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 Industry Information: www.fda.gov/oc/industry	03/17/2014 - 04/01/2014* FEI NUMBER 3010683157

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Roy Eugene Graves, Chief Executive Officer

FIRM NAME	STREET ADDRESS
SCA Pharmaceuticals, LLC	8821 Knoedl Court
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Little Rock, AR 72205-4600	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 I OBSERVED:

OBSERVATION 1

Buildings used in the manufacture, processing, packing or holding of drug products are not maintained in a clean and sanitary condition.

Specifically,

On March 17th, 2014, during an inspection of the ISO 5 Laminar flow hood in Room (b) (ISO 7), we observed the following inside two of your firm's [redacted] (b) (4) Laminar Flow Hoods (hoods 16E and 16F) where sterile injectable drug products are produced:

In Hood 16E: Above the work surface and directly below the hood's HEPA filter, multiple white residue splatters were observed attached to the grate that protects the HEPA filter. One of these splatter marks was approximately 4 inches by 3 inches in surface area and another area had multiple splatterings of ≤¼ inch diameter throughout an approximate 8 inch by 8 inch area. Cefazolin 3 grams in sodium chloride 0.9%, 100 mL intraveneous piggyback bags, Lot No. 20140317@4, was being compounded at the time of observation.

In Hood 16F: Above the work surface and directly below the hood's HEPA filter, multiple white residue splatters were observed attached to the grate that protects the HEPA filter. One of these areas had multiple splatterings of ≤¼ inch diameter throughout an approximate 4 inch by 6 inch area. A (b) (4) [redacted] drug product, was being compounded at the time of this observation.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Zachery L. Miller, Investigator	DATE ISSUED 04/01/2014

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OBSERVATION 2

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

Specifically,

On March 17th, 2014, during an inspection of the ISO 5 sterile compounding area, we observed the following:

i. The HEPA filters in your ISO 7 (surrounding the ISO 5 hoods) and ISO 8 clean rooms were not leak tested during your last two ISO certification inspections on 5/1/2013 and 11/25/2013;

ii. The [redacted] (b) (4) [redacted] used to conduct [redacted] (b) (4) of your [redacted] (b) (4), have never been calibrated;

iii. None of your firm's magnehelic differential pressure gauges used to quantitatively evaluate your ISO 7 (surrounding the ISO 5 hoods) and ISO 8 clean rooms have ever been calibrated, and Room (b) (ISO 7), where caps are added to stoppered vials, has no pressure gauge at all. Further, there is no evidence of your firm's investigations into daily logs of 0.01 inches of water pressure excursions (Pressure specification (b) (4) inches of water) in the ISO 7 room (surrounding the ISO 5 hoods) when they occurred every day from 12/13/2013 through 3/20/2014. Furthermore, [redacted] (b) (4) recording of pressure differentials ([redacted] (b) (4) during static conditions) is an inadequate representation of the pressures in each ISO certified cleanroom throughout the production day.

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	Zachery L. Miller, Investigator	04/01/2014

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OBSERVATION 3

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process.

Specifically,

During periods of production in the ISO 5 hoods, your firm does not conduct active viable air monitoring and work area surface sampling on a daily basis. Further, your firm has no documentation of smoke studies conducted under dynamic conditions to indicate adequate unidirectional air control during sterile compounding.

OBSERVATION 4

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,

i. The Logged Formula Worksheets identified "particles" and "something" found in three vials (two vials from Lot No. 20140310@7, with visual inspection on 3/11/14 and quality release on 3/13/14; and, one vial from Lot No. 20140212@11, with visual inspection and quality release on 2/17/14) of Papaverine HCl 30 mg/mL in 10 mL Preserved Water for Injection. There was never an investigation initiated to determine the root cause and the impact of the contaminants; the remainder of the product was released. Procedure QMS-003, Reporting, Reviewing, Closing Deviations, Effective 9/18/2013, requires reporting deviations from observations suggesting potential quality related problems. The "particles" and "something" found in the vials mentioned above were documented in the Formula Worksheet and destroyed (on their visual inspection dates listed above) by the technician who conducted the visual exam.

ii. During your firm's root cause analysis (RCA No. 14-017) of fentanyl (20140130@2) and atropine (20140130@3) sterility failures, a Gap Analysis identified a particulate inside of a vial and considered it a critical defect. These two drug products were rejected and destroyed; however, there was never an investigation initiated to determine the root cause and the impact of particulates in future lots.

iii. Out-of-specification (OOS) sterility results were not investigated fully in order to determine facility-wide root causes of sterility failures that would lead to adequate corrective/preventative actions, follow-up (verification) and conclusions throughout the entire facility (e.g. ISO 5, ISO 7, and ISO 8 production areas). This is evidenced by the repeatability of your firm's OOS sterility results over a one month timeframe (24 total OOS sterility failures in January 2014), after accepting laboratory error and laboratory environment conditions as root causes, and only correcting laboratory conditions.

Given the inadequate facility and equipment controls in place in the production suites, there is a failure to fully review potential discrepancies in production. In January 2014, your firm was unable to identify a root cause for eleven of the total 24 OOS sterility failures. Without identifying root causes, your firm decided to reject/destroy these products. An example of seven products rejected/destroyed in January 2014 include the following: fentanyl 2000mcg/mL + bupivacaine HCl 30mg/mL (Lot No. 20140109@20); fentanyl 25mcg/mL in NS (Lot No. 20140110@1); oxytocin 10units/mL (Lot No. 20140110@5); sodium phosphate injection (Lot No. 20140113@10); fentanyl 290mcg/mL with baclofen 80mcg/mL (Lot No. 20140120@25); fentanyl 10mcg/mL (Lot No. 20140130@2); and, atropine 0.4mg/mL (Lot No. 20140130@3).

OBSERVATION 5

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,

There is no evidence of content testing to verify preservative systems/antimicrobial agents deployed in your sterile multi-use vials of drug products (e.g. papaverine HCl 30 mg/ml in 10 mL preserved water for injection, contains preservative [redacted] (b) (4) are effective and protect the multi-use vial products over its shelf-life under expected conditions.

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OBSERVATION 6

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

Specifically,

There is no sporicidal disinfectant used to clean and disinfect in the ISO 5 laminar flow hoods used for sterile drug preparation. [redacted] (b) (4) are the only disinfectants used to clean and disinfect in the ISO 5 laminar flow hoods.

OBSERVATION 7

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

Specifically,

Sterile gowning components are reused by employees on a daily basis. Employees remove their sterile gowning components (hanging them in ISO 7 classified, Room (b)) after the morning work period, leave and return from lunch, and then re-gown for the afternoon work period, using the same gowning components from the morning work period.

OBSERVATION 8

The labels of your firm's drug products do not always contain information required in section 503B(a)(10) of the Act.

Specifically,

i. The following drug product labels do not contain the statement "This is a compounded drug": Hydroxyprogesterone Caproate Injection 250 mg/mL Single Dose Vials; Zinc 0.5 mg/mL,

Copper 0.1 mg/mL, Manganese 30 mcg/mL, Chromium 1 mcg/mL 10 mL Multi-Dose Vial for Injection; Hydromorphone HCl 10 mg per mL + Bupivicaine 5 mg/mL + Clonidine 100 mcg/mL, 40 mL Fill Volume in 60 mL Single-Dose Syringe; Fentanyl 335 mcg / mL + Bupivicaine HCl 13 mg/mL PF in 0.9% Sodium Chloride 40 mL; Nalbuphine 10 mg/mL Injection Solution; Papaverine HCL 30 mg/mL in 10 mL Preserved Water for Injection; Morphine Sulfate 50 mg/mL + Bupivacaine 25 mg/mL 41 mL Fill volume in 60 mL Single-Dose Syringe; Glycopyrrolate 0.2 mg per mL, Total Volume-5 mL in 5 mL Single Dose Injectable Syringe; Sodium Phosphates Injection USP; Droperidol Injection USP 5 mg / 2 mL Single Dose Vial (2.5 mg/mL); Potassium Acetate for Injection 100 mEq / 50 mL (2 mEq/mL).

ii. The following drug product label does not contain the statement "Not for resale": Glycopyrrolate 0.2 mg per mL, Total Volume-5 mL in 5 mL Single Dose Injectable Syringe.

iii. The following drug product labels do not contain the address of your outsourcing facility: Hydroxyprogesterone Caproate Injection 250 mg/mL Single Dose Vials; Zinc 0.5 mg/mL, Copper 0.1 mg/mL, Manganese 30 mcg/mL, Chromium 1 mcg/mL 10 mL Multi-Dose Vial for Injection; Hydromorphone HCl 10 mg per mL + Bupivicaine 5 mg/mL + Clonidine 100 mcg/mL, 40 mL Fill Volume in 60 mL Single-Dose Syringe; Fentanyl 335 mcg / mL + Bupivicaine HCl 13 mg/mL PF in 0.9% Sodium Chloride 40 mL; Nalbuphine 10 mg/mL Injection Solution; Papaverine HCL 30 mg/mL in 10 mL Preserved Water for Injection; Morphine Sulfate 50 mg/mL + Bupivacaine 25 mg/mL 41 mL Fill volume in 60 mL Single-Dose Syringe; Glycopyrrolate 0.2 mg per mL, Total Volume-5 mL in 5 mL Single Dose Injectable Syringe; Sodium Phosphates Injection USP; Droperidol Injection USP 5 mg / 2 mL Single Dose Vial (2.5 mg/mL); Potassium Acetate for Injection 100 mEq / 50 mL (2 mEq/mL).

iv. The following drug product labels do not contain the quantity or proportion of each ingredient: Nalbuphine 10 mg/mL Injection Solution; Droperidol Injection USP 5 mg / 2 mL Single Dose Vial (2.5 mg/mL).

v. The following drug product container labels do not contain information to facilitate adverse event reporting www.fda.gov/medwatch and 1-800-FDA-1088 <http://www.fda.gov/medwatch%20and%201-800-FDA-1088>: Hydroxyprogesterone Caproate Injection 250 mg/mL Single Dose Vials; Zinc 0.5 mg/mL, Copper 0.1 mg/mL, Manganese 30 mcg/mL, Chromium 1 mcg/mL 10 mL Multi-Dose Vial for Injection;

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Hydromorphone HCl 10 mg per mL + Bupivicaine 5 mg/mL + Clonidine 100 mcg/mL, 40 mL Fill Volume in 60 mL Single-Dose Syringe; Fentanyl 335 mcg / mL + Bupivicaine HCl 13 mg/mL PF in 0.9% Sodium Chloride 40 mL; Nalbuphine 10 mg/mL Injection Solution; Papaverine HCL 30 mg/mL in 10 mL Preserved Water for Injection; Morphine Sulfate 50 mg/mL + Bupivacaine 25 mg/mL 41 mL Fill volume in 60 mL Single-Dose Syringe; Glycopyrrolate 0.2 mg per mL, Total Volume-5 mL in 5 mL Single Dose Injectable Syringe; Sodium Phosphates Injection USP; Droperidol Injection USP 5 mg / 2 mL Single Dose Vial (2.5 mg/mL); Potassium Acetate for Injection 100 mEq / 50 mL (2 mEq/mL).

*** DATES OF INSPECTION:**
03/17/2014(Mon), 03/18/2014(Tue), 03/19/2014(Wed), 03/20/2014(Thu), 03/21/2014(Fri), 04/01/2014(Tue)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Zachery L. Miller, Investigator	04/01/2014

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."