

From: Sista, Ramani V
Sent: Tuesday, August 19, 2014 1:41 PM
To: Heather Pratt (heather@macopharmausa.com)
Subject: BN125552 - IR

Importance: High

Hi Heather,
Please provide the following information by COB, September 03, 2014.
Regarding Sterilization

1. Please provide the results of your OQ (empty chamber temperature distribution study and heat distribution study) for your (b) (4) autoclaves.
 2. Please compare the subject units of the NDA to the PCD. Specifically, please provide a side-by-side comparison of each unit, including but not limited to, the dimensions, material of construction, and volume.
 3. Please clarify if the PQ was performed on the maximum load.
 4. Please clarify if all of your loads for production purposes will be at the maximum load. If not, provide a justification on why the minimum load was not validated.
 5. Please provide your rationale for the placement of the PCD with biological indicators and sensors.
 6. In the PQ, you placed (b) (4) . Please clarify if this practice is also performed during routine production on the subjected unit.
 7. During the heat penetration study, (b) (4) sensors did not register the correct data (F0-value of (b) (4)). You stated that retesting on those failed sensors would be performed. Please provide the results to those repeated run(s).
 8. Please clarify if product was in the PCD with biological indicators and sensors.
 9. You stated that some of the manufacturing steps can be sub-contracted to (b) (4) or MacoProductions (b) (4) . Please clarify if sterilization will and can be sub-contracted to (b) (4) MacoProductions (b) (4) . If so, please submit the sterilization validation for these sub-contractors.
- Regarding Container Closure Integrity
10. Please provide your rationale for selecting (b) (4) as your challenge organism for your container closure integrity testing (CCIT).
 11. Please clarify if the units tested for CCIT were sterilized.
 12. Please clarify which filling lines the units tested for CCIT were filled on. It appears that you have (b) (4) filling machines. To demonstrate that all filling machines can create an integral unit, units should be filled on each filling machine and tested for CCIT.
 13. Please provide the sensitivity of your CCIT method.

Thanks,
Ramani

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