DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Peter E. Nero, Director of Pharmacy

FIRM NAME	STREET ADDRESS
Central Admixture Pharmacy Services, Inc.	2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Phoenix, AZ 85043-3909	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

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

Specifically, for example, but not limited to:
A. Your Quality Unit failed to:

1. Initiate a Notice of Quality Event (NQE) or conduct an investigation evaluating drug product impact or identify a root cause. For example, but not limited to:

   i. Your firm's Director of Pharmacy was aware of at least 27 instances of data integrity concerns identified at your firm from May 25, 2023 – June 15, 2023, by your third-party consultants. For example, but not limited to, shredding of GMP documents, lack of contemporaneous record keeping, and back-dating.

B. Your Quality Unit failed to ensure comprehensive procedures for quality review of audit trails and electronic data review have not been established. For example, but not limited to, your firm's Supervising Chemist, stated Rocuronium is commonly re-ran for UPLC due to system suitability failures. The injection audit trails extracted from (b) (4) between 01/10/2023 – 06/07/2023, show your firm analyzed at least (b) (4) lots of Rocuronium for potency and re-injected (b) (4) of these lots (b) (4), without written justification. Please refer to **OBSERVATION 11** related to Rocuronium method validation concerns.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Dogbeda F Mackenzie, Investigator June P Page, Investigator Melinda Lee, FDA Center Employee Mary-Jeanet Mcgarry, FDA Center Employee	Dogbeda F Mackenzie Investigator	7/31/2023

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

C. Your Quality Unit failed to investigate and appropriately determine if drug product batches intended to be sterile meet all requirements prior to release for distribution. Please refer to **OBSERVATION 2** and **OBSERVATION 4**.

D. Your Quality Unit failed to ensure your aseptic processing areas are free of infestation of vermin. Please refer to **OBSERVATION 3**.

E. Your Quality Unit failed to ensure your firm's written procedures designed to prevent microbiological contamination of drug products intended to be sterile are followed. Please refer to **OBSERVATION 5**.

F. Your Quality Unit failed to ensure systems for monitoring your aseptic processing areas are adequate to compound drugs intended to be sterile. Please refer to **OBSERVATION 6** and **OBSERVATION 9**.

G. Your Quality Unit failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products. Your Quality Assurance (QA) Supervisor for Process Control provided four names of individuals that are qualified to sign off on final batch release for CAPS Phoenix location. During review of Total Parenteral Nutrition (TPN) products, the documents were signed by individuals not on the list of qualified quality staff to sign off on final batch review and release. For example, but not limited to:

1. Trophamine 3%/Dextrose 10% with low Calcium Gluconate and Heparin 250mL (Lot# (b) (4) produced on 05/08/23 was released by an employee of Lehigh Valley CAPS facility working on location in Phoenix to help as a QC Coordinator on 05/17/2023.
2. Trophamine 3%/Dextrose 10% with low Calcium Gluconate and Heparin 250mL (Lot# (b) (4)) produced on 05/25/23 was released by an employee of Lehigh Valley CAPS facility working on location in Phoenix to help as a QC Coordinator on 06/12/23, additionally, this same QC Coordinator released the environmental monitoring (EM) results on 06/12/23.

3. Trophamine 3%/Dextrose 10% with low Calcium Gluconate and Heparin 250mL (Lot (b) (4) produced on 05/2/23 was released by a quality technician from Lehigh Valley on 05/17/23; additionally, this same technician released the EM results on 05/17/23.
4. Trophamine 3.5%/Dextrose 10% w/Ca Gluconate and Heparin in 250mL (Lot# (b) (4)) produced on May 12, 2023, was released by a quality technician from Lehigh Valley on June 8, 2023

H. Your Quality Unit failed to establish and follow an adequate written stability testing program to determine appropriate storage conditions and expiration dates. Please refer to **OBSERVATION 7**.

I. Your Quality Unit failed to establish adequate written procedures justifying the re-introduction of drug components into your cleanroom an uncontrolled number of times. Please refer to **OBSERVATION 8**.

J. Your Quality Unit failed to perform a method transfer of your sterility test method and follow analytical method validations used for release of drug products. Please refer to **OBSERVATION 11**.

K. Your Quality Unit failed to ensure that your Batch Compounding Records are representative of your approved Master Production Records, referred to by your firm as a "Drug Master Formula" (DMF) and to ensure that the Batch Compounding Records document complete information relating to the production and control of each batch of sterile drug product produced. Please refer to **OBSERVATION 12**.

L. Your Quality Unit failed to ensure appropriate controls are established to assure that changes to CGMP records can only be made by authorized personnel and your product has not undergone unauthorized retesting or whether data has been otherwise manipulated. Please refer to **OBSERVATION 13**.

M. Your Quality Unit failed to maintain a chain of custody for your microbiology samples used for

release testing. Please refer to **OBSERVATION 14**.

N. Your Quality Unit failed to ensure maintenance and/or calibration is completed prior to the equipment being used for commercial production of your firm's 503B products. Please refer to **OBSERVATION 15**.

O. Your Quality Unit failed to follow written procedures designed to assure that correct labels, labeling, and packaging are used for drug products. Please refer to **OBSERVATION 16.**

OBSERVATION 2

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,

A. Your firm's Quality Unit failed to thoroughly investigate, determine root causes, and implement appropriate corrective and preventive actions in response to failing sterility test results. For example, but not limited to:

- NQE-US59-230502-115 was initiated on May 1, 2023, in response to failing sterility test results for del Nido Formula (Plasmalyte) 1052.8mL, Lot # (b) (4) . The organism recovered was identified as *Staphylococcus hominis.*
- NQE-US59-230228-044 was initiated on February 27, 2023, in response to failing sterility test results for Oxytocin 30 Units/500 mL LR, Lot # (b) (4) . The organism recovered was identified as *Rhodococcus spp.*
- NQE- US59-220311-036 was initiated on March 09, 2022, in response to failing sterility test results for Oxytocin 30 Units/500 mL 0.9% Sodium Chloride, Lot (b) (4) . The organism recovered was identified as *Staphylococcus pasteuri.*

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

B. Your Quality Unit failed to investigate environmental monitoring (EM) and personnel monitoring (PM) results that exceed action limits as established in your firm's written procedures. For example, but not limited to, according to data provided by your firm's QA Supervisor of Microbiology, your firm exceeded microbial action limits in the ISO 5 classified areas at least 198 times since November 2022. However, your firm did not initiate an NQE or conduct an investigation for 167 (84%) of these instances, to determine the root cause and take appropriate corrective action to ensure the ISO 5 classified areas are within a state of control during the compounding of drug products intended to be sterile. For example, but not limited to:

1. The following EM excursions were not investigated for mold recovered in your ISO 5 classified area.

Submission Report Number	**Microorganism ID**	**CFU**
R23-0049	*Aspergillus terreus complex*	1
R23-0227	*Penicillium spp. / Alternaria spp. / Micrococcus luteus / Staphylococcus epidermidis*	37
R23-0421	*Aspergillus lentulus*	1
R23-0465	*Staphylococcus epidermidis / Micrococcus luteus / Bacillus subtilis / amyloliquefaciens / vallismortis / Penicillium glabrum*	19
R23-0687	*Chaetomium globosum*	1

2. According to data provided your firm's QA Supervisor of Microbiology, your firm exceeded EM action limits for the ISO 5 classified area and released at least (b) (4) lots of

drug product intended to be sterile without a thorough investigation. For example, but not limited to:

Lot #	Drug Name
(b) (4)	Norepinephrine 8 mg/250 mL NS
	Oxytocin 30 units/500 mL NS
	Oxytocin 30 units/500 mL NS
	Vancomycin 1.5 gram/500 mL NS
	Phenylephrine 100 mcg/mL in NS 10 mL SY
	Succinylcholine 20mg/mL 10 mL SY
	Oxytocin 30 units/500 mL LR
	Phenylephrine 40 mg/250 mL NS
	Phenylephrine 100 mcg/mL in NS 10 mL SY

C. Your firm's Quality Unit failed to investigate and appropriately determine if drug product batches intended to be sterile meet all requirements prior to release for distribution. A review of your firm's microbiology laboratory notebook, "Invalid Tests: Bacterial Endotoxin Testing" found your firm performed over (b) (4) retests of drug products intended to be sterile produced at your firm since February 2022. According to your firm's QA Supervisor of Microbiology, your firm did not initiate an NQE or conduct any investigations for these retests. For example, but not limited to:

1. Your firm documented "HIGH ENDOTOXIN VALUE" as the "invalid description" associated with (b) (4) Endotoxin report, file name: "(b) (4) ", within

your firm's Invalid Tests: (b) (4) logbook. However, your firm's batch record does not contain the failing endotoxin report or any associated documentation, investigation, or reference indicating a failure occurred. Your firm's batch record released by your Quality Unit only contains a passing (b) (4) Endotoxin report, file name: "(b) (4) ". The following lot associated with the original endotoxin failure was released into distribution:

Drug Product	Invalid Description	Bacterial Endotoxin Acceptance Criteria	Result(s) of Failure Prior to Re-Test
(b) (4) : Norepinephrine 4 mg/250 mL D5W	HIGH ENDOTOXIN VALUE	NMT (b) (4) EU/mg	170.7 EU/mg 368.2 EU/mg

2. Your firm documented an "INVALID ENDO. VALUE" as an "invalid description" associated with (b) (4) Endotoxin report, file name: CAPS.23060604 within your firm's Invalid Test - (b) (4) logbook. However, your firm's batch record does not contain all associated endotoxin reports or any associated investigation indicating a non-conformance had occurred. For example, but not limited to, your firm's batch record released by your Quality Unit contains (b) (4) Endotoxin reports and your firm's Invalid Test - (b) (4) logbook contains (b) (4) Endotoxin reports. The following lot associated with the unknown endotoxin non-conformance was released for distribution:

Lot Number	Drug Product

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

(b) (4)	Transplant Solution (Plasmalyte) 165 mL

Additional examples include, but are not limited to, the following lots were released for distribution:

Lot Number/ Drug Product Description	**Invalid Description**	**Bacterial Endotoxin Acceptance Criteria**	**Result(s) of Failure Prior to Re-Test**
(b) (4) del Nido Formula (Plasmalyte) 1052.8 mL	"Endotoxin value higher than limit allowed"	(b) (4) EU/mL	<0.3360 EU/mL
(b) (4) Norepinephrine 4 mg/250 mL D5W	"ENDOTOXIN VALUE HIGH"	NMT (b) (4) EU/mg	438.7696 EU/mg 204.2137 EU/mg
(b) (4) Oxytocin 20 units/1000 mL NS	"High sample endotoxin value"	NMT (b) (4) EU/Unit	77.8599 EU/unit

D. Your firm documented non-conformances in your Sample Analysis for Release UPLC logbook. However, according to your supervising chemist, your firm did not initiate a Notice of Quality Event (NQE) or investigate these concerns. For example, but not limited to:

Sequence Name	**Comment**
(b) (4)	Sample result invalid due to contamination. Sample to be prepared

(b) (4)	and run-on new sequence.
	Sample result invalid due to contamination. Sample to be run on new sequence.
	Sample results invalid due to peak splitting. To be run on future sequence.
	The second injection for (b) (4) #1 T45 was invalid due to low area counts.
	Sample results invalid due to aberrant chromatography - peak missing. To be tested again on future run.
	Sample results invalid due to aberrant chromatography (contamination peaks present). To be tested again on future run.
	Sample results invalid due to peak splitting. To be ran on future sequence
	Sample results invalid due to aberrant chromatography. To be ran on future sequence

E. A review of your firm's (b) (4) Decontamination Cycle Log found the internal clock for (b) (4) chamber, Asset ID# 112727, did not capture cycle time durations for each cycle (b) (4)) as outlined in your firm's written procedures since at least January 2023. Your firm uses the (b) (4) chamber to decontaminate drug components as they are transferred from a non-classified area to the classified area for use in the compounding of drug products intended to be sterile. The (b) (4) Decontamination Cycle Logs are signed by at least 2 personnel. Your firm's Warehouse Lead, who was identified as the (b) (4) subject matter expert by the Regional Director of Quality, stated they were aware of the (b) (4) clock malfunction. However, a Notice of Quality Event (NQE) documenting this non-conformance was

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

not initiated and this (b) (4) chamber was still in use on July 13, 2023. For example, but not limited to, since at least 01/02/2023 through 07/12/2023, your cycle time printout shows the same start and stop time. Therefore, it is not known if components used during aseptic production of sterile injectable drug products during this timeframe were exposed to your firm's required decontamination cycle times.

(b) (4) **Asset ID 112727**		(b) (4) **112727 Jan_07132023151034**	(b) (4) **112727 July_07132023151117**
Cycle Parameter	**Cycle Time Requirements**	**01/02/2023**	**07/12/2023**
(b) (4)	(b) (4)	07:46:01	17:13:28
		07:46:01	17:13:28
		07:46:01	17:13:28
		07:46:01	17:13:28
		07:46:01	17:13:28
Total Cycle		**00:00:00**	**00:00:00**

F. NQE-US59-230210-034 was opened on 02/09/2023 documenting the negative control for the sterility test for Lots (b) (4) and (b) (4) was removed from incubation pre-maturely. The negative control was removed two (2) days before the completion of the entire incubation time ((b) (4)). Three (3) orders from this lot were shipped prior to the completion of the sterility test and the event was inadequately addressed in the investigation.

G. Your firm's Quality Unit failed to open an investigation where your firm exceeded EM action limits when performing sterility testing. For example, but not limited to, *Rhodococcus spp.* was identified in Lot (b) (4) : Oxytocin 30 units/500ml LR.

H. On 01/19/2023, your firm opened NQE-US59-230123-012, documenting *Aspergillus* was recovered from PM sampling of your firm's aseptic technician's right sleeve during the production of (b) (4) : del Nido Formula (Plasmalyte) 1052.8 mL. Your NQE documents the following lots were also involved:

1. (b) (4): del Nido Formula (Plasmalyte) 1052.8 mL
2. : Trophamine 3.5% Dextrose 10% 250mL
3. : Trophamine 3.5% Dextrose 10% 250mL
4. : Induction 8:1 High K (100 mEq) Low Dextrose 500 ml

However, your firm released three (3) of these lots without evaluating the source of the microorganism. Please refer to **OBSERVATION 9** for EM/PM sampling concern.

****** THIS OBSERVATION WAS CITED IN THE PREVIOUS INSPECTION. ******

OBSERVATION 3

Buildings used in the manufacture, processing, packing or holding of drug products are not maintained in a clean and sanitary condition and free of infestation by rodents, birds insects, and other vermin.

Specifically,

According to NQE-US59-221216-358 initiated on 12/15/2022, your IV Technician found a deceased lizard in ISO 7 cleanroom (b) (4), where aseptic processing occurs in (b) (4) ISO 5 hoods.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

OBSERVATION 4

Drug product production and control records, are not reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed.

Specifically,

A. A review of your firm's electronic and paper batch records found your firm released purportedly sterile drug products before reviewing the completed EM results associated with each batch. According to your QA Supervisor of Microbiology, the earliest a batch can be released from the microbiology department is (b) (4). However, your firm's batch release system, " (b) (4) recorded at least 9 instances of lot release prior to (b) (4) from production of each drug product lot. Furthermore, the completed EM data packets are provided as paper records and there is no record of your firm's designated QA personnel reviewing the raw EM data prior to release of each lot. Examples of purportedly sterile drug product lots released within (b) (4) of production, include but are not limited to:

Drug Name	Lot Number
Rocuronium 10 mg/mL 5 mL SY	(b) (4)
Phenylephrine 100 mcg/mL in NS 10 mL SY	
Rocuronium 10 mg/mL 5 mL SY	
Oxytocin 15 units/250 mL NS	
Trophamine 4%/Dextrose 10% w/ Ca Gluc & Heparin 250 mL	
Phenylephrine 100 mcg/mL in NS 10 mL SY	
Phenylephrine 50 mg/250 mL NS	

del Nido Formula (Plasmalyte) 1052.8 mL	(b) (4)
Diltiazem 125 mg/125 mL D5W	

B. Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity of each active ingredient prior to release. For example, according to your firm's supervising chemist, your firm does not perform any impurity testing (e.g., degradation impurities, organic impurities, process related impurities, or stability related impurities) on your sterile drug products. Your firm's logbook, "Sample Analysis for Release - UPLC," documents the presence of an "extra peak" for sample, (b) (4) " (amino acid analysis), which is associated with lot (b) (4) : Trophamine 3.5%/Dextrose 10% 250 mL in 250 mL (b) (4) Bag. However, during our review of your firm's batch record for this lot, we noted the analytical packet containing this extra peak was missing and an analytical packet ran at a later time was included. Your firm did not initiate an NQE, conduct an investigation, or reference there was an unknown peak associated with this batch. This batch was released into distribution by your firm's QA Batch Release personnel.

OBSERVATION 5

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

Specifically,

A. Your procedure, SOP- CAPS-4000175, *Aseptic Technique,* Version 15.0, Effective date: 2023-05-26, Section 6.6. states, (b) (4) ." On 06/26/2023, we observed IV Tech compounding Oxytocin Lot (b) (4) in hood (b) (4) and then transferring finished product bags from the ISO 5 hood onto a cart

located in the ISO 7 area at least five (5) times without sanitizing their gloved hands.

B. Your procedure, SOP- CAPS-4000717, *Repeater Pump Procedure,* Version 23.0, Effective date: 2023-06-26, Section 6.6.2 - 6.6.4 states, "(b) (4) ." On 06/26/2023, we observed your IV tech compounding Oxytocin Lot (b) (4) in hood (b) (4) only spray the (b) (4) side of the IV bags before placing the IV bags onto the bench. After introducing the IV bags into the ISO 5 direct compounding area, the IV tech did not spray the additive ports as directed by your procedure.

****** THIS OBSERVATION WAS CITED IN THE PREVIOUS INSPECTION. ******

OBSERVATION 6

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically,

A. Production areas and equipment were visibly dirty. For example, but not limited to:

1. On 06/26/2023, during a walkthrough of the controlled corridor, we observed what appeared to be rusted casters on at least four bucket carts. Your Assistant Director of Pharmacy stated the stains were "rust or detergent residue" and that the (b) (4) (b) (4) are used for mopping of the ISO 7 cleanroom floors where the ISO 5 hoods are located.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME	STREET ADDRESS
Central Admixture Pharmacy Services, Inc.	2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Phoenix, AZ 85043-3909	Outsourcing Facility

2. On 06/26/2023, we observed orange-brown stains on the ISO 7 cleanroom floor directly below the ISO 5 hoods in Rooms (b) (4) Your Assistant Director of Pharmacy stated the stains were from detergent residue.

B. Your firm does not adequately maintain your ISO 5 hoods used to produce sterile drug products. On 06/26/2023, we observed scratches on the back wall of ISO 5 hoods (b) (4), and (b) (4) during production of drug products. The scratches do not appear to be smooth and cleanable for aseptic operations. For example, but not limited to, the following drug product batches intended to be sterile were produced in these hoods and released for distribution:

Lot number	Hood ID	Prod. name
(b) (4)		Diphenhydramine 25mg/50 mL NS
		del Nido Formula (Plasmalyte)1052.8 mL
		Leesburg BTO Cardioplegia
		Reperfusate NO K 238.75 mL
		Reperfusate NO K 238.75 mL
		del Nido Formula (Plasmalyte)1052.8 mL
		Phenylephrine 20 mg/250 mL NS
		Oxytocin 30 units/500 mL LR
		Oxytocin 40 units/1000 mL NS
		Oxytocin 30 units/500 mL LR
		Oxytocin 30 units/500 mL LR

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

****** THIS OBSERVATION WAS CITED IN THE PREVIOUS INSPECTION. ******

OBSERVATION 7

Results of stability testing are not used in determining expiration dates.

Specifically, your firm's Quality Unit failed to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products and to use results of stability testing to determine appropriate storage conditions and expiration dates.

A. Your firm lacks stability data to support that any of your sterile drug products will remain sterile throughout the labeled expiration date.

B. Your products failed to meet specifications at various timepoints of stability testing. A review of your current stability data for Oxytocin 20 Units - 0.9% Sodium Chloride 1000 mL (Lot (b) (4), compound date (b) (4) and Oxytocin 15 units - 0.9% Sodium Chloride 250 mL (Lot (b) (4), compound date (b) (4)) demonstrated the batches did not meet potency specifications throughout the assigned (b) (4)-day expiration date. For example, but not limited to:

   1. Your established specification range for Oxytocin 20 Units/1000 mL NS is (b) (4) units/mL. "Oxytocin Assay" results for lot (b) (4) include:
      - Day (b) (4) 0.0173 units/mL (86.5% of label claim)
      - Day (b) (4) 0.0176 units/mL (88%) and 0.0177 units/mL (88.5%)
   2. Your established specification range for Oxytocin 15 Units/250 mL NS is (b) (4) units/mL. "Oxytocin Assay" results for lot (b) (4) include:
      - Day (b) (4) 0.0481 units/mL and 0.0489 units/mL

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

A total of (b) (4) lots of Oxytocin 15 units/250 mL NS and (b) (4) lots of Oxytocin 20 units/1000 mL NS were distributed between 02/09/2023 to 06/01/2023, including for example:

Lot #	Drug Product
(b) (4)	Oxytocin 15 units/250 mL NS
	Oxytocin 15 units/250 mL NS
	Oxytocin 15 units/250 mL NS
	Oxytocin 20 units/1000 mL NS
	Oxytocin 20 units/1000 mL NS
	Oxytocin 20 units/1000 mL NS

OBSERVATION 8

Your firm failed to establish written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess.

Specifically,

A. Your firm did not provide scientific justification for re-introducing drug components into the (b) (4) chamber an uncontrolled number of times. For example, on 06/27/2023, during walkthrough of the warehouse, we observed (b) (4) carts filled with raw materials staged in the warehouse labeled "GO BACKS." Your Director of Pharmacy stated that the GO BACKS process is used to return raw materials back into the (b) (4) chamber to be re-introduced to the cleanrooms for use in compounding drug products intended to be sterile. Your firm does not keep a record of which materials were re-introduced and how many times. Your firm also did not conduct a study on how many times raw materials used for compounding drug products can be re-introduced to the (b) (4)

chamber. During discussion of this process, your VP of Quality stated, "a procedure does not exist for this operation."

B. You do not follow your validated method of loading materials on your (b) (4) carts. Your procedure, SOP-CAPS-4000754, *Product Introduction using the* (b) (4) *Chamber*, Version 12.0, Effective: 2022-11-01 states to put (b) (4). However, during our walkthrough of your warehouse, we observed (b) (4) carts packed with (b) (4). This arrangement of carting was not validated to ensure that all items loaded on the cart are properly decontaminated prior to transfer from the unclassified to classified area.

OBSERVATION 9

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

Specifically,

A. Your firm's environmental monitoring (EM) and personnel monitoring (PM) sampling conducted within your ISO 5 classified area is not representative of environmental conditions during aseptic production. Your firm's VP of Quality, Director of Pharmacy, and Director of Quality Systems did not provide any supporting documents justifying why EM/PM sampling is performed under these conditions. For example, but not limited to:

1. According to your firm's QA Supervisor of Microbiology, your firm routinely performs EM/PM sampling after your aseptic operator compounds (b) (4) units (i.v. bags, syringes, etc.) for each batch produced without any additional EM/PM sampling for the remainder of that batch. Your firm produces batch sizes as large as (b) (4) units.
2. On 06/26/2023, we observed PM sampling of your firm's aseptic operator after (b) (4) i.v.

bags were produced of Oxytocin 40 units/1000 mL NS (Lot (b) (4)). Your procedure, SOP- CAPS-4000582, *Environmental Monitoring,* describes the PM sleeve sampling schedule of aseptic operators performing operations within the ISO 5 classified areas, (b) (4)." Your firm's QA Supervisor of Microbiology stated (b) (4)

B. On 06/26/2023, we observed your firm's EM Quality Technician, who routinely conducts EM/PM sampling, failed to employ proper fingertip plating techniques during PM of your firm's aseptic operator for Oxytocin 40 units/1000 mL NS (Lot (b) (4)). The aseptic operator was observed (b) (4) their fingertips to each media plate, rather than rolling their fingers to capture the gloved hands utilized during aseptic production.

OBSERVATION 10

Written production and process control procedures are not followed in the execution of production and process control functions and documented at the time of performance.

Specifically,

Your firm does not keep records pertaining to production of released sterile drug products in accordance with your firm's written procedures, SOP-CAPS-4000212 entitled "Good Documentation Practices.

For example, but not limited to:

A. The Pallet ID is used to document important steps in production, including but not limited to, lot

numbers, product name, hood number, and notes from production staff. According to your firm's QA Supervisor of Process Control, all Pallet IDs were shredded prior to April 2023.

B. You have poor documentation practices. For example, we observed sticky notes on a destruction log form that said, "Checking destruction counts Missing 4 Reach out to (b) (6), (b)(7)(C) about how to document". Your firm's SOP-CAPS-4000212, *Good Documentation Practices*, also states "Records shall not be documented in uncontrolled media (post-it notes, steno pads, scratch paper)".

C. On June 20, 2023, during our walk through of your facility it was noted that sticky notes were placed on official endotoxin reports. Your QA Supervisor of Microbiology stated that this is to inform the reviewer of the concern but that the sticky notes are not maintained.

OBSERVATION 11

The accuracy, sensitivity, specificity and reproducibility of test methods have not been established and documented.

Specifically, but not limited to:

A. Your firm's Quality Unit failed to perform a method transfer of your sterility test method used for release of drug products. Your firm utilizes the (b) (4) for sterility testing. The associated test method was developed and validated at the CAPS Technical Services Laboratory located in Irvine, CA. During our review, we noted your firm failed to conduct a method transfer ensuring the (b) (4) sterility method test method is suitable for release of your sterile drug products.

B. According to your firm's Associate Director of Projects, you conducted a method validation to demonstrate the "non-inferiority" of the (b) (4) sterility test method. We reviewed your (b) (4) Qualification Package with its supporting data and noted the following concerns:

1. Your procedure, TP- CAPS-4000040, *Sterility Testing Using* (b) (4) *for*

CAPS Pharmacies, states to test (b) (4) mL from each collected container for (b) (4) container volumes regardless of the container volume. With the exception of drug products filled in syringes, your container volume for your drug products ranges from (b) (4). However, the compendial USP <71> method for sterility testing requires a minimum of 20 mL sampling size for container volumes greater than 40 mL.

2. According to your procedure, SPEC-CAPS-4000235, *Sterility and Bacterial Endotoxin Test SPECs for CAPS Products*, your firm incubates sterility test samples for release of drug product between (b) (4). Your Associate Director of Projects stated that the incubation time frames were chosen based on the (b) (4). However, the compendial USP <71> method for sterility testing requires 14 days of incubation.

3. Your firm evaluated the (b) (4) in detecting the lowest number of microorganisms in a test sample. We noted negative values for inoculated bottles incubated for (b) (4) days (i.e., lack of recovery of inoculated microorganisms). The (b) (4) failed to support growth of *Aspergillus brasiliensis*, *Pseudomonas aeruginosa*, and *Clostridium sporogenes* in multiple runs. Your firm is unable to provide scientific justification to support the (b) (4) incubation time frame for sterility testing using (b) (4). Additionally, you did not open investigations into these discrepancies.

4. Your firm's Quality Unit failed to demonstrate reproducibility of your sterility method used for release of drug products with the (b) (4). The (b) (4) runs performed were conducted on the same day by the same analyst using the same microbial preparation. For example, the limit of detection using (b) (4) CFUs with *Pseudomonas aeruginosa*, was performed on 07/08/19. (b) (4) replicates were completed for (b) (4) runs and each run was performed by the same individual on the same day with the same

microbial preparation.

Therefore, the use of the (b) (4) has not been established as a sterility indicating method.

C. Your firm's Quality Unit failed to follow the analytical method validation used for release of drug products. For example, but not limited to, Rocuronium Bromide. According to your firm's Supervising Chemist, your firm uses a Testing Procedure (TP) for Rocuronium Bromide that was validated in your San Diego 503B facility. During our review of the method validation for potency analysis by UPLC, transfer of analytical test procedures, and the testing procedure for identification, assay, and purity determination by HPLC/UPLC used at your facility, we noted the following concerns:

1. The target concentration outlined in your testing procedure is not the same as the concentration outlined in your firm's method validation. You have not shown accuracy or precision at the current target concentration of (b) (4) (as outlined in your testing procedure) which is below from target concentration of (b) (4) (as outlined in your method validation). There is no data to reflect an accuracy of (b) (4).
2. The solution preparation for your diluent as outlined in your testing procedure ((b) (4)) is a different diluent mix as outlined in your method validation ((b) (4)
3. Your firm's Transfer of Analytical Test Procedures from CAPS San Diego, CA to CAPS Phoenix, AZ (Report: (b) (4)) states the Injection volume can be " (b) (4) if needed without causing a deviation to provide a successful method transfer.

However, USP <621> states, an increase is permitted provided, in particular, linearity and resolution of the peak(s) to be determined remain satisfactory. Your firm did not provide supporting data for linearity and resolution.

In addition, your firm's method validation states specificity was not included, therefore, this is not a stability indicating method.

Please refer to **OBSERVATION 1** related to repeated Rocuronium failures and subsequent retesting.

OBSERVATION 12

Batch production and control records are not prepared for each batch of drug product produced and do not include complete information relating to the production and control of each batch.

Specifically,

A. The Quality Unit failed to ensure that your Batch Compounding Record is representative of your approved "Drug Master Formula." Your firm's "Drug Master Formula" (Master - Production Record) only supports a batch size up to (b) (4) units. However, your firm exceeded the units supported by your "Drug Master Formula." For example, but not limited to:
   1. Trophamine 3%/Dextrose 10% w/Ca Gluconate and Heparin in 250mL (Lot (b) (4)) compounded on May 2, 2023, yielded a batch size of (b) (4) units. Released by quality on May 10, 2023.
   2. Trophamine 3.5%/Dextrose 10% w/ low Ca Gluconate and Heparin in 250mL ((b) (4)) compounded on May 2, 2023, as a batch size of (b) (4) units. Released by quality on May 17, 2023.

3. Trophamine 3.5%/Dextrose 10% w/Ca Gluconate and Heparin in 250mL (Lot# (b) (4)) compounded on May 12, 2023, as a batch size of (b) (4) units. Released by quality on June 8, 2023. Please refer to **OBSERVATION 1**.

B. Your Quality Unit failed to prepare batch production and control records with complete information relating to the production and control of each batch of sterile drug product produced. Specifically, your firm failed to document the total number of units of each raw material used in the final production of your products. For example, but not limited to:

1. Maintenance 4:1 Low K (20mEq) 810 mL (Lot# (b) (4))
2. Trophamine 3.5%/Dextrose 10% w/Heparin 250mL (Lot# (b) (4))

Oxytocin 15 units/250mL LR (Lot# (b) (4)).

OBSERVATION 13

Input to and output from the computer, related systems of formulas and records or data are not checked for accuracy.

Specifically,

A. Your firm does not have written procedures in place describing the review of analytical data used for final release testing of finished drug products. Currently, your firm uses (b) (4) UPLCs for potency and/or identification testing. Your firm does not conduct a review of the electronic data to ensure manual integrations are not conducted and audit trails are not routinely reviewed to ensure your product has not undergone unauthorized retesting or whether data has been otherwise manipulated.

In addition, according to your firm's supervising chemist, logbook, "Sample Analysis for Release - UPLC", referenced in SOP-CAPS-4000736, is to capture UPLC sample sequences for release. However, not all sequences are captured in this logbook.

For example, but not limited to, during our review of your firm's injection and result trails extracted from (b) (4) we noted sample sets were ran multiple times over multiple days. It is unclear

why your firm repeats testing without documentation.

- Oxytocin, Lot (b) (4), was injected on (b) (4)
- Phenylephrine, Lot (b) (4), was injected on (b) (4), and (b) (4)
- Succinylcholine, Lot (b) (4), was injected on (b) (4).
- Neostigmine, Lot (b) (4), was injected on (b) (4).

B. Appropriate controls are not established to assure that changes to CGMP records can only be made by authorized personnel. Your firm utilizes an electronic documentation management system, (b) (4), for the control, preparation, approval, and distribution of new or modified controlled documents. According to your firm's written procedure, SOP-CAPS-4000227 (b) (4) provides secure and Regulatory-compliant methods of document control and history. Your firm's Director of CAPS Quality System stated only (b) (4) CAPS Phoenix personnel are assigned an administrator role with the ability to modify, edit, and delete documents from your firm's database. However, during our electronic review with the (b) (4), IT Senior Systems Analyst, we noted (b) (4) global users employed by (b) (4) have the access and rights to modify, edit, and delete your firm's controlled documents.

C. Your Quality Unit failed to ensure appropriate controls are not established to assure functions are performed under approved authorized access. For example, your firm utilizes an (b) (4) Compounding System for TPNs and Cardioplegia drugs. On 06/29/2023, we observed your IV Tech 1 perform functions and duties under the IV Tech Lead's credentials.

OBSERVATION 14

Samples taken of drug products for determination of conformance to written specifications are not properly identified.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/21/2023-7/31/2023* FEI NUMBER 3014307835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Peter E. Nero, Director of Pharmacy	
FIRM NAME Central Admixture Pharmacy Services, Inc.	STREET ADDRESS 2200 S 43rd Ave
CITY, STATE, ZIP CODE, COUNTRY Phoenix, AZ 85043-3909	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

Specifically,

Your firm's written procedure, SOP-CAPS- 4000657, defines the collection, retention, testing, and destruction of quality test samples from each lot of compounded products preparation. For example, a "logbook is used to record the compounding date, date received, NDC number, lot number, product name, number of samples received for sterility testing and initialed for destruction." However, your firm's QA Supervisor of Microbiology, confirmed that your firm does not maintain a chain of custody for samples.

OBSERVATION 15

The calibration of instruments, apparatus and recording devices is not done at suitable intervals in accordance with an established written program and with provisions for remedial action in the event accuracy and/or precision limits are not met.

Specifically,

Your firm's Quality Unit failed to ensure maintenance and/or calibration is completed prior to the equipment being used for commercial production of your firm's 503B products. For example, but not limited to, on 06/22/2023, we observed (b) (4) (ID 116307), used for testing particulate matter content of your drug products intended to be sterile, was past due for calibration.

OBSERVATION 16

Procedures designed to assure that correct labels are used for drug products are not followed.

Specifically, your firm's Quality Unit failed to follow written procedures designed to assure that correct labels, labeling, and packaging are used for drug products.

Your firm's SOP CAPS-4000643 entitled "Hold, Test and Release Policy –503B" under section 6.1.8

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Dogbeda F Mackenzie, Investigator June P Page, Investigator Melinda Lee, FDA Center Employee Mary-Jeanet Mcgarry, FDA Center Employee	Dogbeda F Mackenzie Investigator	7/31/2023

states that prior to compounding the pharmacist must approve the labels. On multiple occasions a pharmacy technician released labels for production instead of a pharmacist, per your firm's procedure. For example, but not limited to, Microplegia High K (100 mEq) 200 mL -(Lot# (b) (4)) the label release was conducted by a pharmacy technician, and the batch was released on 6/7/23.

OBSERVATION 17

Adverse drug experience information has not been reported to FDA.

Specifically,

The firm's SOP for Adverse Events entitled "CAPS 503B Adverse Drug Experiences Processing" SOP-CAPS-4000235" Version 5.0 Effective Date: 2022-03-09 states that all customer complaints will be reviewed by CAPS Quality and Operations; however, your firm has failed to document this step.

Additionally, the firm relies on the VP of Quality to determine if a medical assessment is required based on the firm's definition of a reportable event. The medical assessment is obtained by parent company B. Braun. For example, your firm opened NQE-US59-230413-081 and NQE-US59-230505-122 to investigate two customer complaints of unexpected reactions to Oxytocin Lot (b) (4) (30 units/500 mL). The VP of Quality stated that they know this is a common "issue" and that they did not report it.

***DATES OF INSPECTION**

6/21/2023(Wed), 6/22/2023(Thu), 6/23/2023(Fri), 6/26/2023(Mon), 6/27/2023(Tue), 6/28/2023(Wed), 6/29/2023(Thu), 7/11/2023(Tue), 7/12/2023(Wed), 7/13/2023(Thu), 7/17/2023(Mon), 7/18/2023(Tue), 7/19/2023(Wed), 7/20/2023(Thu), 7/21/2023(Fri), 7/25/2023(Tue), 7/26/2023(Wed), 7/27/2023(Thu), 7/28/2023(Fri), 7/31/2023(Mon)

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 judgment, 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."