US Compounding
PHARMACY
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April 11, 2019

VIA ELECTRONIC MAIL

LCDR John W. Diehl,
Director, Compliance Branch
ORA/OPQ – Division 2
Department of Health and Human Services
Food and Drug Administration
Dallas District Office
4040 North Central Expressway, Room 950
Dallas, TX 75204

RE: US COMPOUNDING, INC.
FOLLOW UP TO 2019 INSPECTIONAL OBSERVATIONS

LCDR Diehl:

US Compounding, Inc. ("*USC*") would like to take this opportunity to follow up on its March 1, 2019 Form 483 response. During the January-February 2019 inspection, USC informed FDA that it initiated a number of change control projects to ensure that USC meets FDA's updated 503B Outsourcing Facility expectations as set out in the Agency's recent December 2018 Guidance.[1] As such, USC is supplementing its initial response with the following updates to demonstrate that USC completed, or made substantial progress made towards completion, of its change control projects. Further, USC would like to demonstrate how it continues to assess and improve its quality systems on an ongoing basis. With that background, USC's updates are as follows:

Follow Up to Response to Observation 2B:

As a follow up to Observation 2B, USC committed to executing a feasibility study and method development study to create a specific, accurate and sensitive test method for recovering and quantifying potential testosterone residue with swabs. Since USC submitted its March 1, 2019 Form 483 response, USC focused on the framework for developing and verifying mass spectrometry detection and swab recoveries of testosterone from surfaces. Currently, the third-party contract lab that USC engaged is working on developing and qualifying the testosterone analytical mass spectrometry method, including the limit of quantitation and limit

[1] Current Good Manufacturing Practice – Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act, Revised Draft Guidance, December 2018.

of quantitation. The expected lower limit of quantitation for this assay is 10 ug/mL. As such, the scope of work for the method development and feasibility is underway, and USC anticipates more information will be available by the end of April 2019. USC will therefore provide this information once it becomes available.

Further, dynamic smoke studies were performed on March 19, 2019 for all powder containment hoods, which confirmed their airflow performance and containment. USC anticipates the final summary report will be available by the end of April 2019. USC will also provide this information once it becomes available.

Follow Up to Response to Observation 3:

As a follow up to Observation 3, USC ordered and received Everbuild® Silicone Eater and Everbuild® Everflex® 565 Clean Room Silicone. USC scheduled the first phase of deployment for the materials in April 2019. A more formal update will be provided once the deployment is complete.

Follow Up to Response to Observation 4A:

As a follow up to Observation 4A, on February 25, 2019, USC re-executed extreme dynamic media fill according to the approved batch record. This media fill simulation was executed in accordance with USC's expectations for extreme aseptic processing dynamic conditions, as well as common interventions for aseptic processing activities. Specifically, a total of 3681 1mL in a 3mL syringes were aseptically processed, and inspection of all 3681 units after 7 and 14 days of incubation showed no units with turbidity. This testing confirms qualification of USC's routine aseptic processing activities. As such, USC anticipates that it will provide the media fill batch record and supporting documentation with its next update to FDA.

Follow Up to Response to Observation 4B:

As a follow up to Observation 4B, USC re-executed airflow smoke studies from March 19-21, 2019, under extreme dynamic conditions according to USC's approved protocol. This protocol was executed in accordance with USC's expectations for extreme dynamic conditions as well as common interventions for aseptic processing activities. During the smoke study, USC operational and quality management were present. USC anticipates that the the summary report and video will be available by the end of April 2019. As such, USC will provide this information once it becomes available.

Follow Up to Response to Observation 5A:

As a follow up to Observation 5A, USC engaged a third-party subject matter expert in process qualification and validation to consult on the initial suspension process performance qualification protocol. Due to the complexity and importance of process validation, USC suspended all compounded suspension drug products until the individual process performance

qualification is successfully executed. USC will provide more information on the progress of the process validations as that information becomes available.

Follow Up to Response to Observation 5B:

As a follow up to Observation 5B, all homogenizers are currently going through the comprehensive installation, operational, performance qualification processes described in USC's March 1, 2019 Form 483 response to Observation 5B. Specifically, USC is using a preapproved protocol with defined acceptance criteria. USC will provide documentation regarding these protocols in its next update to FDA.

Further, the initial feasibility assessment referenced in USC's March 1, 2019 Form 483 response is complete. Specifically, the analytical methodology is finalized so that the execution of the formal feasibility and design of experiments, DOE, for particle size distribution can be initiated. This phase is planned to be completed in April 2019, and USC will provide more information regarding this assessment as it becomes available.

Follow Up to Response to Observation 8:

As a follow up to Observation 8, the four tier-transform infrared ("FTIR") spectroscopy instrument that used in performing identity analysis has been sourced, is onsite and undergoing USC's qualification process. USC anticipates that the FTIR implementation will be complete by the end of April 2019, and USC will provide more information regarding this implementation as it becomes available.

Follow Up to Response to Observation 9:

As a follow up to Observation 9, USC ceased 503A patient-specific human drug compounding effective April 1, 2019.

In closing, USC wants to reiterate and emphasize that it is committed to patient safety and to meeting Agency expectations for compliance and quality as it relates 503B Facilities. USC will continue to provide the updates it committed to in its responses to FDA's observations and to implementing those changes as quickly as possible. Thank you for your attention to this matter.

Respectfully,

11 Apr 19

Ron E Antes II
Director of QA/QC
US Compounding, Inc.