MAYO CLINIC

Mayo Clinic Pharmacy
21 Second Street SW
Rochester, MN 55902
Phone: 507-284-2021
Fax: 507-538-1314

Date: January 31st, 2019

To: U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III
Attn: Art Czabaniuk, Program Division Director

Re: Authorization to post Mayo Clinic Pharmacy Response dated August 30th, 2018 to FDA-483

On behalf of Mayo Clinic Pharmacy, 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, 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: Mayo Clinic Pharmacy's letter dated 08/30/2018 excluding attachments/exhibits, which responds to FDA's Form 483 dated 08/15/2018.

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

Sincerely,

Kevin R. Dillon, PharmD
Chief Pharmacy Officer
Mayo Clinic Department of Pharmacy
21 Second Street SW
Rochester, MN 55902
Phone: 507-284-2021
Fax: 507-538-1314

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Date: August 30th, 2018

To: U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III
Attn: Art Czabaniuk, Program Division Director

From: Mayo Clinic Pharmacy
FEI Number: 3005070479
Dates of Inspection: 8/06/2018 - 8/10/2018, 8/15/2018

Re: FDA-483 Response

Mr. Czabaniuk,

Please accept this letter as Mayo Clinic Pharmacy's response to the FDA-483 observations issued August 15, 2018 after detailed assessment of our compounding pharmacy operations and records. We respectfully request that this response, excluding the attachments, be posted on the FDA's website with the Form 483 and be included every time the FDA provides a copy of the Form 483 to any individual or entity outside the FDA. Mayo Clinic Pharmacy is committed to Mayo Clinic's Primacy Value: "The needs of the patient come first". Fundamental to this commitment is the provision of high quality pharmacy services. We appreciate the professional and informative process executed during the inspection, and are confident that our processes and implemented improvements have addressed the stated observations.

OBSERVATION 1

You did not make adequate product evaluation and take remedial action where actionable microbial contamination was found to be present in the ISO 5 classified aseptic processing area during aseptic production.

Specifically,

During the certification by your third-party contractor on 10/30/2017, there were 73 CFUs found in the viable air sample inside your six-foot ISO 5 compounding hood and no identification of the CFUs were done and no evaluation of drug impact were conducted at the time.]

Mayo Clinic Pharmacy Response:

The October 30, 2017 report from our contractor was carefully evaluated taking into consideration historical environmental monitoring data for viable air and surface sampling for the space, batch sterility test results, and overall state of control of the compounding environment during the time. The assessment evidenced that the CFU finding was consistent with an anomaly caused by sample contamination versus a true reflection of air quality in the space, and for that reason identification was not performed at that time.
We have confirmed and further developed our existing SOP (see Attachment A SOP 7.014 Actions to Colony Forming Units (CFUs)) to ensure all CFUs are identified, regardless of our assessment of causality, and a process exists to document an evaluation of potential impact on product, and remedial action taken, if warranted.

Attachment A: SOP 7.014 Actions to Colony Forming Units (CFUs)

OBSERVATION 2

Non-microbial contamination was observed in your production area.
Specifically,

a) On 8/7/2018, during the sterile production of an amphotericin B 0.15% ophthalmic solution, lot #RI 419080718, we observed rust on the wheels of the cart located inside the clean room (ISO 7) adjacent to the six-foot ISO 5 hood.
b) On 8/10/2018, during the daily cleaning of the six-foot ISO 5 hood, we observed duct tape attached to a power cord on the front right side of the six foot ISO 5 hood.

Mayo Clinic Pharmacy Response:

1. The cart was removed from the clean room the same day discovered and a new one has been purchased to replace it. (see Attachment B – Purchase order for new cart)
2. The small piece of duct tape was removed immediately and the area cleaned, as witnessed by the inspectors.
3. We have updated our SOP to include staff vigilance in noticing and bringing forward needed facility updates, and a weekly visual inspection of facilities and fixtures has been added (see Attachment C SOP 8.004 Facilities General Maintenance and Attachment D Cleaning and Facilities Monitoring Records).

Attachment B: Cart Purchase Order
Attachment C: SOP 8.004 Facilities General Maintenance
Attachment D: Form - Cleaning & Facilities Monitoring Records

OBSERVATION 3

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

Specifically,
On 8/10/18, during your daily cleaning of your two ISO 5 hoods, we observed the operator use a non sterile chemical disinfectant inside the ISO 5 classified hoods with sterile wipes.

Mayo Clinic Pharmacy Response:
We have switched to a sterile disinfectant cleaner in the ISO 5 hoods and updated our SOP accordingly (see Attachments E-H & D).

Attachment E:	TexQ Disinfectant Purchase Order
Attachment F:	Certificate of Analysis for Sterility - TexQ – Lot # Example
Attachment G:	7.006 Cleaning of the Compounding Environment
Attachment H:	TexQ Disinfectant Technical Data Sheet
Attachment D:	Form – Cleaning & Facilities Monitoring Records

OBSERVATION 4
Disinfectant contact time (also known as "dwell time") and coverage of the item being disinfected were insufficient to achieve adequate levels of disinfection.

Specifically,
The sporicidal agent used in your ISO 5 area requires a contact time of 180 minutes in order to eliminate spores. Your current procedure, SOP 7.012 Sporicide Hood Cleaning - Weekly Cleaning, states that the sporicide is applied three consecutive times, with a total wet contact time of 15 minutes after each application.

Mayo Clinic Pharmacy Response:
We have implemented use of a sterile sporicide based on manufacturer guidelines for contact time. We have updated our SOP accordingly. (see Attachments G, D, & I-K)

Attachment G:	7.006 Cleaning of the Compounding Environment
Attachment D:	Form - Cleaning & Facilities Monitoring Records
Attachment I:	PeridoxRTU Purchase Order
Attachment J:	Certificate of Conformance and Analysis and Sterility - PeridoxRTU – Lot # Example
Attachment K:	PeridoxRTU Datasheet

OBSERVATION 5
No endotoxin testings are done for multi-dose products which are not produced with a preservative to ensure product sterility.

Specifically,

On 8/7/2018, we observed the production of amphotericin B 0.15% ophthalmic solution, lot #Rl419080718, was produced without an addition of a preservative and labeled with a beyond use date of seven days refrigerated with no testing of endotoxin conducted.

Mayo Clinic Pharmacy Response:
We have changed our amphotericin B 0.15% ophthalmic solution preparations to be dispensed in single use packaging. Our understanding is that endotoxin testing is not required for topical ophthalmic solutions packaged for single use.

We value the opportunity to improve our compounding practices and to respond to the observations with the processes we have in place.

Sincerely,

Kevin R. Dillon, PharmD
Chief Pharmacy Officer
Mayo Clinic Department of Pharmacy