

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 60 Eighth Street NE Atlanta, GA 30309 (404) 253-1161 Fax: (404) 253-1202 Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 03/18/2013 - 04/02/2013*
	FIR NUMBER 3010078541

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: Austin E. Gore, Owner/Pharmacist in Charge

FIRM NAME Clinical Specialties Compounding Pharmacy	STREET ADDRESS 318 Baston Rd, Suite 103
CITY, STATE, ZIP CODE, COUNTRY Augusta, GA 30907	TYPE ESTABLISHMENT INSPECTED Producer of 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 WE OBSERVED:

OBSERVATION 1

Each batch of drug product required to be free of objectionable microorganisms is not tested through appropriate laboratory testing.

Specifically,

Your firm does not perform sterility and endotoxin testing for any sterile drug products produced at and distributed by your firm. As such, there is no assurance that your aseptic process is effective in achieving sterility of finished, critical drug products. For example:

1. Commercially available Avastin 100mg/4-mL vial, lot # (b) (4), was repacked into [redacted] individual 0.1 mL syringes, lot # CABDBDAC:17, by you on 2/13/13. This lot was released without sterility or endotoxin testing. It is associated with 4 cases of bacterial eye infections after intraocular administration in Athens, GA.
2. Commercially available Avastin 100mg/4-mL vial, lot # (b) (4), was repacked into [redacted] individual 0.1 mL syringes, lot # CABDBDAC:69, by you on 2/13/13. This lot was released without sterility or endotoxin testing. It is associated with 1 case of bacterial eye infection in South Bend, IN.
3. Hydroxyprogesterone Caproate (HPC) is produced from non-sterile components at your firm. This drug product is administered to pregnant women at risk of pre-term delivery. No sterility or endotoxin tests have been performed for any finished lots produced and released for records reviewed within the last 6 months.

OBSERVATION 2

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications and identity and strength of each active ingredient prior to release.

Specifically,

Sterile drug products produced at and distributed by your firm have not been assay tested for potency. As such, there is no assurance that these distributed drug products can produce the desired, maximal effect for patients.

SEE REVERSE OF THIS PAGE	EMPLOYER(S) SIGNATURE LaReese K. Thomas, Investigator <i>LaReese K. Thomas</i> Nicole A. Lloyd, Investigator Jawaid Hamid, Investigator <i>Jawaid Hamid</i>	DATE ISSUED 04/02/2013

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OBSERVATION 3

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

Specifically,

- A. Environmental monitoring of the ISO 5 (b) (4) has not been performed adequately and periodically according to an approved written program. For example:
 - 1. SOP No. 4, Environmental Monitoring of the buffer or clean area and anteroom area, has not been approved or implemented by you to date. It states that "in addition to viable and nonviable air sampling, the LAFW and/or Barrier Isolators require contact surface test performed at least (b) (4)." Test results are to be recorded on the sterile product maintenance log. There is no documentation that indicates that you have routinely performed these required tests for microbial organisms.
 - 2. There is no documentation maintained at your firm that demonstrates that the ISO 5 (b) (4) has been surface sampled for microbial contamination from the time period covering 2007 - March 12, 2013. Certification Reports from contract testing facilities covering this time period only report that air sampling for particle counts has been conducted within the (b) (4).
 - 3. The (b) (4) attached to the (b) (4) of the ISO 5 (b) (4) that contact products during sterile operations (a critical area prone to contamination) have not been monitored for microbial contamination. You do not perform environmental monitoring with each daily production run to demonstrate that microbial limits have not been exceeded after each sterile operation is performed in the (b) (4).
 - 4. (b) (4) Certification Reports provided by contract testing facilities are deficient in that they do not provide enough detail regarding the specific locations in the ISO 5 (b) (4) that were sampled for air quality analysis. Additionally, the reports do not delineate whether viable or non-viable air particles were sampled. Moreover, the tests were not conducted in accordance with an approved procedure by your firm.
 - 5. Airflow smoke pattern tests that were performed by a contract testing facility and documented in (b) (4) Certification Reports from 2007 - current are deficient in that they do not demonstrate unidirectional airflow under dynamic conditions.
- B. Personnel monitoring is not performed by you after sterile repacking or production operations.
 - 1. There is no determination as to whether bacterial limits have been exceeded during and after sterile operations in the ISO 5 (b) (4). Also, the efficacy of your aseptic procedures cannot be determined.
 - 2. There is no determination that you have performed media fills at least semi-annually inside the ISO 5 (b) (4). You have not demonstrated that you can perform sterile operations under conditions that closely simulate the most challenging or stressful conditions encountered during repacking or production of sterile products.
 - 3. SOP 7.007.31, Process Simulation Testing, High Risk, has not been approved or implemented by you to date. There is no indication that you have performed this procedure for evaluation of your aseptic technique and the cleanliness of the equipment used in your sterile production operations.

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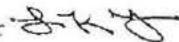
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OBSERVATION 4

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

Specifically,

- A. Initial qualification and routine calibration, maintenance, and cleaning of automatic, mechanical, and electronic equipment is not performed or documented to assure proper performance.
- The (b) (4) used for the sterilization of aqueous injectable solutions has not been qualified, maintained, or cleaned according to the operation's manual or an approved written program. The programmed sterilization cycle (typically (b) (4)) has not been validated. No biological indicators or temperature sensing devices are used to verify the effectiveness of this sterilization process. Further, the identification of non-sterile components that enter the machine or the load sizes are not documented. Moreover, the (b) (4) has not been temperature mapped to demonstrate the capability of the instrument in achieving uniform distribution of temperature.
 - The (b) (4) used for (b) (4) sterilization of aqueous injectable solutions has not been qualified, maintained, or cleaned according to an approved written program. Moreover, the temperature used to achieve sterility of products (typically (b) (4)) has not been validated for each drug product that requires (b) (4) sterilization. No biological indicators or temperature sensing devices are used to gauge the effectiveness of the (b) (4). There is no documentation of the non-sterile components that enter the machine or the load sizes to ensure uniform distribution of temperatures.
 - The medication refrigerator used to store clinic-purchased Avastin 4-mL vials and drug product retains is not real-time monitored for temperature fluctuations. (b) (4) recordings are made (b) (4) on a temperature recording chart. There is no back-up generator or alternate power source in case of a power outage. Moreover, the refrigerator is not monitored over the weekend or when there is no personnel present at the firm to record the temperature.
 - The magnahelic gauges used to measure differential pressure between areas in the IV clean room and the gowning/buffer room lacked calibration records prior to 3/11/13 and 3/13/13. As such there is no assurance that the positive pressure has been working properly to facilitate adequate air quality between the rooms.
- B. Drug products such as Estradiol Cypionate, Progesterone Injectable, Cyclosporin 2% in Corn Oil, and Diazepam Injectable are produced from non-sterile components and require (b) (4) for sterilization. There is no documentation that (b) (4) integrity testing is performed for each (b) (4) or production run.
- C. A caulking gun hangs from a metal rod in the ISO 5 (b) (4). It is manually rigged to add pressure to syringes in order to force oil-based drug solutions (b) (4) for collection into empty, pre-sterilized vials. There is no validated, written procedure for the use of the caulking gun and there is no indication that the caulking gun is sanitized prior to and after its use. Further, there is no evaluation of the pressure generated by the gun. Additionally, the pre-sterilized vials are not disinfected prior to (b) (4) entry.

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OBSERVATION 5

The flow of components, drug product containers, in-process materials, and drug products though the building is not designed to prevent contamination.

Specifically,

A. Avastin

1. Commercially available and sterile vials of Avastin are removed from a refrigerator that does not have real-time temperature monitoring. Without a backup generator or alternate power source, there is no assurance that Avastin products have not been subjected to abnormal, fluctuating temperatures for extended periods of time (i.e. power outages over the weekend when personnel is not present) which could adulterate the products.
2. Materials and supplies such as pre-packaged sterile syringes, needles, Luer locks, and empty vials are removed from the ISO 7 buffer area/gowning room and transferred to the ante chamber of the ISO 5 (b) (4). During a mock demonstration of avastin repacking/unit dosing, it was observed that you did not disinfect any of these supplies prior to their entry into the ante chamber of the (b) (4) or when you transferred them to the work chamber of the (b) (4). Only the top portion of the rubber vial of a saline vial (used in place of Avastin for the mock demonstration) was disinfected with (b) (4) prior to the repacking process. Additionally, approved and implemented SOP 8.080-A, Aseptic Filling and Packaging of Sterile Unit Dose Avastin Syringes, does not include the provision for disinfecting materials and supplies pivotal for sterile drug product production prior to ante chamber entry of the (b) (4).

B. Hydroxyprogesterone Caproate (HPC)

1. Non-sterile components used in the production of sterile Hydroxyprogesterone caproate (HPC) injection are weighed and mixed in a (b) (4) within a non-classified room by you prior to transfer to the ISO 7 buffer area/gowning room. Further, no bioburden limits are established for the non-sterile components used for the production of sterile preparations.
2. You stated that hold times for aqueous, non-sterile mixtures (including HPC) range from (b) (4). However, you do not have written procedures governing these hold times and you do not have batch data to substantiate these hold times.
3. The aqueous mixture of HPC non-sterile components is placed in (b) (4) located in the ISO 7 buffer area. There is no justification for the temperature used and no assurance that the length of time that non-sterile, aqueous mixtures are exposed to the temperature can effectively achieve sterility. Additionally, the bulk solutions contained in beakers are further manipulated in the ISO 5 (b) (4) without disinfection of the beaker prior to (b) (4) ante chamber entry.

C. Medroxyprogesterone

1. Non-sterile components used in the production of Medroxyprogesterone are weighed and mixed in (b) (4) within a non-classified room by you prior to transfer to the ISO 7 gowning room. No bioburden limits are established.
2. Hold times used for Medroxyprogesterone production are not justified with supporting data.

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manual. The non-sterile components made in this (b) (4) will be further processed via sterilization methods (filtration, autoclave, convection oven) for use in sterile drug production.

OBSERVATION 7

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

Specifically,

There is no approved or implemented stability program procedures for Beyond Use Dates (BUDs) assigned to sterile drug products. There is also no stability data to support current BUDs of 60, 90, or 180 days.

OBSERVATION 8

Complaint procedures are deficient in that written complaint records are not maintained in a file designated for drug product complaints.

Specifically,

1. There are no written, approved procedures for handling written or oral drug complaints.
2. Five (5) cases of bacterial eye infections are associated with Avastin lots repacked on 2/13/13. There is no documentation that you conducted an investigation to identify the root cause of the infections.

OBSERVATION 9

The number of qualified personnel is inadequate to perform the manufacture and processing of each drug product.

Specifically,

There is a (b) ratio of Pharmacist in Charge to Pharmacy Technician at the firm and (b) (4) performs sterile drug production at the firm. There is no second person verification of your gowning routine in the buffer area or your aseptic technique during the production of sterile drug products.

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OBSERVATION 10

GMP training is not conducted on a continuing basis and with sufficient frequency to assure that employees remain familiar with CGMP requirements applicable to them.

Specifically,

There are no training records at your firm to document that you and the pharmacy technician are current on aseptic techniques and practices for the production of both sterile and non-sterile drug products.

OBSERVATION 11

A system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary, has not been established.

Specifically,

There are no written, approved procedures in place to facilitate a recall of drug products at your firm. During the inspection, a recall of all sterile products at your firm was requested. Since no recall system was in place, there was a delay in contacting and notifying clinics to make patients aware of potential drug product contamination.

*** DATES OF INSPECTION:**

03/18/2013(Mon), 03/19/2013(Tue), 03/20/2013(Wed), 03/21/2013(Thu), 03/22/2013(Fri), 03/25/2013(Mon), 03/26/2013(Tue), 03/27/2013(Wed), 03/28/2013(Thu), 04/02/2013(Tue)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."