

Information Request for MACI (STN 125603/0)

Sterility using (b) (4) Validation for Drug Substance and Drug Product

The FDA acknowledges the proposed sterility method is the (b) (4), in which the FDA provided recommendations for the validation protocol and approved the validation report as (b) (4). However since (b) (4), the FDA established the Division of Biological Standards and Quality Control (DBSQC) for continued regulatory review improvements in method quality assurance to ensure test methods are appropriately validated and/or suitable for their intended purpose. Thus method validations approved by the FDA in the past, does not necessarily mean they are acceptable by FDA's current standards. Since MACI is a new biological product license application and the proposed alternate sterility test method is the only sterility test that will be performed for product release, the FDA's current standard for the validation of an alternate sterility test method is required.

Based on DBSQC's experience with (b) (4) as an alternate sterility test method, the FDA requests the following:

- Perform a Limit of Detection (LOD) study using (b) (4) in accordance with (b) (4);
- Perform the LOD study using (b) (4) lots of MACI drug substance, to include (b) (4) and at least (b) (4) known environmental microorganisms from your Cambridge, MA manufacturing facility;
- Report results from this study on or before 01 October, 2016 to allow the FDA review of acceptability.

Please contact the FDA immediately if you experience difficulty achieving a successful validation of the method.

During the midcycle teleconference between Vericel and the FDA held on 29 June, 2016 at 12:00 PM EST, Vericel agreed to send the FDA a list of their current known environmental microorganisms from their Cambridge facility to determine which should be included in the validation requirements listed above.