DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612 (949) 608-2900 Fax:(949) 608-4417 Industry Information: www.fda.gov/oc/industry	08/03/2015 - 08/18/2015* FEI NUMBER 3005530267

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Hyun Joon Ro, Pharm D., President & Owner

FIRM NAME	STREET ADDRESS
Pacific Healthcare, Inc dba B&B Pharmacy	10244 Rosecrans Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Bellflower, CA 90706	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 are not followed.

Specifically,

A. On 08/03/15, we observed the technician (b) (6) making Trimix lot # 08032015@2 BUD 01/30/15 from three (b) (4) (Alprostadil, Phentolamine, and Papeverine) in ISO 5 (b) (4) hood # 1 where (b) (6) hands were blocking the airflow over these vials. These (b) (4) vials are multi-use vials with (b) (4) during the production process.

B. The firm's Policy # 1751.1, date effective 11/15/10, date revised 07/29/13 titled "Sterile Injectable Recordkeeping Requirements" is deficient in that it does not state the frequency of media fill requirement. In actual practice, the firm performs media fill on (b) (4) basis. The last media fills conducted were on (b) (4) for ISO 5 (b) (4) hood (b) (4)(b) (4) (not ISO 5 (b) (4) hood # 1) for the following personnel with passing results. Per the owner (ER) and technician (b) (6), the firm uses ISO hood (b) (4) much more frequent than ISO hood # 1 but the firm does not record such information.

   a. ER, owner – only signing off formula worksheets and does not perform sterile production
   b. (b) (6), technician – (b) (4) technician doing sterile production
   c. SM, PIC (pharmacist in charge) – only signing off formula worksheets and does not perform sterile production
   d. (b) (6), staff pharmacist – only signing off formula worksheets and does not perform sterile production

C. The owner stated that the firm followed CA Board of Pharmacy to conduct media fills or (b) (4)

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(b) (4) basis.

D. The firm did not evaluate whether or not their media fill testing simulates actual production environment in accordance with their Media-Fill Testing Notes which states "Media Fill Tests are performed during(b) (4) compounding procedures." For example, the firm made (b) (4) (Alprostadil lot # (b) (4) , (b) (4) Phentolamine lot # (b) (4) (b) (4) and Papaverine lot # (b) (4) (b) (4) and then (b) (4) the final finished drug product (e.g. Trimix lot # 08032015@2, BUD 01/30/2016). This process involves (b) (4) (b) (4) (b) (4) (b) (4) to make the finished drug product. The media fill process per the Media-Fill Testing Notes states

(b) (4)

E. The firm failed to follow policy # 1751.6, date effective 11/15/10, date revise 07/29/13 titled "Training of Sterile Injectable Compounding Staff, Patient, and Caregiver"

a. Section 5.5.2 states to (b) (4) According to the technician (b) (6), they (b) (4) the glassware to (b) (4) to sterilize it. There were no records kept by the firm while they do sterilization.

b. Section 5.5.3 which states "If the glassware is to be stored and remain sterile and free of pyrogens, the following procedures shall be performed."...i. "The glassware shall be allowed to reach room temperature (b) (4) . The

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glassware shall be (b) (4) On 08/03/15, we observed beakers being kept in the ante room area (b) (4) (b) (4) . There is no label on there to show when it was sterilized and when they are expired from usage. The firm does not record when beakers are used in the formula worksheets. Per technician (b) (4), beakers are used to (b) (4) .

c. The (b) (4) (b) (4) used as (b) (4) has not been validated for the depyrogenation.

F. There is no validation for the (b) (4) used for the sterilization of stoppers and seals. There were no (b) (4) used. Stoppers are not tested for endotoxin. Vials are purchased sterile. Per technician (b) (4), stoppers are used to make (b) (4) sterile drug products that are (b) (4) sterilized (b) (4) (b) (4) per (b) (4)

(b) (4)

Per the technician, (b) (4) (b) (4) products are made as followed:

(b) (4)

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OBSERVATION 2

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

Specifically,

A. The firm does not have a written procedure requiring monitoring of non-viable, viable, surface, and personnel monitoring. Per the owner, the firm has not formally done any environmental monitoring for their ISO 5, 7, and 8 areas with exception of a (b) (4) for information only environmental monitoring (fingertip (b) (4) and air) of (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) on 11/12/14 to identify bacteria, mold, and/or fungus. Out of (b) (4) conducted for (b) (4) (b) (4) one test came up positive with 1 CFU for surface sampling of the (b) (4) (b) (4) in ISO 7 room # 1 which was identified as *Chaelomium globosum* on 12/24/14 by a third party lab. The firm (b) (4) (b) (4) (b) (4) which resulted in zero counts for this room # 1.

B. The firm does not conduct any smoke studies (dynamic and/or static) for (b) (4) ISO 5 hoods # 1 (b) (4) and ISO 7 rooms # 1 (b) (4) used to produce drug products. The ISO 5 (b) (4) hoods # 1 (b) (4) were last certified on 05/14/15. The hoods are currently being certified (b) (4) when although firm's policy # 1751, date effective 11/15/10, date revised 07/29/13 states (b) (4) needs to come in and test sterile room (b) (4)

OBSERVATION 3

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

Specifically,

A. On 08/03/2015 we observed two vials of Alprostadil (b) (4) (b) (4) with particulates floating in the vials. One of these vials was used to make a finished drug product, Trimix lot # 08032015@2, BUD 01/30/2016 which had a combination of (b) (4) additional (b) (4) Phentolamine (b) (4) and Papaverine (b) (4) as a sterile to sterile production without

any (b) (4) Each of these (b) (4) (b) (4) were made from active ingredients as non-sterile to sterile process with the following ingredients:

(b) (4)

The firm does not have any data to show that the container closure is not compromised (b) (4)

B. Potency analysis conducted for Trimix Inj lot # 06182013@16, third party assigned (b) (4) and reported on the CoA that "Precipitate of a light color could be seen inside the vial before testing. The vial was gently warmed which removed most of the particles but not all of

them." The firm did not conduct any investigation in regards to the precipitate observed because this lot was prepared only to test the potency of the three components, per the owner.

C. The firm does not have a written procedure requiring visual inspection. Per the PIC (SM), the firm does (b) (4) visual inspection but does not record such information on any of the formula worksheets. We did not observe any white/black background setup used for visual inspection of sterile drug products.

OBSERVATION 4

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

Specifically,

A. Policy # 1751.4, date effective 11/15/10, date revised 07/29/13 titled "Facility and Equipment Standards for Sterile Injectable Compounding" is deficient in that it does not have detailed descriptions of how to conduct cleaning including contact time requirement of cleaning reagents (no contact time studies). Per the PIC, the firm (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) while sterile (b) (4) is used on a (b) (4) basis. Cleaning is conducted on (b) (4) basis (b) (4) with either non-sterile (b) (4) or non-sterile (b) (4) and sterile (b) (4) Cleaning (b) (4) (b) (4) (b) (4) is conducted with sterile (b) (4) .

B. On 08/03/15 we observed the following deficiencies with the firm's cleaning practice of ISO 5, 7, and 8 areas:

a. Use of non-sterile (b) (4)) to clean ISO 5 hoods (b) (4) ISO 7 clean rooms # 1 (b) (4) and ISO 8 ante room.
b. Use of non-sterile wipes (b) (4) to clean ISO 5 hoods with sterile (b) (4)
c. Use of non-sterile gloves while cleaning surfaces including ISO 5 hoods
d. Use of non-sterile gowning inside the ISO 7 and while cleaning ISO 5 Area
e. Use of non-sterile mops to clean ISO 7 rooms (b) (4) Mops are stored upright behind the sink in ISO 8 area when not in used.

f. The operator came out of the clean room area with cleanroom garment to get a trash can and went back to the ISO 8 ante room without changing the gowning.

g. The operator used a liquid from an unidentified container to scrub (b)(6) hands (firm said this was non-sterile(b) (4)while cleaning the ISO 7 and ISO 8 areas.

h. The operator enter (b)(6) head into the hood (ISO 5 (b) (4) hood) to clean the interior of the hood while exposing skin such as neck, forehead, eyes, and eye brows.

i. Goggles are not worn during the cleaning process.

j. On 08/17/2015 we observed that the handsanitizer (b) (4))used inside the Ante room was expired on 09/14.

C. On 08/03/15, we observed the technician (b) (6) cleaned (b)(6) sterile gloves with a non-labeled bottle while making Trimix lot # 08032015@2 BUD 01/30/15. (b)(6) stated that the bottle was sterile(b) (4)

OBSERVATION 5

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

Specifically.

A. Policy # 1751.5, date effective 11/15/10, date revised 07/29/13 titled "Sterile Injectable Compound Attire" is deficient in that it does not require sterile apparel to be worn while working in ISO 5 and 7 areas. The gowning is performed in the Ante Room (ISO 8).

B. In actual practice, the firm used non-sterile gowning and had skin exposure. For example. on 08/03/2015, while performing a sterile production for Trimix lot number 08032015@2, BUD 01/30/2016, in Buffer Zone # 1 or ISO 7 room # 1 and ISO 5 (b) (4) the operator was wearing non sterile gowning with the exception of sterile gloves:

1. Non-sterile labcoat that leave the lower part of the street pants exposed.
2. Non-sterile mask that leave the eyes, eyebrows and part of the forehead exposed.
3. Non-sterile hair cover that, together with the mask, leaves part of the neck exposed.
4. No goggles were worn.

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OBSERVATION 6

Aseptic processing areas are deficient in that ceilings are not smooth and/or hard surfaces that are easily cleanable.

Specifically, on 08/03/15 we observed:

a. A gap between the plastic cover and the frame of the lamp at the ceiling in the ISO 7 area of Clean Room # 1. There were also dark specs inside the housing of the lamp. This lamp is located above the hood at approximately 2 feet away from the edge of the hood.

b. The lamination of the table where the hood of Clean Room # 1 is located had a space that leaves the wood exposed at a corner approximately 1 inch from the hood.

OBSERVATION 7

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

Specifically, the firm does not have a written procedure to address stability such as Beyond Use Date (BUD) assigned on (b) (4) drug products made. The firm sends out sterility and endotoxin testing to third party lab for (b) (4) (non-sterile to sterile) (b) (4). They perform in-house sterility testing (many without endotoxin testing) without any existing sterility testing procedure for some preparations (non-sterile to sterile) that not used for (b) (4) The firm does not perform any endotoxin testing in house. The firm does not perform sterility and/or endotoxin testing for sterile to sterile preparations. Sterility and endotoxin reviewed met specifications and (b) (4) . Per the owner, the firm used BUD given from (b) (4) formula worksheets which states "The Beyond Use Date assigned to the formula is in regard to the stability of the compound and does not address the sterility issue." The following are examples of preparations and/or finished drug products that do not have sterility and/or endotoxin tested at all or not tested at the end of BUD.

A. Alprostadil (b) (4) lot (b) (4) – (b) (4) third party sterility and endotoxin tested (non-sterile to sterile).

B. Phentolamine (b) (4) prepared on (b) (4)

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(b) (4) : third party sterility and endotoxin tested (non-sterile to sterile).

C. Papaverine (b) (4) prepared on (b) (4) – (b) (4) third party sterility and endotoxin tested (non-sterile to sterile).

D. Trimix lot # 08032015@2 (papaverine + PGE1 + Phentolamine Injection 30 mg:20mcg:1mg/ml Injectable) prepared on 08/03/15 with BUD of 01/30/16 – finished drug product: no sterility or endotoxin testing (sterile to sterile).

E. Estradiol Aqueous Injection Suspension 5mg/ml lot # 07272015@2 prepared on 07/27/15 with BUD of 10/25/15 – finished drug product: in house sterility tested (non-sterile to sterile).

OBSERVATION 8

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,

A. Beakers used are sterilized in a (b) (4) (b) (4) that is not qualified. The firm has a (b) (4) (b) (4) (b) (4) (b) (4) but it is used to (b) (4)(b) (4) (b) (4) . (b) (4)(b) (4) (b) (4) are located in the non-sterile production area, approximately (b) (4) apart from the door that access the sterile area. Per policy # 1751.6 section 5.5.2 "You then place the (b) (4) then (b) (4) . If the glassware is to be used immediately, it shall be (b) (4) , and then removed and immediately (b) (4) ." There is no documentation to demonstrate the temperature and the time that the glassware was exposed for depyrogenation. Per the technician, (b) (6), (b) (4) is cleaned (b) (4) using non-sterile (b) (4)

B. The firm has not qualified the incubator (b) (4) used to incubate media for sterility testing. In addition, the firm does not record daily temperature of the incubator.

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C. The firm uses (b) (4) (b) (4) used to crimp (b) (4) that require crimping. The firm does not have any validation study to demostrate the integrity of the container closure after (b) (4) crimping.

(b) (4)

OBSERVATION 9

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

Specifically, policy # 1735.6, date effective 11/15/10, date revised 07/29/13 titled "Compounding Facilities and Equipment" is deficient in that it does not require the firm to calibrate certain equipment and to NIST standards. For example,

A. Thermometers used to measure temperature of the refrigerator/freezer and ISO 7 rooms are not calibrated.

   a. (b) (4) thermometer is located in the (b) (4) refrigerator
   b. (b) (4) thermometer is located in the (b) (4) freezer
   c. (b) (4) are located in ISO 7 clean rooms

B. Gauges used to measure pressure differential in clean rooms are not calibrated. The firm does not document the air pressure differential reading.

C. Scale is calibrated at one weight (b) (4) only, not calibrated through the usage range (~ (b) (4)). The weight used is not calibrated against NIST standard weight.

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OBSERVATION 10

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

Specifically, the firm does not require complete information to be recorded on formula worksheets. Information such as hood # 1, clean room #1 , and stoppers used are not documented. For example,

(b) (4)

OBSERVATION 11

Washing and toilet facilities lack hot and cold water, soap or detergent, and air driers or single-service towels.

Specifically, the firm has a restroom located in pharmacy work area and there's no sink with hot and cold water, soap or detergent, air driers or single-service towels to wash hands. Employees who use this restroom have to go outside to use a lab sink to wash their hands. The lab sink is located in the production area and is also used to wash glassware and other equipment used in for the preparation of products. The firm has two other restrooms with sinks located at the opposite side of the pharmacy, in the break room.

*** DATES OF INSPECTION:**
08/03/2015(Mon), 08/04/2015(Tue), 08/06/2015(Thu), 08/07/2015(Fri), 08/10/2015(Mon), 08/11/2015(Tue), 08/13/2015(Thu), 08/17/2015(Mon), 08/18/2015(Tue)

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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."