DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214)253-5200 Fax:(214)253-5314	9/14/2016-10/14/2016* FEI NUMBER 3004483441

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
James L. McCarley , CEO

FIRM NAME	STREET ADDRESS
Cantrell Drug Company	7321 Cantrell Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Little Rock, AR 72207-4144	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

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

Specifically, the following deficiencies were observed during the current inspection:

1. Cleaning solutions were observed stored on rolling carts adjacent to ISO 5 Hoods inside of ISO 7 Rooms (b) (4) and (b) (4) On 9/15/16 operators inside of ISO 7 Room (b) (4) were observed spraying (b) (4) on sterile wipes to clean equipment and surfaces outside of the ISO 5 Hood. The sterile wipes were stored openly on a rolling cart and came in contact with the spray mist of (b) (4), the container of (b) (4) sleeves of operator gowning and gloves, surface of the metal cart, and paper transferred from the non-classified area. The sterile wipes were subsequently observed being used to clean the inside of the ISO 5 Hoods with (b) (4) and Sterile (b) (4)

   The firm utilizes the following agents for cleaning the ISO 5, 7 and 8 areas:

Cleaning Agent	Area of Use	Contact Time
Sterile (b) (4)	ISO 5 Hoods, sterile gloves	(b) (4)
***Note:** Contact time of (b) (4) is for sterile gloves only. Disinfectant study did not include any other surfaces outside of latex gloves with (b) (4). Contact time for stainless		

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EMPLOYEE(S) SIGNATURE
Latorie S Jones, Investigator
Lisa R Jennings, Investigator
Shelby N Marler, Generic Drug User Fee Amendments (GDUFA)

10/14/2016
X Latorie S Jones
Latorie S Jones
Investigator
Signed by: Latorie S. Jones -S

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steel, plexiglass, and glass surfaces was not established.

(b) (4) (b) (4)	ISO 5 Hoods, ISO 7 Buffer Room, ISO 8 Ante Room	(b) (4)
Non-Sterile (b) (4) (b) (4)	Ceilings, Walls and Floors of ISO 7 Buffer Room and ISO 8 Ante Room	(b) (4)

***Note:** Your PIC (pharmacist-in-charge) stated your (b) (4) is prepared using (b) (4) (b) (4) using (b) (4) Your disinfectant study contact time of (b) (4) is based on using (b) (4) .

Despite your firms use of "sporicidal agent" multiple spore forming microorganisms have been recovered in your ISO 5 environment during periods when your firm was producing products purporting to be sterile. For example,

Date	Location	Identification
9/15/16	Room (b) (4) Hood (b) (4)	Bacillus cereus
9/13/16	Room Hood	Lysinibacillus sinduriensis
9/12/16	Room Hood	Rhizopus oryzae*
9/9/16	Room Hood	Bacillus simplex/Brevibacterium (Bacillus) frigoritolerans
9/1/16	Room Hood	Bacillus amyloliquefaciens/methylotrophicus
9/1/16	Room Hood	Bacillus circulans

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8/24/16	Room (b) (4) Hood (b) (4)	Bacillus cereus
8/17/16	Room Hood	Bacillus cereus
*Note: Recovery was Mold		

Furthermore, your (b) (4) manufacturer's instruction for use states a BUD of (b) (4). However, we observed expiration dates of 28 days and 56 days for (b) (4) used in your cleanrooms without any scientific justification.

2. Your operator failed to adequately sanitize the IV bags, including the "belly button" (needle port) and secondary port, prior to placing them inside of the ISO 5 hood and performing a needle stick or spike while filling Heparin 5,000 units in NS-1,000mL bags, lot #168094, (b) (4) units on 9-15-16. Your non-classified (b) (4) is used to (b) (4) are subsequently (b) (4)

3. Corded and wireless computer mouses with scroll wheels did not contain any protective covering and were observed being used inside of multiple ISO 5 hoods, laptops containing exposed keyboards stored on rolling carts adjacent to the ISO 5 Hoods were observed being used, and portable walkie talkies and wall mounted phones were observed in use in the ISO 7 Buffer Room. The aforementioned did not appear to be easily cleanable surfaces.

OBSERVATION 2

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

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Specifically,

1. Your media fills do not represent the batch size, worst case scenario or the most challenging conditions. For example,

   a. Your firm's average batch size is approximately (b) (4) units with a maximum production up to (b) (4) units. Batches are produced (b) (4) in which operators are allotted to exit the cleanrooms up to (b) (4)

   b. Your firm uses various size containers and closures such as IV bags, syringes, vials, (b) (4) cassettes, (b) (4) vials. However, the most recent media fills in (b) (4) utilized either (b) (4)

This is repeat observation from the last FDA inspection conducted 10/15/13-11/4/13.

2. The following deficiencies in aseptic technique were observed during the inspection:

   a. Operators with their upper body inside of the ISO 5 hood during aseptic filling which could potentially interrupt unidirectional flow and prevents first pass air.

   b. Failure to adequately sanitize gloves. For example,

      i. On 9/14/16 operator (b) (7) (C), (b) (6) was observed touching tubing outside of the ISO 5 hood then re-entering the hood without sanitizing or changing gloves during the filling of Norepinephrine 32mcg/mL in 0.9%NaCl-250mL bag, lot #9042, in hood (b) (4).

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	Latorie S Jones, Investigator Lisa R Jennings, Investigator Shelby N Marler, Generic Drug User Fee Amendments (GDUFA) 10/14/2016 X Latorie S Jones Latorie S Jones Investigator Signed by: Latorie S. Jones -S	10/14/2016

ii. On 9/15/16 multiple operators were observed placing a sterile wipe in one gloved hand and using the opposite gloved hand to spray cleaning solution on to the sterile wipe. The side of the sterile wipe soaked with cleaning solution is then placed into the opposite hand followed by the operator using the same sterile wipe to clean inside of the ISO 5 hood. The gloves were not adequately sanitized or changed prior to exiting and reentry of the ISO 5 hood.

iii. Operator sprayed cloth in one hand with sterile cleaning solution then used proceeded to clean inside of the ISO 5 hood. The second gloved hand of the operator was then placed inside of the ISO 5 hood without sanitizing or changing the gloves.

b. Your operator failed to adequately sanitize all sides of sterile (b) (4) pads prior to placing them inside of the ISO 5 hood while compounding Heparin 5,000 units in NS-1,000mL bags, lot #168094, (b) (4) units on 9-15-16.

c. Operating gowning, especially the sleeves and upper body, continuously come in contact with various items in the ISO 7 Buffer Room which have not been sanitized such as plastic totes moved from the non-classified area, underside of hood and table, and cords and equipment located under the ISO 5 hood. Operator gowning is not changed prior to producing products purporting to be sterile inside of the ISO 5 hood.

d. Exposed skin was observed around the goggles, facemask and neck of multiple operators on 10/12/16.

3. Your firm has not validated the sterilization process ((b) (4) and (b) (4)) for finished drug products and laboratory equipment or (b) (4) used for finished drug products

and laboratory equipment in your firm. Your (b) (4) and (b) (4) are both housed and used in an unclassified area. Your firm sterilizes laboratory equipment (b) (4) and finished product (b) (4) and finished drug product (b) (4) (b) (4). In addition, records reviewed showed various (b) (4) were used for (b) (4) sterilization, for example, two different (b) (4) for the sterilization of Glycerin lot number 165184 (b) (4) followed by (b) (4) at a (b) (4) Glycerin lot number 159520 and 160871 had (b) (4) and Glycerin lot number 167466 and 166419 had (b) (4).

This is repeat observation from the last FDA inspection conducted 10/15/13-11/4/13.

4. All glassware (including (b) (4) and all metal ware (including (b) (4) (b) (4) are (b) (4) washed and dried in a dishwasher using (b) (4) Detergent or (b) (4) rinsed with (b) (4) followed by (b) (4) (b) (4) (b) (4) Your firm has not demonstrated these methods can achieve appropriate log reduction of microbes. Furthermore, your firm does not use any biological indicator during the drying cycle in the dishwasher

5. Your firm failed to conduct smoke studies under dynamic conditions.

OBSERVATION 3

Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to aseptic processing of drug products.

Specifically, your clean room facility design is insufficient in that:

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1. The ceiling tiles in (b) (4) of your ISO 7 clean rooms ((b) (4)) contained approximately ¼"- ½" gaps around the HEPA filters and light fixtures.

2. A blackish substance was observed in the approximately ½" gap of the ceiling light adjacent to the HEPA filter in ISO 8 Ante Room (b) (4) where products such as intrathecals are prepared (b) (4) . The duct work could be seen through the gaps. The products are transferred to the ISO 7 Buffer Room and (b) (4) in an ISO 5 Hood. The following intrathecal syringes were prepared in Room (b) (4) and were released:

Product	Lot
Hydromorphone 20mg/mL intrathecal syringe	168211
Morphine/Baclofen/Clonidine 20mg/90mcg/55mcg/mL intrathecal syringe	168139
Morphine 50mg/mL intrathecal syringe	168240
Fentanyl 100mcg/mL intrathecal syringe	168119
Hydromorphone/Baclofen 20mg/625mcg/mL intrathecal syringe	168213

3. The air returns located in the ISO 8 Buffer Room (b) (4) appeared to be a reddish-brownish color consistent with rust. Additionally, the return above the sink appeared to have a whitish substance.

4. ISO 7 Buffer Room (b) (4) contained exposed porous surfaces from approximately 1" tears in the epoxy flooring throughout the room which included areas in front of the ISO 5 hoods where

products purporting to be sterile are produced. The following products were manufactured in Room (b) (4):

Date Made	Product	Lot
9/15/16	Calcium Chloride 10G in NS 500mL bags	168032
9/19/16	Cardioplegia 4:1Solution-1,00mL bags	168346
9/19/16	Methacholine 0.125mg/mL-6mL syringe	168338

5. (b) (4) (b) (4) were noted as cracked during the inspection and were still being utilized during normal production activities. The firm placed a sign stating "decommissioned" on (b) (4) of the cracked (b) (4) located between ISO 8 Room (b) (4) and ISO 7 Room (b) (4) to prevent further use. This action was taken after the cracked (b) (4) was observed by the FDA investigators.

6. Reddish-brownish colored surfaces were noted at the base of the Plexiglass at the glass-metal juncture in the ISO 5 hoods visible in ISO 7 Buffer Room (b) (4) and ISO 7 Buffer Room (b) (4).

7. Approximately 1" tears in length were observed in the epoxy flooring adjacent to the ISO 5 Hood in ISO 7 Buffer Room (b) (4). Furthermore, scuffed walls were also observed in this room adjacent to the ISO 5 Hood.

8. On 9-16-16, we observed your firm's (b) (4) contained labeled and unlabeled totes containing products at different statuses: finished drug products ready for shipment, rejected products, quarantined products, bulk drugs, retain samples, and samples marked for destruction. Products of all statuses were comingled within the (b) (4) In addition, on 9-15-16,

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we observed the staging area of (b) (4) contained labeled and unlabeled totes containing products at different statuses similar to that of the (b) (4)

OBSERVATION 4

Test procedures relative to appropriate laboratory testing for sterility and pyrogens are not written and followed.

Specifically,

1. Your firm utilizes (b) (4) to conduct sterility testing of drug products purporting to be sterile produced by your firm without performing method suitability for all products tested. Your Policy and Procedure (P&P) 7.200 (R7) titled (b) (4) Testing Protocol, effective 2-1-16 and P&P 7.201(R1) titled (b) (4) Inconclusive, effective 7-2-15 do not establish a threshold of events to be verified (b) (4) as necessary before classifying a result as inconclusive. Your QC specialist stated events are designated as inconclusive if they appear "suspect" or TNTC (too numerous to count).

   Your firm does not maintain examples of what a positive signal that a viable microorganism could produce if present when (b) (4). On 10-5-16 your operator stated "I do not know what fungal would look like".

   Your firm does not always retest inconclusive samples using the remaining sample from the original containers when testing in-house. A new container is always submitted to a 3rd party laboratory for retesting. The following products underwent initial testing and repeated testing until a passing result was achieved prior to being released into the market:

Date Tested	Product	Lot#	Detected Events*	Date Shipped

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9/9/16	Fentanyl Citrate 2mcg/mL & Ropivacaine HCl 0.2% in 0.9% NaCl-100mL bag	167652	23	(b) (4)
8/18/16	Norepinephrine 4mg (16mcg/mL) Added to Dextrose-250mL bag	8917	215	
8/11/16	Ropivacaine HCl 1% Concentrate-50mL syringe	166733	676	
6/24/16	Glycopyrrolate 0.2mg/mL-1mL syringe	8637	61	
6/9/16	Phentolamine Mesylate 5mg/mL-10mL syringe	163913	550	
6/9/16	Heparin Sodium 5,000 USP units added to NaCl-500mL bag	8566	391	
6/3/16	Oxytocin 20 USP added to Lactated Ringer's-100mL bag	8542	1119	
5/24/16	Oxytocin 20 USP added to 0.9% NaCl-1000mL bag	8489	223	
5/24/16	Sodium Citrate 30% in Sterile Water for Injection-55mL vials	163006	2032	
5/18/16	(b) (4) Intrathecal Samples	Multiple**	248	
3/24/16	Fentanyl Citrate 3000mcg (10mcg/mL) in 0.9% NaCl-300mL bag	160875	12***	
4/2/15	Amiodarone 450mg added to 5% Dextrose-250mL bag	6270	9****	

*Detected Events are those detected by (b) (4) which require (b) (4) by the operator. The events could be viable microorganisms, particulates, or (b) (4)

**Individual intrathecal lot numbers:162847, 163050, 162972, 162920, 162867, 162870, 162974, 162976, 163048, 162878, 162969, 163046, 162916

***Product had 12 events detected and 4 events identified as microorganism suspects.

****Product had 9 events detected and 5 events identified as microorganism suspects. Product samples sent to 2 different laboratories: 1 failing result (gram positive rods-Propionibacterium acnes) and 1 passing result.

This is repeat observation from the last FDA inspection conducted 10/15/13-11/4/13.

2. Your P&P 7.190 (R3) titled Endotoxin testing using the (b) (4) effective 3-4-16 and 7.192.0 titled Endotoxin testing using the (b) (4) effective 5-16-16, do not define a criterion for retesting endotoxin levels until a result of passing is achieved. Your

firm routinely fails to initiate or adequately investigate endotoxin failures. Your firm utilizes the (b) (4) (b) (4). Your firm tested the following products 2-5 times prior to receiving a passing result and releasing the product into the market:

Date Tested	Product	Lot#	Number of Fails In-House	Passing Result prior to shipment	Date Shipped
7/7/16	Cardioplegic Solution	164863	1	Yes-In-House	(b) (4)
5/23/16	Sodium Citrate 30% in Sterile Water for injection-55mL vial	163006	2	Yes-3rd party	
5/5/16	Glycopyrrolate 0.2mg/mL Concentrate	8356	4	Yes-3rd party	
1/18/16	Edetate Disodium	158067	2	Yes-3rd party	
1/18/16	Edetate Disodium	157992	2	Yes-3rd party	
12/17/15	Fentanyl Citrate	156801	1	Yes- In-house	
9/14/15	Ethanol 95%-10mL vial	152927	5	Yes- 3rd party	
5/6/15	Zinc Sulfate 1mg/mL Concentrate	148001	4	Yes-3rd party	

Furthermore, on 7-5-16 your firm produced and then performed endotoxin testing on Cardiac Reperfusate Solution ((b) (4), (b) (6)), Lot #165116, 188mL bags three times before submitting

a new bag for sampling to a 3rd party vendor. The endotoxin result from the 3rd party vendor was 28.68 EU/mL (limit (b) (4) . Your firm identified one of the components used in lot#165116 was Monosodium-L-Glutamate (MSG), lot # (b) (4) , which contained an endotoxin level >25EU/mL (limit (b) (4) on 7-18-16. The following products used MSG, lot # (b) (4) were released to the market:

Date Made	Product	Lot #	BUD
7/5/16	Cardioplegia Solution C ((b) (4), (b) (6)) Solution	165132	9/3/16
6/29/16	Cardiplegic Solution	164863	8/28/16
6/27/16	Cardioplegia Physiologic	164740	8/11/16
6/27/16	Cardioplegia Warm Induction	164738	8/11/16
6/10/16	Cardioplegia Solution C ((b) (4), (b) (6)) Solution	164169	8/9/16

Lastly, your firm does not perform endotoxin testing on all finished products.

OBSERVATION 5

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

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Specifically, your firm does not have stability data to support the BUD assigned for all products purporting to be sterile produced by your firm. The following products on the drug shortage list produced by your firm do not have stability studies:

1. Droperidol 2.5mg/mL injection- 2mL vial, BUD 90 days
2. Potassium Acetate 4mEq/mL injection-50mL vial, BUD 90 days
3. Dexamethasone Sodium Phosphate 10mg/mL injection-1mL vial, BUD 90 days

This is repeat observation from the last FDA inspection conducted 10/15/13-11/4/13.

OBSERVATION 6

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,

1. Your firm's policy and procedure 7.390, revision 4, effective 11-9-15, states (b) (4) . Your firm did not perform potency testing for the following (b) (4) :

Product	Lot#	Quantity
Oxytocin 30 USP units added to 0.9%NaCl-500mL bags	9056	(b) (4)
Heparin Sodium 10 USP units/mL in 0.9% NaCl 3 mL in 10 mL BD syringe	9007	

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preserved with 0.9% Benzyl Alcohol		
Heparin Sodium 4,000 USP units added to 0.9% NaCl- 1,000mL bags	8946	(b) (4)
Amiodarone 450mg added to 5% Dextrose-250mL bags	6270	
Methacholine 0.125mg/mL-6mL syringe	168338	

2. Your firm does not visually inspect all products prior to release. Your firm performs a (b) (4) For example,

(b) (4)

Note: Your firm has filled (b) (4) .

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OBSERVATION 7

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

Specifically,

1. Your firm documented 1 CFU for a plate that was observed as too numerous to count (TNTC) during the plate reading of the (b) (4) surface environmental sample taken (b) (4) on 9-12-16. The following products were produced on 9-12-16 and released to the market:

Product Name	Lot#	Units Processed	Quality Release Date	Units Shipped
Cardioplegia 4:1-100mL bags	167961	(b) (4)	9-13-16	(b) (4)
Ephedrine Sulfate 10mg/mL-5mL syringes	168006		9-16-16	

2. On 9/16/2016, I observed Glove Fingertip Sampling during Personnel Monitoring, which consisted of the sterile compounding technician (b) (4) (b) (4) . This Glove Fingertip Sampling method is inadequate in that (b) (4) does not represent an accurate representation of the (b) (4) .

3. During this inspection, I reviewed your firm's performance qualification/validation from September 2014 for incubator number (b) (4) located in the quality laboratory. This incubator is used to incubate environmental fungal samples. Documents reviewed showed that the company your firm hired to conduct the validation failed the equipment and wrote "Due to the recovered results the unit was found to be unable to maintain Temperatures within the acceptance criteria and is considered unreliable to maintain desired temperatures. The recommendation was given that the unit be removed from service and replaced with a more suitable unit." This document is signed by the Director of Quality Assurance. In addition, in the last 3 months the incubator was recorded to have a (b) (4) low temperature below the lower limit of (b) (4) °C eleven (11) times and above the upper limit of (b) (4) °C five (5) times. This incubator was observed to still be in use as of 10/6/2016.

OBSERVATION 8

Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.

Specifically,

1. The ISO 8 Ante Room (b) (4) separating the ISO 7 Buffer Room (b) (4) (positive pressure) from the ISO 8 Labeling Area lacked HEPA filtration from January 2015 to July 2016; the ISO 7 Buffer Room (b) (4) (negative pressure) is connected to ISO 7 Buffer Room (b) (4). Your firm's President stated this was an oversight in design that was not corrected until July 2016.

   Your ISO 8 Ante Rooms (b) (4) leading into ISO 7 Buffer Room (b) (4) did not meet your (b) (4) minimum pressure differential and was observed to be 0.01"w.c. during your (b) (4)

room certification by (b) (4) in (b) (4) Your firm relies on (b) (4) of pressure differentials. The (b) (4) is (b) (4) (b) (4) if a room is not within minimum pressure guidelines (b) (4) (b) (4) Furthermore, your firm does not perform periodical review of the monitoring data to ensure cascading pressure differentials are maintained when drugs purporting to be sterile are produced.

Your firm has produced approximately (b) (4) units from December 2014 to September 2016. No evaluation to product impact has been assessed to date.

2. Your firm failed to allow the (b) (4) on your (b) (4) (b) (4) [serial no. (b) (4)] to maintain room pressure changes after being advised by your 3rd party room and device certification vendor in (b) (4) (b) (4) . The aforementioned (b) (4) are utilized to produce Oxytocin and Cefazolin in ISO 7 Room (b) (4) which opens into ISO 7 Buffer Room (b) (4) where non-beta lactam products are produced.

OBSERVATION 9

The building lacks adequate space for the orderly placement of equipment and materials to prevent mix-ups between different components, drug product containers, labeling, in-process materials and drug products and to prevent contamination.

Specifically, on 9/20/2016, I observed racks of labeled and unlabeled totes in Cleanroom (b) (4) containing Intermediate drug products, saline bags and the finished drug products, "Fentanyl Citrate 10mcg/mL in 0.9% Sodium Chloride 100mL Inj Bag", Lot 9064. For example:

1. Totes labeled as the finished drug product, "Fentanyl Citrate 10mcg/mL in 0.9% Sodium Chloride 100mL Inj Bag", Lot 9064, contain bags labeled as the finished drug product, "Fentanyl Citrate 10mcg/mL in 0.9% Sodium Chloride 100mL Inj Bag", Lot 9064. Your firm's Staff Pharmacist and PIC stated the bags did not contain the finished drug product, "Fentanyl Citrate 10mcg/mL in 0.9% Sodium Chloride 100mL Inj Bag", Lot 9064; but contained the (b) (4) drug (b) (4) . However, the Staff Pharmacist and PIC stated they did not know the concentration of (b) (4)

   a. The batch record revealed the (b) (4) is Fentanyl Citrate with a concentration of (b) (4)

2. Unlabeled totes contain (b) (4) 0.9% Sodium Chloride, Lot (b) (4) , bags without their outer sleeves. These bags are used in the compounding process of the finished drug product, "Fentanyl Citrate 10mcg/mL in 0.9% Sodium Chloride 100mL Inj Bag", Lot 9064.

Totes labeled as the finished drug product, "Fentanyl Citrate 10mcg/mL in 0.9% Sodium Chloride 100mL Inj Bag", Lot 9064, contain (b) (4) 0.9% Sodium Chloride, Lot (b) (4) , bags without their outer sleeves. Your firm's Staff Pharmacist and PIC stated those bags are the finished drug product, "Fentanyl Citrate 10mcg/mL in 0.9% Sodium Chloride 100mL Inj Bag", Lot 9064, but the bags are not labeled as the finished drug product until they leave the cleanroom.

OBSERVATION 10

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically, your firm's Internal Finding Records (IFRs), used to document out-of-specification results for personnel and environmental monitoring samples, potency failures, sterility failures, and endotoxin failures, do not require investigations into issues. 19 out of 19 IFRs reviewed during this inspection revealed your firm does not fully conduct and document investigations. SOP 7.220, "Documentation of

Internal Findings", Revision 2, Effective Date 7/2/2015, does not include the requirement of an investigation of failing testing results.

Date of Occurrence	*Product*	*Lot Number*	*Issue*	*Product Disposition*	*IFR Number*
9/15/2016	Calcium Chloride 20mg/mL in 0.9% Sodium Chloride	168032	EM Failure	Open	5296
9/12/2016	Fentanyl Citrate 2mcg/mL and Bupivacaine HCl 0.125% in 0.9% Sodium Chloride	9029	EM Failure	IFR Open	
9/12/2016	Cardioplegia Solution 4:1	167961	EM Failure	Released	5201
9/10/2016	Hydromorphone HCl 1mg/mL in 0.9% Sodium Chloride	9016	EM Failure	IFR Open	
7/29/2016	Trypan Blue Concentrate	166258	Potency Failure	Destroyed	5096
6/24/2016	Hydromorphone HCl 1mg/mL in 0.9% Sodium Chloride 30mL (b) (4) Vial	163941	BUD Extended	Released	4909
6/21/2016	Magnesium Sulfate 6g added to 0.9% Sodium Chloride 100mL Bag	164289	EM Failure	Released	4902
	Hydromorphone HCl 1mg/mL in 0.9% Sodium Chloride 30mL (b) (4) Vial	163941		Released	

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214)253-5200 Fax:(214)253-5314	9/14/2016-10/14/2016* FEI NUMBER 3004483441

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
James L. McCarley , CEO

FIRM NAME	STREET ADDRESS
Cantrell Drug Company	7321 Cantrell Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Little Rock, AR 72207-4144	Outsourcing Facility

6/15/2016	Betamethasone Sodium Phosphate 2.4mg/mL 5mL vial	163862	Potency Failure	Destroyed	4890
6/15/2016	Betamethasone Sodium Phosphate 6mg/mL 1mL syringe	164175	Potency Failure	Destroyed	4891
5/23/2016	Sodium Citrate 30% in Sterile Water for Injection	163006	Sterility Inconclusive	Released	4854
5/9/2016	Succinylcholine 20mg/mL Injection	162585	PM Failure	Released	4760
5/9/2016	Cefazolin Sodium 3g added to 0.9% Sodium Chloride 100mL Bag	8429	Leaking Bag	Released	4684
3/14 – 31/2016	(b) (4) Cleaning for Rooms (b) (4) not performed from 3/14-31/2016	(b) (4) Lots	The (b) (4) cleaning was not completed in Rooms (b) (4) from 3/14 – 31/2016	No investigations performed or IFRs created for the (b) (4) lots.	4570
3/9/2016	Promethazine 6.25mg/mL Sub formula	160319	Incorrect Formula Made	Destroyed	4387
1/27/2016	Hydromorphone 0.2mg/mL 30mL Barrel	158511	Potency Failure	Destroyed	4186
1/23/2016	ITs Rx (b) (4), (b) (6)	158333, 158331	Endotoxin Failure	Destroyed	4161
1/29/2016	Fentanyl Citrate 25mcg/mL in 5% Dextrose – 2mL Syringe	157929	Sterility Inconclusive	Released	4312
1/21/2016	Fentanyl Citrate 25mcg/mL in 5% Dextrose – 2mL Syringe		Sterility Inconclusive	Released	4310

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Little Rock, AR 72207-4144	Outsourcing Facility

1/20/2016	Fentanyl Citrate 25mcg/mL in 5% Dextrose – 2mL Syringe		EM Failure	Unknown	4182

OBSERVATION 11

The labels of your outsourcing facility's drug products are deficient.

The labels of your outsourcing facility's drug products do not include information required by section 503B(a)(10)(A). Specifically, the following information is not found on your drug product labels:

a) The statement "This is a compounded drug."
Example(s) of drug product labels that do not contain this information:

- Fentanyl Citrate 2 mcg/mL and Ropicacaine HCl 0.1% in 0.9% Sodium Chloride 100 mL bag
- Heparin Sodium 25,000 units added to 5% Dextrose 250 mL bag
- Calcium Chloride 20 mg/mL in 0.9% Sodium Chloride 500 mL bag
- Glycopyrrolate 0.2 mg/1 mL Injection Solution 1 mL
- Heparin Sodium 4,000 units added to 0.9% Sodium Chloride 1000 mL bag
- Cardioplegia Solution 52 mL bag
- Heparin Sodium 1,000 units added to 0.9% Sodium Chloride 1000 mL bag
- Hydromorphone HCl 30 mg/30 mL in 0.9% Sodium Chloride
- Del Nido Cardioplegia 1,092.5 mL
- Heparin Sodium 5,000 units added to 0.9% Sodium Chloride 1000 mL bag
- Morphine Sulfate 1 mg/mL in 5% Dextrose 100 mL bag

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	FEI NUMBER 3004483441

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

James L. McCarley , CEO

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Cantrell Drug Company	7321 Cantrell Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Little Rock, AR 72207-4144	Outsourcing Facility

OBSERVATION 12

Deviations from written production and process control procedures are not recorded and justified.

Specifically, on 10/12/16 we observed Glycopyrrolate 1mg/5mL (0.2mg/mL) syringes, lot 9174, were stored in a (b) (4) touching a portable space heater reading between 91-92°F during the labeling process. Your batch record and labeling both states the product should be stored at room temperature. No impact assessment has been preformed to determine the effect on the identity, quality, strength, and purity of this product.

*DATES OF INSPECTION

9/14/2016(Wed),9/15/2016(Thu),9/16/2016(Fri),9/19/2016(Mon),9/20/2016(Tue),9/21/2016(Wed),9/22/2016(Thu),9/23/2016(Fri),10/04/2016(Tue),10/05/2016(Wed),10/06/2016(Thu),10/07/2016(Fri),10/11/2016(Tue),10/12/2016(Wed),10/13/2016(Thu),10/14/2016(Fri)

10/14/2016

X Shelby N Marler
Shelby N Marler
Generic Drug User Fee Amendments (GDUFA)
Signed by: Shelby Marler -S

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Latorie S Jones, Investigator Lisa R Jennings, Investigator Shelby N Marler, Generic Drug User Fee Amendments (GDUFA)	10/14/2016

10/14/2016
X Latorie S Jones
Latorie S Jones
Investigator
Signed by: Latorie S. Jones -S