DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
New Orleans District Office 404 BNA Drive, Bldg. 200, Ste. 500 Nashville, TN 37217 (615) 366-7801 Industry Information: www.fda.gov/oc/industry	8/24/2015 - 9/23/2015* FEI NUMBER 3006014626

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mark D. Acker, CEO

FIRM NAME	STREET ADDRESS
Medistat RX, LLC	110 East Azalea Avenue
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Foley, AL 36535	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) (WE) OBSERVED:

OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy and 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,

a) Environmental monitoring failures and trends are not adequately addressed and investigated. During the previous 10 months, numerous organisms have been identified, including gram negative bacteria, yeast, and mold, within ISO 5 hoods on both surfaces and in the air.

b) Methylprednisolone 40 mg/mL, Lot 07082015@1, Triamcinolone Acetonide 80 mg/mL, Lot 07072015@1, Tri-Mix (25/10/1.25), Lot 07092015@1, and Tri-Mix (25/10/1.25), Lot 07092015@2, were released after receiving failing sterility results from their contract laboratory. The investigation concluded it was laboratory error. A new sample of the same size for each product was sent to an alternative laboratory, which produced acceptable results. The products were released and distributed.

c) HCG 3000, Lot 12262014@5, IC (50/50/0.175/0.175), Lot 12232014@1, Triamcinolone, Lot 12232014@1, Testosterone Cypionate/Propionate 180/20 mg/mL, Lot 12232014@10 and @11, were released after receiving failing sterility results from their contract laboratory. The investigation concludes analyst error, though there is no evidence to support this conclusion. A new sample of the same size for each product was sent to an alternative laboratory, which produced acceptable results. The products were released and distributed.

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	Samantha J. Bradley	Samantha J. Bradley, Investigator Jason D. Abel, Investigator	9/23/2015

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OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, and followed. Procedures shall include validation of all aseptic and sterilization processes.

Specifically,

a) Injectable drug suspensions are sterilized in (b) (4) located within the ISO 8 Prep Room. The (b) (4) have not been qualified and the sterilization cycles have not been validated. There has been no (b) (4) studies or (b) (4) determinations. The (b) (4) are used to sterilize injectable drug products (b) (4).

b) On 8/31/2015, during observation of compounding of Medroxyprogesterone Suspension Vehicle, Lot 08312015@3, and Medroxyprogesterone Acetate 150 mg/mL, Lot 08312015@2, the following was noted:

i. Operators were observed to handle a keyboard, mouse, scanner, phone, and cabinet handle and resume compounding activities without re-sanitizing their hands within the ISO 8 Prep Room.
ii. An operator poured Benzyl Alcohol into a depyrogenated (b) (4) (b) (4) (b) (4) within the ISO 8 Prep Room. (b) (6) (b) (4).
iii. During aseptic filling within the ISO 5 Hood, Hood (b) (4) the operator was observed to move (b) (6) hand over the open vials prior to filling them with product.
iv. During aseptic filling within the ISO 5 Hood, Hood (b) (4) the operator was observed to place stoppers on filled vials with tweezers and then push them into the vials using (b) (6) fingers.

c) Smoke studies have not been performed in the clean rooms, including the ISO 5 critical areas, in either static or dynamic conditions.

d) The (b) (4) used for (b) (4) testing has no documentation of calibration.

e) There is no viable air monitoring within the ISO 5 hood during aseptic operations.

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f) Media fills are not representative of the most challenging product compounded and aseptically filled. The largest media fill was (b) (4) and the largest batch size made is (b) (4)

g) During a media fill, Lot 10302014@20, growth was found on an operator's left and right sleeve and it was not investigated or identified.

OBSERVATION 3

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

Specifically, on 8/31/2015, after the production of Medroxyprogesterone Acetate 150 mg/mL, lot 08312015@2, an operator was observed to sanitize (b) (6) hands prior to finger plating.

OBSERVATION 4

Acceptance criteria for the sampling and testing conducted by the quality control unit is not adequate to assure that batches of drug products meet appropriate statistical quality control criteria as a condition for their approval and release.

Specifically,

a) Visual inspection of injectable products is limited to the presence of particulate matter (PM) for rejection. For example, apparent product residue was observed around and in the closures of 8 vials of Methylprednisolone Acetate 80 mg/mL, Lot 08052015@2, and 2 vials of Lipostat, Lot 07012015@1. This is not considered significant and vials are accepted.

b) There is no established limit for PM and excessive rejections were noted for the following:

i. MIC 25/50/50/0.175/0.175 mg/mL, Lot 07272015@1, resulted in (b) (4) vials. Two hundred and

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twenty nine (229) vials, or approximately (b) (4) %, were rejected for PM.

ii. Triamcinolone Acetate 80 mg/mL, Lot 05192015@1, resulted in (b) (4) vials. Seventy four (74) vials, or approximately (b) (4) %, were rejected for PM.

iii. Tri-Mix 30/10/1 mg/mL, Lot 08032015@3, resulted in (b) (4) vials. Twenty seven (27) vials, or approximately (b) (4) %, were rejected for PM.

OBSERVATION 5

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

Specifically, the design of the clean room is deficient in that:

a) Pressure differentials between rooms are not monitored during production.

b) There are no gauges between the ISO 8 Prep Room and uncontrolled rooms, and, therefore, no pressure monitoring between the rooms.

c) There are openings between the ISO 7 Large Buffer Room and the ISO 8 Prep Room, but there is no pressure differential monitoring between these two rooms to identify which direction air is moving. The ISO 8 Prep Room does not receive HEPA filtered air.

d) The hand-washing sink and (b) (4) hand dryer are located directly in front of an air return in the ISO 7 Ante Room.

e) Non-sterile (b) (4) is used for all sanitizing activities within the ISO 8 Prep Room.

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OBSERVATION 6

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

Specifically,

a) Non-sterile, non-shedding wipes are used in the clean rooms, including the ISO 5 areas.

b) (b) (4) non-sterile cleaners are used on a (b) (4) within the clean room. Only (b) (4) (b) (4) cleaners acts as a sporicide, which appears to be ineffective or ineffectively used based on the identification of spore-forming bacteria during environmental monitoring.

OBSERVATION 7

The written stability testing program is not followed.

Specifically, the procedure for extending expiration dates with stability data, SOP 3.17, is not followed. Stability data is insufficient to support the expiration dates assigned to injectable drug products, which include expiration dates of up to 570 days. Only (b) (4) (b) (4) with no testing between (b) (4) (b) (4). For example Lipostat, Lipostat Plus, and Sulfa-Free Lipostat are assigned expirations of 570 days and Cyanocobalamin is assigned an expiration of 450 days.

OBSERVATION 8

Drug product containers and closures were not sterilized and processed to remove pyrogenic properties to assure that they are suitable for their intended use using a validated process.

Specifically, vials and glassware used for injectable drug products are sterilized and depyrogenated in-house using

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a non-validated process. Within the ISO 8 Prep Room, vials are (b) (4) (b) (4) They are (b) (4) in the ISO 7 Ante Room prior (b) (4) (b) (4)

(b) (4) (b) (4) (b) (4) located in uncontrolled rooms, and are (b) (4) for (b)(4) (b) (4) There has been no (b) (4) studies for the (b) (4) determined. (b) (4) are used approximately (b) (4) There is no assurance the vials and glassware are adequately sterilized and depyrogenated.

OBSERVATION 9

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

Specifically, on 8/31/2015,

a) During the compounding of Medroxyprogesterone Acetate Suspension Vehicle, Lot 08312015@3, in the ISO 8 Prep Room, I observed personnel to be wearing all non-sterile garb, with the exception of sterile gloves. The gloves are not donned in a sterile manner and are sanitized using non-sterile (b) (4)

b) During the compounding of Medroxyprogesterone Acetate 150 mg/mL, Lot 08312015@2, I observed personnel to be wearing no protective covering over their eyes, cheeks, or forehead, leaving their skin exposed within the ISO 5 critical work zone.

OBSERVATION 10

Batch production and control records do not include complete information relating to the production and control of each batch.

Specifically, records are sometimes or always lacking the following information:

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a) Actual and theoretical yield
b) Label samples and reconciliation
c) Dates for signatures
d) Verification of shortage status prior to production
e) The number of vials produced, sent for sampling, and kept
f) Verification of calculations
g) References to investigations
h) Final batch disposition
i) Batch release signature and date

OBSERVATION 11

The labels and containers of your outsourcing facility's drug products do not include information required by section 503B(a)(10).

Specifically,

The following information is not found on some of your drug product labels:

1. The statement "Not for resale."

Examples of drug product labels that do not contain this information include:

a) Testosterone Cypionate/Testosterone Propionate 180mg/20mg/ml
b) Triamcinolone Acetonide USP 80mg/ml 10ml Vial
c) Trimix (Papaverine 30mg/Alprostadil 10mcg/Phentolamine 1mg/ml) 5ml Vial

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*Dates of inspection: 8/24-28/2015, 8/31-9/3/2015, 9/17/2015, 9/23/2015

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."