

From: Sista, Ramani V
Sent: Tuesday, February 17, 2015 11:37 AM
To: Heather Pratt (heather@macopharmausa.com)
Subject: Macopharma NDA 125552 - IR

Importance: High

Hi Heather,
Please provide the information below by COB March 2:

1. Since you are claiming that the exterior surface of the unit is sterile, please address the following concerns regarding your (b) (4) that you produce in house:

a. Please clarify how you ensure the (b) (4) materials allows for steam penetration. To address this concern, we recommend that you provide the labeling from the (b) (4) manufacturer which indicates that material is intended to be used as a sterile barrier for steam sterilization. If the (b) (4) material is not indicated as a sterile barrier by the manufacturer, then additional testing information should be provided to support this intended use. This information can include:

i. Physical properties testing such as tensile strength, thickness variation, tear resistance, air permanence, burst strength, etc. before and after sterilization. This information should be compared to known sterile barrier (b) (4) materials to ensure adequacy.

ii. Alternatively biological indicator testing (b) (4)

b. Provides a sterile integral barrier over the duration of shelf. This additional testing should include:

- i. Description of sealing process and validated sealing parameters.
- ii. Whole package integrity testing such as dye penetration or bubble testing following shipping stress.
- iii. Accelerated aging to support shelf life claim.

Please let me know if you have questions.
Thanks,
Ramani

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