

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER US Customhouse Rm900 2nd & Chestnut St Philadelphia, PA 19106 (215) 597-4390 Ext:4200 Fax: (215) 597-0875	DATE(S) OF INSPECTION 1/23/2017-2/17/2017* FEI NUMBER 1000121499
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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Joseph G. Bettinger , Owner

FIRM NAME Hieber's Pharmacy	STREET ADDRESS 3500 5th Ave
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CITY, STATE, ZIP CODE, COUNTRY Pittsburgh, PA 15213-3337	TYPE ESTABLISHMENT INSPECTED Producer of Sterile Drug Products
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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

Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to aseptic processing of drug products.

Specifically, aseptic operations are not performed in separate or defined areas or under appropriate controls as necessary to prevent contamination of drug products purporting to be sterile such as Gentamicin 28.8mg/ml 60 ml #45 units Batch 06292016@1, Histamine Phosphate (with Preservative) 2.75mg/5ml Sterile Inj. Batch # 10122016@10, Dexamethasone Sodium Phosphate (MDV) 24mg/ml Injection Batch # 11142016@4, and Hydroxocobalamin B12 A (PF) 1000mcg/ml Injection, Batch # 01202017@3. For example,

a) during certifications for (b) (4), the firm did not qualify the ISO 5 (b) (4) glovebox isolator and the surrounding room as ISO 7 in that certification activities were not conducted under dynamic conditions, did not include documented smoke studies under dynamic conditions, did not include an evaluation of the (b) (4) HEPA filters in the surrounding room, and there was inadequate assessment of the pressure differentials between the (b) (4) glovebox isolator, the surrounding room, and the adjacent uncontrolled area. Additionally, there is no record to indicate that the certification activities performed by at least (b) (4) outside firms were reviewed and found acceptable to meet the reported ISO-5 conditions and how the reported ISO-8 conditions in the surrounding room were found acceptable.

b) there has been no assessment of the impact of the firm's practice of (b) (4) in the (b) (4) isolator glovebox and the surrounding room, (b) (4) and which (b) (4) (b) (4), which may (b) (4)

c) the sole entrance door to the Sterile Compounding Room is through a small vestibule approximately (b) (4) (b) (4) in size, which has carpet on the floor.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Gayle S Lawson, Investigator (CTNH) Lisa B Orr, Investigator	DATE ISSUED 2/17/2017
	X Lisa B Orr Lisa B Orr Investigator Signed by: Lisa Orr -S	

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d) handwashing and partial gowning is performed in a small (approximately (b) (4)) bathroom accessed through the carpeted vestibule, in which a toilet is located and which the sterile compounding technician must walk past, after handwashing and donning the hair bonnet and face mask, to enter the Sterile Compounding Room. The toilet is (b) (4) from the sole entrance door to the Sterile Compounding Room. During handwashing and gowning on 1/26/17, we observed the toilet seat in the open position.

e) the (b) (4) and the (b) (4) (b) (4) used for sterilizing drug products and sterilizing and depyrogenating glass vials used to produce drug products, are located in a room that lacks environmental controls to prevent contamination. (b) (4) is reportedly (b) (4) (b) (4) to protect the components and drug products from contamination.

OBSERVATION 2

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

Specifically,

a) the (b) (4) (b) (4) are not sterile and there are no procedures for the preventive maintenance of the sleeves, to include routine maintenance such as sterilization and inspection of the (b) (4) for acceptability for their intended/continued use.

b) there are no procedures to demonstrate that the (b) (4) used in the (b) (4) are adequately cleaned, and are free of cleaning agents, chemicals and microbiological organisms.

c) the cleaning of the (b) (4) glovebox isolator and sterile compounding room is conducted using (b) (4) types of non-sterile low-lint wipes. (b) (4) and there are no documented contact times for the cleaning solutions such as the (b) (4) the use of which was observed on 01/26/17.

d) (b) (4) cleaning procedures for the sterile compounding room include dry sweeping the floor with a plastic bristle broom and sweeping debris into a dustpan which may cause an increase in airborne particulates immediately preceding production operations.

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e) no environmental monitoring is performed during production in the (b) (4) glovebox isolator or in the sterile Compounding Room.

f) Media fills performed by the firm are inadequate in that they are limited to (b) (4) (b) (4). For example, the media fill performed on (b) (4) following the High Risk Media Fill Logged Formula Worksheet (SOP 1.632 Sterile Compounding Staff Competency – High Risk Media Fill), used (b) (4) samples which were tested and found to be sterile.

OBSERVATION 3

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

Specifically, non-sterile gowning articles are worn by the technician during the (b) (4) Cleaning of the (b) (4) glovebox isolator during which (b) (4) (b) (4) of the isolator. Gowning articles consist of a non-sterile hair bonnet, non-sterile half-face surgical mask (ear-loop style), non-sterile non-shedding knee-length gown that ties at the neck and is open in the back, which (b) (6) wears over street clothes and which leaves exposed skin on (b) (6) neck and face. Sterile gloves are donned for cleaning the isolator; however the technician used (b) (6) gloved hands to crumble the glove wrappings which (b) (6) disposed in the trash.

OBSERVATION 4

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

Specifically, the firm did not perform testing to confirm sterility and/or absence of pyrogens of drug products purporting to be sterile. For example, the firm produced approximately (b) (4) batches of Gentamicin 28.8mg/ml 60 ml during the period from 01/01/2015 to present, for which no testing was performed. For example, the firm produced Gentamicin 28.8mg/ml 60 ml (b) (4) Batch 06292016@1, for which there was no testing to confirm sterility and/or absence of pyrogens.

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OBSERVATION 5

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

Specifically, the firm did not perform testing to confirm the identity and strength of drug products. For example, the firm produced approximately (b) (4) batches of Gentamicin 28.8mg/ml 60 ml during the period from 01/01/2015 to present, for which no testing was performed. For example, the firm produced Gentamicin 28.8mg/ml 60 ml (b) (4) Batch 06292016@1, for which there was no testing to confirm the identity and strength.

OBSERVATION 6

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

Specifically,

a) there is no data to support the beyond use dates assigned to drugs produced by the firm. For example, the firm produced Gentamicin 28.8mg/ml 60 ml (b) (4) Batch 06292016@1, a solution for bladder irrigation, which is labeled to store frozen for 45 days and thawed and refrigerated for up to 3 days. The firm has conducted no testing to demonstrate that the appropriate physical, chemical, and microbiologic properties are stable over the labeled shelf life.

b) the firm produces sterile injectable drug products containing preservatives, such as Progesterone 50mg/ml Injection Batch # 11082016@23, Histamine Phosphate (with Preservative) 2.75mg/5ml Sterile Inj. Batch # 10122016@10, Dexamethasone Sodium Phosphate (MDV) 24mg/ml Injection Batch # 11142016@4, and Hydroxocobalamin B12 A (PF) 1000mcg/ml Injection, Batch # 01202017@3, for which there is no data to demonstrate the antimicrobial effectiveness of the preservative over the course of the labeled shelf life.

OBSERVATION 7

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

Specifically, the firm has not validated the (b) (4) sterilization processes including the (b) (4) process and the (b) (4) process for injectable drugs produced by the firm. For example, the firm produced injectable drugs such as Methylcobalamin (PF) 1000 ug/mL Batch # 12122016@5 and Histamine Phosphate (with

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Pittsburgh, PA 15213-3337	Producer of Sterile Drug Products

Preservative) 2.75mg/5ml Sterile Inj. Batch # 10122016@10, each of which were (b) (4) (b) (4) and Hydroxocobalamin B12 A (PF) 1000mcg/ml Injection, Batch # 01202017@3 which was (b) (4). There are no validation studies to assure the effectiveness of the sterilization processes.

OBSERVATION 8

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

Specifically, the sterilization and depyrogenation process established by the firm (SOP 2.281 and SOP 4.31) for components such as glass vials and vial stoppers have not been validated. For example, glass vials and vial stoppers which are sterilized and/or depyrogenated by the firm are used to produce injectable drugs such as Hydroxyprogesterone caproate Injection Batch # 09262016@11 and Histamine Phosphate (with Preservative) 2.75mg/5ml Sterile Inj. Batch # 10122016@10, for which no sterilization/depyrogenation validation for the components has been conducted. Additionally, there is no data to demonstrate that vials processed in this manner remain sterile and pyrogen free for the labeled time period of six months.

***DATES OF INSPECTION**

1/23/2017(Mon), 1/24/2017(Tue), 1/25/2017(Wed), 1/26/2017(Thu), 1/27/2017(Fri), 2/06/2017(Mon), 2/07/2017(Tue), 2/08/2017(Wed), 2/09/2017(Thu), 2/10/2017(Fri), 2/17/2017(Fri)

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