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01/31/2024

To whom it may concern,
In response to the inspectional observations and form 483 issued on 11/9/2023, the following corrective actions have or will be done as outlined below.

*Observation 1:Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the equipment to produce aseptic conditions.*

All stained filters were replacement and the cleanroom recertified:
A replacement filter was installed in the Air Science LF Series vertical laminar flow cabinet serial #VLF-74051 on December 23, 2023.
Two replacement HEPA filters were installed on December 22, 2023.
The cleanroom suite and the laminar flow cabinet were recertified on December 23, 2023. All HEPA filters passed a leak test and all particle counts were well within limits.
In regards to surfaces that may be difficult to clean, all surfaces -including ceiling, walls and tables- are cleaned at least monthly. Non-viable and viable particles counts are all well below action or alert levels.

The wooden surfaces (door and baseboards) in the ISO-8 prep room were painted with a urethane semigloss on January 5, 2024, allowing them to be easily cleanable.

*Observation 2: Procedures designed to prevent microbiological contamination of drug purporting to be sterile did not include adequate validation of the aseptic process.*

Media fill challenge has been updated. This new process simulates filtering 10L into a depyrogenated beaker, then transferring using sterile tubing into approximately 330 30ml

vials. This will simulate our largest volume (10L) and our largest batch size (300 vials). This media fill was completed on December 8, 2023.

A new smoke flow studies were done in January 2024. These smoke studies demonstrated that the electric outlet in the back of the cabinet does not create turbulence. They also include all aseptic operations including filling and stoppering of the vials.

SOP Module 6-PM-98A, section 7 has been updated so the pass criteria for post fill fingertip sampling to be <1 CFU/plate.

Sterile wipes stored in plastic containers in the ISO -7 buffer room were sterility tested. A random wipe from an open package stored in the container was removed and transferred to the ISO-5 hood. The wipe was then transferred into sterile TSB, USP and incubated at 20-25C per SOP. No turbidity was observed thru day 14. These wipes will continue to be stored this way and used in the ISO-7 areas. Sterile wipes used for ISO-5 surfaces are now stored and opened in the ISO-5 hood.

*Observation 3: Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.*

The sliding windows in the doors separating the drug prep room (ISO -8), the ante room, and the ISO-7 buffer room are needed to maintain proper pressure gradients. If the windows are closed, the pressure in the small anteroom would increase, causing backflow into the ISO-7 buffer room. With the sliding windows open, pressure gradients as well as non-viable particle counts are all well within limits.

Pressure differentials are read and recorded before compounding begins and again during compounding. The digital display has an audible alarm that will sound when pressure in the anteroom or buffer room drops below and acceptable level.

*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.*

The threshold to the powder containment hood located in the ISO-8 prep room has been sealed with an epoxy paint.

Our weighing SOP has been updated to require the time and date on the scale print out. This SOP has also been updated to allow weighing up to 3% over the required amount and that no powders should be returned to the stock bottles.

The tile floor in the ISO-8 prep room is sealed with a cleanroom epoxy paint, allowing for it to be easily cleaned.

*Observation 5: Aseptic processing areas are deficient in that floors, walls and ceilings are not smooth and or hard surfaces that are easily cleanable.*

The flooring underneath the ISO-5 hood is coated with a cleanroom epoxy paint, making it smooth and easily cleanable.

*Observation 6: Your facility compounds drug products using bulk substances that cannot be used in compounding under section 503B of the FD&C act because they (a) are not used to compound drug products that appear on the drug shortage list in effect under section 506E of the Act and (b) do not appear on a list developed by the FDA of bulk drug substances for which there is a clinical need.*

Disodium edetate (EDTA) is no longer being compounded. The pharmacy manager will be checking the list of drugs on the "Bulk Drug Substances Nominated for Use in Compounding Under Section 503B" list for updated on a regular basis (at least monthly).

*Observation 7: Laboratory controls do not include the establishment of scientifically sound and appropriate specifications, standards, sampling plans and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling and drug products conform to appropriate standards of identity, strength, quality and purity.*

The ascorbic acid powder, USP/EP used to make the ascorbic acid for injection, 500mg/ml, is tested by the FDA registered manufacturer for oxalate (impurity E) as per EP standards. EP standards require the amount of oxalic acid in the ascorbic acid API to be less than or = to 0.2%. All ascorbic acid we use to compound the ascorbic acid for injection is USP/EP grade. We also tested several lots of finished products of ascorbic acid for injection 500mg/ml and found no oxalate present. We will test incoming lots of ascorbic acid, USP/EP for oxalate before the API is used in production.

The USP reference standard for ascorbic acid was purchased on 10/26/23 and is now being used as the reference standard. HPLC using the USP reference standard was run on 11/19/2023.

*Observation 8: The accuracy, sensitivity and reproducibility of test methods have not been established and documented.*

The iodometric titration is no longer being used to determine the assay/potency of ascorbic acid for injection for batch release. As of June 2023, we are using the HPLC method to determine assay/potency of ascorbic acid for injection before batch release.

*Observation 9: Testing and release of drug product 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.*

CoA's for all APIs are checked and verified to be within USP standards. All formulas are verified for calculation and determined weights to be used. Theoretical potencies are calculated before batch release.

*Observation 10: Your facility has not submitted a report to FDA identifying a product compounded during the previous six months as required by section 503B(b)(2)(A) of the FD&C Act.*

On 6/23/23, reporting period 2023-1, CMP NAD 5mg/ml, NDC 26436-5472-5, 2 units were submitted and NAD 50mg/ml, NDC 26436-5558-0 1 unit and NDC 26436-558-5 11 units were submitted. These were submitted thru CDER Direct with set ID 7d28eaf6-7b1e-94d2-e053-2a91aa0a18f4 and Root ID fe42e7a1-1938-1699-e053-6294a90ac207.

On 1/5/23, reporting period 2022-2, with root ID 7d28eaf6-7b1e-94d2-e053-2a91aa0a18f4 and set ID f18d6ef8-58cb-296b-e053-2995a90a0418 an SPL was submitted thru CDER Direct. This report included, but was not limited to the following drug products compounded: Ascorbic acid, Combo drops, Cyanocobalamin +MIC, Lidocaine 1% buffered, magnesium chloride, MIC, Glutamine, arginine, and Carnitine, Liposupreme, Myer's Cocktail I and II, progesterone capsules and sermorelin acetate injection. Sermorelin troches were submitted on 3/10/23, reporting period 2022-2, root ID 7d28eaf6-7b1e-94d2-e053-2a91aa0a18f4 and set ID f6902d0f-0f18-2302-e053-2995a90a88ae.

*Observation #11: Master production and control records lack complete manufacturing and control instructions, sampling and testing procedures, specifications, special notations and precautions to be followed.*

Laboratory notebooks have been purchased that are numbered. Those in use that are not numbered will be numbered. QC will review, sign and date each laboratory notebook page.

Multiple forms used for environmental monitoring have been updated. The new forms are more streamlined, simpler to fill out, and will reduce the chance of documentation error. Forms 69A and 69B are now specific for the ISO class being sampled. Forms 75A and 75B have been revised as well.

Form EMT- Production Environmental & Personnel Monitoring Tracking list been created. This form will list the compounded sterile batches done on a specific day and the EM sampling done on that date. This will allow us to link all batch lots to the appropriate environmental sampling forms.

A master list of test methods has been created. Batch records will be updated to reflect the approved test method used. Relevant SOPs will be updated so they reference the appropriate test number from the master list.

The iodometric titration test method for ascorbic acid 500mg/ml for injection is no longer being used as a criteria for batch release.

Thank you,

Ponswamy Rajalingam