WELLNESS PHARMACY

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To: US FDA Nashville District Office
Attn: Kim McMillan, Acting District Director
404 BNA Drive, Bldg. 200 Ste. 500
Nashville, TN 37217-2597

CC: Kari Batey, Compliance Officer
Samantha Bradley, Investigator
Patrick Dooley, Investigator
Susan Alverson, Pharm D., Executive Secretary Alabama Board of Pharmacy

Re: Posting of FDA Form 483 Response

FEI: 1037746
EI: 9/22/2014-9/30/2014

Dear Kim McMillan,

Please accept this letter as authorization to post on the US FDA Internet website Wellness Pharmacy's response to the FDA Form 483 Notice of Observations, dated 9/30/2014, as submitted to Nashville District Office, unredacted but without attachments. We understand this response will be posted under the FDA Form 483 Notice of Observations for Wellness Pharmacy, issued on 9/30/2014.

Thank you,

Rod Harbin, President
Wellness Pharmacy
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Birmingham, AL 35209
Tel: (800) 227-2627
Tel: (205) 879-6551

October 20, 2014

VIA FEDEX OVERNIGHT DELIVERY
AND EMAIL:
Kim McMillan, Acting District Director
US FDA, New Orleans District Office
404 BNA Drive, Bldg 200, Ste 500
Nashville, TN 37217

Electronic copy sent to:
Kim McMillan, Acting District Director, New Orleans District Office
Kari Batey, Compliance Officer, New Orleans District Office
Samantha Bradley, Investigator, New Orleans District Office
Patrick Dooley, Investigator, New Orleans District Office
Susan Alverson, Pharm D., Executive Director, Alabama Board of Pharmacy

*RE: Wellness Pharmacy, Inc.'s Response to FDA Form 483 Issued September 30, 2014*

Dear Kim McMillan,

This letter responds to the FDA Form 483 issued Wellness Pharmacy, Inc. (Wellness Pharmacy) on September 30, 2014, which is located at 3401 Independence Dr., Birmingham, AL 35209. FDA inspected Wellness Pharmacy between September 22, 2014 and September 30, 2014. At the end of the inspection, Wellness Pharmacy received a FDA Form 483 listing nine (9) observations from FDA Investigators Samantha Bradley and Patrick Dooley. The observations were based upon CGMP requirements.

**Introduction:**

Wellness Pharmacy is a 3rd generation family owned and operated pharmacy established in 1964 and accredited by the Pharmacy Compounding Accreditation Board (PCAB), a voluntary body representing the gold standard of compounding pharmacy. PCAB accredited Wellness Pharmacy in August 2010 and reissued its accreditation in August 2013. PCAB inspected Wellness prior to accrediting it, and found Wellness Pharmacy to be in compliance with applicable regulations. Wellness Pharmacy focuses on sterile and non-sterile compounding, in addition to being a retail pharmacy. The pharmacy is compliant with all state pharmacy laws pertaining to compounding as well as federal regulations. For example, when Wellness Pharmacy compounds medications, it does so pursuant to a valid prescription for an individual patient in compliance with the United States Pharmacopoeia (USP) chapters on pharmacy compounding, USP 795 and USP 797, using bulk drug substances that comply with USP or National Formulary (NF) monographs. Additionally, Wellness has continually passed inspections at the state level, including, most recently, inspections by the Alabama Board of Pharmacy, as well as the California Board of Pharmacy, and National Boards of Pharmacy

(NABP). Wellness Pharmacy was found to be in compliance with applicable pharmacy laws during these inspections.

Please see below for a complete list of our responses to the FDA Form 483. Our responses are not an acknowledgement that Wellness Pharmacy is subject to CGMP requirements. Nonetheless, as it had done in the past during a recall resulting from an inspection of Front Range Laboratories, Wellness Pharmacy will fully cooperate with FDA to the agency's concerns.

**Observation 1**

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

Specifically,

a) Your firm has not validated the process used in the sterilization of filters used in the sterile filtration of drugs. The autoclave cycle used is based on manufacturer recommendation; however your firm has not performed any testing to ensure your autoclave sterilizes these filters under your conditions of use. The autoclave cycle is run at 121° C for 20 minutes.

**Observation 1.A. Response:** Wellness Pharmacy's policy and procedure for use of the autoclave is based on USP 797 standards which concern the compounding of sterile preparations. USP 797 states "to achieve sterility, all materials are exposed to steam at 121 degrees C under a pressure of about 1 atmosphere or 15 psi for a minimum of 20 minutes." Wellness Pharmacy performs sterilization of filters by autoclaving the filters for 20 minutes at 121 degrees C. To verify the autoclave cycle, Wellness Pharmacy uses 3M Comply SteriGage (a chemical indicator), ProSpore2 (a biologic indicator), and Madgetech (a thermocouple which measures temperature and time) which verifies exposure of the filters to appropriate conditions for sterilization. In addition, all sterile preparations are sent to an independent testing laboratory for sterility testing and are quarantined until confirmation of a passed sterility test result. Accordingly, we are confident that our procedures for our filters prevent microbiological contamination of our sterile preparations. Nonetheless, Wellness Pharmacy is investigating a resource to validate our process used in the sterilization of filters used in sterile filtration of preparations. **See attachment #1**

**Time Line:** To be completed by November 30, 2014.

b) Your firm has not validated the oven cycle used in the depyrogenation of glassware and utensils used during compounding of drug products intended to be sterile. The oven cycle is run at 250° C for 45 minutes; however, your firm has not performed any testing to ensure your equipment is depyrogenated under your conditions of use. Additionally,

no time limits have been established for how long depyrogenated equipment can be used past their depyrogenated dates.

**Observation 1.B. Response:** Wellness Pharmacy's policy and procedure for depyrogenation is based on USP 797 standards. USP 797 states that "dry heat pyrogenation shall be used to render glassware or containers such as vials, free from pyrogens as well as viable microbes. A typical cycle would be 30 minutes at 250 degrees C." Depyrogenation of glassware and utensils is performed at Wellness Pharmacy by exposing glassware and utensils to 250 degrees C for 30 minutes in a convection oven. Wellness uses DriAmp (a dry heat biologic indicator) and Madgetech (a thermocouple which measures temperature and time) to verify the oven reached the appropriate temperature for the necessary amount of time to achieve depyrogenation. In addition, all sterile preparations are sent to an independent testing laboratory for endotoxin testing and are quarantined until confirmation of passed endotoxin test result. Accordingly, we are confident that our procedures for the depyrogenation of glassware and utensils prevent microbiological contamination of our sterile preparations. Nonetheless, Wellness Pharmacy is investigating a resource to validate our process used in the depyrogenation of glassware and utensils. Further, Wellness Pharmacy will establish time limits for how long depyrogenated equipment can be used past their depyrogenation dates. **See attachment #2**

**Time Line:** To be completed no later than November 30, 2014.

c) On 9/23/2014, I observed an operator working in an ISO 5 hood filling PAP+2, lot 140923@40. During set-up for filling, the operator was observed to lean into the vertical flow hood over stoppered, pre-sterilized vials, disrupting air flow.

**Observation 1.C. Response:** Wellness Pharmacy discussed with the pharmacy technician appropriate work processes in the ISO 5 environment. Documentation of the training is stored in the Employee Training documents. Out of an abundance of caution, Wellness Pharmacy also chose to discard the lot 140923@40 PAP+2. The lot was sent for destruction on October 1, 2014.

**Time Line:** Complete

**Observation 2**

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

Specifically, the sporicidal in use at your firm, Sporgon made by Decon, is not appropriate for use over large surface areas. Your firm uses Sporgon for the purpose of sanitizing controlled room surfaces and hoods on a routine basis. Sporgon is designed for soaking and requires a 3 hour contact time.

**Observation 2 Response:** Wellness Pharmacy discontinued use of the sporocidal agent Sporgon and implemented Sporklenz made by Steris as our sporocidal agent. Per the Sporklenz label,

contact time required is 30 minutes and is used to clean all surfaces in the ISO 5, ISO 7, and ISO 8 areas once weekly. **See attachment #3**

**Time Line:** Complete. We began using the Sporklenz on September 29, 2014.

**Observation 3**

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

Specifically, your firm does not perform endotoxin testing on 100% of the products purporting to be endotoxin free. Endotoxin testing is limited to the largest finished volume container of product produced from each bulk batch, which means this only affects stock solutions that were used to fill more than one vial size.

**Observation 3 Response:** Wellness Pharmacy implemented a policy to perform endotoxin testing on 100% of sterile preparations purporting to be endotoxin free. In addition to performing endotoxin testing on the largest vial, endotoxin testing will be performed on all vial sizes. **See attachment #4**

**Time Line:** Complete on September 25, 2014.

**Observation 4**

Protective apparel is not worn as necessary to protect drug products from contamination.

Specifically, the personnel working in the ISO 7 area and under ISO 5 hoods are garbed in a hair net, non-sterile mask, sterile gown, dedicated shoes, disinfected safety glasses, and sterile gloves. The non-sterile mask and glasses leave areas of exposed skin of the operator's face. Sterile gowns are re-used throughout the day for a full day; gowns are stored in the ISO8 ante room when operators leave the ISO 7 area.

**Observation 4 Response:** Wellness Pharmacy has ordered a larger face mask to cover a larger portion of the face and allow minimal skin exposure. An evaluation will be performed to determine if the larger face mask in adequate to prevent skin exposure, and if not, further investigation will be performed for a different solution. Wellness Pharmacy ceased the re-use of sterile gowns. A new policy was implemented to replace sterile gowns upon re-entry into the ISO 7 area. **See attachment #5 and #6**

**Time Line:** To be completed no later than November 30, 2014.

**Observation 5**

Buildings used in the manufacture, processing, packing, or holding of a drug product do not have the suitable construction to facilitate cleaning, maintenance, and proper operations.

Specifically, the ceiling in the ISO 7 and ISO 8 rooms are not cleanable. Drop-tiles, which appear to be non-porous, are caulked in place causing the tiles to be uneven. Additionally, metal inlets for HEPA filter maintenance and fire sprinklers protrude from the ceiling in numerous places.

**Observation 5 Response:** The ceiling tiles in the ISO 7 and ISO 8 rooms are Envirogard Gypsum ceilings which are specifically designed for low particulate emission and maximum cleanliness. They are constructed of a gypsum core with vinyl facing, vinyl backing and sealed edges. Wellness Pharmacy is in the process of replacing and resealing the ceiling tiles that have uneven surfaces. The 4 fires sprinklers located in these rooms were installed based on local municipality fire codes regulations. Wellness Pharmacy will investigate the possibility of having the fire sprinklers recessed. Additionally Wellness Pharmacy has purchased a Sanosil HaloFogger which delivers hydrogen peroxide through a dry-mist fog system allowing the disinfectant to reach and clean all surfaces. **See attachment #7**

**Time Line:** To be completed no later than November 30, 2014.

**Observation 6**

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

Specifically,

a) Surface and air monitoring of the ISO 5 environment are not performed each day sterile drug products are produced. Currently, surface monitoring is performed once every 2 weeks and viable and non-viable air monitoring is performed once every 6 months under static conditions.

**Observation 6.A. Response:** Wellness Pharmacy exceeds USP 797, which requires "surface sampling to be performed frequently and viable air sampling to be performed with a frequency of once every 6 months." Wellness Pharmacy has a written surface sampling plan which occurs once every 2 weeks. Air monitoring is performed currently once every 6 months by an independent clean room certification company. A microbial air sampler has been purchased so that air monitoring can occur more frequently than every 6 months as required. Wellness Pharmacy will perform air sampling of the ISO 5 environment every 2 weeks, on the alternate week of the surface sampling plan. All plates will be incubated for the appropriate time. If growth is found, the plates are sent to a laboratory for identification of the microorganism. This information is compiled and trended to ensure the effectiveness of the disinfectant schedule, create a database of microorganisms found in our environment, and for investigation of environmental monitoring results. Wellness Pharmacy is confident that through these practices, appropriate environmental monitoring is maintained. **See attachment #8 and #9**

**Time Line:** To be completed no later than November 30, 2014.

b) Personnel monitoring is not performed each day sterile drug products are produced. Currently, finger-tip testing is performed once every 6 months.

**Observation 6.B. Response:** Wellness Pharmacy is compliant with USP 797 standards which states finger-tip testing is to be performed once every 6 months. In an effort to enhance the level of training of our employees, Wellness Pharmacy has implemented a policy to perform finger-tip testing once every 3 months which will exceed USP 797 standards. **See attachment #10 and #11**

**Time Line:** Additional finger-tip testing will be performed in December 2014 in accordance with the current training schedule.

c) Smoke studies have not been conducted in all ISO 5 hoods where sterile drug products are produced and they were not performed under dynamic conditions.

**Observation 6.C. Response:** Wellness Pharmacy will be conducting additional smoke studies in all ISO 5 hoods and under dynamic conditions.

**Time Line:** To be completed no later than November 30, 2014.

d) Media used for surface sampling and personnel monitoring is not growth promoted; media used for media fills is not appropriately growth promoted.

**Observation 6.D. Response:** Wellness Pharmacy exceeds USP 797 in our policy and procedure used for surface sampling and personnel monitoring. Wellness Pharmacy is investigating the purchase of the appropriate growth promoting bacteria to be used in media used for environmental and personnel monitoring.

**Time Line:** To be completed no later than November 30, 2014.

e) Temperature and relative humidity conditions are not continuously monitored in controlled production rooms or in the freezer and refrigerator which contain media, raw materials, and finished drug products purporting to be sterile.

**Observation 6.E. Response:** Wellness Pharmacy has purchased a continuous monitoring system called AseptRx which will be implemented over the next 30 days.

**Time Line:** To be completed no later than November 30, 2014. **See attachment #12**

f) Pressure differentials between controlled rooms are not continuously monitored. Currently, your practice is to document these values once per day.

**Observation 6.F. Response:** Wellness Pharmacy has purchased a continuous monitoring system called AseptRx which will be implemented over the next 30 days. **See attachment #12**

**Time Line:** To be completed no later than November 30, 2014.

**Observation 7**

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

Specifically, potency testing is not performed on every batch of drug product purporting to be sterile. Currently, your firm performs potency testing on every fourth batch of drug product purporting to be sterile.

**Observation 7 Response:** Wellness Pharmacy exceeds USP 797 with our policy and procedure on end product potency testing. Currently potency testing is performed on any new formulation, on every fourth batch of sterile preparation made, and when any change occurs to a formulation. Wellness Pharmacy only compounds with USP or NF bulk drug substances purchased from a FDA registered facility. Each USP or NF bulk drug substance is accompanied by a certificate of analysis stating purity of the drug substance. As a commitment to continued quality, Wellness Pharmacy is considering performing more frequent potency testing.

**Time Line:** Complete

**Observation 8**

Routine calibration of mechanical and electronic equipment is not performed according to a written program designed to assure proper performance.

Specifically, thermometers, hygrometers, and pressure gauges are not routinely calibrated by your firm. These instruments are used for temperature and relative humidity monitoring in controlled rooms, refrigerators holding components and finished products, incubators used for routine environmental monitoring activities, an autoclave used for terminal sterilization of one drug product and one type of filter, and an oven used to depyrogenate glassware and utensils used for compounding. The pressure gauges are used for controlled room monitoring and bubble point testing of filters.

**Observation 8 Response:** Wellness Pharmacy has purchased a continuous monitoring system called AseptRx. Calibration will be performed on thermometers, hygrometers, and pressure gauges per manufacturer guidelines upon installation and once annually. **See attachment #12**

**Time Line:** To be completed no later than November 30, 2014.

**Observation 9**

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

Specifically, stability data is either unavailable or limited for numerous drug products purporting to be sterile. There is no written testing program for on-going stability monitoring. Injectable, preservative free drug products are assigned dates as long as 6 months. Some products have data from studies to support their dates, while other expirations are assigned based on literature.

**Observation 9 Response:** Wellness Pharmacy will be implementing a written stability testing program that will allow for ongoing and additional stability testing to establish appropriate beyond use dates for sterile preparations.

**Time Line:** To be completed no later than November 30, 2014.

Sincerely,

Rod Harbin, President
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Birmingham, AL 35209
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