with 5mL in each vial, of Trimix 1A Lot # 04212015@10 were produced on 4/21/2015; however testing does not include endotoxin results.

OBSERVATION 4

Equipment and utensils are not maintained at appropriate intervals to prevent malfunctions and contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically, balance (b) (4) Model # (b) (4), which is used to weigh non-sterile ingredients has not been calibrated to ensure that the scale can accurately weigh across its minimum range (b) (4) The minimum weight used to calibrate the balance was (b) (4) in 2014 and (b) (4) in 2015. Examples of ingredients which have been weighed that are less than (b) (4) include: (b) (4) g procaine (b) (4) to compound procaine (buffered) (PF) 1% Lot # 04212015@17 and (b) (4) of sodium molybdate (b) (4) for Molybdenum (P) 25mcg/mL Lot # 06022015@5.

OBSERVATION 5

Employees are not given training in the particular operations they perform as part of their function.

Specifically,

A. There is no documented microbiological training for the following tests and individuals who perform them:
   1. Sterility and environmental testing by Pharmacist, (b) (6)
   2. Reading of microbiological assay results by Pharmacy Technician, (b) (6)
   3. Performance of (b) (4) by Pharmacist Intern, (b) (6)

B. There is no documented training for Pharmacist (b) (6) who performed physical testing for sterile compounded finished products.

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C. There is no documented training for Pharmacist (b) (6) who performed (b) (4) testing.

OBSERVATION 6

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

Specifically,

A. Procedure *SOP 3.03 Environmental Monitoring (EM) of the Sterile Compounding Area (Date Effective: 01-01-07)* provides instructions on surface sampling technique and incubation; however, this procedure is not being followed. For example: use of sampling environemental monitoring sampling supplies are not the same as described in the procedure, (b) (4) (b) (4) was observed to be sampling multiple locations in the (b) (4) and all EM samples are not being incubated for the (b) (4) temperature requirement.

Additionally, incubators, used for incubation of EM samples and sterility testing samples, have not been qualified and the thermometers have not been calibrated since installation of an unknown date.

B. Non-viable particulate monitoring, performed under static conditions, is limited to (b) (4) during the certification of the (b) (4) There is no monitoring of non-viable air particulates under operating conditions within the ISO 5 (b) (4)

C. Environmental monitoring of viable particulates is not performed within the ISO 5 (b) (4)

D. The personnel working within the sterile area and the surfaces of the ISO 5 (b) (4) are monitored (b) (4) and not on a daily basis or after every batch of drug product produced.

OBSERVATION 7

There is a failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically, for at least two products which the firm has tested, including Alprostadil 10mcg/mL Lot # 01242012@1 and Methylcobalamin(P) 25mcg/mL Lot # 12042013@59, the testing for these lots resulted in a potency outside of 139% and 72%, respectively. Methylcobalamin(P) 25mcg/mL Lot # 12042013@59 was not dispensed; however the firm has produced this formulation since and has dispensed it as Lot # 06042015@37 without ensuring that the potency is within specifications.

Specifically, investigations have not been initiated for out of specification potency testing results for at least two products:

- Alprostadil 10mcg/mL Lot # 01242012@1, tested on 1/26/2012, resulted in a potency of 139%. The product was dispensed to a patient on 1/23/2012.
- Methylcobalamin(P) 25mcg/mL Lot # 12042013@59, tested on 1/16/2014, resulted in a potency of 72.2%. The lot

was not dispensed; however the firm has produced this formulation since without investigating the failure. Most recently, Methylcobalamin(P) 25mcg/mL has been dispensed as Lot # 06042015@37.

OBSERVATION 8

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

Specifically, the firm has not demonstrated the efficacy of their disinfectants, [redacted] (b) (4), Sterile [redacted] (b) (4) and Sterile [redacted] (b) (4) %, which are used to clean the firm's [redacted] (b) (4) and ISO 8 anteroom.

Additionally, we did not observe personnel adhering to the established contact times for their disinfectant agents as noted in procedure *SOP 3.02 Cleaning and Maintenance of the Clean Room Facility (Date Effective: 01-01-07).*

OBSERVATION 9

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,

A. Visual inspection of Alprostadil 20mcg/mL Lot # 06252015@31 on 6/29/2015 was not documented within the batch record as per procedure *SOP 6.02 Sterile Compounding Finished Preparation Testing (Date Effective: 01-01-07)*. This product was delivered to the customer on 6/30/2015.

B. During compounding of TriMix STD Mayo Lot # 06302015@14, we observed that the operator did not conduct a visual check of [redacted] (b) (4) to [redacted] (b) (4) of Phentolamine. There are no procedures to ensure that this quality control step is taken [redacted] (b) (4). We observed non-dissolved particles in the [redacted] (b) (4)

OBSERVATION 10

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

Specifically, media fill simulations are not representative of the preparation of aseptically filled sterile products. For example, the sterile preparation of [redacted] (b) (4) Trimix 1A RX (PAPAV/PHENTOL/PGE1) 30MG/1MG/10MCG/mL has [redacted] (b) (4) [redacted] (b) (4) [redacted] however, the media fill simulation is [redacted] (b) (4)

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OBSERVATION 11

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

Specifically, you have not qualified or audited your contract testing laboratories, used for potency, endotoxin, and sterility testing of Trimix finished products; however rely on their results.

OBSERVATION 12

The flow of components, drug product containers, in-process materials, and drug products though the building is not designed to prevent contamination.

Specifically, the ISO 8 anteroom contains a sink sourced with tap water that is located [redacted] *(b) (4)* which is used as the [redacted] *(b) (4)* the firm's [redacted] *(b) (4)*

*** DATES OF INSPECTION:**
06/29/2015(Mon), 06/30/2015(Tue), 07/01/2015(Wed), 07/06/2015(Mon), 07/16/2015(Thu)

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