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	08/04/2014 - 08/08/2014 FEI NUMBER 3004378804

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Mr. William D. Jones, Regional Director

FIRM NAME	STREET ADDRESS
Central Admixture Pharmacy Services Inc	7935 Dunbrook Rd Ste C
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
San Diego, CA 92126-6322	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

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, your firm does not perform sterility and endotoxin testing of every batch of human drug products intended to be sterile.

On August 4 and 5, 2014, we observed your firm process and release the following drug products without sterility and endotoxin testing:

1. Midazolam; Lot #17-040222; [redacted] (b) (4); 1mg/mL; 100mL Bag
2. Glycopyrrolate; Lot #17-40287; [redacted] (b) (4); 0.2mg/mL; 5 mL syringe
3. Vecuronium; Lot #17-40300; [redacted] (b) (4); 1mg/mL; 10mL syringe

Per SOP # TP-CAPS-4000037, Version 10.0, Effective Date 2014-05-06 titled "CAPS-TP-Test Procedure-Infection Control-Sterility Testing Using [redacted] (b) (4)" section 2.5 states "sterility testing must be conducted for each process batch, which is the [redacted] (b) (4) [redacted]"

OBSERVATION 2

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

Specifically, your firm has not adequately validated your aseptic production procedures through adequate media fills. Per

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"Process" Manual Addition Process Media Fill Validation Summary Report: Low Risk Compounding, the firm used TSB media to simulate vial to bag, vial to vial, and bag to bag with a goal of simulating up to [redacted] aseptic connections. However, actual batch aseptic connections may exceed that number. For example,

A. On 07/04/14, Hydromorphone injectable product lot #17-39444 has [redacted (b) (4)] filled by [redacted (b) (4)] (b) (4). This is approximately [redacted (b) (4)] aseptic connections per technician during actual manufacturing.

B. On 07/16/14, Morphine injectable product lot # 17-39685 has [redacted (b) (4)] filled by [redacted (b) (4)] which is approximately [redacted (b) (4)] aseptic connections.

C. On 08/04/14, Hydromophone injectable product lot # 17-40294 has [redacted (b) (4)] filled by [redacted (b) (4)] which is approximately [redacted (b) (4)] aseptic connections.

OBSERVATION 3

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

Specifically, your firm does not adequately monitor the bio-burden of Laminar Air Flow hoods, cleanrooms, and personnel who perform aseptic operations. Your firm is not monitoring every batch or every shift of production for surface, air, and personnel samples. This monitoring is performed only [redacted (b) (4)] per SOP # CAPS-4000172, version 12, effective date May 5, 2014 titled "CAPS-SOP-Sys Environ Control-Infection Control-Environmental Monitoring." With the current [redacted (b) (4)] monitoring, the firm has recovered the following samples with microbial growth from ISO 5 surfaces and personnel samples between January and July of 2014.

Sample Description	Date Sampled	Micro ID	Submission #	Microorganism ID	Media Type
[redacted (b) (6)] RF (right finger)	2/27/2014	[redacted]	[redacted (b) (4)]	*Paenibacillus glucanolyticus*	Personnel
[redacted] RF (right finger)	3/15/2014	[redacted]	[redacted]	*Bacillus vallismortis*	Personnel
TPN hood [redacted (b) (4)]	5/5/2014	[redacted]	[redacted]	*Bacillus fentus*	Surface
TPN hood [redacted (b) (4)]	5/19/2014	[redacted]	[redacted]	*Staphylococcus epidermidis*	Surface
[redacted (b) (4)] RF (right finger)	6/9/2014	[redacted]	[redacted]	*Bacillus firmus*	Personnel
hood [redacted (b) (4)]	6/30/2014	[redacted]	[redacted]	*Arcanobacterium haemolyticum*	Surface
[redacted (b) (6)] RF (right finger)	6/30/2014	[redacted]	[redacted]	*Brevibacillus choshinensis*	Personnel
[redacted] RS (right sleeve)	6/30/2014	[redacted]	[redacted]	*Penicillium spp.*	Personnel
[redacted] LS (left sleeve)	6/30/2014	[redacted]	[redacted]	*Verticillium spp.*	Personnel

In addition, the following 1 cfu/ml hits were not investigated.

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PERSONNEL FINGERTIP TOUCHPLATES		
Date	Sample ID	CFU
1/24/2014	(b) (6) R. Finger	1
2./13/14	[redacted] R. Finger	1
2/13/2014	[redacted] R. Finger	1
3/15/2014	[redacted] R. Finger	1
4/17/2014	[redacted] L. Finger	1
4/23/2014	[redacted] L. Finger	1
5/7/2014	[redacted] L. Finger	1
6/9/2014	[redacted] R. Finger	1
6/20/2014	[redacted] L. Finger	1
6/20/2014	[redacted] L. Sleeve	1
6/23/2014	[redacted] R. Sleeve	1
6/30/2014	[redacted] R. Finger	1
6/30/2014	[redacted] L. Sleeve	1

ISO 5 HOOD TOUCHPLATES		
Date	Sample ID	CFU
1/2/2014	Hood (b) (4) [redacted]	1
1/2/2014	Hood [redacted]	1
3/13/2014	Hood [redacted]	1
3/15/2014	Hood [redacted]	1
5/5/2014	Hood [redacted]	1
6/30/2014	Hood [redacted]	1
7/28/2014	Hood [redacted]	1

OBSERVATION 4

Clothing of personnel engaged in the processing of drug products is not appropriate for the duties they perform.

Specifically, your pharmacy technicians performing aseptic processing of human drug products do not adequately cover their face around the eyes and their shoes per SOP-CAPS-4000171, Version 7.0, Effective 2014-04-14 titled "CAPS - SOP-Sys Environ Control - Infection Control - Gowning Requirements." The technicians have exposed skin including eye lashes and eye brows on their faces during aseptic processing of human drug products intended to be sterile. The exposed skin is due to not wearing a guard such as sterile goggles. All technicians in the ISO 7 clean room were observed wearing upper sterile gowns and blue-non sterile foot covers with exposed facility shoes on August 4 and 5, 2014.

Examples of drug products processed by these technicians are:

1. Midazolam; Lot #17-040222; (b) (4) [redacted]; 1mg/mL; 100mL Bag

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2. Glycopyrrolate; Lot #17-40287; [redacted] (b) (4); 0.2mg/mL; 5 mL syringe
3. Vecuronium; Lot #17-40300; [redacted] (b) (4); 1mg/mL; 10mL syringe

OBSERVATION 5

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Specifically, your firm's Beyond Use Dates study is inadequate in that

A. Central Admixture Pharmacy Services (CAPS) Beyond Use Dating Extension Study For Controlled Substances (CAPS Document # V0211) dated 10/09/08 does not require the firm to perform endotoxin testing and does not specify what types of container and closure systems were used. This protocol only states the different sizes (e.g. 30 ml and 60ml syringes, 100ml and 250ml bags) of the container/closure systems. The firm has not performed any periodic BUD studies for any of the drug products compounded since this protocol written in 2008. Examples of products without documented packaging types in the report include:

1. Midazolam; Lot #17-040222; [redacted] (b) (4); 1mg/mL; 100mL Bag
2. Glycopyrrolate; Lot #17-40287; [redacted] (b) (4); 0.2mg/mL; 5 mL syringe
3. Vecuronium; Lot #17-40300; [redacted] (b) (4); 1mg/mL; 10mL syringe

B. Central Admixture Pharmacy Services (CAPS) The Report of 90-Day Study For Beyond Use Dating (BUD) For Controlled Substances (CAPS Document # V0211 and [redacted] (b) (4) Document # [redacted] (b) (4)) dated 03/02/09 listed Lorazepam 0.1mg/ml with failed chemical analysis (potency - 40%) at day # 30 and lack of 30 day sterility study due to potency failure using [redacted] (b) (4) containers. The firm later changed its container to [redacted] (b) (4) and still assigned a 30 day BUD at 24°C based on literature. The firm has no BUD study conducted up to date to support the use of [redacted] (b) (4) containers to validate a 30 day BUD at room temperature for Lorazepam 1mg/1ml (NDC #66647-4121-21).

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OBSERVATION 6

Equipment and utensils are not cleaned at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically, your firm does not adequately clean and inspect grills covering the HEPA filters in Laminar Air Flow hoods between processing of batches or during [redacted] (b) (4) cleaning. On August 5, 2014, we observed white residue adhered to the inner circumference of the circular perforations in the grill covering HEPA filters in three different hoods. Two of these hoods were being used for production of human drug products intended to be sterile:

1. Ketamine lot # 17-40298
2. Hydromorphone lot # 17-40328

Based on SOP-CAPS-4000155 dated 08/05/14, these hoods were cleaned with [redacted] (b) (4) prior to the production of these products. Your QA Regional Manager provided documentation that this white residue is being investigated as a result of our visual observation in Deviation #23-140806-25.

OBSERVATION 7

Written procedures are not established for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically, your firm does not verify the effectiveness of sanitizers adequately to the conditions found in the processing facility. For example,

A. Project 00133J-1 dated 2/17/2004 titled "Final Report on the Evaluation of the Effectiveness of the Disinfective Agents Used in the Laboratory, Cleanroom and Manufacturing Areas" conducted by Corporate in Irvine, CA has not been verified here at CAPS San Diego to demonstrate that cleaning agents used continue to be effective against different microorganisms. This study indicates the following D-value (minutes) data for [redacted] (b) (4) and [redacted] (b) against *Bacillus subtilis*.

Substrate	[redacted] (b) (4)		
Stainless Steel	NLR*	7.27	4.05
Epoxy Paint	35.21	7.09	6.41

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Floor Material	21.19	19.46	8.80

*NLR: No Log Reduction

B. The firm uses [redacted] (b) (4) to clean ISO 5 and ISO 7 areas per SOP-CAPS-4000183, Version 10.0, Effective Date 2014-06-09 titled "CAPS-SOP-Sys Environ Control-Infection Control-Cleaning Procedure" section 2.6 which states [redacted] (b) (4) [redacted] " In actual practice, the firm only uses [redacted] (b) (4) as sporicidal agent and not [redacted] (b) (4)

OBSERVATION 8

Strict control is not exercised over labeling issued for use in drug product labeling operations.

Specifically, your firm does not adequately reconcile labels used for the production of human drug products intended to be sterile. For example,

A. On August 4 and 5, 2014, we observed your firm releasing the following drug products for distribution without conducting a reconciliation of labels after the labeling operation was completed:

1. Midazolam; Lot #17-040222; [redacted] (b) (4); 1mg/mL; 100mL Bag
2. Glycopyrrolate; Lot #17-40287; [redacted] (b) (4); 0.2mg/mL; 5 mL syringe
3. Vecuronium; Lot #17-40300; [redacted] (b) (4); 1mg/mL; 10mL syringe

Your Regional Director stated the typical process is to conduct a reconciliation of the labels issued to the production area, but there is no document or written procedure for conducting reconciliation by the personnel who perform labeling or reconciliation after all product units are labeled.

Additionally, your firm has received two complaints dated August 30, 2011 where six pediatric patients were infused with mislabeled drug product (list mislabeled products); and March 9, 2014 where a hospital customer reported mislabeled drug product (list mislabeled products) prior to patient infusion.

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OBSERVATION 9

Laboratory controls do not include the establishment of scientifically sound and appropriate specifications designed to assure that components conform to appropriate standards of identity, strength, quality and purity.

Specifically, your firm has not established a justified specification for water used in Total Parenteral Nutrition Products intended to be sterile injectable.

All TPN's are compounded using (b) (4) solution instead of Sterile Water for Injection. The label for (b) (4) "

OBSERVATION 10

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

Specifically the information to facilitate adverse event reporting: www.fda.gov/medwatch and 1-800-FDA-1088; is not included on individual unit labeling such as syringes, bags, and vials. The following drug products' labels do not contain such statements: Ketamine (lot #17-40299), Midazolam (lot #17-40222), Lorazepam (lot #17-40223), Vecuronium (lot #17-40288), and Glycopyrrolate (lot #17-40287).

Your Quality Assurance Director stated the labels are considered too small to include all of this information on the unit dose containers.

Additionally, your firm labels products without the FDA contact information specified above, such as:

1. Cardioplegia Solution; total volume 955mL; exp 06 SEP 2014; lot #23-117811-0-1
2. Peripheral Neonate TPN; volume 338mL; use by 10 AUG 2014; CAPS Rx: (b) (4)

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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."