Guardian Pharmacy Services
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June 8, 2018

LCDR John W. Diehl, M.S.
Director, Compliance Division
Office of Pharmaceutical Quality Operations, Division II
FDA/Office of Regulatory Affairs
Dallas District Office
4040 North Central Expressway, Suite 300
Dallas, TX 75204

RE: Guardian Pharmacy Services. WAIVER for Publication of Response to FDA Form 483 Issued on April 23, 2018; FEI No. 3012669715: AMENDED RESPONSE

Dear Mr. Diehl;

On behalf of Guardian Pharmacy Services (hereafter referred to as GPS), located in Dallas, Texas, I hereby authorize the United States Food and Drug Administration (FDA) to publicly disclose the information described below on FDA's website. 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. §3310), 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: GPS' Response to FDA Form 483 issued April 23, 2018; FEI No. 3012669715. The waiver shall extend only to GPS' Response to the FDA Form 483 issued April 23, 2018, and not to any of the supporting or underlying documents implicated or involved in the FDA Form 483 issued April 23, 2018 such as Attachments and Exhibits.

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 GPS, and my full name, title, address, telephone number, and facsimile number is set out above for verification.

In the event there are any questions regarding the disclosure of such information, I hereby request pre-disclosure notification so that we can address any such questions prior to disclosure of the material. Thank you.

Sincerely,

Jack R. Munn, RPh
Owner

June 8, 2018

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Director, Compliance Division
Office of Pharmaceutical Quality Operations, Division II
FDA/Office of Regulatory Affairs
Dallas District Office
4040 North Central Expressway, Suite 300
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RE: Response to Inspectional Observations Issued to Guardian Pharmacy Services (GPS) on April 23, 2018; FEI No. 3012669715: AMENDED RESPONSE

GPS would like to take this opportunity to respond to the inspectional observations listed within Form 483 dated April 23, 2018; FEI No. 3012669715. During FDA's inspection, GPS engaged cooperatively and constructively with FDA as GPS would like to assure FDA that it is committed to providing patients with the highest quality compounded preparations and takes FDA's observations and its professional responsibilities very seriously

GPS is a Texas licensed compounding pharmacy, which compounds medications in compliance with Texas law, USP Chapter 795 and USP Chapter 797 respectively, and in compliance with Section 503A of the Federal *Food, Drug, and Cosmetic Act* (hereafter referred to as Section 503A). For the past years, GPS has been providing the highest quality compounded medications to its patients for a multitude of conditions to fulfill their otherwise unmet medical needs.

As a Section 503A pharmacy compliant with Texas state law, we would like to note that many of the observations included within the Form 483 are based on current good manufacturing practices ("cGMP"). Section 503A specifically exempts 503A pharmacies compliant with state law from complying with Section 501(a)(2)(B) of the Federal *Food Drug and Cosmetic Act*, which requires compliance with cGMP. Therefore, GPS is not required to meet the cGMP regulations that are cited within the Form 483. FDA's guidance, published July 2, 2014 reiterated that drugs compounded in compliance with Section 503A will be exempt from certain sections of the *Food, Drug, and Cosmetic Act*, including cGMP requirements. FDA further recognized this to be correct within the released FDA inspections notice stating that FDA will not cite violations based on cGMP regulations for 503A pharmacies.

GPS takes great satisfaction in compounding in compliance with Texas state pharmacy law as well as in compliance with Section 503A. As such, GPS is fully entitled to the exemption from cGMP set forth in Section 503A and objects to any observation in the Form 483, which inappropriately relies on cGMP regulations. While GPS is addressing all of FDA's inspectional observations, its cooperation with FDA should not be interpreted as GPS' admission or agreement that it is required

to comply with cGMP regulations, thereby leaving GPS exposed to repeat citations for failing to confirm with cGMP regulations.

Without conceding that any of the Observations are applicable, set forth below are FDA's Observations, followed by GPS' responses thereto.

GUARDIAN PHARMACY SERVICES RESPONSE TO FDA INSPECTION OBSERVATIONS

Observation 1

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

Response to Observation 1:

1. SOP 3.030, "Environmental Monitoring of the Clean Room Facility, ver. 2.0., eff 2/1/2013, is current as of 5/15/2018 and will be followed. Monthly personnel sampling and ISO 5 surface sampling will be documented appropriately. Documentation of same will be monitored by PIC or Quality Control Officer. **(Revised SOP 3.030 attached)**

2. Semi-annual recertification or the ISO 5 laminar flow hoods, ISO 7 buffer room, and ISO 8 anteroom contracted with AirScanTech was conducted 5/14/2018. The results of the certification process report showed the sterile processing areas passed all requirements; specifically, particle counts in ISO 8 ante room were 802 particles per cubic foot (allowed 100,000 particles per cubic foot); particle counts in the ISO 7 buffer room were 353 particles per cubic foot (allowed 10,000 particles per cubic foot). Biological testing in all areas of the sterile processing area showed no growth.
(AirScan Tech Performance Evaluation and Certification of Clean Room and Equipment is attached)

Observation 2

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

Response to Observation 2:

1. Sterile IPA is being used in the cleaning and disinfecting of the ISO 5 laminar flow hoods, ISO 7 buffer room, and ISO 8 anteroom effective 4/15/2018. **(Invoice and Label attached)**

2. Effective 4/15/2018, sterile IPA 70% is used for cleaning and disinfecting all appropriate areas when and where Sterile IPA is designated. The Sterile IPA 70% used comes in sterile unit of use containers. The containers are used one time and discarded.

3. The cleaning procedure effective 4/15/2018 reflects the use of sterile Hypo-Chlor as a disinfectant which has replaced BruClean. The rinsing procedures use sterile water and sterile IPA as referenced above. If necessity compels a change from this product, an equivalent replacement will be used.
   (Invoice, technical information and Certificate of Sterility attached)

4. Decon Spore 200, a sterile sporicidal agent has replaced Texcide. The sporicidal agent is used alternately with Hypo-Chlor disinfectant. If necessity compels a change from this product, an equivalent replacement will be used.
   (Invoice, technical information and Certificate of Sterility attached)

5. The firm uses the manufacturers recommendations for preparation, dilution, concentration, application and contact times for these products. Documentation from the manufacturers is on file at the firm's office.
6. Sterile Criti-Clean, lint free wipes moistened with Sterile IPA (as described above) are used for cleaning purposes within the ISO 5 laminar airflow workbench where aseptic processing of sterile preparations occur. If necessity compels a change from this product, an equivalent replacement will be used.
   (Invoice and label attached)

7. Effective 4/17/2018 the daily, weekly, and monthly cleaning activities are regularly verified and documented to ensure the cleaning is performed and is effective. Historic records have been located, collated, and logged appropriately.

Observation 3

Air is recirculated to production areas without adequate measures to control recirculation of dust.

Response to Observation 3:

The room is in compliance with TSBP standards as evidenced by the recertification of the rooms by AirScan.

1. Successful smoke test studies performed within the ISO 5 laminar flow hoods were documented by video on 5/14/2018.
   (Video of smoke test performed by AirScan Tech included)

Observation 4

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its cleaning and maintenance.

Response to Observation 4:

1. The Nuaire ISO 5 laminar airflow workbench (model 301-630) has been removed from the sterile processing environment.

Observation 6

Written records are not always made if investigations into unexplained discrepancies.

Response to Observation 6:

1. Discrepancies will be noted, investigated and documented.

2. Service technicians were sent from the company that maintains the air conditioning system who fixed the malfunction. In the event the sterile processing area is shut down due to an air conditioning malfunction, the area will be cleaned according to SOP prior to resuming compounding.

Observation 7

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

Response to Observation 7:

Annual review of SOP manual will be documented. Updates to SOP will be documented. Review and monitoring records have been updated reviewed and signed by PIC or Quality Control Officer. Equipment calibration has been performed and documented. Processing data generated during the production of drug preparations, Logged Formula Worksheets, are reviewed and initialed for each compounded preparation dispensed.

Observation 8

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

Response to Observation 8:

1. The current procedure, SOP 9.110, conforms with the requirements in USP and the Texas State Board of Pharmacy. Our firm will continue to re-evaluate all SOPs in order to continue to improve processes. All personnel that compound sterile preparations will be evaluated and monitored for adherence to the SOP.
   (SOP 9.110 attached)

2. All sterile processing personnel have completed media fill as required by SOP and will be monitored to assure compliance.
   (Media Fill test for sterile operator attached)

3. Biological indicators are placed in various sites of the autoclaves and dry heat oven to verify proper function of the equipment. All processes are documented and monitored by PIC or Quality Control Officer.
4. Current procedures for bubble point testing have been updated to an SOP 8.050, Filter Integrity Test (Bubble Point). All sterile processing personnel will follow SOP. Documentation of bubble point tests are currently documented and monitored by PIC, Quality Control Officer or designee.
   (Revised SOP 8.050 attached)

5. All sterile processing personnel have been counseled as to the proper function of disinfecting devices and equipment during sterile processing. Educational observational review of the sterile operator in question has been performed by PIC or pharmacist designee.

Observation 9

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested t determine conformance to such requirements.

Response to Observation 9:

GPS is a Texas licensed compounding pharmacy, which compounds medications in compliance with Texas law, USP Chapter 795 and USP Chapter 797 respectively, and in compliance with Section 503A of the Federal *Food, Drug, and Cosmetic Act* (hereafter referred to as Section 503A). As a result GPS is not held to certain requirements of cGMP.

1. Endotoxin testing is currently being performed according to revised SOP 9.123b using the Cape Cod system. Some of the preparations undergoing terminal

sterilization by autoclave or dry heat oven have been deleted from our production line. Oil based preparations and suspensions will be evaluated for testing when suitable methods are available.
(Revised SOP 9.123 attached)

2. Sterility testing is currently being performed according to revised SOP 9.120. Some of the preparations undergoing terminal sterilization by autoclave or dry heat oven have been deleted from our production line. Our firm has begun to perform sterility tests on all sterile preparations to which we are extending beyond use dates.
   (Revised SOP 9.120 attached)

3. Sterility testing is currently being performed according to revised SOP 9.120.
   (Revised SOP 9.120 and purchase order attached)

4. Our firm has ordered appropriate ATCC organisms for use in growth promotion testing of in-house prepared growth media. Tryptic Soy Broth (TSB) agar plates and Fluid Thioglycollate Medium (FTM) agar plates will be challenged with the appropriate organisms.
   (Our firm has obtained the appropriate organisms and have consulted with a microbiologist from a nearby college to assist in this process. Documentation of organism acquisition attached)

5. The test sample sent to Pharmetrics Laboratory was a small sample from a preparation compounded for a specific patient with a 24 hour beyond use date (BUD). The process was in compliance with USP 797 for a patient specific prescription.

Observation 10

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

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Response to Observation 10:

A. Potency testing is required if an extended BUD is assigned to the finished preparation. BUD dating is assigned according to USP 797, data found in appropriate literature and GPS sponsored testing by out sourced laboratories.
B. Our firm will find suitable methods of testing of non-sterile preparations according to USP 795.
C. Antimicrobial effectiveness tests for drug preparations containing preservatives are not a requirement of USP Chapter 795 and USP Chapter 797.

Observation 11.

Written procedures are not followed for the cleaning and maintenance of equipment, including utensils, use in the manufacture, processing, packing or holding of a drug product.

Response to Observation 11:

GPS is a Texas licensed compounding pharmacy, which compounds medications in compliance with Texas law, USP Chapter 795 and USP Chapter 797 respectively, and in compliance with Section 503A of the Federal *Food, Drug, and Cosmetic Act* (hereafter referred to as Section 503A). As a result, GPS is not held to certain requirements of cGMP. GPS does not manufacture drug products.

A. GPS will investigate the availability of a pharmaceutical grade detergent for use in the dishwashing system currently in operation. Improvements to the current procedure will include a second rinse cycle to further remove any residue that may be on the glassware, stir bars and utensils.
B. GPS has revised SOP 8.040 to reflect current practice and will investigate a test method to evaluate hold time integrity.

Observation 12

There is a failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Response to Observation 12:

1. All appropriate personnel have reviewed SOP 9.080 for clear understanding. In the event a recall is indicted, the SOP will be followed.
   (SOP 9.080 attached)

2. A second endotoxin test was performed on Ropivacaine 2mg/ml, Lot# 53550:42 which passed, therefore no recall was required.
3. As a result of a consumer complaint, a recall was performed on Glycopyrrolate 0.2mg/ml, Lot# 53766:14. All remaining doses were retrieved from the facility.
4. Mitomycin 1ml syringe 0.4mg/ml, Lot# 55337:00 was sent to Eagle Analytical Services. The test was performed 4 days after the BUD assigned to the preparation.

Observation 13

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

Response to Observation 13:

1. BUD dating is assigned according to USP 797, data found in appropriate literature and GPS sponsored testing by out sourced laboratories.
2. GPS SOP 9.050 clarifies the method used to assign BUD to compounded preparations.
   (SOP 9.050 attached)

Observation 14

Procedures describing the handling of all written and oral complaints regarding a drug product are not followed.

Response to Observation 14:

All personnel have reviewed SOP 5.030. A close adherence to the compliance software in place so as to be timely in such reviews.
(SOP 5.030 attached)

Observation 15

Records of calibration check of automatic, mechanical or electronic equipment, including computers or related systems are not maintained.

Response to Observation 15:

GPS is a Texas licensed compounding pharmacy, which compounds medications in compliance with Texas law, USP Chapter 795 and USP Chapter 797 respectively, and in compliance with Section 503A of the Federal *Food, Drug, and Cosmetic Act* (hereafter referred to as Section 503A). As a result, GPS is not held to certain requirements of cGMP.

The minihelic pressure gauges of the ISO 5 laminar airflow workbenches were located on the two ISO 5 workbenches that have been removed from the ISO 7 buffer room.

New SOP 1.070 attached to clarify certain new procedures as it pertains to not providing prescription medication designated as "office use".