DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue Stoneham, MA 02180 (781)587-7500 Fax:(781)587-7556	8/6/2019-8/29/2019* FEI NUMBER 3012039582

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Michael Roberge, Owner

FIRM NAME	STREET ADDRESS
Compounded Solutions in Pharmacy	810 Main St
CITY, STATE, ZIP CODE, COUNTRY Monroe, CT 06468-2809	TYPE ESTABLISHMENT INSPECTED Producer of Non-Sterile and Sterile Drug Products

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

OBSERVATION 1

You used a non-pharmaceutical grade component in the formulation of a drug product.

Specifically, your firm failed to appropriately use drug substances that are components of approved drugs or ingredients to produce sterile and non-sterile drug products. For example:

- On 8/6/2019, a partially used reconstituted 1-gram vial of Ceftazidime for Injection USP was found in your firm's stock refrigerator. The Ceftazidime for Injection (NDC 44567-235-25) Lot 06072019@(b)(4) vial was reconstituted with (b)(4) of (b) (4) on 6/7/19 and assigned a 90-day BUD. The reconstituted vial was subsequently used for sterile to sterile production of (b)(4) drug products (b)(4) eye drops and (b)(4) intravitreal products) on 6/7/19, 6/11/19, 7/8/19, and 8/5/19, and each drug product was assigned a 14-day BUD. According to the Ceftazidime package insert, Ceftazidime for Injection is supplied as a "*single-dose vial*" and "*Ceftazidime for injection, when constituted as directed with Sterile Water for Injection or Bacteriostatic Water for Injection maintains satisfactory potency for 12 hours at room temperature or for 3 days under refrigeration. Solutions in Sterile Water for Injection that are frozen immediately after constitution in the original container are stable for 3 months when stored at -20°C. Once thawed, solutions should not be refrozen*."

- On 8/6/2019, a partially used 30ml vial of Acetylcysteine Injection 6g/30ml (NDC 00574-0805-30) Lot B-18-036 was found in your firm's stock refrigerator. This Acetylcysteine vial was acquired by your firm as part of a four pack of vials (4x30ml vials, all Lot B-18-036) on

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05/30/2019. The Acetylcysteine vial found in your refrigerator and one additional Acetylcysteine vial from the four pack were used for sterile to sterile production of (b) (4) ophthalmic drug products on multiple days between 6/4/2019 and 8/2/2019, including several ophthalmic drug products with 90-day BUDs. According to the Acetylcysteine Injection package insert, "*Acetylcysteine Injection is available as a 20% solution in 30mL single dose glass vials*", "*do not use previously opened vials*", and "*store unopened vials at controlled room temperature*".

- On 8/16/2019, several containers of stock capsules used for encapsulating non-sterile drug products were found in your firm's stock room and observed to be expired. Firm management stated the firm will use these expired capsules for production of non-sterile drug products.

OBSERVATION 2

The ISO 5 classified aseptic processing areas had difficult to clean, particle-generating and visibly dirty equipment or surface.

Specifically,

- Your firm's hazardous ISO Class 5 BSC (b) (4) was observed to have what appeared to be duct tape along the entire circumference of the shield frame grove adhering the (b) (4) frame to the (b) (4) sash (shield). Several cracks were observed in the (b) (4) sash (shield) as well.

- Your firm's non-hazardous ISO Class 5 BSC (b) (4) was observed to have scratching on the inside of the (b) (4) sash (shield) as well as rouging on the (b) (4) deck.

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- Your firm uses (b) (4) caulking guns inside ISO Class 5 BSCs to perform (b) (4) (b) (4) of multiple (b) (4) drug products such as Triple P Injection, Double P Injection, DMSO Injection, and several other drug products containing oils. Firm personnel use the caulking guns to compress syringes with attached (b) (4) because (b) (4) compression of syringes with attached (b) (4) is difficult. The caulking guns were observed to be stored (hanging on a shelving unit) in the non-hazardous ISO Class 7 buffer room. Firm personnel stated the caulking guns are sprayed with sterile (b) (4) prior to being placed into the ISO-5 area of the BSC; however, the caulking guns have multiple mechanical intricacies that are challenging to properly sanitize. In addition, the caulking guns were observed to have what appeared to rust, chipped paint, and original manufacturer stickers on them. Further, firm management stated the caulking guns are only used for (b) (4) and not for facilities repair; however, what appeared to be white caulking was observed adhered to one of the caulking gun's plunger.

OBSERVATION 3

Non-microbial contamination was observed in your production area.

Specifically,

On 8/6/2019, rust was observed on the exterior of both the hazardous and non-hazardous ISO Class 5 BSCs. In addition, on 8/7/2019 and 8/8/2019, rust was observed on a chain attached to the top of the non-hazardous ISO Class 5 BSC (b) (4)). The rusty chain was observed stored on a horizontal ledge on the front of the non-hazardous ISO Class BSC and is used to prop open the (b) (4) sash (shield) during cleaning of the non-hazardous ISO Class 5 BSC. A (b) (4) hook at the end of the chain aligned with the scratching on the inside of the (b) (4) sash (shield) of the ISO Class 5 BSC (b) (4)).

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OBSERVATION 4

Unsealed, loose ceiling tiles were observed in your cleanroom.

Specifically,

Ceiling tiles, including ceiling mounted lights and HEPA filters, located in both the firm's ISO Class 7 non-hazardous buffer room and ISO Class 7 hazardous buffer room, were observed unsealed or with caulking which appeared to be pealing back or not properly adhered. In addition, paint on the corners of ceiling tiles/lights in the firm's ISO Class 7 non-hazardous buffer room appeared to be chipped and or flaked off. The firm's ISO Class 7 non-hazardous buffer room supports an ISO Class 5 BSC (b) (4) used to produce non-hazardous sterile drug products such as Triple P Injection and the firm's ISO Class 7 hazardous buffer room supports an ISO Class 5 BSC (b) (4) used to produce hazardous drug products such as Testosterone AQ (PF) suspensi

Deficiencies regarding loose and or unsealed cleanroom ceiling tiles was also noted during the 2017 FDA inspection.

OBSERVATION 5

The ISO 5 classified aseptic processing area was located within a non-classified room (segregated production area).

Specifically,

Your firm's ISO Class 5(b) (4) an ISO Tech (b) (4) is in an unclassified room. Firm personnel open the ISO Class 5(b) (4) (b) (4) to perform cleaning, exposing

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the inside of the (b) (4) to the unclassified air in the surrounding room. Your firm uses this (b) (4) exclusively to produce sterile autologous serum eye drops and since 10/23/2018, your firm has produced (b) (4) lots of sterile autologous serum eye drops. Autologous serum eye drops are assigned 90 day beyond use dates (BUD).

OBSERVATION 6

Disinfecting agents and used in the ISO 5 classified aseptic processing areas were not sterile.

Specifically,

Cleaning practices and disinfecting agents used by the firm for cleaning of ISO Class 5 areas such as the firm's BSCs and (b) (4) are not adequate and do not support appropriate environmental cleanliness for sterile drug production. The firm uses (b) (4) from manufacturer (b) (4); however, this cleaning agent is not labeled as sterile. In addition, firm personnel who perform cleaning of critical ISO Class 5 BSCs bend at the waist and reach into and or enter the ISO Class 5 BSCs to perform cleaning of the equipment's back and side walls instead of using an extension mop/wipe handle, therefore exposing non-sterile gowning and exposed skin into the critical ISO Class 5 areas.

OBSERVATION 7

The use of sporicidal agents in the ISO 5 classified aseptic processing area was inadequate.

Specifically,

Your firm does not follow manufacturer recommended dwell times for sporicidal cleaning agents used within ISO Class 5 critical environments to assure elimination of spore forming microbes. Firm

personnel use (b) (4) to perform cleaning of the firm's ISO Class 5 BSCs and ISO Class 5 (b) (4) however, sporicidal dwell times as identified by the cleaning agent manufacturer is not followed. For example: per (b) (4), the minimum efficacy data for (b) (4) is (b) (4) for sporicidal. Your firm personnel use (b) (4) with only a (b) (4) contact time, and in addition, your firm personnel do not reapply cleaning agents when ISO Class 5 surfaces appear dry prior to reaching the manufacturer's recommended dwell time.

OBSERVATION 8

You produced beta-lactam drugs without providing adequate cleaning of work surfaces and cleaning of personnel to prevent cross-contamination.

Specifically,

Your firm reconstitutes and utilizes beta-lactam drugs, such as cephalosporins (e.g. Ceftazidime), to produce sterile drug products. Your firm has not established and does not follow specific standard operating procedures to prevent and or mitigate the risk of cross-contamination between beta-lactams and other sterile products produced within your firm's non-hazardous ISO Class 5 BSC (b) (4). For example, your firm has not determined the suitability of the cleaning agents used to decontaminate beta-lactam residues or spills remaining in the ISO-5 BSC following production of sterile drug products such as Ceftazidime eye drops.

OBSERVATION 9

You had inadequate HEPA filter coverage and airflow over the area to which sterile product was exposed.

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Specifically,

Your firm's smoke studies conducted within the ISO Class 5 areas are inadequate. The studies were conducted by (b) (4) under dynamic conditions in July 2019; however, the smoke study videos only include syringe to syringe transfer/mixing of sterile drug products and did not include the transfer of starting components and materials into the ISO Class 5 areas, transfer of product into final container closure systems, or retrieval of product from the ISO Class 5 areas to demonstrate unidirectional airflow and sweeping action over and away from sterile product under dynamic conditions.

***DATES OF INSPECTION**

8/06/2019(Tue), 8/07/2019(Wed), 8/08/2019(Thu), 8/09/2019(Fri), 8/13/2019(Tue), 8/14/2019(Wed), 8/15/2019(Thu), 8/16/2019(Fri), 8/26/2019(Mon), 8/29/2019(Thu)

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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 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."