DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
404 BNA Dr., Bldg. 200, Ste. 500 Nashville, TN 37217-2597 (615) 366-7801 Fax:(615) 366-7802 Industry Information: www.fda.gov/oc/industry	03/04/2013 - 03/07/2013
	FEI NUMBER 1000221951

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Jody K. Grooms, Regional Director, Pharmacy Operations

FIRM NAME	STREET ADDRESS
Central Admixture Pharmacy Services, Inc.	211 Summit Parkway #122
CITY, STATE, ZIP CODE, COUNTRY Homewood, AL 35209	TYPE ESTABLISHMENT INSPECTED 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

Each batch of drug product required to be free of objectionable microorganisms is not tested through appropriate laboratory testing.

Specifically, the firm fails to ensure that each batch of aseptically processed sterile drugs, which it distributes, passes sterility and endotoxin testing before batch distribution. According to in process Investigation #06-130214-005, the firm received failing sterility testing results representing 18 orders of Cardioplegia that had already been released and distributed. For example, two of those 18 orders (numbers 690848 and 690849) of Cardioplegia with a BUD of 30 days were shipped to (b) (4) [redacted]

OBSERVATION 2

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 fails to assure that each batch of aseptically processed sterile drugs it distributes, meets predetermined specifications (i.e. assay, pH, osmolality, etc.) by way of relevant chemical analysis, before batch distribution. For example, Oxytocin and Cardioplegia are released with no assay testing prior to distribution.

OBSERVATION 3

Investigations of an unexplained discrepancy did not extend to other drug products that may have been associated with the specific failure or discrepancy.

The" Investigative/Corrective Action Reports" identified as 06-120709-005 and 06-121102-008 were intitiated based on action limits for (b) (4) personnel environmental monitoring specifications that were exceeded. These samples are taken on (b) (4) [redacted], however, the results are not known until the following (b) [redacted]. In the interim the employee produces product during (b) (4) [redacted]. These investigations did not assess the impact to product produced during the timeframe between

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when the sample was taken and the result was determined.

OBSERVATION 4

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

Specifically, personnel conducting aseptic operations within the ISO 5 laminar flow hood were observed to have exposed face and neck skin as well as exposed beard hair.

OBSERVATION 5

Equipment for adequate control over air pressure is not provided when appropriate for the manufacture, processing, packing or holding of a drug product.

Specifically, the firm lacks a system of continuous monitoring of positive pressure differential limits during aseptic processing of sterile drug products. The firm's current practice is to log their reading from their positive differential pressure gauges representing their clean rooms and adjacent rooms, (b) (4) . Because these gauges are located outside of the clean rooms themselves, if a loss of positive pressure in a clean room occurs during aseptic processing, the firm may not notice until the clean room differential pressure gauges are read again (b) (4) . The firm's current clean room differential pressure system has no audible alarm; thus, transient excursions of (b) (4) pressure would not be observed or recorded.

OBSERVATION 6

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

A) The firm lacks adequate environmental monitoring controls within the aseptic processing facility (including personnel gowning areas). The firm does not conduct environmental monitoring (i.e. viable/non-viable air sampling, surface touch plates, microbial settling plates, operator fingers/sleeves) within the laminar flow hood during and after the aseptic processing operations of each batch of finished sterile drug product.

B) No positive controls are included in media fill process validation batches.

C) No formal bacterial retention testing has been completed on the (b) sterile (b) used in the (b) (4) of the non-sterile to sterile processing of Sodium Chloride, Magnesium Sulfate, and Potassium Phosphate sterile solutions.

D) The procedure "Environmental Monitoring" #SOP-CAPS-4000172 effective 9/5/12 is inadequate in that:

1) the specified action and alert limits for monitoring of particulate counts, air bioburden counts, and gloved fingertip

bioburden counts, are not based upon the site specific bioburden studies. The following environmental monitoring action limits are used by the firm:

i. ISO 5 Workstation air particle count action limit is (b) (4) [redacted]
ii. ISO 5 Workstation microbial action limit is [redacted] (b) [redacted]
iii. ISO 5 Workstation surface bioburden action limit is [redacted] (b)
iv. Employee fingertip action limit is [redacted] (b)
v. Employee sleeve cover action limit is > [redacted] (b)

2) the action to take if alert/action limits are exceeded in section 4.11.13 "All employees exceeding alert and action limits (b) (4) [redacted] however according to management the procedure should state 'exceed the alert limit (b) (4) [redacted] and the action limit (b) (4) [redacted]'.

OBSERVATION 7

Written procedures are lacking for the use of cleaning and sanitizing agents designed to prevent the contamination of drug products.

Specifically, the firm does not use sporicidal cleaning agents in their ISO 5 laminar flow hoods, where aseptic processing of sterile drugs occurs.

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, tape was observed holding up clipboards on the outside sash of the ISO 5 TPN hood in the room identified by the firm as area (b) [redacted]

OBSERVATION 9

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

Specifically, the firm has no written stability program which requires *ongoing* stability studies to show that the aseptically processed sterile drug products which they distribute, continue to meet all relevant chemical and sterility specifications all the way to product expiry, or beyond use dates (BUD).

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OBSERVATION 10

Procedures describing the handling of all written and oral complaints regarding a drug product are not followed.

Specifically, the procedure "Inquiry/Complaint Handling and Reporting" #SOP-CAPS-4000217 effective 8/25/2012, section 4.5.7, was not followed for a complaint involving a Cardioplegia product in that a sample of the product was returned for assay, but no analysis was conducted on the product.

OBSERVATION 11

The establishment of laboratory control mechanisms including any changes thereto, are not drafted by the appropriate organizational unit.

Specifically, on a (b) (4) basis samples of positive growth from air bioburden, fingertip touch plates, surface contact plates or sleeve cover bioburden touch plates are sent to (b) (4) [redacted]. There is no written procedure describing the packaging and shipment of these samples to maintain sample integrity.

OBSERVATION 12

Reserve samples for drug products are not retained for one year after the expiration date of the drug product.

Specifically, the firm fails to retain and store reserve samples for each lot of aseptically processed sterile drug product it distributes.

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