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SUMMARY

This was a directed inspection conducted to evaluate sterile assurance of sterile drug products under FACTS Assignment no. 1495040 and CDER 2/6/2013 assignment. The inspection was conducted per Compliance Program 7356.002, Drug Manufacturing Inspections. This was not a comprehensive inspection.

The previous inspection of 8/9-27/2007 was the initial inspection of this firm. It was conducted at the request of Center for Drug Evaluation and Reporting (CDER) / Division of New Drugs and Labeling Compliance (HFD-317). The inspection was in follow-up to a consumer complaint of an adverse event associated with the use of Colistimethate (premixed for inhalation via a nebulizer) by a Cystic Fibrosis (CF) patient supplied by Foundation Care LLC (Foundation Care).

At the conclusion of the 8/9-27/2007 inspection, a nine item FDA 483, Inspectional Observations, was issued and included: no discrepancy report or investigation was generated when a "Not Sterile" test result was received for Colistimethate. Sterility and endotoxin tests are not conducted on (b) (4) (b) (4) of compounded product per their procedure and potency of the active ingredient is not

routinely tested for Colistimethate. The only potency test conducted for Colistimethate was with the stability study in September 2005. The stability study for Colistimethate was inadequate.

The Clean Room was not in operation during the first two days of the inspection due to the installation of a new air conditioner in the Cleanroom. Operations started back on 08/11/2007 without requalification of the air handling unit. Surface and airborne microorganism samples were not collected between 11/17/06 and 08/11/07 as required by their procedure. The temperature of the incubator is not documented (b) (4) during the incubation period of environmental samples as required by procedures. Not all surfaces in the Cleanroom are smooth surfaces for cleaning: there is tile on the floor, a stereo with speakers on a cart and multiple plastic bins used to hold supplies. Two Pharmacy Techs had been assisting with operations in the Cleanroom and neither had completed their aseptic training. Some verbal observations included: the shipping procedure and study are inadequate. No documentation was provided to show respules used in the compounding process for Colistimethate are sterile. Management was warned of their responsibilities under the FD&C Act. Management stated they would respond in writing within a week. The final inspection classified was VAI. Corrective actions to the previous FDA 483 were not covered during the current inspection.

Foundation Care LLC has been in business since March 2004. The firm continues to supply sterile drug products to Cystic Fibrosis (CF) patients. Some of the products they supply are sterile Tobramycin, Colistimethate, TOBI and Hypertonic Saline in ampules for inhalation.

A seven item FDA 483 was issued at the conclusion of the current inspection and included multiple examples of procedures not established or followed to prevent microbiological contamination and include the following: inadequate media fill; environmental & personnel monitoring are not performed daily; cleaning in the Cleanroom (Class 100) area was inadequate; the firm does not have any documentation of a smoke study to demonstrate the air flow in the Cleanroom; the frequency or intervals to change gloves has not been defined; procedure for hand washing were not followed; gowning for sterile operations found exposed skin around the face & neck and not all the gowning supplied are labeled as sterile. Potency is not conducted on a routine basis for several products and sterility & endotoxin test for Hypertonic Saline was last performed in June 2012. The firm does not track components used in the process such as TPN and ampules. Glassware used in the cleanroom for waste & cleaning is only cleaned and stored in an open area above the hand wash sink. One disinfectant used in the cleanroom is not labeled as sterile and no disinfectant effectiveness studies have been conducted to show the disinfectants reduce bioburden on the different surfaces in the Cleanroom. Management only mentioned correction of two points of the FDA 483.

No samples were collected. The firm was reminded of their responsibilities under the FD&C Act. Refusals were encountered during the inspection. The PIC refused to provide us with photocopies of documents then said he was wrong and allowed us photocopies. He also refused to allow us to take pictures in the Cleanroom or to allow us to take paper into the room. See Refusal section of this report for additional refusal related issues.

ADMINISTRATIVE DATA

Inspected firm:	Foundation Care LLC
Location:	[redacted]
Phone:	
FAX:	
Mailing address:	
Dates of inspection:	3/11/2013, 3/12/2013, 3/13/2013, 3/14/2013, 3/18/2013, 3/19/2013
Days in the facility:	6
Participants:	Shirley J. Berryman, Investigator Michele Perry Williams, Investigator Anthony Bucks, Investigator

Michele Perry-Williams, Investigator, was present 3/11-14/2013. Steven S. Smith, R.Ph, Inspector with the Missouri Board of Pharmacy accompanied us on the inspection all days except for 3/19/2013. Anthony Bucks, Investigator, was present on 3/18-19/2013. I (Shirley J. Berryman, Investigator) was present the entire inspection.

There were three, FDA 482, Notice of Inspection, issued during the inspection and all were issued to Daniel P. Blakeley, R.Ph, CEO and Pharmacist-in-Charge. Mr. Blakeley is the most responsible individual and should receive FMD-145 and official correspondence at the firm address. On 3/11/2013, Investigator Perry-Williams and I presented our credentials and issued the initial FDA 482. On 3/12/2013 we issued another FDA 482 when we inspected the firm's warehouse located near the facility at 4090 Wedgeway Court, Earth City, MO 63045. On 3/18/2013, when Investigator Bucks joined the inspection, Investigator Bucks and I presented our credentials and issued the third FDA 482.

Daniel P. Blakeley, R.Ph, CEO, Pharmacist-in-Charge & Co-owner; Michael A. Schultz, R.Ph., CFO, Quality Control & Co-owner; Lindsay Wessels, Manager Marketing & Regulatory and (b)(6); (b)(7)(C), Regulatory & Documentation Specialist were present at the close-out meeting along with Investigators Bucks and me. The Original FDA 483, Inspectional Observations was issued to Mr. Blakeley on 3/19/2013. Firm management informed us they have documentation to support the observation. The FDA 483, Amendment 1 was then issued to remove the item. See General Discussion with Management for further discussion. The Original FDA 483 was collected from the firm.

Investigator Perry-Williams wrote **Recall Procedure** section, **FDA 483 Items 1.a-1.i; 3, 4** and **6** and co-authored the narrative for the FDA 483 sections. The rest of the sections were written by me, Investigator Berryman.

HISTORY

Foundation Care LLC started in business in March of 2004. The firm was incorporated in the State of Missouri on March 1, 2004. Mr. Daniel P. Blakeley, R.Ph. is Managing Partner, CEO and Pharmacist-In-Charge and Mr. Michael A. Schultz, R.Ph. is also a Managing Partner, Quality Control and the CFO. Mr. Blakeley and Mr. Schultz are co-owners of the business. Mr. Blakeley is the most responsible individual at the firm and should receive all correspondence.

The pharmacy provides prescriptions primarily to Cystic Fibrosis patients. Mr. Blakeley stated they are licensed and ship to 50 states. They have (b) (4) employees and their business hours are 8:00 a.m. to 6:00 p.m. Monday through Friday.

The last Missouri Board of Pharmacy inspection at Foundation Care LLC was 8/16/2012 and reported no observations.

The firm is not registered with the Food and Drug Administration as a drug establishment.

The firm has had a recall last year. See heading "Recall Procedure" for additional information.

INTERSTATE COMMERCE/ JURISDICTION

Mr. Blakeley stated approximately (b) (4) % of finished products are distributed outside the State of Missouri. According to Mr. Blakeley, the pharmacy is licensed in 50 states.

The firm continues to produce ampules of drug products from sterile drug products and components for Cystic Fibrosis patients. According to Mr. Blakeley, the (b) (4) products are Tobramycin, Colistimethate and Hypertonic Saline. A list of all products is attached as **Exhibit 1** and lists the following information for the (b) (4) products:

- Tobramycin 150mg/3ml 0.45% NaCl; Tobramycin 170mg/3.4ml 0.45% NaCl
- Colistimethate 75mg/3ml 0.225% NaCl; Colistimethate 150mg/4ml 0.225% NaCl
- Hypertonic Saline 3% 3ml, 4ml & 5ml
- Hypertonic Saline 4% 3ml & 4ml
- Hypertonic Saline 5% 3ml, 4ml & 5ml
- Hypertonic Saline 6% 3ml, 4ml & 5ml
- Hypertonic Saline 8% 3ml, 4ml & 5ml
- Hypertonic Saline 10% 3ml

During the inspection Mr. Blakeley stated they fill 3%, 4%, 5%, 6% and 9% Hypertonic Saline. He said 3% was just recently commercially available. However, I did not confirm this and at least three batches of Hypertonic Saline were filled in December 2012. He said 7% is also commercially available.

Examples of the labeling for Tobramycin, Colistimethate and Hypertonic Saline can be viewed on the first page each of **Exhibit 13-17 and Exhibit 39** (note the labels are not in color). The firm's labels are color coded as follows:

- Green – Tobramycin
- Orange – Colistimethate
- Yellow – Hypertonic Saline
- Red – all other products

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

Daniel P. Blakeley, R.Ph, CEO, is a co-owner, Pharmacist-In-Charge, and the most responsible individual at the firm and should receive the FMD-145 and official correspondence at the firm address. He accompanied us the entire inspection and directed Ms. Wessels and Ms. (b)(6); (b)(7)(C) to provide documents for our review, provide explanation of documents and provide requested copies. He was present the entire inspection. See the Refusal heading for issues during the inspection.

Michael A. Schultz, R.Ph, CFO and Quality Assurance Officer, is a co-owner and was not present the entire inspection. His participation in the inspection was limited. He attended the close-out meeting.

(b)(6); (b)(7)(C) Pharmacist, provided information during the inspection relating to documents and the process. The organizational chart shows Ms. (b)(6); (b)(7)(C) reports to both Mr. BIakeley and Mr. Schultz.

There are (b) (4) individuals listed under the Compounding Staff on the organizational chart. During the inspection we observed sterile fill operations by (b) (6)
The organizational chart shows they both report to Ms (b)(6); (b)(7)(C) along with the rest of the Compounding Staff.

Lindsay Wessels, Manager Marketing & Regulatory and (b)(6); (b)(7)(C) Regulatory & Documentation Specialist were both present during the entire inspection including the close-out meeting. Mr. Blakeley referred to them to supply us requested procedures and documents. The organizational chart shows Ms. (b)(6); (b)(7)(C) reports to Ms. Wessels and Ms. Wessels reports to both Mr. Blakeley and Mr. Schultz. A copy of the organizational chart was obtained and is attached as **Exhibit 2**.

MANUFACTURING/DESIGN OPERATIONS

The firm is located in a business park. They process primarily antibiotics for Cystic Fibrosis patients along with Hypertonic Saline. A copy of the firm's product list for 2012 was obtained is attached as **Exhibit 1**. The facility has expanded since the previous inspection and is currently at (b) (4) sq. ft. (the 2007 EIR reports (b) (4) - (b) (4) sq. ft.) The facility includes: Class 100 Cleanroom (ISO-5), Class 10,000 Anteroom (ISO-7), pharmacy where drugs are stored and prescriptions are filled, shipping & receiving dock, and walk-in cooler & freezer. Finished sterile products are stored in the cooler. A facility diagram is attached as **Exhibit 3**. Compounding of non-sterile products is conducted in a hood in the Pharmacy area.

Quality System:

The Quality System was covered through the review of procedures and documents. The firm reports no complaints since January 2012. The Complaint procedure was reviewed and discussed under the Complaint heading. The firm does not routinely conduct stability and no stability failures were noted (see Laboratory Control System/Stability and General Discussion with Management for additional information regarding stability). The firm does have designated areas for quarantine products. Training was covered as far at the media fills they conduct as part of the training program. The firm has had one recall since January 2012 for Tobramycin. The firm determined the positive sterility failure was due to laboratory error. See heading Recall Procedure of the EIR for further discussion.

Facilities and Equipment System:

The Facilities and Equipment System was covered through visual observation, review of procedures and documents. The facility appeared visually clean. No objections were noted with the pest control system. The last pest control visit was 2/22/2013.

There is a (b) (4) at the entry to the Anteroom and a (b) (4) to the Cleanroom. Procedure "8B.12, Positive Pressure Monitoring" (**Exhibit 4**) requires a (b) (4) to be logged during compounding activities. Compounding Formula Records reviewed found the Cleanroom Positive Pressure and Clean Room Temperature documented. Procedure "8B.3 Use of Anteroom" (**Exhibit 5**) states it is for storage of Cleanroom supplies. It is also where employees gown, wash their hands prior to entry to the Cleanroom, clean equipment and sanitize products containers prior to entry into the Cleanroom.

Exhibit 6 is a diagram of the Anteroom and Cleanroom. The Cleanroom has a long work bench on the back wall and two smaller tables on each side. Table 2 is where products are filled. The tables have a lower shelf where non-solid side plastic bins hold supplies and components. An outdoor stereo speaker is located on the lower shelf on Table 1. There are two stools in the room that we observed the operators to use as table tops during the cleaning process. There is a plexiglass-type box opened at the bottom for the exit air. During the previous inspection a FDA 483 item was issued for not having smooth surface on the Cleanroom floor (tiled flooring). The current inspection found

the flooring is now a smooth surface. The anteroom has a sink for cleaning and hand washing. The Cleanroom does not have any sink or drains.

The firm continues have the HEPAs for the Cleanroom quarterly recertified quarterly by Ace Electric Laboratory Systems (Ace), St. Louis, MO. The Cleanroom is classified Class 100, ISO-5 and the Anteroom is classified Class 10,000 or ISO-7. The firm has no documentation of a smoke study to verify the airflow in the Cleanroom since its installation in 2004. Mr. Blakeley stated (b) (4) conducted a smoke study but did not video record it. The firm installed a new air conditioning unit in 2007 and no new smoke study was conducted. See **FDA 483 Item 1.d.** for objection noted.

Equipment used in the sterile processed appeared adequate for the intended use. No new equipment was noted since the previous inspection. Cleaning procedures were reviewed. **FDA 483 Item 7** describes concerns with the firm's use of disinfectants not labeled as sterile in the Class 100 /ISO 5 areas and the lack of disinfectant effectiveness studies to assure disinfectants used are effective at reducing bioburden on the various surfaces in the Cleanroom. Equipment and surfaces in the clean room are cleaned / sanitized at the beginning of each product and at the end of each product. See **FDA 483 Item 1.3** for additional information.

Materials System:

The coverage of the Materials System focused on the receipt and handling of raw materials by observation and review of procedures & records.

We observed the movement of supplies, materials and personnel into the cleanroom on the first day of the inspection and again on 3/14/2013. **Exhibit 4**, "8B.3 Use of Anteroom" instructs to gather all supplies onto a cart and remove the outer boxes before entering the anteroom. The carts are not allowed to enter the anteroom as well as no cardboard or loose paper (the batch record is placed in a plastic paper holder which is wiped with IPA prior to entry into the Cleanroom). We observed components and prepackaged supplies sanitized in the pharmacy area and sprayed with (b) (4)% Sterile Isopropyl Alcohol in the Anteroom. Components / supplies are used on a first in-first out basis. **See FDA 483 Item 7** for issued noted with re-used glass beakers for waste and cleaning.

We observed only the surgical gown and gloves to be labeled as sterile. Note the surgical gown does not cover the operator's legs and operators have exposed skin on the face and neck. In addition, employees are allowed to launder their own scubs they wear underneath the surgical gown. See **FDA 483 Item 2** for objections noted with gowning. Mr. Blakeley stated they occasionally get certificate of analysis for the sterile gowns. We were shown recent Certificate of Product Conformance and Sterility for a large and XL gowns from (b) (4) We reviewed the (b) (4) packaging for the hair covers, shoe covers and dust-type mask and found them not labeled as sterile. See **Photos 1** and **2**, **Exhibit 7** for photographs after fill on 3/13/2013.

We noted the use of pre-sterilized / deprogenated single-use equipment: tubing, TPN bags for pooling, etc. They do not sterilize any equipment, containers, or closures on site. We did not observe any non-sterile components in the process. Mr. Blakeley stated they do not ship products on (b) (4) since all the sterile products are shipped refrigerated.

Production System:

We (Investigators Berryman and Perry-Williams) evaluated the Production System. This system was covered through observation, review of procedures & related documents and included: observing set-up, fill operations and cleaning in the Cleanroom and 3/11/2013 and Investigator Perry-Williams observed operations on 3/14/2013. On 3/11/2013 we watched a simulation for about 1½ hours. The process started in the Pharmacy where the operators collected the Hypertonic Saline and other components. The cart and components are sanitized. We followed the operators to the Anteroom where they gowned and prepared for the sterile fill. I informed the operators although this was a simulation they should handle it as if it was actual sterile fill as we might not have another opportunity to observe operations. We observed several unacceptable practices during the sterile fill of Hypertonic Saline lot "4HS4-130311". Investigator Perry-Williams observed a portion of the process for Tobramycin lot "ta150-130314" on 3/14/2013. See **FDA 483 Items 1.e, 1.f, 1.g, 1.h, 1.i,** and **2** for conditions observed.

We asked Mr. Blakeley what the (b) (4) products were according to volume produced. He said (b) (4) We requested a list of all sterile products produced in January, March and August for 2012. We were provided with January 2013. After checking with my supervisor we did not review January 2013 and requested January 2012. We selected the following products as a result of the total amount produced in the months: Colistimethate for January 2012 (**Exhibit 8**), Tobramycin for March 2012 (**Exhibit 9**) and Colistimethate for August 2012 (**Exhibit 10**). I asked Ms. Wessels about the low volume products produced in August. She said we were missing a page. But we didn't change to the product for August. We later collected 15 prescriptions for December 2012 (Tobramycin **Exhibit 11**) at the request of my supervisor. Review of these prescriptions found them to contain the patient name, date of prescription, drug product name and date of the prescription pre-dates the shipment date.

Initially we received a list of batches for January, March, August and December 2012. I later informed Mr. Blakeley we need a list of batches for 2012. He said it would take some time to generate it but if we really needed it he would provide it. After I reminded him for the third time he said he hadn't forgotten. He e-mailed me the list on 3/15/2013. I was provided with a copy when I returned to the firm on 3/18/2013 which is attached to this report as **Exhibit 12**.

We did not observe any anticipatory products and record review of four batches found the entire lot went out under prescriptions and was accounted for the lots listed below. From the "2012 Compounded Products" list, we (Investigators Berryman and Perry-Williams) selected one batch from January, March, August and December 2012. We requested the batch record and related prescriptions and confirmed. The documents also included the Pharmacy Work Order /

Compounding Record and Foundation Care Delivery Ticket. See **Table 2** for the number of batches filled in January, March, August 2012 and total for the year for Tobramycin, Colistimethate and Hypertonic Saline.

- January 2012, Tobramycin 50mg/ml 0.45% NaCl, lot TA170-120103B, (b) (4) units 5ml neb ampules, (b) (4) prescriptions totaling (b) (4) units, Beyond use Period 60 days/Exp 03/03/12 (**Exhibit 13**).
- March 2012, Tobramycin 50mg/ml 0.45% NaCl, lot TA170-120327B, (b) (4) units 5ml neb ampules (b) (4) prescriptions totaling (b) (4) units, Beyond use Period 90 days/Exp 06/27/12 (**Exhibit 14**).
- August 2012, Colistimethate 75mg/3ml 0.225% NaCl, lot C75-120816, (b) (4) units 5ml neb ampules (b) (4) prescriptions totaling (b) (4) units, Beyond the Period 60 days/Exp 10/16/12 (**Exhibit 15**).
- December 2012, Tobramycin 50mg/ml 0.45% NaCl, lot TA170-121211A, (b) (4) units 5ml neb ampules (b) (4) prescriptions totaling (b) (4) units, Beyond the Period 90 days/Exp 03/11/13 (**Exhibit 16**).
- December 2012, Hypertonic Saline 4%/4ml, lot 4HS4-121213, (b) (4) units 5ml neb ampules (b) (4) prescriptions totaling (b) (4) units, Beyond the Period 180 days/Exp 06/13/13 (**Exhibit 17**).

The firm states they perform 100% visual exam of the ampules in the Cleanroom and then another 100% visual exam in the pharmacy area. "8B.10 Quality Assurance of Sterile Compounded Product" (**Exhibit 18**) states there are (b) (4) quality assurance checks to ensure conformance standards are met. The (b) (4) and the (b) (4) of the compounded product. We did observe this inspection in the Cleanroom but it is not documented on the batch record. On 3/14/2013, we inspected products in the cooler and did not find any signs of growth or particulate matter.

We did not observe any production phases with extended periods of hold time. Products are on hand approximately (b) (4) They deny the use of bulk chemicals. The firm reports all products go out with patient's name except for samples or products destroyed due to past expiration date. Products are labeled as refrigerate/light sensitive. No admixing or repackaging was noted. All products covered were observed made from sterile ingredients, sterile to sterile which they report makes them a medium risk with the Missouri Board of Pharmacy. They wait for verification by the pharmacy for release.

Laboratory Control System:
The Laboratory Control System was covered through the observation, review of procedures and related documents. The firm incubates personnel and environmental monitoring samples and the media plates are read on site. Personnel monitoring is conducted (b) (4) and environmental monitoring occurs (b) (4) We did not observe personnel or environmental monitoring during the inspection. Media fills are conducted as part of the operator's training program. See **FDA 483 Item 1.a.** for observation regarding media fills.

The firm uses Analytical Research Laboratories (ARL) located at 840 Research Parkway, Suite 546, Oklahoma City, OK 73104 for periodic (b) (4) for products compounded. The last FDA inspection was at (b) (4) (b) (4) was conducted 10/12-11/8/2012. Foundation Care LLC has not audited (b) (4) ". The firm has recently started using a second contract testing laboratory: Dynalabs LLC, 2327 Chouteau Avenue, St. Louis, MO 63103. The only out of specification result was a sterility failure which resulted in a recall. Foundation Care's investigation determined it was a laboratory error. See the Recall Procedure section for details.

The firm does not routinely perform potency tests for products filled (see **FDA 483 Item 3**) and Sterility and Endotoxin Testing was last conducted on Hypertonic Saline in June, 2012 (see **FDA 483 Item 4**).

Stability / Beyond Use Dating (BUD)

The firm does not have a formal stability program. They do not have a stability procedure on how to conduct stability nor a protocol when to conduct stability. See the General Discussion with Management section of this report for additional details. They do have test data for Tobramycin and Hypertonic Saline. The Colistimethate data is from September, 2005.

At one point during the inspection we were informed they can't use preservatives for inhalation products. I asked for the "Compounded Drug Reimbursement Information" list to be updated to include whether or not the drug products used in their process have preservative or are preservative free. Mr. Blakeley asked why we needed this information. I said it is related to Beyond Usage Date (BUD). He then provided package inserts for the following and our review found the products were all preservative free:

- (b) (4) Tobramycin for Injection, USP
- (b) (4) Vancomycin Hcl for Injection
- (b) (4) Amikacin
- (b) (4) Colistimethate for Injection
- (b) (4) Gentamicin Injection USP
- (b) (4) Levofloxacin Injection
- (b) (4) Ceftazidime for Injection
- (b) (4) Hypertonic Saline (Sodium Chloride Injection USP 23.4% 4meq/mL Concentrated
- (b) (4) Amphotericin B for Injection USP
- TOBI (repack it don't compound it per Dan – later said they don't repack anything)

The firm is producing preservative-free products with a beyond use date on the batch record and identified as expiration date on the label. "8B.11 Beyond Use Dates of Sterile Compounded Product" (**Exhibit 19**) states "Beyond use dates (BUD) are determined according to the USP Chapter 797, scientific literature, or stability, potency and sterility data from a contracted analytical

laboratory." It also shows the BUD is documented on the master compounding formula record and entered into the inventory management system in (b) (4) which is used for dispensing the medication. A list of the Expiration Date is listed for all products on the Compounded Drug Reimbursement Information list attached as **Exhibit 1**. Products that were a focus of the inspection are listed below:

Table 1

Product	Expiration Date
Colistimethate	60 days
Hypertonic Saline	180 days
Tobramycin	90 days*

*A post-inspection observation noted on **Exhibit 1** outside the Exp Date column for Tobramycin it shows "120 days testing".

Foundation Care LLC, 4090 Wedgeway Court, Earth City, MO

On 3/12/2013 we visited the firm's wholesale warehouse located across the parking lot at: 4090 Wedgeway Court, Earth City, MO. Credentials were presented and FDA 482 was issued to Mr. Blakeley. Ms. (b)(6), (b)(7)(C) also accompanied us. Mr. Blakeley stated the warehouse is (b) (4) sq. ft. and included the office space as well as the storage area. This site is licensed with the Missouri Board of Pharmacy. We observed warehouse staff loading a pallet of (b) (4) upon our arrival. There is a designated holding area. There are two overhead doors. There is a walk-in refrigerator. The warehouse has controlled temperature. Products were stored on wooden pallets and plastic pallets on metal shelving. We noted a "HT" stamp on wooden pallets which we believe to mean heat treated. There are security cameras. This warehouse is also on a (b) (4) before it kicks on in case of a power outage. This warehouse has a (b) (4) product, (b) (4) Mr. Blakeley and the Pharmacists have access to this controlled facility. The warehouse primarily stored (b) (4) stored for (b) (4) a local company. (b) (4) is distributed to physicians, clinics and hospitals for ophthalmic surgery. Foundation Care LLC does not manipulation the (b) (4) We also noted Sodium Chloride Inhalation Solution, (b) (4) drug/device (b) (4) kit, (b) (4) parts for insulin pump, (b) (4) disinfectant a (b) (4) product, ultra sonic cleaning for electronics (purchased for a study which never started). They do have a (b) (4) pest control service by (b) (4) who visits for pest control. I reviewed documentation of the last visit by (b) (4) and found it to be signed off by (b) (6) Accounting / Corporate Services. No objections were noted with the pest control documentation.

MANUFACTURING CODES

A lot number is assigned to each batch produced. The lot numbering system has changed since the previous inspection. The (b) (4) (b) (4) For example: C75121228 is (b) (4)

COMPLAINTS

Mr. Blakeley reports no complaint for 2012 and 2013. A copy of "7A.13 Complaint" procedure was reviewed and a copy is attached as **Exhibit 20**. All employees are trained on how to handle complaints. Their complaint form includes the person reporting the complaint, summary of the complaint including date received, summary of actions taken to resolve the complaint and signature of supervisor. A written response is to be provided to the complainant within (b) (4) calendar days. Copies of complaints and investigations are to be kept on file for (b) (4) The complaint procedure does not require obtaining the lot number of products. This was not listed on the FDA 483.

RECALL PROCEDURES

Exhibit 21, is the SOP (Standard Operating Procedure) "11.1 Recall Procedure – Pharmacy Product". Documentation regarding the recall of Tobramycin Sulfate, lot no. 9150-130305, was reviewed during this establishment inspection. One of their contract testing laboratories, (b) (4) reported a sterility failure on 5/17/12. This product had been compounded on 5/1/12 and dispensed on 5/7 and 5/11/12. Their Recall SOP, Recall Strategy for this Recall, and verification that communication was made through e-mail and telephone was reviewed. The firm provided information on each of their customers who received this product and documentation to show they had been contacted and information on the quantity of product which had been returned. The firm received product back which was tested by another contract testing lab which was found acceptable. The conclusion of the information conducted as a result of this Recall found the reported failure was due to a laboratory error. The investigation appeared adequate.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

OBSERVATION 1

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

Specifically,

a. **Your media fill procedure and documentation, which are used to validate your sterile processing operations, are inadequate. You failed to a perform media fill simulation, including documenting the following kinds of information:**
   1) **Average and worst case processing times.**
   2) **Document the different kinds of interventions, along with the average and maximum number of interventions.**
   3) **The maximum number (under worst case scenario) or personnel in the cleanroom (Class 100 i.e. ISO 5 zone) during dynamic processing operations.**

b. **Your SOP 8B.16 "Environmental Testing for Cleanroom" fails to include instructions on daily monitoring under dynamic conditions (when processing occurs) in your Class 100 (ISO 5 zone) cleanroom as it instructs for monthly environmental monitoring only for equipment and air sample (viable and non-viable monitoring).**

   In addition, this SOP does not include all of the equipment contained in your Class 100 cleanroom to be included in your monthly monitoring program. For example it fails to include and you fail to monitor the following (this is not an inclusive list):
   1) **One (1) BAXA Pump**
   2) **Two (2) Chairs**
   3) **Fifteen (15) plastic storage bins located on the lower shelf of one of your long tables;**
   4) **Five (5) black plastic vial racks used to hold your ampules which are passed into the heat sealer for ampule sealing operations;**
   5) **Speaker located on the bottom shelf of your short table;**
   6) **Door knobs, walls, and floors.**

c. **You failed to perform daily environmental monitoring (or when processing occurs) of your personnel. Your SOP 3C.4 "Compounding Personnel Training" instructs you to conduct annual personnel monitoring activities only. For example: (b) (6) was last monitored 10/19/2012 and (b) (6) was last monitored 10/18/2012.**

d. **You failed to have a smoke study procedure used to evaluate your cleanroom suite (Class 100) under dynamic conditions and employee (b) (6) stated you have not conducted a smoke study since the room was installed in 2005.**

Additionally, you failed to conduct a smoke study after a new air handling unit was installed in 2007.

e. **You failed to use appropriate aseptic cleaning practices as you do not always use overlapping cleaning strokes, cleaning from the top to the bottom, from the back to the front and from the inside/outside of your cleaning areas and equipment as observed on 3/12/2013.**

f. **Your firm has not defined a frequency or intervals where gloves must be changed out. "8B.4 Compounding Garb" only states to spray gloves with "Sterile 70% ISA". On 3/11/2013 during the fill of Hypertonic Saline 4% Lot 4HS4-130311, employee (b) (6) dropped the disinfectant bottle once at the end of processing and once during cleaning. He sprayed the bottle with Sterile IPA (Isopropyl Alcohol), placed it back on the lower shelf, continued to work and did not change his gloves. Neither pharmacist technicians changed their gloves during the process and they only wore one pair of gloves.**

g. **While observing cleaning operations on 3/11/2013 in the anteroom employee (b) (6) left the door between the cleanroom (Class 100) and anteroom (Class 10,000) open at least 3 times for over 5-10 second after cleaning/sanitization of the Clean Room. The door does not automatically close nor is there an airlock between the rooms.**

h. **You failed to follow your SOP 8B.5 "Hand Washing -Sterile Compounding". On 3/11/13 and 3/13/13, your employees (b) (6) and (b) (6) both failed to allow "water to run from fingertips toward elbows" during the rinsing of their hands as required by the procedure.**

i. **There is no clock or time instrument in the anteroom to make sure employees preparing for aseptic production scrub their hands for a minimum of 30 seconds in accordance to their procedure 8B.5 "Hand Washing -Sterile Compounding."**

Reference: 21 CFR 211.113(b)

Supporting Evidence and Relevance:

1.a. Documents provided for media fill is attached as **Exhibit 22** and includes a copy of (b) (4) (b) (4) Test Kit which includes a laminated card that comes with the test kit from (b) (4) (b) (4) The exhibit also includes the Media Fill Testing Log for documentation Mr. Blakeley, Ms. Heyde and (b) (6) completed a media fill in October 2012.

This documentation was the information they currently have in place to show they perform media fill evaluations. When questioned about their documentation regarding the amount of time including the longest amount of time, number of personnel present, including the maximum number of personnel present, and the number of interventions, including the maximum number of interventions which occur, firm management stated this documentation along with the copy of the "(b) (4) (b) (4) Test Kit" (**Exhibit 22**) was the only documentation they had for their media fills performed at this time. The "(b) (4) Test Kit", was the information provided when asked about their sterile room qualification activities including media fill SOPs, media fill simulations and documentation to support these activities. Mr. Blakeley and Ms. Wessels stated they were currently developing this program but this was what they had in place.

Firm management was also questioned about the SOPs for their sterile room qualification (i.e. media fill) activities. Ms. Wessels stated they are working on them but they did not have documentation procedures for these tasks available during this inspection.

1.b. and 1.c. **Exhibit 25** SOP "8B.16 Environmental Testing for Cleanroom" fails to include the requirement for daily or monitoring while the sterile operations are occurring. This SOP also only lists some of the furniture and items included in the sterile compounding suite (Class 100 area) and fails to include information on environmental monitoring tasks performed on all items included in the Class 100 area.

The current procedure requires monthly monitor of the work surface of Table 1, 2, or 3 and refers to the diagram. The diagram only shows one chair in the room (there were two chairs on 3/11/2013). The procedure states to allow (b) (4) minutes. They also provided a revision, **Exhibit 26** Draft SOP "8B.16 Environmental Testing for Cleanroom" states to monitor (b) (4) collect a (b) (4) . The procedure also has a heading "Post-Compounding (b) (4) Testing" which only requires (b) (4) to be monitored. The Draft procedure does not give a time frame but instructs "On a regular basis, (b) (4) and post compounding (b) (4) are performed and the results are recorded on the Environment Testing Log."

Exhibit 27 is Cleanroom Environmental Testing Logs for November 2012 and January 2013. The log documents the media lot number, date, temperature of the incubator and results. **Exhibit 23** SOP "3C.4 Compounding Personnel Training" requires annual (b) (4) assessment, (b) (4) and (b) (4) working in the Class 100 only as opposed to personnel monitoring every day. Test results for Employee (b) (4) /Aseptic Technique Validation Tests (b) (4) Testing Log; (b) (4) Testing Logs and (b) (4) Validation Test, all for 2012, are attached as **Exhibit 24**. This information documents the environmental monitoring which is performed on the employees working in the sterile suite (Class 100 area) which is only performed annually.

1.d. The firm supplied a drawing of the air flow dated 5/13/04 prior to installation attached as **Exhibit 44**. "8B.14 Cleanroom & Anteroom Certification" (**Exhibit 45**) requires recertification

quarterly. The Exhibit includes the 7/24/2012 recertification and test data. Test conducted for both the Anteroom and the Cleanroom are: (b) (4) (b) (4)

1.e. **Exhibit 28** SOP "8B.19 Anteroom & Cleanroom Cleaning Procedures" and **Exhibit 29** SOP "8B.20 Cleaning and Maintenance of Cleanroom Equipment" were not followed and or failed to include instructions for a Class 100 area for the following: use overlapping strokes when cleaning; clean from the inside toward the outside of the equipment and work stations and clean from the top toward the bottom of work spaces. In addition, neither SOP 8B.19 nor 8B.20 requires cleaning of the chairs in the Cleanroom. Other related procedures reviewed during the inspection: **Exhibit 32** SOP "8B.7 General Aseptic Procedures Used at the Clean Room Workbench".

1.f. **Exhibit 30** SOP "8B.4 Compounding Garb" has not defined a frequency or intervals where gloves must be changed out. This SOP only states to spray gloves with "Sterile 70% ISA". During the operations we observed poor aseptic practices being used on 3/11/2013 during the fill of Hypertonic Saline 4% Lot 4HS4-130311. Employee (b) (6) dropped the disinfectant bottle once at the end of processing and once during the cleaning process. He sprayed the bottle with Sterile IPA (Isopropyl Alcohol), placed it back on the lower shelf, continues to work and did not change his gloves. Neither pharmacist technicians changed their gloves during the process and they only wore one pair of gloves. **Exhibit 32** SOP "8B.7 General Aseptic Procedures Used at the Clean Room Workbench" states under 9. Use sterile 70% IPA on the surface of gloved hands, as necessary.

1.g. **Exhibit 5**, Copy of SOP "8B.3, Use of Anteroom" explains the route of getting product in the Cleanroom. It also states that (b) (4) of doors (b) (4) (b) (4) and under 6.b. (b) (4) door should only be open for a minimal amount of time.

1.h. and 1.i. See firm's procedure attached as **Exhibit 33** "8B.5 Hand Washing—Sterile Compounding" and **Exhibit 31,** Compounding Formula Record for Hypertonic Saline 4% lot 4HS4-130311. SOP 8B.5 was not followed. On 3/11/13 and 3/14/13, your employees (b) (6) and (b) (6) both failed to allow "water to run from their fingertips toward elbows" during the rinsing of their hands as required by the procedure. Additionally, there is no clock or time instrument in the anteroom to make sure employees preparing for aseptic production scrub their hands for a minimum of 30 seconds in accordance to this SOP.

Discussion with Management:

Regarding 1.a. Mr. Blakeley said this information was provided to us during the inspection. He stated he didn't know what an intervention was. Investigator Bucks explained and Mr. Blakeley stated they call that manipulations. I said you are performing the media fill as part of employee training and not to validate the process.

1.b. This item should be conduct daily to show they have a sterile process. Management stated they follow state laws and exceeding guidelines for pharmacies. Mr. Blakeley agreed he should have a list of what equipment is in the Cleanroom.

1.e. Mr. Schultz stated they use soapy water, disinfectant and IPA. So they are wiping down the surfaces three times. He said one of his audits found their method acceptable since they were wiping down the surfaces three times.

1.g. Management didn't seem to think this was an issue with the Cleanroom being at positive pressure and said they won't get a back flow.

OBSERVATION 2

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

Specifically, during processing of Hypertonic Saline on 3/11/2013 and Tobramycin on 3/14/2013 both employees (b) (6) and (b) (6) were observed with exposed skin around the neck and face. The operators do not wear the jumpsuit style but Royal Silk Surgical Gown which wraps around, ties on the side and not totally closed in the back. In addition, the bouffant cap, surgical mask, shoe covers they wear are not sterile to protect pharmaceuticals which are preservative free such as Tobramycin, Colistimethate and Hypertonic Saline. The Pharmacist-in-charge stated the scrubs worn underneath the Gown are laundered at home by the employees.

Reference: 21 CFR 211.28(a)

Supporting Evidence and Relevance:

Exhibit 7 Photo 1 is a front view of Pharmacist Tech (b) (6) preparing to exit the Anteroom and Photo 2 is a back view of Pharmacist Tech (b) (6) preparing to exit the Anteroom. The photographs were taken on 3/13/2013. It is unknown if the employees working in the Cleanroom wear facility dedicated shoes.

Exhibit 30 "8B.4 Compounding Garb"

Exhibit 31 Compounding Formula Record for Hypertonic Saline 4% lot 4HS4-130311

Discussion with Management:

We observed the pharmacist technician's gown in the anteroom during the inspection on 3/11/2013 during a "simulation". Investigator Perry-Williams observed the process of Tobramycin on 3/14/2013, and I took the picture of (b) (6) gowned on 3/13/2013.

When we asked to observe filling operations in the Cleanroom Mr. Blakeley asked if we had our own scrubs. Investigator Perry-Williams asked Mr. Blakeley if the employees purchase their own scrubs and he stated they did. He also stated employees are required to launder their own scrubs. He said they change into the scrubs at the firm. (b) (6) changes into her scrubs either in the bathroom or in a cubicle, uncontrolled areas. On the first day of the inspection we conducted an inspection of the facility by following the process, from the pharmacy, where components are received, then I asked to go to the Cleanroom to watch filling operations. Mr. Blakeley stated we couldn't go into this area as we didn't have our own scrubs and we would disrupt the air flow. Eventually he stated we could observe before operations or at the end of the day as they would have to do a thorough clean after we were in the Cleanroom and they would have to throw away the product. We contacted our office and obtained white jumpsuit type over cover and he agreed we could wear the jumpsuit over our clothes. They agreed we could watch the process at the end of the day. I stated they should operate as if it was the actual process as it might be our only opportunity to watch the process.

The hand wash sink is in the anteroom and the water temperature is controlled by foot pedals for both hot and cold. The pharmacist technicians stated the temperature is difficult to regulate. While washing my hands, I agree it was either very hot or cold. I finished washing my hands and was informed by (b) (6) that I had not washed my hand long enough so I continued to wash my hands. It is the firm's responsibility to assure we are following their procedures when we go through their process.

OBSERVATION 3

Laboratory controls do not include the establishment of scientifically sound and appropriate designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically,

a. Potency is not performed on a routine basis. Your procedure 8B.13 Contract Laboratories & Sample Testing Frequency states "Potency testing may be done on a random basis or at the Pharmacist-in-Charge's or Quality Assurance Officer's discretion." For example:

1) Hypertonic Saline potency was last tested in July 2009.

2) **Tobramycin potency was last tested in December 2012.**
3) **Colistimethate was last tested for potency in September 2005.**

Reference: 21 CFR 211.160(b)

Supporting Evidence and Relevance:

The following are documentation of the last potency test provided:

Exhibit 34 (b) (4) Certificate of Analysis for Hypertonic Saline 3%/3mL for 7/29/2009 documenting this product was last tested in July 2009.

Exhibit 35 Copy of (b) (4) Certificate of Analysis for Tobra 170mg/3.4ml 0.45 NaCl for 6/21/2012

Exhibit 36 Stability of Colistimethate September 2005 documenting this product was last tested in September 2005.

Exhibit 37 "8B.13 Contract Laboratories & Sample Testing Frequency" procedure states "(b) (4) (b) (4) is tested for (b) (4)." It also states "A sample from (b) (4) lot of sterile compounded product is sent for testing according to USP 797 requirements for sterility and fungal."

The values in the **Table 2** were manually tabulated from the 2012 Compounded Products spreadsheet provided by the firm (attached as **Exhibit 12)** and represent approximate values.

Table 2

Product	Month/year	Number Batches	Largest lot (units)	Smallest lot (units)	Total units for month	Total Units for 2012
Tobramycin	January 2012	(b) (4)				
Tobramycin	March 2012					
Tobramycin	August 2012					
Colistimethate	January 2012					
Colistimethate	March 2012					
Colistimethate	August 2012					
Hypertonic Saline	January 2012					
Hypertonic Saline	March 2012					
Hypertonic Saline	August 2012					

Discussion with Management:

Mr. Schultz stated the Colistimethate is a sophisticated potency test as it is a "Pro-Drug". He also stated it was a (b) (4) dollar test. Both Mr. Blakeley and Mr. Schultz indicated FDA had tested for potency and sterility for them on the samples I (Investigator Berryman) collected during the inspection of 2007. Mr. Blakeley stated they exceed the Board of Pharmacy requirements for testing. Mr. Bucks asked Mr. Blakeley how they were making sure they are making their potency specifications with (b) (4) . At one point Mr. Schultz stated you count the product you have when you start and count the finished product when you are done to see if it is all accounted for.

OBSERVATION 4

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

Specifically, you do not perform sterility and endotoxin test on a routine basis for Hypertonic Saline which was last tested for sterility in June 2012.

Reference: 21 CFR 211.165(b)

Supporting Evidence and Relevance:

Exhibit 37 "8B.13 Contract Laboratories & Sample Testing Frequency" procedure states '(b) (4) (b) (4) is tested for (b) (4) " It also states "A sample from (b) (4) lot of sterile compounded product is sent for testing according to USP 797 requirements for sterility and fungal."

Exhibit 38 (b) (4) Microbiology Report dated 7/28/2009, page 1. In addition, page 2 is Colistimethate Microbiology Report is dated 8/31/2012. Pages 3-7 are 2012 results from (b) (4) for Tobramycin.

Exhibit 47 Microbiology Report from (b) (4) for Hypertonic Saline sterility test in June 2012; Endotoxin and Sterility Certificate of Analysis from (b) (4) for Tobramycin dated 3/15/2013 and Colistimethate 3/15/2013.

Discussion with Management:

Management provided additional information prior to the conclusion of the inspection included above.

OBSERVATION 5

The records for components and drug product containers or closures do not include the supplier's lot number.

Specifically,

a. **You did not document the lot number of the TPN bags used in the sterile drug process for the following but not limited to: Tobramycin Lot TA170-120103B, TA170-120327B, TA170-121211A, TA170-130312B; and Colistimethate Lot C75-120816.**
b. **Ampule lot numbers used in sterile drug products are not documented. Ampules used in the process are received from the sterilization company have a list of lot number on the shipping carton but do not have lot numbers on the individual bags.**

Reference: 21 CFR 211.184(a)

Supporting Evidence and Relevance:

Exhibit 39 Copies of Compounding Formula Records for Tobramycin lot TA170-130312B and ta150-130312A and TA170-130312A. Also, please note the first page of **Exhibits 13 – 16,** Compounding Formula Record lists "TPN Bag" and "(b) (4) Ampules" without recording a lot number. If the manufacturer of the TPN bags or Ampules had a recall it would be difficult to identify the specific lot. In addition, it would be difficult to conduct an adequate investigation if the firm had an issue relating to either the TPN bags or the Ampules.

Discussion with Management:

Management did not comment on this observation.

OBSERVATION 6

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

Specifically, there is no documented cleaning of the glassware prior to use in the cleanroom. You failed to render glassware re-used in your Cleanroom (Class 100 area) in a sterile condition prior to being introduced into your Cleanroom. This re-used glassware is located on the tables in close proximity to your processing area which includes opened ampules before sealing activities occur. Your SOP 8B.21 "Washing Glassware for use in the Cleanroom" instructs your employees to rinse the glassware using tap water, wash with liquid detergents, wipe with IPA, etc. After the washing/drying steps this SOP instructs them to hang the glassware "on rack to dry". This rack is located in the anteroom (class 10,000) area which does not have documented cleaning of this storage area. We observed this practice on 3/11/2013 during the cleaning process after the sterile fill of Hypertonic Saline.

Reference: 21 CFR 211.67(a)

Supporting Evidence and Relevance:

Related exhibits:

Exhibit 40 SOP "8B.21 Washing Glassware for use in the Cleanroom". This glassware was observed to be used for cleaning activities along with being placed on the tables where sterile activities occur during the process. This glassware has not been rendered sterile and is used and manipulated during sterile operations.

Exhibit 41 Compounding Area Cleaning Log does not provide evidence that this glassware is sterilized and is being introduced to the firm's cleanroom (Class 100). This glassware is also placed on the counter during sterile compounding operations. The log is an example of the current cleaning of the Cleanroom and Anteroom. Daily cleaning is checked off for the room, machines, carts & tablets, waste removal, tacky mat removal and floors. The month cleaning documents a check mark for walls, ceilings storage units and supplies. It is important to note, the two chairs noted in the Cleanroom on 3/11/2013 are not on the list for cleaning. We observed the chairs used as tables during the cleaning process. We did not observe either operator sitting on the chairs during the process on 3/11/2013.

Discussion with Management:

Management stated they only use the glassware for cleaning and product(s) to be discarded. Mr. Schultz stated it was no different than cleaning the vials. The vials are cleaned in the Pharmacy and again prior to use. The glassware is placed on a rack above the sink until their next use. The glassware beaker sizes are(b) (4) .

OBSERVATION 7

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

Specifically,

a. You have not conduced disinfectant effectiveness studies to show the disinfectants used can reduce bioburden on the different surfaces in the cleanroom (Class 100) where you produce sterile products including the following but limited to: Tobramycin, Colistimethate and Hypertonic Saline.

b. The Cavicide used to disinfect the surfaces in the cleanroom (Class 100) (where sterile Tobramycin, Colistimethate, and Hypertonic Saline are filled) is not labeled as sterile.

Reference: 21 CFR 211.42(c)(10)(v)

Supporting Evidence and Relevance:

During the inspection I asked Mr. Blakeley if they had performed any disinfectant studies to show what they use are effective on their surfaces in the cleanroom. Mr. Blakeley stated "Why should I, they are already tested and approved by FDA". We responded we believe they are regulated by EPA. In addition, their environmental monitoring is inadequate in that they only conduct environmental monitoring on a monthly basis. Review of the label on the bottle of Cavicide in the Cleanroom did not indicate the product is sterile. The Cavicide is used as the second cleaning of surfaces prior to sanitizing with Sterile Isopropyl Alcohol.

Discussion with Management:

Mr. Schultz indicated they follow the USP guidance on this.

REFUSALS

During the initial walk-through inspection of the facility I asked to observe operations in the Cleanroom and was informed by Mr. Blakeley that he didn't want us to disrupt the air flow. He later said they could provide a simulation either before 8:00am or after 6:00pm as they would need to do a major clean afterwards. He asked if we had scrubs. Investigator Perry-Williams asked Mr. Blakeley if the employees purchase their own scrubs and he stated they did. He stated employees are required to launder their own scrubs. He also said they change into the scrubs at the firm. We were able to provide our own disposable jumpsuit and observed a simulation of Hypertonic Saline lot 4HS4-130311 late on the first day of the inspection. We were not allowed to take any paper or our camera in the Cleanroom. The design of the Anteroom and Cleanroom does not allow viewing area as there are no windows in the room or in either of the doors. I informed the operators they should operate as if it was the actual process as it might be our only opportunity to watch the process.

Mr. Blakeley didn't believe we had the authority to inspect his facility unless we had a product complaint or drug recall. On the first day of the inspection I read 704(a)(1) and then Mr. Blakeley pointed out 704(a)(2) from the FDA 482. On 3/12/2013 I informed Mr. Blakeley we have authority under 21 U.S.C. 374(a)(1) to enter the cleanroom, take photos and enter the warehouse where drugs are stored. I informed him it is our job to review his record to determine if he was except from 21 U.S.C. 374(a)(2)(A) that we just can't take his word that his company is exempt. Mr. Blakeley stated this was not his understanding. He requested a list of documents we wanted. Investigator Perry-Williams informed him we could provide it verbally. Once we outlined our requested documents he stated that is everything that is regulated by the Board of Pharmacy and questioned why we need that information.

Initially Mr. Blakeley refused to provide us with copies of requested documents. Later, Mr. Blakeley said he was wrong and started providing copies when requested.

At one point I informed Mr. Blakeley it would be easier to have our FDA attorneys speak with his attorney to "hammer out these issues". He requested to speak direct with the FDA attorneys. I informed him the FDA attorneys could not speak with him as if he has counsel it is against their ethic rules. Mr. Blakeley stated he had not talked to an attorney since we have been at his firm, does not have one on staff or one on retainer. However, the organizational chart attached as **Exhibit 2** shows "Legal" and lists (b) (4) *. "Outside Counsel December 2012" is located next to the asterisk. On 3/18/2013 Mr. Blakeley notified the inspectional team in an e-mail that he contacted legal counsel and provided the name of (b) (4)

On 3/13/2013, Mr. Blakeley asked if FDA will "pay me for the drugs I'm going to have to throw away" with us being in the Cleanroom. We indicated FDA would not pay for the drugs. On 3/14/2013 he did allow Investigator Perry-Williams to observe set up for sterile fill of Tobramycin.

Mr. Schultz stated he would have some questions for us at the end of the day. He mentioned they follow the USP <797>. I stated we were not following USP <797> for the current inspection. At the end of the day Mr. Blakeley read from a list of questions and some were: request for the FDA attorney contact information, an FDA organizational chart, asked if we had gowning/gloving experience, if we were familiar with USP <797>, if we were familiar with Low/Medium/High risk with the Board of Pharmacy, and if we had knowledge of the Missouri Board of Pharmacy Rules, Regulations, etc. He also wanted to know if he needed to file a formal protest against the inspection after the inspection or before we close-out. I referred him to the FDA website and stated he should type in Ombudsman. I said I believe FDA organizational charts are available on the internet. I informed him John Thorsky is our District Director and our contact information is on the FDA 482 and FDA 483.

At the conclusion of 3/18/2013, Mr. Blakeley stated if we post our findings he will seek legal counsel and come at us with a vengeance, anyone involved.

GENERAL DISCUSSION WITH MANAGEMENT

The FDA 483, Inspectional Observations, was issued to Daniel P. Blakeley, CEO and Pharmacist in Charge. Also present during the close-out meeting were Michael A. Schultz, CFO and Quality; Lindsay Wessels, Manager Marketing & Regulatory and (b) (6), (b) (7)(C) Regulatory & Documentation Specialist. Before the FDA 483 was issued to the firm I informed them these are our observations by following our assignment. I also read the initial paragraph on the 483.

Mr. Blakeley asked if he could ask us a question. He wanted to know if we had seen the FDA Frequently Asked Questions on the FDA website. He went on to say nothing they are doing shows their product is adulterated. I said from what they are not doing the products could become contaminated. He continued with another question. I said requested no more questions and said we need to continue with the close out.

Mr. Blakeley asked that we walk through each item one at a time. Other comments made during the close-out meeting are listed with the observation in the Objectionable Conditions and Management's Response section of this report.

Mr. Blakeley asked with each observation where could he find information to comply, what regulations applied, etc. He said he didn't want to wait until he got the report to get this information so he could respond. At one point I recommended the Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice. Mr. Bucks stated this is one of the guidance documents they could use but there are others.

One observation initially listed on the FDA 483 was the lack of stability for Tobramycin, Colistimethate and Hypertonic Saline but removed when the FDA 483 was amended. Mr. Blakeley

and Mr. Schultz were adamant they provided us data during the inspection. They also provided additional data prior to the conclusion of the inspection. Due to the lack of time, this item was not re-written but removed from the FDA 483. However, the firm does not have a formal stability program. They have some recent stability data for Tobramycin and Hypertonic Saline. They only have a 2005 stability study for Colistimethate. Data provided during the inspection included the following:

Table 3

Product	Lot	Test points	Date	Sample size	Storage conditions	Specs	Test Results
Tobramycin Sulfate 170mg/ 3.4mL 0.45% NaCl	TA170-090721B	(b) (4)	July-Sept. 2009	(b) (4)			
Tobra 170mg/ 3.4mL 0.45% NaCl	TA170-111115B		Feb-Mar 2012				
Hypertonic Saline 4%/4mL	4HS4-090720		July-2009				
Hypertonic Saline 4%/4mL	4HS4-090720		Aug 2009				
Hypertonie Saline 4%/4mL	4HS4-090720		Sept 2009				
Hypertonic Saline 4%/4mL	4HS4-090720		Jan 2010				
Colistimethate 25mg/mL 0.225%	*		Sept 2005				
Colistimethate 25mg/mL 0.225%	*		Sept 2005				

The only document the firm has related to stability is potency tests for the following products: **Exhibit 42**, Tobramycin, (b) (4) Certificate of Analysis for 2009 and 2012 as reported in **Table 3**.

Exhibit 43, Hypertonic Saline (b) (4) Certificate of Analysis for 2009-2010 as reported in **Table 3**.

Exhibit 36, Stability of Colistimethate at (b) (4) September 2005. *Note on Page 4 the Exhibit shows Colistimethate in (b) (4) – 75mg/3ml: Lot 050527. They have not conducted any stability studies for Colistimethate since 2005. The last potency test for Colistimethate was in 2005. The previous FDA report states this study was conducted by (b) (4), Ph.D, of the (b) (4) This study was not signed by Ms. (b) (4) or anyone from Foundation Care. See **Table 2** for Tobramycin, Colistimethate and Hypertonic Saline the amounts filled in January, March and August 2012 and total for the year.

The conclusion of the inspection I stated any further questions could be directed to our Compliance Branch or through the attorneys. Investigator Bucks and I both stated during the close-out they are not being treated any differently than any other compounding pharmacy.

I read the following warning to firm management: I am required to warn you of your responsibility to be in compliance with the FD&C Act. Failure to do so could result in an action including seizure, injunction, and civil or criminal penalties. Please keep in mind this inspection is not considered all-inclusive nor should the FDA 483 be considered all inclusive.

SAMPLES COLLECTED

No samples were collected.

EXHIBITS COLLECTED

1. Compounded Drug Reimbursement Information list, 3 pages
2. Foundation Care organizational chart, 1 page
3. Foundation Care 4010 Facility diagram, 1 page
4. 8B.12 Positive Pressure Monitoring, 1 page
5. 8B.3 Use of Anteroom, 2 pages
6. Clean Room Layout (and Ante Room), 1 page
7. Photographs of employee, 2 pages
8. 15 prescriptions for January 2012, 45 pages
9. 15 prescriptions for March 2012, 39 pages

10. 15 prescriptions for August 2012, 45 pages
11. 15 prescriptions for December 2012, 45 pages
12. 2012 Compounded Products list, 21 pages
13. Prescriptions, Pharmacy Work Order / Compounding Record and Foundation Care Delivery Ticket used to fill from Compounding Formula Record Tobramycin Lot TA170-120103B, 47 pages.
14. Prescriptions, Pharmacy Work Order / Compounding Record and Foundation Care Delivery Ticket used to fill from Compounding Formula Record Tobramycin Lot TA170-120327B, 56 pages.
15. Prescriptions, Pharmacy Work Order / Compounding Record and Foundation Care Delivery Ticket used to fill from Compounding Formula Record Colistimethate Lot C75-120816, 35 pages.
16. Prescriptions, Pharmacy Work Order / Compounding Record and Foundation Care Delivery Ticket used to fill from Compounding Formula Record Tobramycin Lot TA170-121211A, and Quality Control Inspection to explain discrepancy with unit amount, 48 pages.
17. Prescriptions, Pharmacy Work Order / Compounding Record and Foundation Care Delivery Ticket used to fill from Compounding Formula Record Hypertonic Saline Lot 4HS4-121213, 43 pages.
18. 8B.10 Quality Assurance of Sterile Compounded Product, Revision 1, signed 7/17/2012, 1 page
19. 8B.11 Beyond Use Dates of Sterile Compounded Product, Revision 1, signed 7/17/2012, 1 page
20. 7A.13 Complaint, 4 pages
21. 11.1 Recall Procedure – Pharmacy Product, 4 pages
22. Media fill test kit instructions and Media Fill Testing log, 5 pages
23. 3C.4 Compounding Personnel Training, 2 pages
24. (b) (4) results, 12 pages
25. 8B.16 Environmental Testing for Cleanroom, 3 pages
26. 8B.16 Environmental Testing for Cleanroom Draft, 4 pages
27. Cleanroom Environmental Testing Log for November 2012 and January 2013, 2 pages
28. 8B.19 Anteroom & Cleanroom Cleaning Procedures, 2 pages
29. 8B.20 Cleaning and Maintenance of Cleanroom Equipment, 1 page
30. 8B.4 Compounding Garb, 2 pages
31. Compounding Formula Record for Hypertonic Saline 4% lot 4HS4-130311, 1 page
32. 8B.7 General Aseptic Procedures Used at the Clean Room Workbench, 1 page
33. 8B.5 Hand Washing—Sterile Compounding, 1 page
34. (b) (4) Certificate of Analysis for Hypertonic Saline 3%/3mL for 7/29/2009

35. (b) (4) Certificate of Analysis for Tobra 170mg/3.4ml 0.45 NaCl for 6/21/2012, 1 page
36. Stability of Colistimethate September 2005, 11 pages
37. 8B.13 Contract Laboratories & Sample Testing Frequency, 2 pages
38. (b) (4) Microbiology Reports, 7 Pages
39. Compounding Formula Record for Tobramycin lot TA170-130312B and ta150-130312A / TA170-130312A, 2 pages
40. 8B.21 Washing Glassware for use in the Cleanroom, 1 pages
41. Compounding Area Cleaning Log, 1 page
42. (b) (4) Certificate of Analysis (COA) for Tobramycin, 5 pages
43. (b) (4) Certificate of Analysis (COA) for Hypertonic Saline, 4 pages
44. Letter with replacement estimates for (b) (4) with projected air flow.
45. 8B.14 Cleanroom & Anteroom Certification and Test data for 7/24/2012
46. CD of photographs taken with an FDA digital camera and officially sealed.
47. Microbiology Report from (b) (4) for Hypertonic Saline sterility test in June 2012; Endotoxin and Sterility Certificate of Analysis from (b) (4) for Tobramycin dated 3/15/2013 and Colistimethate 3/15/2013.

ATTACHMENTS

- FACTS Assignment ID: 1495040 Operation ID 6608238
- Inspection request memo from CDER/OMPQ, dated 2/6/13.
- FDA 482, Notice of Inspection, dated 03/11/2013 to Daniel P. Blakeley, R.Ph, CEO/Pharmacist in Charge
- FDA 482, Notice of Inspection, dated 03/12/2013 to Daniel P. Blakeley, R.Ph, CEO/Pharmacist in Charge
- FDA 482, Notice of Inspection, dated 03/18/2013 to Daniel P. Blakeley, R.Ph, CEO/Pharmacist in Charge
- Original FDA 483, Inspectional Observations issued on 3/19/2013 to Daniel P. Blakely, R.Ph, CEO/Pharmacist in Charge
- Amendment 1, FDA 483, Inspectional Observations issued on 3/19/2013 to Daniel P. Blakely, R.Ph, CEO/Pharmacist in Charge

SIGNATURES

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