DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US Customhouse, Rm 900 2nd & Chestnut St Philadelphia, PA 19106 (215) 597-4390 Fax:(215) 597-0875 Industry Information: www.fda.gov/oc/industry	06/04/2014 - 06/11/2014* FEI NUMBER 3009590582

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Jody Grooms, R.Ph., Regional Director, Pharmacy Operations

FIRM NAME	STREET ADDRESS
Central Admixture Pharmacy Services, Inc.	6580 Snowdrift Rd Suite 100
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Allentown, PA 18106	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

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

1) The "low/medium risk" area of the facility is a large ISO 7 area with (b) areas that are called bays. Each bay has a bank of HEPA filters over stainless steel tables roughly 5 feet below. There is a solid shield angled outward from the bank of HEPA filters to the edge of the table stopping roughly at head level depending on the height of the operator. Air flow studies conducted September of 2012 in the "low/medium risk" area show patterns of turbulent upward air movement in bays (b) (4). This turbulent upward air movement was observed near the solid shield that is angled outward from the HEPA bank in the video for workstations (b) (4). Furthermore, each of the dynamic air flow studies for the "low/medium risk" area was conducted on a single (b) (4) unit at a single workstation in a bay. These studies did not include the activities of the room and the adjacent workstations. These studies failed to demonstrate the air flow over any aseptic connection and there could be up to (b) (4) aseptic connections for the set up on a single (b) (4) unit.

2) Poor aseptic technique was observed as follows:
   a) Observed the compounding of Cefazolin on June 6, in bay (b). During this compounding an operator performing at least (b) (4) sterile connects in a downward manner into vials that were positioned on the work surface. The motion blocked the protection of HEPA filtered air. The pharmacist did not intervene until instructed by management.
   b) Observed the reconstitution of Vancomycin on June 6, in bay (b). During this process the operator performing each sterile connect in a downward manner into vials that were positioned on the work surface. The motion blocked the protection of HEPA filtered air. The pharmacist did not intervene until instructed by management.
   c) Observed the set-up of 2 (b) (4) units (workstations (b) (4) on June 6, in bay (b) (4). On the (b) (4) unit the manifold is orientated (b) (4) on the top (b) (4). The sterile connections were made (b) (4) with gloved hands and no use of sterile tools. Each connection was made in a downward motion blocking the protection of HEPA filtered air. In addition, the operator in workstation (b) (4) moved the (b) (4) exposed without a covering. Furthermore, the sterile connection of the (b) (4) component was observed in a downward motion into the component that was positioned on the workstation. This blocked the protection of HEPA filtered air.
   d) In the "high risk" area on June 4 an operator who was training personnel was observed placing the handles of the

clamp under the balance between uses which placed the exposed connection adjacent to the balance between filling units. Also observed the operator infrequently sanitizing hands when re-entering the ISO 5 area and speaking in direct proximity to the ISO 5 while training.

e) Sterile connects into IV bags were not made with proper aseptic technique: IV bags were positioned at roughly a 15 degree angle when the connections were made, IV bags that were laid upon the work surface in close proximity to equipment, and sterile connections into the IV bags were seen taking quick movements and twisting to obtain the connection.

3) The media fill simulations for the process in the "low/medium risk" area do not include the activities of the ISO 7 room. The ISO 7 area has [redacted] bays and a common area in the back of the room that services [redacted] bays. There are [redacted] material transfer bays in the common area. Each bay can support up to [redacted] filling operations and [redacted] operators at a time. The ISO 7 room could have up to [redacted] operators and [redacted] filling operations occurring at a time. The media fills are conducted independently in each bay. The media fills included [redacted] operators in the simulation, but did not include media to challenge all [redacted] workstations. Generally, only [redacted] workstations were represented in the simulations.

4) In the "low/medium risk" area, observed a media fill to qualify individuals on the [redacted] equipment. [redacted] was added to the media in the process simulation. There was no data available to support that the commercially obtained media was not impacted by the dilution with [redacted]

5) The units produced in a media fill are not reconciled for full accountability.

6) In the benches [redacted] during the production of the Cardioplegia Solution an employee was observed on multiple occasions not wiping down IV bags with [redacted] prior to placing them in the ISO5 hood. Also, the employee proceeded to label the filled unwiped bags within the ISO5 hood. This occurred during the production of the following lots of Cardioplegia Solution:
Lot 37-42040
Lot 37-42041
Lot 37-42188
Lot 37-42117

7) Between the dates 2-28-14 and 4-30-14 no media qualification (growth promotion) or sterility testing was performed for each of the lots of media listed below.

TSA Agar Strips
[redacted]

TSA Contact Plates
[redacted]

(b) (4)

TSA Settle Plate
(b) (4)

TSB 100mL Vials
(b) (4)

TSB 500mL Bags
(b) (4)

Review of additional media lots received from 4/30/2014 to date revealed these lots were tested for sterility and growth promotion.

OBSERVATION 2

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

1) On June 6th, observed operators gowning. During gowning the operators placed the sterile hoods on while on the dirty side of the growing room prior to crossing over to the clean side of the gowning room. This was done per procedure, SOP-CAPs-4000516, Gowning Requirements- LHV. Also, the operator's gowning does not fully cover their face. Operators were observed with exposed skin around their eyes and on their cheeks between the hood and the face mask. SOP-CAPs-4000516, also allows for the reuse of gowns throughout the day. On June 4th, a gown without protective wrap from the supplier was observed hanging on the rack in the gowning room.

OBSERVATION 3

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

Specifically, rooms WS1 and WS2 is where the injectable drugs Sodium Phosphate, Tromethamine and MSA/MSG are produced and final packaged. WS1 is used for batch (b) (4) and WS2 is used for final filling of during the production of these products. WS1 is classified ISO7. WS2 is classified ISO7 and houses (b) (4) ISO5 hoods. During the production of the high risk products the following was observed in rooms WS1 and WS2:

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In WS1 (ISO 7)
(b) (4) cleaning solution was stored directly next to an uncontrolled graduated cylinder, causing a possible cross contamination with an adulterant. The graduated cylinder is used for (b) (4)
A used dirty mop and pile of unwrapped sterile wipes stored uncovered and open to the ISO 7 environment.

In WS2 (ISO 7 and ISO5 during production)
Inside the ISO 5 hood during production it was observed that there were approximately (b) (4) possibly blocking the laminar air flow path.
On a shelf, directly under the ISO 5 hood certain items were being stored. Extra (b) (4). Also, extra (b) (4) were located on this shelve.
This was observed during the production of high risk sterile injectable drugs. Specifically, Tromethamine DS 0.6M compounded solution, 150 liters, Lot (b) (4).

OBSERVATION 4

The control systems necessary to prevent contamination or mix-ups are deficient.

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

1) Specifically, the fingertip monitoring was observed for the operator that was processing in workstation (b) of the "high risk" area on June 4, 2014. The finger tips were gently tapped to the surface of the media.

2) Pressure differentials for the ISO 7 clean room (housing all of the ISO5 hoods) and ISO 8 areas are monitored throughout the facility utilizing magnehelic gauges #'s (b) (4). All pressure differential readings are to be documented on the CAPS document -4000117, titled Compounding Room Magnehelic Gauge Monitoring Log. Review of this log from 03/03/14 through 05/01/14 contained numerous mistakes and was illegible. Specifically, cross outs and annotations were made of the ISO room locations. Locations where pressure readings are required to be read (b) (4) were changed by personnel without proper change control or authorized. Additionally, the gauge numbers were not identified in the logs for pressures readings between the ISO 7 (housing all of the ISO5 hoods) and ISO 8 areas. Additionally, the firm did not have any backup records such as continuous monitoring readings for review. Also, manual readings are taken (b) (4).

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

Specifically,

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1) The walls, solid shield on the front of the ISO 5, IV bars, IV hooks, and brackets that hold up the IV bars that run horizontally the length of the ISO 5 are not surfaces included in the daily cleaning in the "low/medium risk" area. Operators were observed touching the IV hooks during processing. On June 6, at the end of the weekly production and prior to the (b) (4) cleaning, upon request an operator took a clean wipe across the surfaces of the IV pole and brackets. Residue was noted in (b) (4) and a label with signs of wear and filth was recovered in bay (b)(4). It was confirmed that the label was from a bracket that holds up the IV poles.

2) Bulk sterile (b) (4) is applied to product and the facility surfaces from (b) (4). These (b) (4) use (b) (4). Also, there are no defined periods of use for (b) (4) and operators noted degradation with use.

3) Transfer carts staged to enter the ISO 7 material transfer area for transfer to the ISO 7 cleanroom were observed to have visible residue.

4) Specifically, The beta-lactam Cefazolin antibiotic syringe is produced in the non-dedicated (b) (4) (ISO-5) hood on Fridays. (b) (4) is not dedicated to beta-lactam Cefazolin. Other low risk products such as Oxytocin, Heparin and TPN are also produced in (b) (4). The Antibiotic Cleaning Method Validation final report # V0376 dated 05/01/13 requires the use (b) (4) for effective cleaning and the deactivating beta-lactam products. Cleaning records for (b) (4) (b) (4) does not reflect the current validated cleaning study report # V0376. Review of the current cleaning SOP (CAPS 4000515 version-6) and compounding records for Cefazolin only document the use (b) (4). Additionally, the site specific cleaning SOP-CAPS 4000515 version-6 titled Cleaning Procedure does not include instructions for cleaning (b) (4) of beta-lactam Cefazolin. Additionally, there is no record in the daily, (b) (4) cleaning logs of which of the Bays (b) (4) are cleaned.

OBSERVATION 5

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

Specifically, 100 % visual inspection is performed by the pharmacist that supervises the operators. The pharmacist reviewed the labels and then viewed each unit produced under the lighting conditions of the room with no additional illumination. The visual inspection was observed to take around (b) seconds for each unit against a black and white background. The quality AQL inspection was performed (b) (4), but units were (b) (4) causing bubbles and operators viewed each unit for around (b) seconds per unit.

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OBSERVATION 6

The flow of components, drug product containers, closures, and drug products though the building is not designed to prevent contamination.

Specifically, in the warehouse where sterile components and non-sterile components are received bags of solutions were observed being removed from the tertiary and secondary packaging and placed on warehouse carts. For (b) (4) Normal Saline lot # (b) (4) expiration of 04/2016 the primary packaging was exposed to the unclassified warehouse and touching the warehouse carts. These bags of Saline solutions were then sprayed down with (b) (4) within the warehouse and left uncovered exposed to the environment. Multiple large dumpsters were observed adjacent or near to the wetted Saline bags and carts. These components then enter into the manufacturing areas (ISO8, ISO7 and ISO5 environments).
Additionally, warehouse carts are not labeled as dedicated to the warehouse. Similar carts were observed in the ISO8, ISO7 and ISO5 areas.
Also, the multiple lights in the warehouse are not covered to prevent broken glass from coming in contact with components stored in the warehouse. Multiple component boxes were not closed or sealed throughout the warehouse. Also debris and broken pallets were observed in the warehouse.

OBSERVATION 7

Written records of investigations into unexplained discrepancies do not always include the conclusions and follow-up.

Specifically, alert levels limits were exceeded in the following critical ISO5 areas or during personnel monitoring:
Right Glove date of the exceeded alert 01/16/14 (result 2 cfu) and re-tested 01/29/14
Bench (b)(4) Viable Air date of the exceeded alert 01/17/14 (result 1cfu) and re-tested 01/24/14
Bench (b)(4) Viable Air date of the exceeded alert 03/06/14 (result 1 cfu) and re-tested 03/07/14
Bench (b)(4) Viable Air date of the exceeded alert 03/14/2014 (result 1 cfu) and re-tested 03/21/2014
Bench (b)(4) Viable Air date of the exceeded alert 04/05/14 (result 1 cfu) and re-tested 04/11/2014

All alerts results were classified as invalid (non-confirmed). The firm re-tested the same areas and upon second re-testing received passing results. Re-testing was conducted (b) (4) later for 4 of the 5 alerts listed above. There were no investigation reports completed for the alerts. The SOPs are incomplete and do not describe how and when re-testing is to be performed and documented. Additionally, corrective actions or preventive actions were not implemented.

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OBSERVATION 8

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

Specifically, while observing the "high risk" production of the sterile drug product, Sodium Phosphate, lo[redacted (b) (4)], on June 6, 2014 components were staged on the table in the compounding room near the (b) (4) [redacted] in unmarked plastic bags. The bags did not have the component name or item code, receiving or control number, weight or measure, or identify the batch for which the component was dispensed. While being observed the operator charged the unmarked components to the batch. A second operator did not verify the components or the addition. The operator who charged the component did not document the addition of the component in the batch record. The operator began the (b) (4) of the batch and did not document the time the (b) (4) commenced. A review of the executed record showed the operator documented the time in a non-contemporaneous manner. Also, the master batch records for two other "high risk" products, MSA/MSG and Tromethamine, do not require dispensed components to be identified.

OBSERVATION 9

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

Specifically, stability testing is not conducted on Vancomycin or Cefazolin (expiry of 45 and 30 days refrigerated, respectively) which are transferred to less protective plastic container closures from glass commercial containers. There are no ongoing stability studies for any products. The active ingredient for Potassium Sulfate was not measured in the January 2009 stability study.

OBSERVATION 10

Each lot of is not withheld from use until the lot has been sampled, tested, examined, and released by the quality control unit.

Specifically, CoA's for components, containers and closures, or disposable equipment used in "low/medium risk" area are not reviewed by QA. QA does review CoA's for components, containers and closures, or disposable equipment used in the "high risk" area. There was no rational provided for the difference in practice.

OBSERVATION 11

The labels for the drug products you produce do not contain information required by section 503B(a)(10).

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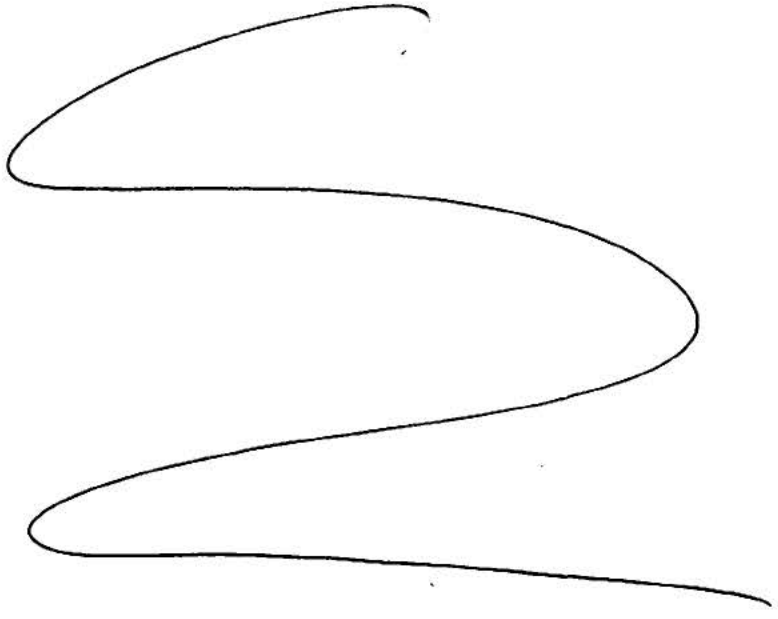
Specifically, the statement, "This is a compounded drug" is not present on your drug product labels as required in the statute. Labels for the following drug products do not contain this statement:

- Magnesium Sulfate 1 g in dextrose 5% 50mL
- Oxytocin 15 units in 0.9% sodium chloride 250 mL
- Bupivacaine PF 0.25%
- Epinephrine 2 mg in dextrose 5% 250 ml

*** DATES OF INSPECTION:**
06/04/2014(Wed), 06/05/2014(Thu), 06/06/2014(Fri), 06/09/2014(Mon), 06/11/2014(Wed)



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