DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US Customhouse Rm900 2nd & Chestnut St Philadelphia, PA 19106 (215)597-4390 Ext:4200 Fax:(215)597-0875	6/28/2016-8/1/2016* FEI NUMBER 3012124155

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Tari E. Shapiro , Pharmacist in Charge

FIRM NAME	STREET ADDRESS
ImprimisRx Pharmacy LLC	780 Primos Ave Ste E
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Folcroft, PA 19032-2000	Producer of Non-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

Adequate lab facilities for testing and approval or rejection of components, drug product containers and drug products are not available to the quality control unit.

Specifically, no testing is performed for aqueous solutions and suspensions for inhalation, encapsulated powders for inhalation, and capsules for oral administration to determine if they meet specifications for potency and appropriate levels of microbiological organisms. For example,

a) there is no testing to demonstrate that individual units of drug products produced by the firm contain the intended, labeled dose of active drug ingredient. For example, Budesonide 0.6mg/2ml Solution Lot 06292016:44 is a suspension produced in a batch size of (b) (4) [redacted] process is not defined in the master batch production record.

b) there is no testing to demonstrate that the drug products meet the microbiological specifications established by the firm to be (b) (4) [redacted] for aqueous solutions and suspensions intended for inhalation through the nasal passage with the use of an atomizer or nebulizer device and encapsulated powders for dissolution by the patient, intended for inhalation through the nasal passage with the use of an atomizer or nebulizer device.

c) the firm has conducted no testing of non-sterile aqueous solutions and suspensions and encapsulated powders for dissolution by the patient, intended for inhalation through the nasal passage with the use of an atomizer or nebulizer device to determine the particle size of the aerosolized drug to ensure that the non-sterile drug is not delivered to the lower airway.

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d) there is no testing to demonstrate that the Pentosan Polysulfate Delayed Release 150mg and 200mg Capsules are formulated to provide the patient with a time-released delivery of this drug which is produced from a (b) (4) Pentosan Polysulfate (b) (4) (b) (4)

OBSERVATION 2

An adequate number of batches of each drug product are not tested nor are records of such data maintained to determine an appropriate expiration date.

Specifically,

a) the firm has not conducted testing of drug products that were produced by the current production methods in the current production facility to support the 30-day, 60-day, and 90-day beyond use dates (BUDs) for aqueous solutions and suspensions intended for inhalation through the nasal passage with the use of an atomizer or nebulizer device, the 180-day BUD for encapsulated powders for dissolution by the patient for inhalation through the nasal passage with the use of an atomizer or nebulizer device, or the 180-day BUD for capsules for oral administration.

Data to support the current BUDs of drug products, such as aqueous solutions and suspensions for inhalation Budesonide 0.6mg/2ml, Betamethasone 0.5mg/2ml, and Vancomycin 200mg/2ml, was limited to laboratory result reports for batches of drug products that were made in other pharmacies or in the decommissioned production room of this pharmacy, for which no supporting documentation, including production records, have been maintained or discussed in the report. Additionally, testing was limited to (b) (4) and included no scientific rationale to demonstrate that these tests alone are stability-indicating.

In addition, the firm has not conducted testing to demonstrate the stability of aqueous solutions and suspensions intended for inhalation, which are packaged in clear colorless plastic unit-dose ampules, and labeled to "protect from light".

b) APIs and excipients are used in the manufacture of compounded drugs, where the BUD assigned to the compounded drug product exceeds the expiration date of the API or excipient incorporated into the batch. For example, API Betamethasone (b) (4) with expiration date of August 31, 2016 was used by the firm on 6/22/16 to compound Betamethasone Solution 0.5mg/2mL for Inhalation Lot 06222016:36, which was assigned a 90-day BUD of September 20, 2016.

OBSERVATION 3

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically, appropriate production practices are not established and/or followed for the preparation of drug products to preclude the contamination by microbiological organisms, foreign particulates, or cross-contamination from other drug products. For example,

a) The firm has failed to follow their procedure, SOP P-6.10: Clean Room Certification, which requires certification of the Clean Room HEPA filters and ISO-5 hoods in the drug production area, reportedly to ensure that drug production is conducted in a low-particulate environment. The current production area, used for production of all drug products, has been operational since approximately 5/11/2016, without certification. Records show that the HEPA filter directly behind and above the primary weighing and mixing work surface for drug production is damaged beyond repair and is reportedly awaiting replacement. Furthermore, the primary weighing and mixing work surface for drug production is performed in a (b) (4) hood, which (b) (4) (b) (4)

b) The certification of the ISO-5 hood, required per the firm's procedures for the unit-dose ampule filling process, is inadequate in that the certification activities did not show dynamic conditions in the hood and do not include an assessment of viable particulates. The smoke study video of (b) (4) laminar flow hood (b) (4) in which the (b) (4) (b) (4) (b) (4) (b) (4) (b) (4)

c) The firm has failed to establish adequate procedures for the use of the non-dedicated (b) (4) to preclude contamination and/or cross-contamination of drug products, in that:

i) The (b) (4) are stored in an (b) (4) (b) (4)

ii) (b) (4) is selected and used (b) (4) for the ampule-filling operation of different drug products, wherein initial set-up of the (b) (4) is limited to wiping (b) (4) with non-sterile (b) (4) with a non-sterile disposable wipe, followed by a (b) (4) (b) (4)

iii) The batch to batch changeover of different drug products is (b) (4) (b) (4) (b) (4) (b) (4)

d) The firm has failed to establish adequate gowning procedures to prevent particulates from becoming incorporated into drug products, in that gowning articles do not cover all skin, and articles are donned at the discretion of the operator, including no gowning, or partial gowning. Gowning articles are limited to disposable lab coat, hair net, face mask, beard covers and gloves.

e) Unrestricted personnel movement with no re-gowning, into and out of the drug production area was observed, whereby airborne particulates in the production area may become incorporated into the drug products. Additionally, personnel wearing clothing dragging on the floor, were observed walking into and out of the drug production area, whereby particulates swept from the floor may become airborne.

f) Two open trash receptacles located on both sides of the primary weighing and mixing work surface for drug production, contain exposed waste including disposed wipes used to clean powders from the work surface between batches of different drug products, which powders may become airborne upon the drying of the wipe and movement of the operator.

g) The procedures for the seal integrity inspection (b) (4) do not ensure that each unit-dose vial is sealed to prevent contamination of the product or changes in concentration of the drug product due to evaporation. The seal integrity check is (b) (4) (b) (4) The pharmacist reportedly (b) (4) (b) (4) however detection of seal integrity failures observed during the inspection, required (b) (4)

OBSERVATION 4

Separate or defined areas to prevent contamination or mix-ups are deficient regarding the manufacturing and processing operations.

Specifically,

a) Penicillin and/or related beta-lactam drug products are produced on the same equipment in the same production areas used for the production of other drugs produced by the firm in the absence of appropriate measures to eliminate the potential for cross-contamination. For example,

i) On 4/04/16, Clindamycin 150mg/3ml Solution Lot 7120 was produced at the same time as Ceftazidime 600mg/4ml Solution Lot 7121.

ii) On 6/02/16, Cefepime 200mg/2mL Lot 06012016:88, Mupirocin 15mg/4mL Lot # 06022016:97, Vancomycin 200mg/2mL Lot # 06022016:41, and Chelating Agent PX 15mg/2mL Lot # 06022016:48 were produced.

iii) On 6/29/16, Cefuroxime 300mg/4mL Lot # 06292016:38, Levofloxacin 100mg/4mL Lot # 06292016:19, and Budesonide 0.6mg/2mL Lot # 06292016:44 were produced.

Additionally, no testing of compounded drugs is performed for drugs that may unintentionally contain beta-lactam and sulfa drugs.

b) Multiple batches of different drug products being produced are present at the same time in the production area and the ampule-filling production area, including the containers of active drugs and

other raw materials, for which limited labeling is present on the (b) (4) and for which (b) (4) in the production area without status labeling to indicate the phase of production, (b) (4). For example, on 6/28/16, Budesonide 0.6mg/2ml Solution Lot 06282016:19, Amphotericin B 5mg/3ml Solution Lot 06282016:13, and Tobramycin 100mg/2ml Solution 06282016:57 were observed in the drug production (b) (4) area at the same time, including all raw materials used to produce the batches.

OBSERVATION 5

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

Specifically, established personnel gowning in the drug production and ampule-filling areas is practiced at the discretion of the pharmacy technicians and pharmacists, including no gowning, or partial gowning consisting of disposable lab coat, hair net, face mask, beard covers and gloves. No garments for complete skin coverage are available. Personnel move from the uncontrolled surrounding room into each of the (b) (4) and exit and reenter the (b) (4) without removing and re-donning gowning articles. Gowning articles are not sterile and are reportedly used primarily as personal protective equipment to prevent operator exposure to the drug products.

OBSERVATION 6

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use.

Specifically, the (b) (4) hood) located in the (b) (4) production area is used for (b) (4) n the production of drug products. The unit (b) (4) (b) (4) (who is partially gowned or

not gowned with exposed skin areas and non-sterile garments, see Observation 3), (b) (4) [redacted]

OBSERVATION 7

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

Specifically,

a) there is no data to demonstrate that the cleaning of the non-dedicated (b) (4) [redacted] is adequate to prevent contamination of aqueous drug products. The non-dedicated (b) (4) [redacted], with an approximate (b) (4) [redacted], is used to (b) (4) [redacted] from a (b) (4) [redacted]. The (b) (4) [redacted] are reportedly used on (b) (4) [redacted] basis.

i) (b) (4) [redacted] non-dedicated (b) (4) [redacted] is selected and used (b) (4) [redacted] for the ampule-filling operation of different drug products, wherein cleaning of the (b) (4) [redacted] is limited to spraying and wiping the exterior of the (b) (4) [redacted] with non-sterile (b) (4) [redacted] with a non-sterile low-lint disposable wipe, (b) (4) [redacted]

ii) Cleaning in between batches of different drug products and at the end of the production day is limited to the (b) (4) [redacted]. The drug solution uptake end of the (b) (4) [redacted] is (b) (4) [redacted] At the end of the production day, (b) (4) [redacted]

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iii) The (b) (4) is (b) (4) inspected (b) (4) on the (b) (4) and are reportedly (b) (4) . The dates of (b) (4) for the (b) (4) currently in service are unknown.

b) there is no data to demonstrate that the cleaning of the glassware used for the compounding of drug products is adequate to prevent contamination of aqueous compounded drug products. For example, glassware is washed (b) (4) (b) (4) (b) (4) (b) (4) , the glassware is reportedly (b) (4) placed on a cart, which is rolled into the drug production area, through the uncontrolled Pharmacy Lab area.

OBSERVATION 8

Approved components, drug product containers and closures are not retested or reexamined as appropriate for identity, strength, quality and purity after storage for long periods with subsequent approval or rejection by the quality control unit.

Specifically, (b) (4) clear plastic ampules, reportedly (b) (4) are not retested to establish the time period that the vials remain in an acceptable status for the intended use. The (b) (4) are used in the unit-dose packaging of aqueous solutions and suspensions for inhalation through nasal passages with the use of an atomizer or nebulizer device, including some of which are not (b) (4) , contain no preservative, and are stored at ambient temperatures with a BUD of 90 days, such as Budesonide 0.6mg per 2 ml Solution Lot 06292016:44, produced on 6/29/16. In addition, opened and partially used packs of the ampules are stored on a cart in the (b) (4) area for packaging of subsequent batches.

*DATES OF INSPECTION

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X Lisa B Orr

Lisa B Orr
Investigator
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