DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
300 River Place, Suite 5900 Detroit, MI 48207 (313) 393-8100 Fax:(313) 393-8139 Industry Information: www.fda.gov/oc/industry	02/19/2013 - 02/22/2013
	FEI NUMBER 1000306306

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Glenn J. Pangrazzi, R.Ph., MBA, Director of Pharmacy

FIRM NAME	STREET ADDRESS
Central Admixture Pharmacy Services, Inc.	37497 Schoolcraft Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Livonia, MI 48150-1007	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:

Facilities & Equipment

OBSERVATION 1

Air-handling systems for the processing of penicillin are not completely separate from those for other drug products for human use.

Specifically,

The air handling system for the Antibiotic room where penicillin and cephalosporin products are compounded also supplies air to the firm's Ante Room, Gowning Room, and Product room. The exhaust from the Antibiotic room is into the surrounding non-classified area housing the operations suite. This same non-classified area also provides air to the Air Handling Unit supplying air to the TPN room ([redacted] human compounding room). Additionally review of pressure differential monitoring points on 2/19/2013 revealed the Antibiotic room was at a higher pressure then the adjacent and connected TPN compounding room.

Products compounded in the Antibiotic room include:
Ceftriaxone 1g/10mL lot 13-797560-0 on 2/18/2013
Cefazolin 2gm/20mL lot 13-797670-0 on 2/18/2013
Penicillin G potassium lot 13-793827-0 on 2/05/2013

Other human products compounded on these same days include:
Oxytocin 20 units lot 13-797570-0 on 2/18/2013
Oxytocin 30 units lot 13-793650-0 on 2/05/2013

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OBSERVATION 2

The operations relating to the processing of penicillin are not performed in facilities separate from those used for other drug products for human use.

Specifically,

Procedures have not been established for the separation of tasks and segregation of personnel handling penicillin and cephalosporin drug products from those for all other human drug products. For example:

i-On 2/19/2013, compounding personnel were observed entering and exiting the Antibiotic room during compounding operations. Specifically, we observed an employee entering the Antibiotic room to retrieve a cart of bagged diluents from the Antibiotic room that were subsequently used in the compounding of Oxytocin lot 13-797566-0 within Hood # 8 of the TPN room. Ceftriaxone 1g/10mL lot 13-797560-0 was compounded in this Antibiotic room on 2/18/2013.

ii- On 2/19/2013, non-sterile gowning was observed in the gowning room for re-use by operators on this same day. There was no segregation of the re-usable gowning observed hung on a rack in this space, including the compounding operator stated to have been operating in the antibiotic room on this day. An example product compounded on 2/19/2013 is Oxytocin lot 13-797566-0.

iii-The 2/15/2013 transfer of (b) (4) [redacted] from bulk containers into spray bottles was stated to have last occurred within Hood # 16 within the Antibiotic room. These filled spray bottles are then placed at each ISO 5 work station within the TPN compounding room. On 2/19/2013, we observed the spraying from one of the 2/15/2013 refilled bottles of (b) [redacted] onto components used during compounding of Cardioplegia lot # 13-79790802, Cardioplegia lot # 13-797625-0-2, and Oxytocin lot 13-797566-0, as examples.

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OBSERVATION 3

There is a lack of written procedures describing in sufficient detail the methods, equipment and materials to be used for sanitation.

Specifically,

Written procedure SOP-CAPS-4000183, Cleaning Procedure, does not clearly establish all minimum exposure times as supported by validation/effectiveness data. Specifically, the "Total Cleandown" that is performed weekly does not specify:
- the agent to be used in mopping of the clean room suite floors and the exposure period for the same.
- the exposure time for the dilute bleach rinsed trash barrels within the compounding suite, before replacement of the liner.

The last cleandown was performed on 2/15/2013. Subsequently compounded products include:

-Oxytocin 20 units, lot 13-797566-0
-Cardioplegia lot 13-797625-0
-Cardioplegia lot # 13-7979080-2

OBSERVATION 4

Buildings used in the processing of a drug product are not maintained in a good state of repair.

Specifically,

The face of the HEPA grate covering the HEPA filter over ISO 5 workstation # (b) was observed with a small amount of a brownish residue, noted during compounding operations on 2/19/2013. This residue was later stated to have been easily removed with a cloth wipe, but the identity of the residue was not confirmed. Products

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compounded in this work station on this day are all TPN products, including lot # 13-79762004 and lot# 13-79793101. Other products compounded in the TPN room at this time included Oxytocin lot 13-797566-0.

Production

OBSERVATION 5

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

Specifically, operations at this facility include the compounding of sterile products from purchased sterile finished dosage forms into sterile diluents or new sterile container closures. Pertaining to these operations, the following was noted:

1- Procedures are not fully established. For example:

i- Gowning used in protection of personnel working at the ISO 5 workbenches was observed to incompletely cover all exposed skin surfaces. Specifically, no covering over the face and neck beyond a mouth/nose mask was observed worn by compounding personnel during all compounding operations from 2/19-21/2013. Only sleeve covers and gloves were provided with certification supporting sterility. Products compounded during these same days include:

Cardioplegia lot 13-778554-0 on 2/21/2013

Cardioplegia lot 13-797960-0 on 2/20/2013

Cardioplegia lot 13-797625-0 on 2/19/2013

Oxytocin 20 Units lot 13-797566-0 on 2/19/2013

ii- According to written procedure and as shown in supporting records, Environmental monitoring of the ISO 5 workspaces and personnel monitoring of compounding employees working in the same occurs only (b) (4) [redacted]

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(b) (4) [redacted] Daily Non Viable Particulate (NVP) monitoring in the ISO 5 compounding work spaces does not occur during compounding operations. Specifically, this site houses (b) (4) [redacted] ISO 5 work spaces used for sterile compounding operations. NVP monitoring was not provided for these same ISO 5 work spaces during daily, compounding operations. Examples of compounded products compounded within these same ISO 5 work spaces include:

Cardioplegia "High K" lot 13-797960-0 on 2/20/2013

Cardioplegia lot 13-797625-0-2 on 2/19/2013

Oxytocin 20 Units lot 13-797566-0-1 on 2/19/2013

iii-(b) (4) [redacted] dispensing occurs according to written procedure SOP-CAPS-4000159 (b) (4) [redacted] Filtration and Filling, and includes direction for the filling of (b) (4) [redacted] into non-sterile, re-usable spray bottles ((b) (4) [redacted] disinfected spray bottles). This refilling activity of (b) (4) [redacted] from the source containers occurs in an ISO 5 hood, and was last performed on 2/15/2013 in Hood # 16. These refilled spray bottles are then stationed at each ISO 5 work station (and elsewhere) and were observed in use in spraying septa of vials prior to compounding (needle puncture), gloved hand sanitization, and ISO 5 bench surface wipe down during all observed operations. Compounded drug products observed impacted under this observation include:

-Oxytocin 20 units, lot 13-797566-0

-Cardioplegia lot 13-797625-0

2- Procedures are not followed: Specifically, written procedure SOP-CAPS-4000175, Aseptic Technique and/or SOP-CAPS-4000158, Clean Room Compounding Area - Product Intro/Removal, were not followed on the following occasions:

i-On 2/19/2013, a compounding employee was observed stretching sterilized tubing from the ISO 5 workbench space into the ISO 7 surrounding space. This tubing is used as a conduit for components utilized in compounding

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Cardioplegia lot # 13-79790802.

ii-On 2/19/2013, a writing utensil (pen), was observed used outside of the ISO 5 hood at work station #(b) brought into the ISO 5 space by pharmacist during review/signing of Magnesium Sulfate lot 13-02-19-MGSO4-01.

iii- Labeling was observed brought from outside the ISO 5 hood to inside the ISO 5 hood and set atop an opened, sterile IV bag during preparation for compounding Cardioplegia lot 13-797960-0 on 2/20/2013.

iv-The upper torso and head of an employee was observed entering into the ISO 5 hood of workstation #(b) during staging of Diluent bags for compounding Oxytocin lot #13-797566-0.

v-Over ten large sterile syringes in packaging were observed brought into the ISO 5 work space of station #(b) (4) without any sanitization of the outer packaging during compounding preparation of Magnesium Sulfate Syringes, lot 13-02-20-MAGSO4-01 on 2/20/13.

vi- Sterile tubing used in connection with the Cardioplegia pump at the ISO 5 Workstation #(b) was observed carried into the ISO 5 work space without any sanitization during compounding of Cardioplegia lot # 13-797960-0.

vii-As observed during compounding operations during the morning 2/19/2013, "Slow deliberate" motions were not always noted. Specifically, compounding personnel were observed moving briskly through the ISO 7 surrounding space within the 'TPN' compounding room, passing beside ISO 5 workbenches (b) (4) Products compounded at this time included:

Cardioplegia lot # 13-797625-0

Oxytocin lot 13-797566-0

Laboratory

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OBSERVATION 6

Acceptance criteria for the sampling and testing conducted by the quality control unit is not adequate to assure that batches of drug products meet each appropriate specification as a condition for their approval and release.

Specifically,

There is no routine, batch specific quality control analysis for anticipatory compounded products including Oxytocin and Nor-epinephrine required according to any written procedure as part of a batch release. For example, no batch specific sterility testing was performed (or initiated), and no QC chemical analysis was performed prior to the release of Oxytocin lot 13-797570-0 and Cardioplegia lot # 13-797625-0.

Materials

OBSERVATION 7

Reports of analysis from component suppliers are accepted in lieu of testing each component for conformity with all appropriate written specifications, without establishing the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.

Specifically,

(b) (4) [redacted] is utilized in compounding operations for injectable compounded products, and is received with a Certificate of Analysis from your firm's supplier. The reliability of this supplier's analyses was not demonstrated by your firm through appropriate validation of the supplier's test results at appropriate intervals. For example, (b) (4) [redacted] USP lot (b) (4) [redacted] was received and released for use in your firm on 2/1/2013. This same lot of (b) (4) [redacted] was used in compounding Cardioplegia High K lot # 13-79796003. ~~and Penicillin G Potassium lot 13-793827-0.~~

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