

From: Sista, Ramani V
Sent: Monday, September 22, 2014 11:11 AM
To: Heather Pratt (heather@macopharmausa.com)
Subject: Macopharma NDA 125552 - IR

Importance: High

Hi Heather,
Thanks for organizing the call today. From our end the attendees were:
Ellen Huang, CSO, DMPQ\OCBQ
Mari on Michaelis, Branch Chief, DMPQ\OCBQ
Ramani Sista, RPM, OCTGT

Please provide response to the following by COB, October 3, 2014:

1. Regarding IR Question 1, it was not clear from your empty chamber study if there were any cold spots. Please provide a summary of your data or the probe locations to clarify this information.
2. Regarding IR Questions 2 and 6, please explain why (b) (4) is placed (b) (4). Please clarify if the (b) (4). Please clarify if there are any standard reference methods or published papers using this method of placing (b) (4) for sterilization. Please provide a picture of where the (b) (4) is in comparison to the unit. Please explain why (b) (4) is the worst-case (versus the (b) (4) that is used for production).
3. You have indicated during the teleconference that you are performing minimum load validation studies. Please submit the summary reports for the minimum load. Please provide a timeframe of when that will be completed.
4. Regarding IR Question 7, please provide a timeframe of when you will have the data for the repeated runs for the (b) (4) sensors.
5. Regarding IR Question 12, since the units are (b) (4) the bags, how do you account for variability between operators?
6. Regarding IR Question 13, please clarify if any other CCIT tests are performed (stability testing, in-process testing, and/or final product testing), such as pressure tests to supportive of the integrity of the unit. If so, please provide a description of the test method and the number of units tested.
7. Please clarify if the bags are 510(k) cleared. If they are cleared, please provide the 510(k) number.
8. Regarding parametric release for sterilization, your Poland facility does not have a compliance history with the Agency. Per FDA's Compliance Policy Guides Section 490.200 (Parametric Release – Parenteral Drug Products Terminally Sterilized by Moist Heat), "A firm may rely on a parametric release strategy and need not perform end-product sterility testing when the firm meets and documents assurances for both of the following conditions: First, the firm's sterility assurance program must be in a state of control, for application products, the firm must have submitted all appropriate regulatory filings to FDA and be operating in conformance with its approved application." Additionally, per FDA's Guidance for Industry Submission of

Documentation in Applications for Parametric Release of Human and Veterinary Drug Products Terminally Sterilized by Moist Heat Processes (February 2010), the firm should have "prior manufacturing experience and knowledge were incorporated into the risk assessment." Since the Agency does not have an established history with this facility, we cannot approve you for parametric release for this NDA. Please ensure you perform sterility testing of your final units. Please clarify if you have submitted your sterility test method in the submission, and if so, please indicate what section it is in your submission. If not, please submit it.

Thanks,
Ramani

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