RE: FDA Disclosure of Warning Letter Response on FDA's Web Site

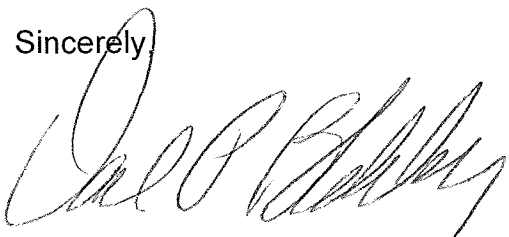
Dear Ms. Melissa Pickworth
melissa.pickworth@fda.hhs.gov.
(301) 796-5323.

On behalf of Foundation Care LLC, I authorize the United States Food and Drug Administration (FDA) to publicly disclose the information described below on FDA's web site. I understand that the information that is disclosed may contain confidential commercial or financial information or trade secrets within the meaning of 18 U.S.C. § 1905, 21 U.S.C. § 331(j), and 5 U.S.C. § 552(b)(4) that is exempt from public disclosure under those statutory provisions and/or relevant FDA regulations. I agree to hold FDA harmless for any injury caused by FDA's sharing the information with the public.

Information to be disclosed: Foundation Care 's letter dated April 9, 2013, which responds to FDA's Form 483 dated March 19, 2013.

Authorization is given to FDA to disclose the above-mentioned information which may include confidential commercial or financial or trade secret information. As indicated by my signature, I am authorized to provide this consent on behalf of Foundation Care LLC and my full name, title, address, telephone number, and facsimile number is set out below for verification.

Sincerely,



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FOUNDATION CARE

April 9, 2013

U.S. Food and Drug Administration
Kansas City District Office
8050 Marshall Drive, Suite 205
Lenexa, KS 66214

Attention: Shirley J. Berryman, Investigator
Michelle Perry Williams, Investigator
Anthony Bucks, Investigator
John Thorsky, District Director

Re: Foundation Care LLC, Earth City, Missouri (FEIN #3005364771)
Response to FDA Form 483 Issued March 19, 2013

Dear Investigators Berryman, Perry Williams and Bucks and Director Thorsky:

The FDA conducted an inspection of Foundation Care, LLC ("Foundation Care") located at 4010 Wedgeway Court, Earth City, Missouri 63045 between March 11, 2013 and March 19, 2013. At the conclusion of the inspection, Foundation Care received an FDA Form 483 (the "Form 483") listing seven observations.

We provide to you this response to the Form 483. We request that this response, excluding the attached SOPs, is included with the Form 483 anytime the FDA provides a copy of the Form 483 to anyone outside the FDA. The attached SOPs are proprietary and confidential and should not be released.

Before we respond to each of the observations listed in the Form 483, we believe that it is important to discuss the FDA's inspection and application of the Form 483 to Foundation Care. Since 2004, Foundation Care has operated as a pharmacy licensed by and subject to the jurisdiction of the Missouri Board of Pharmacy. Foundation Care engages in pharmacy-based compounding pursuant to and in compliance with the compounding guidelines set forth by the Missouri Board of Pharmacy.

It is critical to note that at no time during its existence has Foundation Care engaged in drug manufacturing. Rather, Foundation Care is a specialty pharmacy servicing the unique needs of the cystic fibrosis (CF) patient population nationwide. We provide our CF patients with FDA-approved drugs, devices and, when prescribed by a physician, compounded unit dose respiratory medications. The compounding performed at Foundation Care is considered low and medium risk by the Missouri Board of Pharmacy, USP <797>, and our accrediting body, the PCAB (Pharmacy Compounding

Accreditation Board). Notably, all of the medications used in our compounding process are FDA-approved commercially available, sterile products. Equipment utilized in our compounding areas is designed for small volume unit dosing. All compounded products are prescribed by a physician and dispensed directly to our patients. Foundation Care does not compound drugs for office use. Foundation Care does not compound any medications for intramuscular (IM), intravenous (IV), epidural or intraocular injections. Foundation Care does not compound high risk, non-sterile to sterile products.

Foundation Care respects and understands that the FDA maintains the authority to regulate the manufacture of drugs in furtherance of the public's health and safety. Foundation Care, however, does not engage in the practice of manufacturing drugs. This distinction is important because the FDA's regulation of drug manufacturers and the Missouri Board of Pharmacy's regulation of compounding pharmacies are not uniform and differ significantly. Foundation Care complies with the regulatory demands of its oversight agency, the Missouri Board of Pharmacy.

In addition to complying with the regulations of its oversight body, Foundation Care also complies with the very stringent, nationally-accepted quality control, quality assurance and quality improvement standards defined in the USP <797>, some of which are specifically referenced in the Missouri Board of Pharmacy regulations. Further, Foundation Care's distinguished accreditations demonstrate our dedication to quality and safety. In 2009, we became the first pharmacy in Missouri to achieve accreditation from the Pharmacy Compounding Accreditation Board. In 2010, we were awarded Specialty Pharmacy Accreditation by the Accreditation Commission for Health Care.

Although Foundation Care, to its knowledge, has never compounded a contaminated sterile product, Foundation Care strives for excellence and will use this as an opportunity to review our procedures and identify any area for improvement. We provide this response and plan of action to the Form 483.

Observation 1: *Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established and followed. Specifically,*

- ***Observation 1(a):*** *Your media fill procedure and documentation, which are used to validate your sterile processing operations, are inadequate. You failed to perform a 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.

- **Response to Observation 1(a):** Foundation Care complies with all Missouri Board of Pharmacy and USP <797> requirements for sterile compounding products. Foundation Care is not a pharmaceutical manufacturer. In USP <797> and the Missouri Board of Pharmacy requirements, the processing times, interventions and number of personnel are not required.

    - ***Corrective Action*:** Although not required by the Missouri Board of Pharmacy or USP <797> requirements, Foundation Care will revise SOP 8B.2 Conduct for Cleanroom Personnel to mandate that the maximum number of personnel in the clean room during dynamic processing operations shall be four. (*See* Attachment No. 1, SOP *(amended April 5, 2013)).*

    - ***Timeline*:** Completed April 8, 2013.

    - ***Responsible individual*:** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(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.*

- **Response to Observation 1(b):** Foundation Care complies with Missouri Board of Pharmacy and USP <797> requirements for sterile compounding products. Foundation Care is not a pharmaceutical manufacturer. Specifically, Foundation Care meets the Missouri Board of Pharmacy requirements for environmental monitoring as provided in Rule 20 CSR 2220-2.200 (5)(B) which requires that controlled areas for Risk Level 2 compounding:

  > ...meet Class 10,000 clean room standards; cleaning supplies should be selected to meet clean room standards; critical area work surface must be cleaned between batches; floors should be disinfected daily; equipment surfaces weekly; and walls monthly; with applicable environmental monitoring of air and surfaces.

  Foundation Care also meets and exceeds the USP <797> guidelines for environmental monitoring which require that "*[a]ir sampling shall be performed at least semiannually (i.e., every 6 months) as part of the re-certification of facilities and equipment.*" (*See* USP <797>, section titled "Environmental Viable Airborne Particle Testing Program, Air Sampling Frequency and Process"; p. 54).

  - ***Corrective Action:*** As Foundation Care's monitoring complies with the regulations of its oversight body, we do not believe that corrective action is necessary at this time. We have, however, taken this opportunity to revise our SOP to include the equipment in our cleanroom. Foundation Care has revised its SOP 8B.16 "Environmental Testing Cleanroom" to include all equipment contained in the cleanroom, including those noted in Observation 1(b). (*See* Attachment No. 2, SOP 8B.16 (revised April 5, 2013)).

  - ***Timeline:*** Completed April 8, 2013.

  - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(c):*** *You failed to perform daily environmental monitoring (or when processing occurs) of your personnel. Your SOP 3C.4 "Compounding Personnel Training" instruct you to conduct annual personnel monitoring activities only. For example: ES was last monitored 10/19/2012 and CS was last monitored 10/18/2012.*

- **Response to Observation 1(c):** As documented in SOP 3C.4, Foundation Care complies with Missouri Board of Pharmacy and USP <797> requirements for compounding sterile products. Specifically, Foundation Care complies with Rule 20 CSR 2220-2.200(8)(A) and (B) which requires for Risk Levels 1 and 2 compounding:

> (A) Risk Level 1: All pharmacy personnel preparing who prepare sterile products shall pass a process validation of aseptic technique before compounding sterile products. Pharmacy personnel competency must be reevaluated by process validation at least annually, or whenever the quality assurance program yields an unacceptable techniques are observed ....
>
> (B) Risk Level 2: In addition to Risk Level 1 requirements, process simulation procedures shall cover all types of manipulations, products and batch sizes.

Further, Foundation Care meets the USP <797> requirements for training of compounding personnel which requires:

> Media-fill testing of aseptic work skills shall be performed initially before beginning to prepare CSPs and at least annually thereafter for low-and medium-risk level compounding and semiannually for high-risk level compounding.

(*See* USP <797>, "Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices, and Cleaning/Disinfection Procedures").

  - ***Corrective Action:*** Foundation Care does not believe that corrective action is necessary as Foundation Care is in compliance with applicable requirements. Consistent with SOP 3C.4, Foundation Care will continue to monitor and test its personnel and provide annual evaluations. (*See* Attachment No. 3, SOP 3C.4).

  - ***Timeline*:** Completed April 8, 2013.

  - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(d):*** *You failed to have a smoke study procedure used to evaluate your cleanroom suite (Class 100) under dynamic conditions and employee DB 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.*

- **Response to Observation 1(d):** Foundation Care has engineered its cleanroom to meet and/or exceed specifications outlined by the Missouri Board of Pharmacy in Rule 20 CSR 2220-2.200(1)(G) and (H), which specify as follows:

> (G) Clean room: A room—1. In which the concentration of airborne particles is controlled; 2. That is constructed and used in a manner to minimize the introduction, generation, and retention of particles inside the room; and 3. In which other relevant variables (e.g., temperature, humidity, and pressure) are controlled as necessary.
>
> (H) Clean zone: Dedicated space—1. In which the concentration of airborne particles is controlled; 2. That is constructed and used in a manner that minimizes the introduction, generation, and retention of particles inside the zone; and 3. In which other relevant variables (e.g., temperature, humidity, and pressure) are controlled as necessary. This zone may be open or enclosed and may or may not be located within a clean room.

Additionally, Foundation Care meets the requirements for a cleanroom for medium risk compounding as outlined in USP <797>'s Environmental Quality and Control section.

In addition to its compliance, Foundation Care uses an external approved environmental monitoring company, Ace Electric Laboratory Systems of St. Louis, Missouri, to perform all cleanroom certifications on a quarterly basis. This procedure exceeds the requirements of USP <797> as outlined in the section titled "Environmental Viable Airborne Particle Testing Program, Air Sampling Frequency and Process." This section requires that "[a]ir sampling shall be performed *at least semiannually (i.e., every 6 months) as part of the re-certification of facilities and equipment.*"

The 2004 and 2007 versions of the USP <797>, which were applicable at the time the cleanroom was installed and since that time, do not discuss the necessity of a smoke study. The most recent version of the USP <797>, however, does discuss a smoke study. Thus, although not required, Foundation Care will conduct a smoke study in the second quarter of 2013.

- ***Corrective Action:*** Foundation Care's procedures are legally compliant with the requirements. Although not required by the Missouri Board of Pharmacy or USP <797> requirements, Foundation Care will move forward with conducting a smoke study to ensure the cleanroom meets the requirements under dynamic conditions.

- ***Timeline:*** Foundation Care plans to conduct a smoke study within the second quarter of 2013.

- ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(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.*

- **Response to Observation 1(e):** Foundation Care believes that Observation 1(e) may be incomplete. The cleaning process utilized by Foundation Care and mandated in SOP 8B.19 Anteroom & Cleanroom Cleaning Procedures is actually repeated three times to include the following three steps:

  (1) Wipe surface with sterile water and soap.
  (2) Wipe surface with an antibacterial agent.
  (3) Spray and wipe surface with isopropyl alcohol.

  Foundation Care's process complies with the Missouri Board of Pharmacy requirements for cleaning and disinfecting the compounding area as provided in Rule 20 CSR 2220-2.200(5):

  > (A) The area(s) used for the compounding of drugs shall be maintained in a sanitary condition and shall be free of infestation by insects, rodents and other vermin. Trash shall be held and disposed of in a timely and sanitary manner.

  Our process also meets USP <797> requirements. *See* USP <797>, p. 73, "Cleaning and Disinfecting the Sterile Compounding Areas":

  > The cleaning and disinfecting practices and frequencies in this section apply to ISO Class 5 (see Table 1) compounding areas for exposure of critical sites as well as buffer areas, ante-areas, and segregated compounding areas. Compounding personnel are responsible for ensuring that the frequency of cleaning is in accordance with the requirements stated in Table 3 and determining the cleaning and disinfecting products to be used (see Appendix II). Any organizational or institutional policies regarding disinfectant selection should be considered by compounding personnel. All cleaning and disinfecting practices and policies for the compounding of CSPs shall be included in written SOPs and shall be followed by all compounding personnel.

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The selection and use of disinfectants in healthcare facilities is guided by several properties, such as microbicidal activity, inactivation by organic matter, residue, and shelf life (see Appendix II). In general, highly toxic disinfectants, such as glutaraldehyde, are not used on housekeeping surfaces (e.g., floors, countertops). Many disinfectants registered by the EPA are one-step disinfectants. This means that the disinfectant has been formulated to be effective in the presence of light to moderate soiling without a pre-cleaning step.

Surfaces in LAFWs, BSCs, CAIs, and CACIs, which are intimate to the exposure of critical sites, require disinfecting more frequently than do housekeeping surfaces such as walls and ceilings. Disinfecting sterile compounding areas shall occur on a regular basis at the intervals noted in Table 3 when spills occur, when the surfaces are visibly soiled, and when microbial contamination is known to have been or is suspected of having been introduced into the compounding areas.

When the surface to be disinfected has heavy soiling, a cleaning step is recommended prior to the application of the disinfectant. Trained compounding personnel are responsible for developing, implementing, and practicing the procedures for cleaning and disinfecting the DCAs written in the SOPs. Cleaning and disinfecting shall occur before compounding is performed. Items shall be removed from all areas to be cleaned, and surfaces shall be cleaned by removing loose material and residue from spills; for example, water-soluble solid residues are removed with sterile water (for injection or irrigation) and low-shedding wipes. This shall be followed by wiping with a residue-free disinfecting agent such as sterile 70% IPA, which is allowed to dry before compounding begins.

Cleaning and disinfecting surfaces in the LAFWs, BSCs, CAIs, and CACIs are the most critical practices before the preparation of CSPs. Consequently, such surfaces shall be cleaned and disinfected frequently, including at the beginning of each work shift, before each batch preparation is started, every 30 minutes during continuous compounding periods of individual CSPs, when there are spills, and when surface contamination is known or suspected from procedural breaches.

Work surfaces in the ISO Class 7 (see Table 1) buffer areas and ISO Class 8 (see Table 1) ante-areas as well as segregated compounding areas shall be cleaned and disinfected at least daily, and dust and debris shall be removed when necessary from storage sites for compounding ingredients and supplies using a method that does not degrade the ISO Class 7 or 8 (see Table 1) air quality (see Disinfectants and Antiseptics □1072□).

- ***Corrective Action:*** Foundation Care believes that it is in compliance with all applicable regulations. Foundation Care, will, however, revise SOP 8B.19 to indicate that the staff is to use overlapping strokes. (*See* Attachment No. 4, 8B.19 (revised April 8, 2013)).
- ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(f):*** *Your firm has not defined a frequency or intervals were 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 CS 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 the only wore one pair of gloves.*

- **Response to Observation 1(f):** Foundation Care's compounding personnel apply 70% isopropyl alcohol whenever nonsterile surfaces are touched, as directed by the Missouri Board of Pharmacy and USP <797> in their requirements for sterile compounding products (see below).

  Foundation Care also meets the Missouri Board of Pharmacy requirements for gloving as stated in Rule 20 CSR 2220-2.200(6), "Apparel," which require:

  > (A) Risk Level 2: … During sterile preparation gloves shall be rinsed frequently with a suitable agent and changed when integrity is comprised.

Further, Foundation Care meets the USP <797> requirements with respect to gloves outlined in its section titled "Personnel Cleansing and Garbing," which requires:

> Sterile gloves shall be the last item donned before compounding begins. Gloves become contaminated when they contact nonsterile surfaces during compounding activities. Disinfection of contaminated gloved hands may be accomplished by wiping or rubbing sterile 70% IPA to all contact surface areas of the gloves and letting the gloved hands dry thoroughly. Only use gloves that have been tested for compatibility with alcohol disinfection by the manufacturer. Routine application of sterile 70% IPA shall occur throughout the compounding process and whenever nonsterile surfaces (e.g. vials, counter tops, chairs, carts) are touched. Gloves on hands shall also be routinely inspected for holes, punctures, or tears and replaced immediately if such are detected.

- ***Corrective Action:*** Foundation Care has taken this opportunity to review its oversight body's requirements and analyze its procedures. At this time, Foundation Care believes that its procedures are in compliance and that no action is required.

- ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(g):*** *While observing cleaning operations on 3/11/2013 in the anteroom, employee ES 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.*

- **Response to Observation 1 (g):** Foundation Care has engineered its cleanroom to meet and/or exceed specifications outlined by the Missouri Board of Pharmacy in Rule 20 CSR 2220-2.200(1)(G) and (H). The over-engineering of the cleanroom allows the environment to maintain positive pressure between the cleanroom and anteroom during entry and exit from the cleanroom. Additionally, Foundation Care exceeds the requirements stated in the "Environmental Quality Control" section of the USP <797> for medium risk compounding.

  - ***Corrective Action:*** Foundation Care complies with the Missouri Board of Pharmacy and USP <797> requirements regarding the engineering of the cleanroom. Accordingly, we do not believe corrective action is required for Observation 1 (g).

  - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(h):*** *You failed to follow your SOP 8B.5 "Hand Washing–Sterile Compounding". On 3/11/13 and 3/13/13, your employees ES and CS both failed to allow "water to run from fingertips toward elbows" during the rinsing of their hands as required by the procedure.*

- **Response to Observation 1(h):**

  - ***Corrective Action:*** In order to ensure personnel compliance with SOP 8B.5 "Hand Washing–Sterile Compounding," Foundation Care reviewed the requirements of SOP 8B.5 and hand washing procedures with all the compounding pharmacists and pharmacy technicians. Foundation Care further emphasized to its personnel the importance of strict adherence to SOP 8B.5 and proper hand washing procedures. This review of information was documented on the Employee Training Form. (*See* Attachment No. 5, Employee Training Form).

  - ***Timeline:*** Completed April 8, 2013.

  - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

- ***Observation 1(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.*

- **Response to Observation 1(i):** Foundation Care's compounding personnel will continue to follow SOP 8B.5 "Hand Washing – Sterile Compounding," which states "hands should be scrubbed for a minimum of 30 seconds." (*See* Attachment No. 6, 8B.5). To ensure that the staff properly monitors their hand washing and meets the 30 second requirement, a clock will be installed above the sink in the anteroom.

  - ***Corrective Action:*** Foundation Care installed a clock with a second hand in the anteroom to monitor the hand washing time as outlined in SOP 8B.5.

  - ***Timeline:*** Completed April 8, 2013.

  - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

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 ES and CS 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 that scrubs worn underneath the Gown are laundered at home by the employees.*

- **Response to Observation 2:** The requirements and procedures detailed in Foundation Care's SOP 8B.4 "Compounding Garb" comply with Missouri Board of Pharmacy and USP <797> requirements. (*See* Attachment No. 7, SOP 8B.4).

  Specifically, Foundation Care meets the Missouri Board of Pharmacy requirements for garbing as stated in Rule 20 CSR 2220.2.200(6)(A), which requires for Risk Level 2 compounding that:

  > In the controlled area, personnel wear low particulate, clean clothing covers. Head and facial hair is covered. Gloves, gowns and masks are required. During sterile preparation gloves shall be rinsed frequently with a suitable agent and changed when integrity is comprised.

  Further, Foundation Care personnel comply with USP <797> requirements for garbing as outlined in the "Personnel Cleansing and Garbing," section requiring:

  > Personnel shall don the following PPE in an order that proceeds from those activities considered the dirtiest to those considered the cleanest. Garbing activities considered the dirtiest include donning of dedicated shoes or shoe covers, head and facial hair covers (e.g. beard covers in addition to face masks), and face masks/eye shields. Eye shields are optional unless working with irritants such as germicidal disinfecting agents or when preparing hazardous drugs...[A] nonshedding gown with sleeves that fit snugly around the wrists and enclosed at the neck is donned.

  After careful review of Foundation Care's relevant SOP, the requirements of the Missouri Board of Pharmacy, USP <797> and Observation 2, Foundation Care believes that its personnel are in compliance with the guidelines for a compounding pharmacy.

  - ***Corrective Action:*** Foundation Care complies with the Missouri Board of Pharmacy and USP <797> requirements regarding garbing. Accordingly, we do not believe corrective action is required for Observation 2.

  - ***Responsible individual*:** Pharmacist-In-Charge, Daniel P. Blakeley.

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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.

- **Response to Observation 3:** Potency is performed to establish beyond use dating of sterile compounded product. As evidenced by SOP "8B.13 Contract Laboratories and Frequency" and SOP "8B.11 Beyond Use Dates for Sterile Compounded Product," Foundation Care complies with Missouri Board of Pharmacy and USP <797> requirements for sterile compounding products. (*See* Attachment Nos. 8 and 9, SOP 8B.13 and SOP 8B.11). Foundation Care is not a pharmaceutical manufacturer, nor does it compound from bulk chemicals. Foundation Care utilizes FDA approved products that have established potency and beyond use dates for the physician prescribed formulations. SOP 8B.13 (referenced in Observation 3) indicates that products will be tested initially to certify the accuracy and completeness of the formula. In addition, SOP 8B.13 states that potency will be completed if there is a change to the Master Compounding Formula.

  As demonstrated above, Foundation Care meets the Missouri Board of Pharmacy requirements for potency testing as stated in Rule 20 CSR 2220-2.200(11)(A) and (B), which require:

  > (A) Risk Level 1: All sterile products must bear a beyond-use date. Beyond-use dates are assigned based on current drug stability information and sterility considerations.
  >
  > (B) Risk Level 2: All requirements for Risk Level 1 must be met.

  As established in the above-referenced SOPs, Foundation Care additionally meets the USP <797> requirements for beyond use dating provided in its section titled "Determining Beyond-Use Dates."

  > BUDs and expiration dates are not the same (see General Notices and Requirements). Expiration dates for the chemical and physical stability of manufactured sterile products are determined from results of rigorous analytical

and performance testing, and they are specific for a particular formulation in its container and at stated exposure conditions of illumination and temperature. When CSPs deviate from conditions in the approved labeling of manufactured products contained in CSPs, compounding personnel may consult the manufacturer of particular products for advice on assigning BUDs based on chemical and physical stability parameters. BUDs for CSPs that are prepared strictly in accordance with manufacturers' product labeling shall be those specified in that labeling or from appropriate literature sources or direct testing.

- ***Corrective Action:*** Foundation Care complies with the Missouri Board of Pharmacy and USP <797> requirements regarding potency testing for beyond use dating. Accordingly, we do not believe corrective action is required for Observation 3.

- ***Responsible individual*:** Pharmacist-In-Charge, Daniel P. Blakeley.

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.*

- **Response to Observation 4:** Foundation Care complies with Missouri Board of Pharmacy and USP <797> requirements outlined below for sterile (low and medium risk) compounded products. SOP 8B.13 "Contract Laboratories and Sample Testing Frequency," followed by Foundation Care, incorporates all requirements as discussed below. (*See* Attachment No. 8, SOP 8B.13).

  Foundation Care meets the Missouri Board of Pharmacy requirements for product validation as stated in Rule 20 CSR 2220-2.200(12)(A) and (B), "End-Product Evaluation," which requires:

  > (A) Risk Level 1: The final product must be inspected for container leaks, integrity, solution cloudiness or phase separation, particulates in solution, appropriate solution color, and solution volume. The pharmacist must verify that the product was compounded accurately as to the ingredients, quantities, containers, and reservoirs. Background light or other means for the visual inspection of products for any particulate and/or foreign matter must be used as part of the inspection
  >
  > (B) Risk Level 2: All Risk Level 1 requirements must be met.

Foundation Care also meets the USP <797> requirements for product validation as stated in "Finished Preparation Release Checks and Tests," which requires:

> Finished CSPs are individually inspected in accordance with written procedures after compounding. If not distributed promptly, these CSPs are individually inspected just prior to leaving the storage area. Those CSPs that are not immediately distributed are stored in an appropriate location as described in the written procedures. Immediately after compounding, and as a condition of release, each CSP unit, where possible, should be inspected against lighted white or black background or both for evidence of visible particulates or other foreign matter. Prerelease inspection also includes container–closure integrity and any other apparent visual defect. CSPs with observed defects should be immediately discarded or marked and segregated from acceptable products in a manner that prevents their administration. When CSPs are not distributed promptly after preparation, a predistribution inspection is conducted to ensure that a CSP with defects, such as precipitation, cloudiness, and leakage, which may develop between the time of release and the time of distribution, is not released.

As a pharmacy compounding only Risk Level 2 products, Foundation Care is not required to conduct end-product sterility testing. Foundation Care, however, significantly exceeds this regulation and routinely tests our compounds.

- ***Corrective Action:*** Foundation Care complies with the Missouri Board of Pharmacy and USP <797> requirements regarding product validation. Accordingly, we do not believe corrective action is required for Observation 4.

- ***Responsible individual*:** Pharmacist-In-Charge, Daniel P. Blakeley.

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.*

- **Response to Observation 5:** The information noted in Observation 5 is not specifically required by the Missouri Board of Pharmacy or USP <797>.

    - ***Corrective Action:*** Although this information is not specifically required by the Missouri Board of Pharmacy or USP <797>, Foundation Care will amend our process for documenting this information in our compounding records. More specifically, our compounding records will include the components and lots utilized with each prescription. *See* Attachment No. 10, Documenting Process).

    - ***Timeline:*** Foundation Care is currently in the process of amending its process for documenting and expects to have this completed by April 8, 2013.

    - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

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 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.*

- **Response to Observation 6:** Glassware is utilized in the cleanroom for product waste and cleaning. Foundation Care only uses single use, disposable components in the compounding of medications for our patients. No glassware is utilized in the compounding of any prescription. Glassware is cleaned and maintained in the ante-room and disinfected prior to use in the cleanroom. Foundation Care will amend SOP 8B.21 "Washing Glassware for Use in the Cleanroom" to make it clear the purpose and function of glassware in the cleanroom.

    - ***Corrective Action:*** Foundation Care amended SOP 8B.21 to clarify the purpose and function of glassware in the cleanroom and further emphasize that glassware is not to be utilized to compound any prescription. (*See* Attachment No. 11, SOP 8B.21 (revised April 5, 2013)).

    - ***Timeline:*** Completed April 8, 2013.

    - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

FOUNDATION CARE

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 conducted disinfectant effectiveness studies to show the disinfectants used can reduce bioburden on the different services in the cleanroom (Class 100) where you produce sterile products including the following but limited to: Tobramycin, Colistimethate and Hypertonic Saline.*

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

- **Response to Observation 7:** The Missouri Board of Pharmacy and USP <797> do not require disinfectant effectiveness studies to show the validity of the cleaning agents.

  However, Foundation Care proves the effectiveness of the cleaning agents utilized in the compounding process by randomly testing the sterile compounded product. (Slee Attachment No. 8, SOP 8B.13). Foundation Care also utilizes two different independent testing laboratories, ARL Laboratories of Oklahoma City, Oklahoma, and Dyna Labs of St. Louis, Missouri. Foundation Care's Quality Assurance Program documents that the testing conducted by these mentioned laboratories on the results of the sterile compounded product have been within appropriate ranges to date.

  - ***Corrective Action:*** Foundation Care complies with the Missouri Board of Pharmacy and USP <797> requirements regarding cleaning agents. Accordingly, we do not believe corrective action is required for Observation 7.

  - ***Responsible individual:*** Pharmacist-In-Charge, Daniel P. Blakeley.

I hope that the FDA appreciates the extra steps that Foundation Care has taken to ensure patient safety. We sincerely appreciate the investigator's suggestions. Thank you for considering this response. If you should have any questions, please do not hesitate to contact me at 314-291-1122, x229.

Sincerely,

Daniel P. Blakely, R.Ph.
CEO, Pharmacist-In-Charge

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