

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED 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.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

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

Specifically:

A.) Unexplained discrepancies are not always investigated. During visual inspection of finished sterile products, the firm has identified particulates described as “lint”, “particles” or “fibers”. Regardless of whether or not the visual defect limits are exceeded, or when products are exempt from defect limits, these particulates have not been identified, and their source has not been determined. For example, the following batches, which were made between December 1, 2016 and June 30, 2017, had the following visual reject rates due to defects:

- 1.) Trimix 150/5/50 Injectable, Formula (b) (4) (No visual defect limit established):
 - a.) Log Number (b) (4) units
 - b.) Log Number (b) (4) units

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L. Cook-S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

c.) Log Number (b) (4) units

d.) Log Number (b) (4) units

e.) Log Number (b) (4) units

2.) Betamethasone 8 mg/ml Injectable, Formula # (b) (4) (No visual defect limit established):

a.) Log Number (b) (4) units

b.) Log Number (b) (4) units

c.) Log Number (b) (4) units

d.) Log Number (b) (4) units

e.) Log Number (b) (4) units

3.) Baclofen 3000mcg/ml (Intrathecal) Injectable, Formula (b) (4) (Major visual defect limit (b) (4) units based on pharmacists' experience):

a.) Log Number (b) (4) units

b.) Log Number (b) (4) units

c.) Log Number (b) (4) units

Additionally, your firm has not established visual defect limits for all sterile products. Examples of products without visual defect limits include Papaverine/Phentolamine/Prostaglandin (Trimix) combinations, Dexamethasone Sodium Phosphate, and Betamethasone Sodium Phosphate. For products

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L. Cook -S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

with set visual defect limits, limits are set based on pharmacists' experience and not historical or product specific data. Despite the above rejection rates the batches were still released.

B.) Investigations into sterility failures of products produced by your facility were not thoroughly reviewed and evaluated to determine the root cause of the event and to identify and implement appropriate corrections to prevent reoccurrence.* During the current inspection we reviewed Out-Of-Specification (OOS) Investigation Summary Reports for six out of the seven sterility failures that have occurred since the previous inspection:

- Ophthalmic Dilating (1 mL) Gel Lot # LG33788, sterility failure April 2015
- Avastin (Bevacizumab) 2.5 mg/0.1 mL PF Lot # LG34509, sterility failure April 2015
- Baclofen PF Injection (20mL) 4000 mcg/mL Lot # LG36025, sterility failure June 2015
- Ophthalmic Dilating (1 mL) Gel Lot # LG37400, sterility failure July 2015
- Avastin (Bevacizumab) 2.5 mg/0.1 mL PF Lot # LG40706, sterility failure November 2015
- Ophthalmic Dilating (1 mL) Gel Lot # LG41745, sterility failure December 2015

None of these investigations identified a root cause. Additionally, corrective actions were not required to be implemented to prevent reoccurrence.

*Note: This is a repeat observation from the Form FDA 483 that was issued on 9/22/2014.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L Cook -S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
--	---

CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility
---	--

OBSERVATION 2

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically:

A.) SOP 2.830, Version 6, Visual Inspection Policy and Procedure, is deficient or is not fully followed in that:

- 1.) The procedure states, “(b) (4) [REDACTED] (b) (4) [REDACTED] (b) (4) [REDACTED] (b) (4) [REDACTED]”

However, despite observing particulates in the following lots of intrathecal FGUs, they were still reprocessed and distributed:

- a.) Bupivacaine HCL 30 mg/Clonidine HCl 300 mcg/Morphine Sulfate 2 mg/mL PF Injectable, Log ID: 57278, made 6/16/2017.
- b.) Bupivacaine HCL 10 mg/Morphine Sulfate 5 mg/mL PF Injectable, Log ID: 57067, made 6/06/2017.
- c.) Baclofen 2000 mcg/Hydromorphone HCl 3.5 mg/mL PF Injectable, Log ID: 56155, made 5/02/2017.
- d.) Morphine Sulfate (PF) 20 mg/mL Injectable, Log ID: 56033, made 5/01/2017.
- e.) Hydromorphone PF 20 mg/mL Injectable, Log ID: 56029, made 5/01/2017.
- f.) Bupivacaine HCl 30 mg/Clonidine HCl 300 mcg/Morphine Sulfate 1mg/mL PF Injectable, Log ID: 55931, made 4/25/2017.
- g.) Hydromorphone PF 20 mg/mL Injectable, Log ID: 55034, made 3/28/2017.
- h.) Bupivacaine HCl 22 mg/Hydromorphone HCl 16 mg/mL PF Injectable, Log ID: 55032, made 4/03/2017.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L. Cook -S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

Drug product production and control records, are not reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed.

The Quality Assurance Unit does not review or approve sterile or non-sterile drug products produced for specific patients pursuant to a prescription; these products are only reviewed and approved by a pharmacist. The firm's SOP entitled, "Batch Release of Sterile Drug Products" is only applicable to office use sterile drug products.

OBSERVATION 4

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

Specifically:

- A.) On 06/26/2017, we observed a cleanroom technician spray gloved hands with (b) (4) [redacted] to gloved-finger plate sampling at the end of conducting sterile compounding operations.
- B.) Your firm does not monitor air pressure in your ISO classified areas and adjacent areas during sterile drug production in order to ensure a proper pressure cascade to minimize the risk of product contamination. There is no system in place to alert personnel of any pressure reversals or otherwise unacceptable pressure differentials, nor is there an engineering control in place to prevent more than one door in an ISO classified area from being opened at the same time. Additionally, there have been numerous instances where the pressure differentials between areas in which a positive pressure differential should be maintained have either gone negative or been zero inches water column (wc). None of these instances have been investigated to determine the risk posed to the product or the facility. Some such instances include, but are not limited to:
- 1.) Batching to gowning pressure differential on (b) (4) [redacted]
 - 2.) Batching to gowning pressure differential on (b) (4) [redacted]
 - 3.) Batching to gowning pressure differential on (b) (4) [redacted]

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L. Cook -S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

- 4.) Batching to gowning pressure differential on (b) (4)
- 5.) Batching to gowning pressure differential on (b) (4)
- 6.) Batching to gowning pressure differential on (b) (4)
- 7.) Batching to gowning pressure differential on (b) (4)
- 8.) Batching to gowning pressure differential on (b) (4)
- 9.) Batching to gowning pressure differential on (b) (4)
- 10.) Batching to gowning pressure differential on (b) (4)
- 11.) Batching to gowning pressure differential on (b) (4)
- 12.) Batching to gowning pressure differential on (b) (4)
- 13.) Batching to gowning pressure differential on (b) (4)
- 14.) Batching to gowning pressure differential on (b) (4)

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, your firm does not perform testing to ensure that all finished drug products meet the specifications they are purported to meet prior to release. You do not perform testing on drug products produced for specific patients pursuant to a prescription. For example, your firm does not perform the following tests on products produced for specific patients:

- A.) Endotoxin
- B.) Particulate
- C.) Potency

OBSERVATION 6

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

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L. Cook -S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

Specifically:

A.) Upon a review of (b)(4) aseptic process simulations (APS) that have occurred since the previous inspection for the purpose of validating your aseptic and sterilization processes as well as to qualify your sterile compounding operators according to SOP 8.101 – Validation Plan for Aseptic Process Simulation and SOP 8.103 – Policy for Qualification of Personnel Performing Aseptic Processes, it was found that process simulations were deficient.** This deficiency is due to APS not being conducted under the most challenging circumstances. Examples of circumstances either not documented or not occurring include: ingress and egress of operators to/from the hood, changing of environmental monitoring plates, writing in a batch record, retrieving more materials to complete an operation, remove bags of filled units, changing gloves, etc. These interventions were observed during production activities. Additionally, of the (b)(4) APS reviewed, in (b)(4) run units without integral errors (e.g. lint particles, dark particles, over/underfills, scratches, etc.) were removed from the study prior to incubation. Finally, Quality review of some APS is deficient due to not addressing errors in documentation such as the error in pump delivery documentation found in the APS performed by employee (b)(6) for Process 1 ((b)(4)mL Batch Volume, (b)(4)mL Vials) on 15 APR 2016.

**This is a repeat observation from the 3/01/2013 Form FDA 483.

B.) Your firm has not established a written requirement for smoke studies to be performed in your ISO-5 Laminar Flow Hoods under dynamic conditions representing the most challenging sterile drug production process. The dynamic smoke study performed on September 15, 2016 do not represent the most challenging processing conditions because the following items, which are typically present during sterile drug processing, were not present during the dynamic smoke studies:

1. The (b) (4)
2. Settle plates
3. Additional syringes on the work surface
4. The non-viable particle counting machine

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L. Cook -S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

Additionally, the most recent smoke study, which was performed on September 15, 2016, revealed areas of turbulence in your ISO-5 Laminar Flow Hoods, yet your firm deemed the hoods suitable for use for sterile drug production.

OBSERVATION 7

Failure to reject any lot of components that did not meet the appropriate written specifications for identity, strength, quality, and purity.

Specifically, your firm has used (b) (4) USP in sterile drug products intended for injection including L-Cysteine HCl PF 50 mg/mL Injectable and Betamethasone Sodium Phosphate (PF) 8 mg/mL Injectable. The (b) (4) label states, "(b) (4)", and (b) (4) "

OBSERVATION 8

Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.

Specifically, your firm failed to conduct container enclosure integrity studies to ensure container closure systems provide protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.

*Note: This observation was noted in the Warning Letter dated 11/02/2015.

OBSERVATION 9

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, (b) (4), which is used to sterilize equipment and utensils used in the processing of sterile drug products, has failed to complete its sterilization cycle on approximately 25%

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L Cook -S Date Signed 7/13/2017 X _____	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

of runs since January 4, 2017. You have not determined the root cause of the (b) (4) malfunctioning or had the (b) (4) repaired and you have continued to use the (b) (4) for sterilizing equipment and utensils used to process sterile drug products.

OBSERVATION 10

Filled drug product containers which are set aside and held in an unlabeled condition are not identified and handled to preclude mislabeling of individual containers, lots or portions of lots.

Specifically, on 6/26/2017 we observed approximately (b) (4) five mL unlabeled vials of Trimix (Super) 150/5/50 mg/5 mL Injectable, Log: 55732, made 4/19/2017, in refrigerator (b) (4). These vials were not adequately identified with product information or quarantine status so as to prevent inadvertent mix-up or dispensing.

OBSERVATION 11

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

Specifically, your firm uses non-sterile (b) (4) packaged in cardboard boxes which are not non-shedding in your ISO-7 cleanrooms. These wipes are not suitable for use in cleanrooms.

***DATES OF INSPECTION**

6/26/2017(Mon),6/27/2017(Tue),6/28/2017(Wed),6/29/2017(Thu),6/30/2017(Fri),7/10/2017(Mon),7/13/2017(Thu)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	<input checked="" type="checkbox"/> Rachael L Cook Investigator (CTNH) Signed By Rachael L Cook-S Date Signed 7/13/2017	DATE ISSUED 7/13/2017

**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	DATE(S) OF INSPECTION 6/26/2017-7/13/2017*
	FEI NUMBER 3004969894

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Danny M. Barnes , President and CPO

FIRM NAME Triangle Compounding Pharmacy Inc	STREET ADDRESS 3700 Regency Pkwy Ste 140
--	---

CITY, STATE, ZIP CODE, COUNTRY Cary, NC 27518-8696	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility
---	--

X Seneca D Toms
Investigator
Signed By: 2000592667
Date Signed: 7/13/2017

X Adam R Cooke
Investigator
Signed By: 2001332542
Date Signed: 7/13/2017

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rachael L Cook, Investigator (CTNH) Seneca D Toms, Investigator Adam R Cooke, Investigator	Rachael L Cook Investigator (CTNH) Signed By Rachael L Cook-S Date Signed: 7/13/2017 X	DATE ISSUED 7/13/2017

Date: September 14, 2017

Danny M. Barnes
Triangle Compounding Pharmacy Inc
3700 Regency Pkwy Ste 140
Cary, NC 27518-8696

Subject: System Notification

Dear Danny M. Barnes,

We are notifying you that due to a technical error related to a software update, the FDA Form 483 you received recently inadvertently included a sentence meant only for medical device firms. That statement says, "Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements."

This statement refers to quality system requirements applicable only to medical device establishments, but was inadvertently included on certain Form 483's issued to non-device establishments for a brief period of time. Please note that the statement has no bearing on the inspection observations themselves, which remain applicable as of the date that you were issued the Form FDA 483.

Should you have any questions, please send to AskORAIT@fda.hhs.gov.

Sincerely,



Lisa Creason
Director, Office of Information Systems Management
Office of Regulatory Affairs
Food and Drug Administration