DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	02/23/2016 - 03/02/2016
	FEI NUMBER 3012038236

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Rene F. Garza, CEO/Partner

FIRM NAME	STREET ADDRESS
Stonegate Pharmacy LP	2501 W. William Cannon Drive, Ste 203
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Austin, TX 78745-5255	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 do not include adequate validation of the sterilization process.

Specifically,

a) Your firm has not validated the sterilization process for any of the drug products that you prepare. Your firm prepares various drug products from bulk non-sterile active pharmaceutical ingredients (API) and excipients that are then either (b) (4) (b) (4) or processed (b) (4) The drug products that are (b) (4) or (b) (4) include Testosterone pellets (various strengths), Testosterone/Anastrozole pellets (various strengths), Estradiol pellets (various strengths) and Tacrolimus. Your firm has no documentation of the qualification of the (b) (4) and (b) (4) or how the (b) (4) for the pellets were developed.

b) Your firm does not (b) (4) of drug products and equipment/utensils that are (b) (4) as required by your SOP 8.010 Sterilization and Depyrogenation, version 1.0 effective 8/1/15.

c) Your firm does not follow the manufacturer's instructions for (b) (4) (b) (4) when used. The manufacturer's package insert states that the (b) (4) are to be (b) (4) for (b) (4) sterilization processes. Your firm does not (b) (4) nor do you have a (b) (4) to ensure that the (b) (4) has (b) (4) . According to your technician, the (b) (4) is checked for (b) (4) by a "Pharmacist" after (b) (4) (b) (4) .

d) Media fills performed by your firm with each of the operators that work preparing

injectable drug products do not closely simulate actual production conditions or cover worst case or most challenging conditions. In routine production, your firm fills various size vials ((b) (4)) and batch sizes can be in excess of (b) (4) . The media fill your firm performs has the operator filling (b) (4) vials and (b) (4) vials Your firm also does not perform any environmental monitoring (viable air or surface) during the media fill.

OBSERVATION 2

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

Specifically,

a) Your firm is not performing environmental monitoring of the ISO 5 area every day that your firm is preparing drug products. Your firm is collecting viable surface samples (b) (4) .

A review of the Clean Room Facility Surface Sampling Logs from August 2015-January 2016 showed that your firm failed to document the date the samples are taken, how long they are incubated and at what temperature. In addition, your firm failed to document the results (b) (4) , and for (b) (4) failed to document the lot number and type of media used.

Viable air monitoring is only performed every (b) (4)

b) Your firm is not monitoring each operator working in the ISO 5 area and ISO 7 clean room each day that drug products are prepared. Your firm is currently sampling the fingertips of operators (b) (4) .

c) There is no documentation of the actual pressure differential measurement between the ISO 7 Cleanroom (where the (b) (4)) and the ISO 8 Ante Room (b) (4)) and between the ISO 8 Ante Room and the ISO 8 Non-Sterile (b) (4) Room (b) (4) during operations. The documentation of the (b) (4) check of the

pressure differential only documents "pass" or "fail" for the reading.

OBSERVATION 3

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

Specifically,

a) Your firm is using non-sterile wipes when disinfecting the ISO 5 laminar flow hood (LFH).
b) Your firm is (b) (4) of Sterile (b) (4) for disinfection of the ISO 5 laminar flow hood. Your firm is using Sterile (b) (4) for disinfection of the floors and walls in the ISO 7 Cleanroom. Neither the (b) (4) nor the (b) (4) is sterile. Your firm is not documenting which disinfectant is being used (b) (4). Your technician said the contact time for the disinfectants used in the hood is approximately (b) (4) (b) (4). Your firm does not have documentation to demonstrate that these products are effective in cleaning/disinfecting the laminar flow hood and the room.
c) For the (b) (4), there is no documentation of when the product was (b) (4) and no expiration date given to the product. Your firm has no documentation to show the product is stable for the approximately (b) (4) it is used after preparation (b) (4)

OBSERVATION 4

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

Specifically,

a) The general gowning attire for entry into the ISO 5/ISO 7 classified areas consists of the following: scrubs worn from outside the facility, a disposable lab coat, a single hair net, a single ear-loop face mask, gloves and dedicated shoes. All are non-sterile with the

exception of sterile gloves. The general gowning requirements leave exposed skin around the eyes, forehead and neck of the person preparing the drug product.

On 2/23/16, we observed your firm prepare the following injectable drug products:

- Lot #02232016:01@4 of Trimix (Papaverine/Phentolomine/Alprostadil) 30/0.01mg/mL injectable, Beyond Use Date: April 8, 2016
- Lot #02232016:58@5 of Trimix (Papaverine/Phentolomine/Alprostadil) 30/0.012mg/mL injectable, Beyond Use Date: April 8, 2016
- Lot #02232016:73@6 of Trimix (Papaverine/Phentolomine/Alprostadil) 30/0.5/0.02mg/mL injectable, Beyond Use Date: April 8, 2016
- Lot #02232016:81@8 of Trimix (papaverine/Phentolomine/Alprostadil) 23/0.77/0.038mg/mL injectable, Beyond Use Date: April 8, 2016

b) The general gowning attire for the preparation of the Testosterone, Testosterone/Anastrazole and Estradiol pellet drug products performed in a (b) (4) in the Non-Sterile (b) (4) Room (b) (4) (ISO Class 8) is scrubs worn from outside the facility, a disposable lab coat, a single hair net, a single ear-loop face mask, booties and gloves. All are non-sterile. On 2/24/16, we observed your firm prepare (b) (4) pellets of lot #02242016:76@14 (Beyond Use Date: August 22, 2016).

OBSERVATION 5

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) During the certification of the ISO 5 Laminar Flow Hood (LFH) and the ISO 7 Cleanroom on (b) (4), there was an environmental monitoring failure reported by the 3rd party vendor for viable air. There were 6 CFU found in the (b) (4), 12 CFU in the (b) (4), 2 CFU found in the (b) (4) and 24 CFU in the (b) (4) The organisms found were Cladosporium and Yeasts in the (b) (4),

Aspergillus niger, Cladosporium and Yeasts in the (b) (4), Penicillium in the (b) (4) and Cladosporium, Yeasts, Fusarium and Non-sporulating fungi in the (b) (4) No investigation into the failure was performed by your firm to determine the cause of the failure. The 3rd party vendor returned (b) (4) to re-sample and no colonies were detected. From (b) (4) approximately (b) (4) lots of drug products were prepared by your firm in the ISO 5 LFH.

b) Your firm has no documentation of an investigation being performed when Methylcobalamin 1mg/ml Injection, Lot #07302015:33@26 failed potency testing on 9/25/15. The test revealed that the product had a potency of 18.8% whereas the product specifications are (b) (4). This lot was distributed to a customer.

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, your firm packages the Testosterone, Testosterone/Anastrazole and Estradiol pellets into non-sterile/non-depyrogenated (b) (4) (b) (4). Your firm has no documentation to show that this packaging and container/closure system is suitable to protect the drug product from external factors that may affect the quality and sterility of the drug product over time.

OBSERVATION 7

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

Specifically, your firm packages the Testosterone, Testosterone/Anastrazole and Estradiol pellets into non-sterile/non-depyrogenated (b) (4) (b) (4). Your firm does not process the (b) (4) prior to packaging to remove pyrogenic properties. Your firm has not validated the sterilization (b) (4) for the pellets and has no documentation to show that the (b) (4) are rendered sterile after being (b) (4).

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OBSERVATION 8

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

Specifically, your firm does not conduct routine sterility or endotoxin testing for all injectable drug products produced. Per your SOP 9.120 Sterile Compounding Finished Preparation Testing, version 2.0 effective 8/1/15, sterility testing is to be performed for (b) (4) The procedure also states that endotoxin testing is to be performed for sterile drug products that are (b) (4) Your firm is not following your written procedure for sterility or endotoxin testing.

OBSERVATION 9

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

Specifically, your firm does not have a written stability testing program to determine Beyond Use Dates (BUD) placed on all your drug products. For example,

Your firm has no documentation to justify the following BUDs placed on these injectable drug products prepared by your firm.

I. Estradiol 6.25mg pellet Lot #01152016:60@10, BUD: 180 days
II. Testosterone 80mg pellet (all lots) BUD: 180 days
III. Hydroxyprogesterone Caproate 250mg/mL Oil Injectable Solution (all lots) BUD: 90 days
IV. Methylcobalamin 1mg/ml Injection Solution Lot #12292015:47@23, BUD: 60 days. Your firm also does not label this product to be refrigerated as stated in the Formula Worksheet.
V. Lipo-B Injection (Methionine/Choline Chloride/Inositol/Methylcobalamin 15/100/50/0.02mg/mL) Lot #12142015:62@1, BUD: 90 days. Your firm also does not label this product to be refrigerated as stated in the Formula Worksheet.
VI. Chorionic Gonadotropin Multidose Vial 1000U/ML Solution Lot

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#01142016:49@20, BUD: 90 days

OBSERVATION 10

Written procedures are not established for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically,

a) Your firm cleans (b) (4) and other utensils such as (b) (4) used to process drug products prior to sterilization, by (b) (4) with (b) (4) brand household dishwashing detergent and then in a household style dishwasher using (b) (4) (b) (4) brand dishwashing gel. The water supplied to the dishwasher is (b) (4) (b) (4) water. Your firm has not validated this cleaning process to demonstrate that it is adequate and that no residue or cross contamination of drug substances or cleaning products occurs.

b) SOP 8.010 Sterilization and Depyrogenation, version 2.0 effective 8/1/15, states that equipment must be "(b) (4) (b) (4)" to achieve depyrogenation. Your firm is placing (b) (4) used for making sterile injectable drug products in the (b) (4). Your firm has no documentation to show that the (b) (4) will be depyrogenated using that (b) (4)

OBSERVATION 11

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, your firm does not conduct routine testing for potency for all drug products produced by your firm. Per your SOP 9.120 Sterile Compounding Finished Preparation Testing, version 2.0 effective 8/1/15, potency testing is to be performed (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Margaret M. Annes, CSO Margaret M. Annes Patty P. Kaewussdangkul, CSO Patty P. Kaewussdangkul	03/02/2016

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OBSERVATION 12

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

Specifically,

a) Your firm does not calibrate (b) (4) used to monitor the following:

i) The (b) (4) Testosterone/Anastazole pellets and depyrogenation of glassware.
ii) The (b) (4) used to (b) (4) drug products and equipment/utensils.
iii) Refrigerator and freezer used to store finished sterile drug products
vi) (b) (4) Incubators used to incubate environmental monitoring samples, personnel monitoring samples and media fill vials

b) Your firm does not calibrate the pressure gauges used to monitor the measurement of the pressure differential between the ISO 7 Cleanroom (where the (b) (4)) and the ISO 8 Ante Room (where (b) (4)) and between the ISO 8 Ante Room and the ISO 8 Non-Sterile (b) (4) Room (b) (4)

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