

## Sterility

Sterility testing of products is common throughout the pharmaceutical, biotechnology and medical device industries. The USP procedures are followed as the standards for the assays required.

Even products produced in the cleanest of environments are vulnerable to microbial contamination from numerous sources including the actual process, the systems and equipment used, the environment the process is occurring in and in the majority of cases the operators performing the process.

The validation of the sterilization process and/or aseptic processing procedures together with a rigorous environmental monitoring program combined with strictly adhered to SOPs can generally provide a high degree of confidence that any contamination is identified and controlled.

We often refer to sterility as an absolute condition that is taken to mean the absence of any active microorganisms that can reproduce under fixed conditions. Practically we provide documented evidence of this by testing by methods validated to provide at least a six log reduction of the load ( $10^{-6}$ ). Testing must be designed to allow a statistically relevant sampling of the product or environment. Cambridge Biomedical understands that not all products and environments can be addressed by a single sampling protocol. We work with our clients to assure that the all of the parameters in the process are evaluated and if needed the protocol is adjusted to reflect the individual process.

Cambridge Biomedical offers two methods for testing of sterility. It is recommended that regardless of the method selected, bacteriostatic or fungistatic testing is performed to ensure there is no antimicrobial materials that may affect the growth of organisms.

### Direct Inoculation

The appropriate medium is selected for the product being tested. Inoculation of the test article is made directly into the appropriate medium. The inoculum is then incubated and observed at multiple time intervals for growth. This test is usually selected when it is important to minimize the volume of product used in testing or when non liquid test articles such as creams. Ointments or medical devices must be tested.

One limitation to this method is that unlike membrane filtration where washing of the collected organisms can eliminate any antimicrobial materials such as antibiotics, the presence of these materials may effect the growth of the organisms.

### Membrane Filtration

A filter is used in which the test article is passed through allowing the organisms of interest to be retained on the filter while the test article passes through. The advantage of this test is that large volumes of the test article can be analyzed increasing the relevance of the sampling. This method also allows any anti-microbial materials that can inhibit growth, such as antibiotics, to be washed away by simply rinsing the filter with sterile medium. The

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disadvantage of the method is the requirement of large volumes of final product and the limitation of only testing liquids.

### Test Article

1. All test articles should be collected aseptically, and shipped, in a sterile container.
2. All test articles should be shipped at a temperature appropriate for that particular article.

### Control Article

1. All control articles should be collected aseptically, and shipped, in a sterile container.
2. All control articles should be shipped at a temperature appropriate for that particular article.

### Test Article Preparation and Administration

1. The test article is prepared by the Sponsor. It is recommended that the number of articles to be tested be in relation to the number of articles in the batch. The minimum volume (mL, for liquid articles) or minimum quantity (g, for solid articles) taken from each container, for each medium, is related to the container content. The final volume to be tested will be decided by the Sponsor. It is advised before instituting the use of the sterility test procedure for a test article, ensure that any bacteriostatic and fungistatic activity inherent in the article does not adversely affect the reliability of the test and that the test procedure is suitable for use with the test article.
2. Special treatment of the test article will only be performed at the written request of the Sponsor.

### Control Article Preparation and Administration

1. The control article is prepared by the Sponsor. It is recommended that the number of articles to be tested be in relation to the number of articles in the batch. The minimum volume (mL, for liquid articles) or minimum quantity (g, for solid articles) taken from each container, for each medium, is related to the container content. The final volume to be tested will be decided by the Sponsor. It is advised before instituting the use of the sterility test procedure for a control article, ensure that any bacteriostatic and fungistatic activity inherent in the article does not adversely affect the reliability of the test and that the test procedure is suitable for use with the control article.
2. Special treatment of the control article will only be performed at the written request of the Sponsor.

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