



Sterility Testing

Sterility testing is one of the most crucial steps in pharmaceutical product release. False positives, false negatives, equipment failure and human error cost time, money and ultimately the end product. The two types of product sterility testing are pre-release testing and quality assurance testing. In general, microbiological quality control includes pre-release testing to prevent non-sterile admixtures from being dispensed. Ongoing quality assurance programs include testing random samples of the product, testing the environment where the products are processed to monitor sterile conditions, and testing personnel for proper aseptic technique.

Validation is essential to both quality control and quality assurance programs. Validation verifies that the other variables – the procedures, materials and personnel – inherently do not introduce contamination into the process and that the program is adequate to detect contamination during production of sterile products.

Other Bacteriology Testing Services Offered

- Growth promotion
- Biological indicators
- Endotoxin
- Total viable count
- Antibiotic assay
- Mycobacterium

Your
 partner for
 critical testing in
 microbiology

What Products Should be Tested?

All sterile (end) products required to comply with the test for sterility, including cytotoxic products.

- Cell lines
- Bulk product materials
- Final products
- Harvest

When Should Testing be Performed?

Pre-Release Testing

Pre-release sterility tests are performed promptly on completed batch-prepared products as a condition for releasing certain products. This includes batches that are compounded using non-sterile

drug substances or products, sterilized with filtration apparatus built or sterilized in-house or prepared using open exposure. Batches cannot be released until negative test results confirm sterility. A positive result requires an immediate investigation to determine and correct the cause of the failure.

Quality Assurance Testing

Low risk drugs need not be pre-release tested, but must be sterility tested as a part of an ongoing quality assurance program. Samples are tested according to a planned random selection scheme. This testing enables the evaluation of aseptic technique, the equipment, the environment and the personnel.

Study Design

Upon the request of a customer, the routine studies are performed according to the European Pharmacopeia or the United States Pharmacopeia or CPMP/ICH/294/95. The tests are performed in an isolator, according to Good Manufacturing Practice (GMP) standards as described in the EU GMP guidelines, Annex 1 or GLP.

Two kinds of test could be performed.

1. Membrane filtration method using the Millipore Steritest® system for all filterable products.

The method does not depend on product type, container volume or concentration of microorganisms to provide a statistically valid sample. With membrane filtration, the entire volume can be filtered, which captures all the microorganisms present, removes product components that could cause the growth medium to appear turbid and can decrease the inhibition of microorganism growth due to anti-microbial agents in the product since they are filtered away during this method.

2. Direct inoculation method applicable to non-filterable products and cell banks.

With direct inoculation, a small sample can be taken and then added to a growth medium and incubated.

Validation of the method for the product to be tested can be performed prior to or in parallel with the test.

Assay Duration: 14–18 days

Sample Requirement: Dependent upon production size and volume

Regulatory Compliance

- EP 2.6.1
- USP <71>
- CPMP/ICH/294/95 (ICH Topic Q5D Quality of Biotechnological Products: Derivation and Characterization of Cell Substrates Used for Production of Biotechnological/Biological Products section 2.3.2).

Final Report

MicroSafe Services from Millipore can provide each client with the following final reports:

- GLP report that includes all raw data, protocol methods and final result.
- GMP report that includes a certificate of results.

Identification

All isolates recovered from microbiological tests of critical process and samples can be identified by MicroSafe Services from Millipore. It is important to demonstrate that critical processes are free from objectionable microorganisms.

The culture delivered for identification is checked for purity. A gram stain is performed from a pure and fresh cul-

ture. A biochemical profile is made of the organism, using the API® system (bioMérieux®) and, where applicable, additional confirmatory tests are performed.

In 2007, MicroSafe Services from Millipore will be introducing Nucleic Acid Techniques (NAT) for Identification by Sequence Analysis.

Custom Assays

We understand that no production plant is identical and that every process is unique. Using a combination of practical experience and a scientific approach, we will customize sterility testing methods to meet your specific requirements including scientifically sound data that will be accepted by regulatory authorities around the globe.

Your Partner in Microbiology

MicroSafe Services from Millipore delivers a complete range of critical testing and consultancy services for the development and production of biopharmaceuticals. Leaders in the field of microbiology including *in vitro* virology testing, our staff of accomplished scientists, engineers and microbiologists will help you meet your specific critical testing requirements throughout every phase of drug production. All testing is conducted under GMP and/or GLP certifications as well as our own internal quality system.

SAFETY RELIABILITY QUALITY CUSTOMER RELATIONSHIP FEEDBACK & SUPPORT

MILLIPORE

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