

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

Denver District Office
Denver Federal Center Bldg. 20 W 6th Ave & Kipling St.
Denver CO. 80225-0087
303-236-3017

DATE(S) OF INSPECTION

8/8/16 - 8/22/16

FEI NUMBER

3012248071

Industry Information: www.fda.gov/oc/industry

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Tony E. Jones, Owner

FIRM NAME

Maplerose Enterprises LLC dba Pencol Pharmacy

STREET ADDRESS

1325 S. Colorado Blvd.

CITY, STATE AND ZIP CODE

Denver CO 80222

TYPE OF ESTABLISHMENT INSPECTED

Producer of Sterile and Non-Sterile Drugs

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

Facilities and Equipment System

Observation 1

Buildings used in the processing of a drug product are not maintained in a good state of repair.

Specifically, your firm's ante room as well as clean rooms where your ISO 5 laminar air flow workbench and biosafety cabinet are located have not been maintained in a good state of repair. For example,

A. A ceiling tile in the positive pressure room was observed to be pushed into the ceiling space creating a $\frac{3}{4}$ inch gap on one side. The tile is located directly above and one tile to the right of the LAF.

B. Just above the ante-room pass through, the west wall of the ante-room had the outer paint/paper layer of missing drywall exposing a 2" x 3/4" oblong shape.

Observation 2

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

Specifically,

Environmental monitoring is never conducted during aseptic filling operations in order to give information on the quality of the aseptic processing environment.

A. Dynamic particulate monitoring is never performed.

B. Dynamic viable air sampling has not been performed prior to August 2016.

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REVERSE
OF THIS
PAGE

EMPLOYEE(S) SIGNATURE

Zachary A. Bogorad

EMPLOYEE(S) NAME AND TITLE (Print or Type)

Zachery L. Miller, Investigator
Zachary A. Bogorad, Investigator
Michael E. Maselli, Microbiologist

DATE ISSUED

8/22/16

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C. Passive air sampling is never performed.

D. Pressure, temperature, and humidity monitoring devices installed in each clean room of the suites are not monitored or recorded during sterile operations. Pressure devices are not monitored during sterile operations. Although the data is recorded electronically, the data files have never been utilized due software malfunctions.

Observation 3
Routine calibration, inspection and checking of mechanical and electronic equipment is not performed according to a written program designed to assure proper performance.

Specifically, equipment used to ensure the quality, strength, and purity of drug substances are not calibrated. All drugs manufactured on site are manufactured using a scale and are stored in a space monitored for temperature and humidity.

A. Ongoing calibrations of 14 analytical scales used to measure ingredients and finished drugs in the non-sterile pharmacy were not maintained between 2/5/16 and 8/8/16.


B. Calibration has never been performed for the analytical scale located in the sterile clean room. This scale is used to weigh raw materials.

C. Temperature, humidity, and pressure monitoring equipment including the Holland Safety Equipment door monitoring pressure system and the magnahelic analog pressure gauge calibrations have never been performed.

D. The Millipore pressure gauge used to perform sterile filter integrity testing after manufacturing has never been calibrated. More than 75% of sterile drugs manufactured on site require sterile filtration. Approximately 30% of drugs manufactured on site are sterile.

E. Temperature monitoring devices built into the sterility testing media incubator and environmental sample incubators have never been calibrated.

1. Binder Incubator HSS#0032681 – surface and personnel sample storage

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2. Boekel Scientific Incubator HSS#0012813 – anaerobic sample storage
3. Boekel Scientific Incubator Model 133000 – aerobic sample storage
4. Quincy Lab Model 10-140 – active air sample storage

Observation 4

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

Specifically,

A) The autoclave sterilization cycle has not been shown to be effective. The glassware sterilization cycle and load patterns have not been performed in at-use conditions. Equipment qualifications and load patterns have not been performed.

B) Hand washing of multi-use equipment (beakers, stirrers, stirring rods) has not been shown to be effective.

C) You failed to perform room disinfection with Spore-Klenz. Spore-Klenz sanitizer labeling requires an undiluted chemical contact time of 30 minutes. The sterile technicians stated that a 10 minute contact time is used for the sporicidal treatment of the aseptic processing room and equipment surfaces.


Production System

Observation 5

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

Specifically,

A) Your firm does not perform a bubble point post-filtration integrity testing of the sterilizing filter.

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B) Your firm has not conducted dynamic smoke studies in either cleanroom or the laminar-flow hood in service in cleanroom 1 or the biosafety cabinet in service in cleanroom 2.

C) From 8/8/16 – 8/12/16 equipment used in the production of sterile injectables including glassware, utensils, and stir equipment was not processed in a way that eliminates pyrogens. The following sterile drugs were manufactured during the course of the inspection using non-depyrogenated glassware and utensils:

1. Methylcobalamin, Folic Acid Injection 1 mg / 0.4 mg / 0.12 ml solution, lot MTFA2206, compounded 8/8/16
2. Methionine Inositol Choline with Hydroxocobalamin 25 mg / 50 mg / 175 mcg / 1ml Solution, lot MICH2236, compounded 8/11/16

D) Validated sterility and bacterial endotoxin testing is performed only on products whose batch size is greater than 24 units. Approximately 5% of products have a batch size greater than or equal to 24 units. In conjunction with this, media used for sterility testing for products whose batch size is less than 24 units is not tested for growth promotion prior to use.

Observation 6


Protective apparel is not worn as necessary to protect drug products from contamination. Specifically, on 8/8/16 sterile processing gowning material (hoods, suits, masks, and booties) were donned using non-gloved hands. Gowning was stored rolled up in an ante-room drawer, inside-out, for re-use. In conjunction with this, gowning materials do not completely cover skin. Exposed skin was noted around the face of the operator. At this time lot MICH2206 of Methionine-Inositol-Choline-Hydroxocobalamin was being sterile filled and compounded.

Quality System

Observation 7

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

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A. Procedures outlining the responsibilities of the quality control unit to approve or reject all components, drug product containers, closures, in process materials, packaging material, labeling, and drug products have not been established.

B. Procedures to approve and reject all procedures or specifications impacting the identity, strength, quality, and purity of drug products have not been established. There are no procedures for:



1. The assessment of personnel qualifications or responsibilities
2. Adequate buildings and facilities
3. Equipment qualification, cleaning, and maintenance
4. Control of components, drug product containers, and closures
5. Production and Process controls
6. Packaging and Labeling controls
7. Holding and Distribution controls
8. Laboratory Controls
9. Records and Reports
10. Complaint Handling
11. Returned and Salvaged Drug Products
12. Change Controls
13. Specifications for components, drug product containers, closures, packaging materials, and in-process materials.

C. There are no written procedures which describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval, and rejection of components, drug product containers, and closures.

Observation 8

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

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A. Your firm's beyond use date (BUD) is not based upon completed stability studies. There is no sterility program that 1) Establishes the number and size of batches to be tested, 2) addresses accelerated studies and test intervals, 3) speaks to storage conditions (e.g. store ambient in an upright position) and the integrity of the container closure system; and 4) specifies the testing attributes of the drug products that are susceptible to change during storage.

B. There is no justification for only one batch being used to determine the BUD of all of your sterile drug products. There is no BUD sterility data for any of your sterile drug products – sterility is only performed on day 0. Additionally, there is no antimicrobial effectiveness testing data for any sterile drug products containing preservatives.

For example:

a. Pumice 2.35mg/mL Lidocaine HCl 5mg/mL Injection has a BUD of 206 days. This BUD is based solely on an un-validated potency analysis of the active ingredient lidocaine.

b. Cardioplega Concentrate Injectable Solution has a BUD of 96 days. This BUD is based solely on an un-validated potency analysis of the active ingredients: lidocaine, magnesium sulfate heptahydrate, mannitol, and potassium chloride.

c. Methylcobalamin PF 25mg/mL Solution (dispensed in a syringe) has a BUD of 200 days. This BUD is based solely on a non-validated potency analysis of the active ingredient: methylcobalamin.


Laboratory System

Observation 9

Each lot of a component, drug product containers and closures liable to objectionable microbiological contamination is deficiently subjected to microbiological tests before use.

Specifically,

No procedures exist and your Lead Sterile Pharmacist confirmed that none of your drug components or drug product containers and closures are subjected to any microbiological testing or bioburden assessment, after receipt from supplier. No certificate of analysis is received or reviewed for any lot of incoming components.

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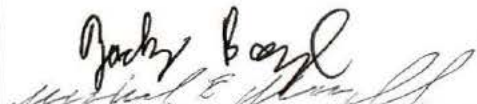
Observation 10

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

Specifically, not all of your sterile products are released with testing for active ingredient identification and potency. Furthermore, it is indeterminable how many formulations have been shipped without identity and potency determinations as approximately 95% of manufactured drugs are patient specific.

For example:

- a. The Tri-mix 30mg/1mg/10mcg/mL (Papaverine, Phentolamine, Prostaglandin) finished drug product is dispensed without determining the identification and potency of each active ingredient of the final product.

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