



Fairview
Pharmacy Services, LLC

711 Kasota Avenue SE
Minneapolis, MN 55414

June 26, 2018

SENT VIA EMAIL

Mr. Art Czabaniuk, Program Division Director
U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III
300 River Place, Suite 5900
Detroit, MI 48207

Re: Fairview Pharmacy Services, LLC, a wholly owned subsidiary of Fairview Health Services, doing business as Fairview Compounding Pharmacy Food and Drug Administration (FDA) inspection FEI Number 3013468187

On behalf of Fairview Pharmacy Services, 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 (0), 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: Fairview Pharmacy Services' letter dated 05/08/2018 excluding attachments/exhibits, which responds to FDA's Form 483 dated 04/18/2018.

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 Fairview Pharmacy Services and my full name, title, address, telephone number, and facsimile number is set out below for verification.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Robert Beacher".

Robert Beacher, RPh
President
Fairview Pharmacy Services
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Fairview
Pharmacy Services, LLC

711 Kasota Avenue SE
Minneapolis, MN 55414

May 8, 2018

SENT VIA EMAIL

Mr. Art Czabaniuk, Program Division Director
U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III
300 River Place, Suite 5900
Detroit, MI 48207

Re: Fairview Pharmacy Services, LLC, a wholly owned subsidiary of Fairview Health Services, doing business as Fairview Compounding Pharmacy Food and Drug Administration (FDA) inspection FEI Number 3013468187

Mr. Czabaniuk,

Per FDA Investigator Tenzin Janchup's instructions, this letter comprises Fairview Compounding Pharmacy's response to the FDA Form 483 Observations which were issued on April 18th, 2018 following an inspection of Fairview Compounding Pharmacy.

Fairview Compounding Pharmacy is a pharmacy preparing both sterile and non-sterile compounded drug products, and operating pursuant to rules and regulations of Minnesota State, the Minnesota Board of Pharmacy, and relevant United States Pharmacopeia (USP) Chapter 795 and 797 standards. Fairview Compounding Pharmacy prepares compounded preparations for identified patients upon receipt of a patient-specific prescription order, and prepares some compound preparations in anticipation of the receipt of a patient-specific prescription.

Fairview Compounding Pharmacy appreciates the thorough investigation by FDA investigators Tenzin Janchup and Anthony Ladner, and has made and will continue to make improvements in our processes as described below. We believe the following actions will fully satisfy all FDA concerns.

OBSERVATION 1

Non-sterilized and non-depyrogenated equipment was used in sterile drug preparation.

Specifically,

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On April 3rd, 2018, we observed an employee use non-sterile aluminum foil to cover a non-sterile product and transport it from the unclassified area into the ISO 5 aseptic processing area. The employee removed the aluminum foil inside the ISO 5 area and continued aseptic processing of Triple Agent UTZ (Papav, Phentol, Alprost) injectable product with Lot # 180403-28. The firm conducted non-sterile production of the papaverine stock solution and phentolamine mesylate stock solution in the non-sterile area which is unclassified. The depyrogenated glassware was also stored in the unclassified area.

RESPONSE

On April 3rd, 2018, Fairview Compounding Pharmacy immediately ceased using non-sterile foil to cover non-sterile products for transport into the ISO 5 aseptic processing area. All non-sterile product is now packaged into sterile syringes or viaflex bags to be transported into the ISO-5 area. This packaging is easily wiped down prior to entering the classified space and wiped down prior to entering the ISO 5 aseptic processing area. See CAP –Aluminum Foil Entry into the Clean Room, provided to inspectors on April 4, 2018 (included here as Attachment 1-001).

The master batch record for the Triple Agent UTZ and its two stock solutions have been updated to reflect the new process for packaging the nonsterile components in a closed system that is easily cleanable. See Attachment 1-002.

Fairview Compounding Pharmacy has adopted a non-sterile to sterile compounding policy and procedure. This policy and procedure reflects the process of packaging for transport into the cleanroom. Staff training on this policy began on May 4, 2018. See Attachment 1-003 and 1-004. Staff training will be completed by May 18, 2018.

Lot #180403-28 was quarantined on April 3rd, 2018. On April 24th, 2018, USP <71> sterility testing and endotoxin testing was completed and found to have no growth. See Attachment 1-005.

We have engaged our vendor to calibrate and certify our dry heat oven and to validate our depyrogenation cycles for effectiveness, specific to the load used. Once calibrated and certified, Fairview Compounding Pharmacy will recertify the oven on a frequency recommended by the manufacturer and certifying vendor to ensure effective

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depyrogenation of our glassware used in the production of non-sterile to sterile products. We anticipate that the oven will be calibrated and certified by July 2, 2018.

We have adopted a policy and procedure on dry heat sterilization & depyrogenation to specify storage times of glassware and the use of indicators during cycles. Glassware will be packaged in sterilization bags or covered in foil. The maximum storage time will be limited to 30 days if packaged in a sterilization bag and 7 days if covered in aluminum foil. Glassware that exceeds the maximum storage time will not be used for production of non-sterile to sterile products and be required to be run through the depyrogenation cycle again before using. See Attachment 1-006. Staff training on the policy and procedure began on May 4, 2018. See Attachment 1-007. Staff training will be completed by May 18, 2018.

We will incorporate specific load diagrams and instructions for the dry heat sterilizing and depyrogenating oven based on the recommendations from the manufacturer, and the vendor who will be certifying the equipment. We anticipate that these load diagrams will be available July 2, 2018, and we plan to train all staff who operate the oven for sterilization and depyrogenation by July 7, 2018.

OBSERVATION 2

The use of sporicidal agents in the cleanrooms and ISO 5 classified aseptic processing area was inadequate.

Specifically,

On April 3rd, 2018, we observed your daily cleaning of ISO 5 aseptic processing areas were done without the use of any sporicidal agents. Also, on April 6th, we observed your weekly deep cleaning of the ISO 5 and 7 areas were done without the use of any sporicidal agent. Currently, you do not use a sporicidal agent on a regular basis.

RESPONSE

USP <797> and <1072> recommend use of a sporicidal weekly on all surfaces in ISO 7 and ISO 5 areas. Investigators did not observe the use of sporicidal agents during our regular staff cleaning activities. In response we have reviewed our historical environmental monitoring to review the incidence of spore forming microorganisms to

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better understand our cleaning processes effectiveness and assess for possible risk to patients.

On April 5th, 2018, policy “Cleaning Program: Fairview Compounding Pharmacy & Fairview Home Infusion Cleanroom” was finalized to update our cleanroom cleaning program and to incorporate frequent use of sporicidal agents in our cleaning procedures. See Attachment 2-001. Training on the new policy was conducted on April 13, 20, 27 & May 1, 2018 with staff, followed by use of PeridoxRTU according to policy Appendix 1 – Daily/Weekly Staff Cleaning Tasks as part of the weekly clean. Sterile PeridoxRTU was applied to a sterile, non-shedding wipe when used in the ISO 5 area. After the prescribed minimum dwell time of 3 minutes, area was wiped with a presaturated sterile IPA wipe.

We have included the following to support these corrections:

1. Proof of the training conducted April 13, 20, 27, and May 1, 2018. See Attachment 2-002.
2. The policy “Cleaning Program: Fairview Compounding Pharmacy & Fairview Home Infusion Cleanroom.” Appendix 1 of the policy lists that the cleaning products for the weekly clean is “1) Detergent/Sporicidal – Sterile Peridox)” (peracetic acid based product) with a 3 minute dwell time, followed by “2) Disinfectant – Sterile IPA.” See Attachment 2-003.
3. The weekly cleaning checklist from April 13, 2018. See Attachment 2-004.
4. Technical data sheet for PeriodoxRTU. See Attachment 2-005.

In addition, bleach is used weekly on floors, walls and ceilings. The mixing and diluting is documented in the Housekeeping Weekly Cleaning Tasks checklist. USP <1072> Table 2 states that 0.5% Sodium Hypochlorite is classified as a sporicidal agent. The housekeeping staff for Fairview Compounding Pharmacy have used 0.5% Sodium Hypochlorite on floors, walls and ceilings every week for several years. We have updated our Housekeeping Weekly Cleaning Tasks checklist to include the concentration of the Sodium Hypochlorite (8.25%) in the dilution documentation. See Attachment 2-006 (page 4).

We will continue to monitor cleaning processes, ensuring proper cleaning and disinfecting agents are used and according to policy. We will continue to monitor and

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trend cleaning effectiveness through existing environmental monitoring processes. Both will be reviewed at our existing Fairview Home Infusion & Fairview Compounding Pharmacy Cleanroom Committee, which meets every two weeks.

OBSERVATION 3

Personnel did not disinfect and change gloves frequently enough to prevent contamination.

Specifically,

On April 2, 2018, we observed:

- a) An employee producing various allergy serums in an ISO 5 classified aseptic processing hood remove their hands from the hood and touch the supply cart located in the ISO 7 classified area. The employee then re-engaged in aseptic processing in the hood without changing or sanitizing gloves.
- b) A separate employee producing Acetylcysteine (PF) 10% Ophthalmic drops, lot #180402-05 remove their hands outside of the ISO 5 classified aseptic processing area numerous times to discard items from the hood to a bin in the ISO 7 area and re-engage in aseptic processing without changing or sanitizing the glove.

RESPONSE

Our policy Pharmaceutical Compounding-Sterile Preparations, requires personnel to sanitize their gloves frequently. In both instances that the FDA witnessed, personnel were not following policy. See Attachment 3-001.

On April 2, 2018, all compounding staff were emailed a reminder to re-sanitize their gloves when they move their hands between ISO 7 and ISO 5 space, and staff were verbally reminded of this on April 3, 2018.

Fairview Compounding Pharmacy will require its staff to complete an online training read and acknowledge program with a test to demonstrate competency, as a one-time correction for all current staff following the FDA inspection. This will in part focus on routinely disinfecting gloves after contacting non-sterile objects prior to re-engaging in aseptic processing. We intend for this training to be completed by June 30, 2018.

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Fairview Compounding Pharmacy has an aseptic training program that all new staff must complete. This training program specifically calls out the need to routinely sanitize hands during compounding. See Attachment 3-002, for select parts from this program. Further, all staff must demonstrate competency as part of our training program and media fill personnel testing, upon hire and every six months thereafter. See Attachment 3-003.

Fairview Pharmacy Services' sterile compounding trainers will also implement a quarterly audit program, where the trainers will observe at least 90 percent of Fairview Compounding Pharmacy's technicians preparing sterile compounds and score them based on personnel and aseptic technique observations. We intend to complete the first quarterly audit by June 30th, 2018. See Attachment 3-004

OBSERVATION 4

Disinfecting agents and cleaning wipes used in the ISO 5 classified aseptic processing areas were not sterile.

Specifically,

On April 3rd, 2018, we observed an employee clean the IOS 5 hood with sterile 70% IPA and non-sterile wipes before starting aseptic processing of Triple Agent UTZ (Papav, Phentol, Alprost) with lot #180403-28.

RESPONSE

Fairview Compounding Pharmacy follows USP <797> and its policy on sterile compounding requires the use of a sterile, non-shedding wipes in its ISO 5 areas. During the inspection on April 3, 2018, a gap was identified when the employee was noted using non-sterile wipes to clean with sterile 70% IPA.

We have resolved this gap by training and educating staff during our weekly staff meeting beginning on May 4, 2018, on using sterile, non-shedding wipes to clean with detergents and sporicidals. All staff who go into the cleanroom or oversee cleanroom staff have completed the training. See Attachment 4-001.

Fairview Compounding Pharmacy received a package of the TX3210 sterile, non-shedding dry wipes from a different Fairview Pharmacy Services' cleanroom on April 13,

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2018, and has been using them since that date. On April 24th, 2018, Fairview Compounding Pharmacy ordered TX3210 sterile, non-shedding dry wipes for use inside the ISO 5 area when cleaning with a detergent or sporicidal. We have included a copy of the purchase order and delivery ticket for the TX3210 sterile, non-shedding dry wipes, Attachment 4-002 and the technical data sheet for the TX3210 sterile, non-shedding dry wipes, Attachment 4-003.

OBSERVATION 5

Biological indicators were not used to verify the adequacy of the sterilization cycle.

Specifically,

- a) Progesterone 100 mg/mL in ethyl oleate injection sterilization cycle of 150 Degrees Celsius for 150 minutes does not include the use of a biological indicator to verify adequacy of the sterilization cycle.
- b) Glassware used for aseptic processing is sterilized and depyrogenated with a cycle of 250 Degrees Celsius for 150 minutes and does not include the use of a biological indicator to verify adequacy of the sterilization cycle.

RESPONSE

We have engaged a vendor to validate our dry heat sterilization and depyrogenation oven, and to validate the depyrogenation cycle. We anticipate that the dry heat sterilization and depyrogenation oven will be validated by July 2, 2018.

We have adopted two policies, “Dry Heat Sterilization & Depyrogenation”, Attachment 5-001, and “Biological and Chemical Indicators for Validation of Dry Heat Sterilization and Depyrogenation Cycles”, Attachment 5-002. Staff training on the new policies will be completed by May 18, 2018. For drug products that are sterilized in the dry heat sterilization and depyrogenation oven, we will use biological indicators with each lot to validate the cycle. Staff will be trained on the load diagrams specific for sterilization and depyrogenation cycles by July 7, 2018.

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For glassware, we will be implementing the use of indicators for the sterilization and depyrogenation cycles, and intend to work more with the vendor who will be certifying the equipment for specific recommendations based on our needs and equipment. See Attachment 5-003 for the biological indicators that have been ordered. We intend to start using the biological indicators as soon as they are received, on May 9, 2018.

The most recent batch of progesterone ethyl oleate was made on March 28th, 2018 and passed sterility and endotoxin testing. See Attachment 5-004. We have halted production of further batches of progesterone ethyl oleate until the dry heat sterilization and depyrogenation oven is validated and staff are trained on its use. We have reviewed the past year of progesterone ethyl oleate sterilized by dry heat and found no failures in sterility testing.

OBSERVATION 6

ISO 5 classified areas were not certified under dynamic conditions.

Specifically,

The certification documents for your ISO 5 aseptic processing areas do not describe the dynamic conditions under which they were tested.

RESPONSE

USP 797 requires facilities and primary engineering controls (PECs) to be certified under dynamic working conditions. April 24th, 2018 we completed our semi-annual certifications of our room and PECs. Dynamic conditions that were representative and exceeding normal operating conditions were present during the room certification. See Attachment 6-001.



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Thank you for allowing us the opportunity to respond to the observations noted during the FDA inspection. We respectfully request that this letter of response be publicly posted when the FDA form 483 observations are posted on the FDA website.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Robert Beacher".

Robert Beacher, RPh

President

Fairview Pharmacy Services