

**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](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

02/19/2013 - 03/01/2013

FEI NUMBER

3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

**TO:** Danny Barnes, Pharm D., Pharmacist In Charge/Owner

FIRM NAME

Triangle Compounding

STREET ADDRESS

550 New Waverly Pl Ste 110

CITY, STATE, ZIP CODE, COUNTRY

Cary, NC 27511-7412

TYPE ESTABLISHMENT INSPECTED

Producers of Sterile Drug Product

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**

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,

Investigations into sterility failures reported by the firm for Sodium Bicarbonate 8.4% PF Inj (4/5/12) and Avastin 2.5 mg Lot# 77711-LG4973(10/27/12) and #80623-LG4973 (10/20/12) are not supported by data in order to substantiate the firm's reported actions of re-testing samples in order to release the lot from quarantine status and make them available for use. Initial reported sterility failures were not attributed to laboratory error or to sample handling, but additional samples were re-tested to determine that the batch was sterile without determination of root cause for the failure or full documentation of the investigation process. Avastin Lot 77711-LG4973 and Sodium Bicarbonate Lot 11035-29 were subsequently distributed.

Furthermore, a formal procedure for handling out of specification tests results or non-conforming tests is not available. Policies in place for "Outside Lab Testing, 6.080", and "Skip Lot Random COA Testing, 6.070", include provisions for the evaluation of a compound not meeting expected parameters, but include actions such as re-tests, modification of compounding areas or alteration of storing/shipping conditions to address failures on tests. Root cause determination is not required by the policies in place to ensure adequacy of corrective/preventive actions or full documentation of such activities.

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EMPLOYEE(S) SIGNATURE

Bonita S Chester, Investigator  
Noreen Muniz, Investigator

*Bonita S. Chester*  
*Noreen Muniz*

DATE ISSUED

03/01/2013

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**OBSERVATION 2**

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

Specifically,

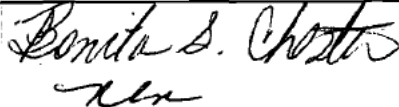
- a. Sterilization cycles executed on the (b) (4) (b) (4) (b) (4) for products and instruments during routine processing have not been validated to ensure that the cycles are capable of producing sterile products. For example, the following products are sterilized in the (b) (4): Bupivacaine For Compounding 30mg/ml; Cyclosporine Ophth 0.5% Suspension, Triamcinolone Hexacetonide 3mg/ml injectable. Instruments sterilized include small items used during aseptic processing such as spatulas.
- b. Sterilization cycles executed on (b) (4) have not been validated to ensure cycles are capable of producing sterile products or instruments and or containers. For example, the following products are sterilized in the (b) (4): Hydroxyprogesterone Caproate 250mg/ml injectable, Hydroxyprogesterone Caproate 250mg/ml PF injectable, and Phenol Oil 5% injectable. Containers sterilized include beakers used during aseptic processing.

**OBSERVATION 3**

The control systems necessary to prevent contamination or mix-ups are deficient.

Specifically, your current environmental program for monitoring and controlling the ISO 5 clean room areas are inadequate in that:

- a. (b) (4) Process Simulation Testing conducted to qualify compounding technicians and aseptic operations are deficient. Simulation tests do not support routine processing operations or evaluate worst case activities that could provide a challenge to manual aseptic operations and present a risk to product sterility (i.e. interventions, representative container/closure systems used; maximum personnel, etc).
- b. (b) (4) surface sampling is not being conducted in areas adjacent to the aseptic processing room, which is also classified as ISO 5.

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c. (b) (4) surface samples are not incubated at optimal temperatures and duration to detect the growth of fungal organisms. In addition, these samples are only being collected on a (b) (4) basis and not during periods of daily routine sterile processing activities. The records are also deficient in that they do not accurately represent surfaces monitored. SOP 6.045.1 "Surface Sampling Testing", states that samples are to be collected on "(b) (4)", however, results are reported for for the left and right areas, but they do not definitively define the locations sampled.

d. (b) (4) viable air sampling has not been conducted in accordance with written procedures. SOP 6.035, "Air Sampling", requires the use of (b) (4) control plates to be exposed in the outside area of the clean room. No controls were used in the months of January-September 2012, nor on 10/12,19,31/2012, nor on 11/2,16,30/2012, nor on 12/14/12, or January - Feb. 2013. In addition, (b) plates were not exposed within rooms identified by the firm and as documented in records provided as: the Ante room, Gowning room, or the Compounding room between January-July 2012, 11/1,2/2012, or on 12/16/12 as required.

e. Environmental monitoring of the ISO 5 aseptic processing area including the laminar air flow hood, and personnel monitoring (i.e. fingertip touch plates) are not being performed during daily routine processing. Currently viable air samples are collected (b) (4) and personnel monitoring is performed (b) (4). In addition no addition there are no monitoring conducted of personnel gowning.

f. The unidirectional flow of air in the aseptic processing room and adjacent ISO 5 classified areas (including the laminar flow hood) has not been confirmed through visual mechanisms (such as smoke studies) to ensure adequacy for use.

g. The efficacy of disinfectants and cleaning agents used on site for routine operations in the aseptic processing rooms and Laminar Flow Hoods has not been verified to ensure that current cleaning procedures are effective as defined on procedure # 5.161.0, Clean Room Routine Maintenance.

g. A dark stain was observed in one of the ceiling HEPA filters inside the ISO 5 aseptic processing during the first day of this inspection.

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**OBSERVATION 4**

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

Specifically,

Poor aseptic techniques and practices were observed being executed during routine operations held on 02/19/13 inside the sterile compounding room (ISO 5) and associated with repackaging of Avastin (Bevacizumab 2.5 mg/1 ml PF CP Syringe) lot 02192013%77711 into 1 ml syringes as follows:

1. Operator's full body suits used for routine operations in the ISO 5 room in order to prevent contamination of materials handled inside and while aseptic fill operations are conducted were reported during the inspection as "non-sterile".
2. Operator was observed transferring material from (b) (4) inside the laminar flow hood with abrupt movements and abrupt placement of filled 1 ml syringes the working surface.
3. Operator was observed leaning against and pushing the portable laminar flow hood with enough strength to cause it to shake while aseptic filling 1 ml syringes of Avastin.
4. Exposed skin was observed on the operator's forehead and face while aseptic filling operations were being conducted in the ISO 5 Room. Operator conducting the operation was observed wearing a face mask which left exposed skin on the sides. Hair was observed outside the hair piece (full body suit).

**OBSERVATION 5**

Equipment and utensils are not maintained at appropriate intervals to prevent malfunctions and contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

Records are not kept for the maintenance and inspection of equipment. Specifically,

- a. Records documenting the qualification of the (b) (4) and most recent calibration of Nov 2012 are not available to ensure adequate (b) (4) during

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routine cycles executed on site. This (b) (4) is used on site for sterilization of products and utensils on site associated to sterile fill operations.

b. Records documenting the qualification of the (b) (4) are not available to ensure adequate (b) (4) during routine cycles executed on site. This (b) (4) is used on site for routine (b) (4) Cycles of containers for aseptic processes and Sterilization of products handled at the ISO 5 Room.

c. No calibration has been conducted or documented to ensure that the (b) (4) used in conducting (b) (4) testing of sterilizing (b) (4) is operable for its intended purpose.

**OBSERVATION 6**

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically,

Your firm does not have real time stability data to support Beyond Use Dates (BUD) assigned to products filled on site for further use on solutions or sold as finished products. No stability studies have been conducted on site to support assigned dates up to 6 months, as described on Procedure 2.600.2, Beyond Use Dating.

Furthermore, products aseptically filled on site can be assigned a Beyond Use Date that exceeds the expiration date of active ingredients or drug components used to formulate the product. For example, Hydroxyethylcellulose (Sterile) 2% Gel Lot# 02012013%71646@2, made on 02/1/13 was assigned a Beyond Use Date of 180 days after the fill date of 7/31/13. However, the Hydroxyethylcellulose NF Powder used as ingredient included an expiration date of 3/3/13 (the ingredient expires 4 months before the actual finished product's assigned date).

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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."