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	03/16/2015 - 03/20/2015
	FEI NUMBER 3009422393

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Tina B. Aramaki, Vice President, Banner Pharmacy Services, LLC

FIRM NAME	STREET ADDRESS
Banner Pharmacy Services, LLC	7300 W Detroit St
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Chandler, AZ 85226-2410	503(B) 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 WE OBSERVED:

OBSERVATION 1

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

Specifically, monitoring of the firm's ISO 5 areas and ISO 7 area used to produce sterile drug products is not done during actual production, for example:

(a) Lack of active monitoring of differential pressures in the ISO 5 areas. There is no monitoring of the cleanroom pressure differential during aseptic processing of drug products. There are no devices to read pressure differentials between the ISO 5 areas to the ISO 7 area. The firm's ISO 5 areas are separated only by plastic curtains from the ISO 7 area.

(b) Lack of routine personnel monitoring for operators conducting compounding operations of aseptically processed drug products. Sampling of personnel gloves is not routinely conducted after daily operations. Sampling of personnel gloves is conducted (b) (4) .

(c) Insufficient frequency of environmental monitoring of the ISO 5 and ISO 7 environment surfaces. Surface sampling is not routinely conducted after daily operations. Surface sampling is conducted on (b) (4)

(d) Lack of viable particulate air monitoring in the ISO 7 area. There is no monitoring of the viable air particulates during aseptic processing of drug products in the ISO 7 environment. Viable air sampling is only conducted by an outside contractor (b) (4)

OBSERVATION 2

Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.

Specifically,

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(a) Your firm has never performed filter leak testing of the (b)(4) HEPA filters located in the ISO 5 areas. In our review of the past three room qualification reports, we observed a downward trend in HEPA filter air velocities coming from these HEPA filters and air exchanges in the surrounding ISO 7 area. In particular, initial room testing from 10/03 - 04/2013 showed average velocities of 54 feet per minute on the sterile compounded drug (east) side of the room and 80 feet per minute on the Total Parenteral Nutrition (west) side of the room, and 34.90 air exchanges per hour in the surrounding ISO 7 area. Testing on 03/24/2014 showed average velocities of 49 feet per minute on the east side and 48 feet per minute on the west side, and 27.63 air exchanges per hour in the surrounding ISO 7 area. Testing on 09/03/2014 showed average velocities of 34 feet per minute on the east side and 44 feet per minute on the west side, and 18.68 air exchanges per hour in the surround ISO 7 area. Per the firm's procedure SOP 02-02.01, "Sterile Facility Maintenance and Management", the firm's specification for air exchanges per hour is (b) (4) The firm has not replaced any HEPA filters since beginning operation in the cleanroom and has not performed any investigation regarding the room air exchange failure.

(b) The (b) (4) qualification of your ISO 5 areas is deficient in the following ways:

1. The viable air sampling was not always conducted under dynamic conditions.
2. The non-viable particulate count for the ISO 5 areas in the room qualification report is one average value for all (b)(4) HEPA filters comprising the ISO 5 areas: (b)(4) HEPA filters over work benches on the east side of the room and (b)(4) HEPA filters over work benches on the west side of the room. The dynamic count provided in the report is an average of all (b)(4) HEPA filters, although some of the work benches may not have been in use at the time of sampling.
3. There is no specification set for adjacent HEPA filter air velocities. HEPA filter air velocities inside the ISO 5 areas were found to have significant differences between adjacent filters.
4. Smoke studies are conducted during (b) (4) ; however, these studies are handled in static conditions and do not show adequate coverage of the ISO 5 area or the ISO 7 / 8 entryway and pass throughs. The smoke studies are not reviewed by your personnel and there is no final report regarding the adequacy of the airflow.

(c) There are no electronic (airlock) or procedural controls surrounding the opening / closing of doors between your unclassified space / ISO 8 Gowning Area / ISO 7 Compounding Area.

(d) Your ISO 5 area is not separated from the ISO 7 area in a way that allows for pressure differentials between areas of different air cleanliness. Additionally, the differential pressure from the ISO 7 Non-Hazardous Compounding Room to the ISO 8 Gowning Room consistently does not meet your firm's specification (b) (4) of water column pressure. For example, differential pressures taken in five minute increments from 02/15/2015 - 03/18/2015 were consistently below (b)(4) inches of water column pressure.

(e) The pass through areas and pass through refrigerator that open directly into your ISO 7 compounding area are unclassified spaces and open into unclassified areas. You do not monitor differential pressure or airflow from the ISO 7 area to the pass through spaces.

(f) You have not established a limit for the number of people that can be in any of the classified areas.

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OBSERVATION 3

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

Specifically:

(a) You have not performed process simulations (media fills) under the most challenging conditions for any of your compounding processes; your use of process simulations is limited to qualifying personnel in which they prepare [redacted] (b) (4) For example, you have not performed a process simulation for your current practice of [redacted] (b) (4) ropivacaine solution from [redacted] (b) (4)

(b) We noted the following departures from aseptic technique on 03/16 and 03/17/2015:

1. We observed that your firm does not sanitize items introduced into the ISO 5 hood such as tubing, bags and vials to be repackaged in a controlled environment.
2. We observed that your technicians do not consistently sanitize their gloved hands prior to entering the ISO 5 areas.
3. We observed that technicians do not work using slow, deliberate movements inside the ISO 5 areas. For example, your firm's technicians were observed sliding vials across the work bench located in the east ISO 5 area.
4. We observed that it is your firm's practice to label product in the ISO 5 area.

OBSERVATION 4

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

Specifically, your gowning practices and procedure are deficient in that:

(a) Gloves donned in the ISO 8 gowning area are removed after gowning is complete and replaced within the ISO 7 area. There is no restricted area where the change of gloves can take place; we witnessed operators with ungloved hands walking about the ISO 7 area.

(b) Gowning does not appear to be complete in that operators' foreheads were visibly exposed in the ISO 7 area.

(c) Your gowning procedure 05-04.01 10/14 "Sterile Hand Hygiene and Garbing Procedure" does not require operators to sanitize safety glasses before entering the ISO 7 area.

(d) Similarly, the gowning procedure states that operators should "Avoid coveralls making contact with the floor", however there is no requirement to regown if coveralls do touch the floor.

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OBSERVATION 5

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

Specifically, while your procedure 02-04.01 "Cleaning and Disinfecting of the Sterile Compounding Area" discusses the use and rotation of disinfectants, you have not specified a disinfectant contact time within your procedure. Additionally, the (b) (4) Disinfectant Cleaner that you currently use in your cleaning regimen is non-sterile.

OBSERVATION 6

Buildings used in the manufacture, processing, packing or holding of drug products are not maintained in a clean and sanitary condition.

Specifically, during our walk-through inspection on 03/16/2015, we noted that the ISO 5 area of the room used for aseptic processing had apparent peeling paint, dark yellow residues and rusty surfaces.

OBSERVATION 7

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, your firm does not have a procedure or process in place to thoroughly review sterility, potency, yield or environmental monitoring failures. For example,

(a) On 09/11/2014 you determined that lot (b) (4) of VANCOmycin 1.5 gram added to 0.9 % Sodium Chloride 500 ml BAG failed sterility testing with one positive result. You speciated the growth and found contamination with Rhodococcus baikonurensis / erythropolis / globerulus / qingshengii. You did not conduct any investigation to determine the potential root cause nor determine if any other lots could be affected by this failure.

(b) On 01/27/2015, you prepared lot (b) (4) of VANCOmycin 1.5 gram added to 0.9 % Sodium Chloride 500 ml BAG. You noted that you ran out of (b) (4) Vancomycin solution (b) (4) bags before completing your lot of (b) (4) bags. You sent (b) (4) bags for potency testing and determined that 3 bags were superpotent (at 123%, 121% and 122%). You rejected the batch, but did not conduct an investigation to determine potential root cause of this failure or initiate a corrective action.

(c) On 08/04/2014, your firm had alert levels met for personnel gloved fingertip samples, surface samples inside the ISO 7 Non-Hazardous Compounding Room, and surface samples inside the ISO 8 Gowning Room. Bacteria

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recovered from samples taken on 08/04/14 included *Paenibacillus xylanexedens*, coag-negative staphylococcus species, *Bacillus clausii*, bacillus species, *Micrococcus luteus*, *Staphylococcus cohnii*, *Staphylococcus hominis*, *Bacillus licheniforms*, corynebacterium group, *Corynebacterium pilosum*, and *Bacillus pumilus / safensis*. Your firm compounded cefazolin 2 gm added to 0.9% sodium chloride 100 mL bag, lot (b) (4) on 08/04/14, but did not conduct an investigation to see if any of the environmental monitoring failures affected product safety.

(d) On 02/03/2015, you determined that your technician (b) (6) had failed (b) (4) unit dose media fill qualification. You did not perform a root cause investigation, speciate the microorganism found nor determine if this failure could affect other product lots.

OBSERVATION 8

Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to the quarantine storage of drug products prior to release.

Specifically,

(a) We observed a quarantined lot of oxytocin 30 units in bags of 500ml 0.9% normal saline, lot number (b) (4) located in the Banner AZRX product distribution area. The batch was prepared on 3/12/2015 and your firm was still awaiting sterility results prior to release.

(b) You have no written or procedural controls to mitigate the potential for product mix-ups for your operations in the packaging area, which include (b) (4) of finished products.

OBSERVATION 9

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

(a) Your firm does not visually inspect all compounded products or commercial product that is used and is intended to be used in compounding operations. For example, there is no record of visual inspection of lot (b) (4) of Oxytocin 30 units added to 0.9% Sodium Chloride 500 ml Bag prepared on 02/25/2015 and lot (b) (4) of Norepinephrine 16 mg add to 0.9% Sodium Chloride Bag prepared on 02/17/2015. Both these products were found in the Banner AZRX distribution warehouse.

(b) Your firm does not have a procedure or practice in place to test or review testing of components for sterility or endotoxin levels. For example, your firm did not have the Certificate of Compliance / Sterilization on hand for (b) (4) (b) (4) bag, lot (b) (4) manufactured by (b) (4) which was being used in the compounding

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of Ropivacaine (PF) 0.2% (2 mg/mL) 100 mL Cassette that was being compounded on 03/17/2015 at Workbench [redacted]. The Ropivacaine Cassette is labeled "FOR EPIDURAL USE".

(c) Your firm does not have a procedure in place that specifies how labeling is checked prior to use and you do not document your practice of checking [redacted] (b)(4) labels released to compounding. For example, your firm did not have any records indicating that the labels were checked before their application on the Cephazolin 2 Gm added to 0.9% Sodium Chloride 100 ml Bags that were compounded and labeled on Workbench [redacted] on 03/17/2015.

OBSERVATION 10

The master production and control records are deficient in that they do not include complete instructions.

Specifically, master production and control records (batching information labels) for:

- Norepinephrine 8 mg added to 0.9% Sodium Chloride
- Norepinephrine 16 mg added to 0.9% Sodium Chloride
- OXYtocin 30 units added to 0.9% Sodium Chloride
- Ropivacaine (PF) 0.2% (2 mg/mL) 100 mL CASSETTE
- Vancomycin 2 Gm added to 0.9 % Sodium Chloride
- Lidocaine 1% Buffered 0.2 ml J-Tip Syringe
- VANCOmycin 1.75 gram added to 0.9% Sodium Chloride

contain no compounding instructions.

OBSERVATION 11

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

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

1. The statement, "This is a compounded drug."
2. The name, address, and phone number of the applicable facility.
3. The lot or batch number.
4. The established name of the drug.
5. The dosage form and strength.
6. The statement of quantity or volume, as appropriate.

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7. The date that the drug was compounded.
8. The storage and handling instructions.
9. The statement, "Not for resale."
10. The statement, "Office Use Only."
11. The inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

Furthermore, the following information is not found on the container labels for some drug products you produce:

1. Information to facilitate adverse event reporting: www.fda.gov/medwatch and 1-800-FDA-1088
2. Directions for use, including, as appropriate, dosage and administration.

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

- Total Parenteral Nutrition (TPN)
- Oxytocin 30 Units added to 0.9% Sodium Chloride 500 ml BAG
- Cefazolin 2 Gm added to 0.9% Sodium Chloride 100 ml BAG
- Midazolam BAG 100 mg (1 mg/mL) in 0.9% Sodium Chloride 100 mL
- Midazolam CASSETTE 100 mg (1 mg/mL) in 0.9% Sodium Chloride 100 mL
- Vancomycin (all strengths)
- Norepinephrine (all strengths)
- GI Cocktail Oral Suspension
- Lidocaine 1% Buffered 0.2 mL
- Magnesium Sulfate 10 Gm added to Lactated Ringers 250 mL BAG
- Ropivacaine (PF) 0.2% (2mg/mL) 100 mL CASSETTE
- Diltiazem HCL 125 mg added to 0.9% Sodium Chloride 100 mL BAG

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