

Information Request for MACI (STN 125603/0)

Sterility Test

1. In section 3.2.P.5.1, please change the acceptance criterion from (b) (4) to (b) (4).
2. As a back-up for the alternate (b) (4) method, sterility is performed by the (b) (4) method on MACI samples for (b) (4) final product. For the (b) (4) qualification report (13-058-TR), please provide:
 - MACI lot numbers tested
 - (b) (4).
3. Based on review of sections 3.2.S.4. (Control of Drug Substance), 2.3.P. (Drug Product), and two validation reports ((b) (4)), the (b) (4) validation study is incomplete for the following reasons:
 - The validation study did not include the evaluation of (b) (4) as listed under (b) (4). Please include an evaluation of these microorganisms using the (b) (4) test method.
 - The limit of detection (LOD) acceptance criterion of (b) (4) for each challenge microorganism is unacceptable. The LOD should be assessed by demonstrating (b) (4). Thus, we request that the (b) (4) LOD test be repeated for all microorganisms used in the (b) (4) validations using the (b) (4) to demonstrate equivalency of the (b) (4) alternate method in accordance with LOD section (b) (4).
 - Please provide lot numbers for each sample used in the validation.
 - Please note that we are concerned that the current (b) (4) system (b) (4) may not detect all microorganisms at LOD values comparable to the compendial sterility method within the proposed (b) (4) days detection time.
4. For validation of the sample configuration (validation report 13-027-TR), please provide:
 - Lot numbers for each sample type ((b) (4) final product test samples); and
 - Information on the media used and their incubation condition for each microorganism tested.

Endotoxin Testing

With regard to the (b) (4) test qualification report (GTR-541-04-12) please include:

- (b) (4)
- Positive product control percent recoveries
- Lot numbers with their respective endotoxin test results
- The final testing dilution selected

In addition, please provide the following:

- The sensitivity range of (b) (4) used.
- Clarification of how the (b) (4) was determined.
- Appendix 1 (endotoxin qualification protocol [SOP VA2-017] and Appendix 2 (Test Records) listed in the table of contents of the method validation report.
- Justification for the bacterial endotoxin release specification.