Basics of Sterility Testing
Andrew Taylor, Microbiology Supervisor

According to research data from Pew Charitable Trusts, over 50 compounding errors with 1,227 adverse events and 99 deaths have been reported from 2001-2017. Contamination of sterile products was the most common compounding error.

Testing the finished drug product is important to ensure drugs delivered to patients are free of contamination.

USP <797> Pharmaceutical Compounding – Sterile Preparations states that certain compounded sterile preparations (CSPs) must undergo sterility testing prior to being dispensed. This requirement is based on multiple factors, including batch size, risk level, and storage conditions.

A validated sterility test can detect microbial contamination in a drug product.

When must pharmacies test?

USP <797> requires sterility testing for:

- Drug products exceeding USP storage periods
- High Risk products prepared in groups greater than 25
- Multiple dose vials prepared for administration to multiple patients; and
- Preparations exposed to longer than 12 hours at 2°C to 8°C before sterilization or longer than 6 hours at greater than 8°C before sterilization

The Food and Drug Administration (FDA) requires 503B Outsourcing facilities to perform sterility testing for all drugs reported to be sterile and/or non-pyrogenic. Refer to FDA Current Good Manufacturing Practice — Interim Guidance for Human Drug Compounding Outsourcing Facilities for deviations. Even if it is not specifically mentioned in the regulatory documents, sterility testing should be performed any time a process changes or new personnel begin compounding. This should be done in addition to testing on a regular recurring basis as part of an overall quality system.

How is sterility testing performed?

Sterility Test Methods
Two distinct methods are used for sterility testing. First is membrane filtration, which is defined in USP <71> as the preferred method, provided the drug product being tested is filterable. This method involves passing a quantity of drug product through two canisters, each housing a filter designed to retain microorganisms. This is followed by a rinse to ensure no drug product remains on the filter, as that can potentially inhibit the growth of microorganisms. The final step is to fill each canister with one of the two media types described below. The second sterility testing method is direct inoculation. This consists of introducing the drug product directly into each of the two growth media using a defined quantity of drug product sample to growth media.-The dilution used must be sufficient to overcome any antimicrobial properties present in the drug product being tested. Regardless of the method chosen, method suitability must be performed prior or concurrent to any USP <71> sterility test. Method

suitability is a validation of the test process, which demonstrates that the method chosen works correctly for the specific drug product formulation.

Sterility Growth Media

A USP <71> sterility test utilizes two growth media. The two media, and the temperatures in which they are incubated, are designed to grow different types of bacteria, yeast, and mold. First, Tryptic Soy Broth (TSB), incubated during the test at 20°-25°C, is designed for the culture of both fungi and aerobic bacteria (requires oxygen). Second, Fluid Thioglycollate Medium (FTG), incubated during the test at 30°-35°C, is primarily intended for the culture of anaerobic bacteria (requires absence of oxygen). FTG will also support aerobic bacterial growth.

ARL Bio Pharma's Sterility Testing Process

ARL Bio Pharma first performs growth promotion testing to demonstrate that each lot of ARL's media can grow the six microorganisms stated in USP <71> Sterility Tests. Second, our laboratory performs method suitability for each specific product formulation prior to conducting a USP <71> sterility test. Third, ARL uses either a membrane filtration method or a direct inoculation method for sterility testing. The test containers are incubated at the appropriate temperatures for at least 14 days. At the end of the incubation period, each drug product is examined for signs of microbial growth, generally turbidity or cloudiness of the media.

At the conclusion of the test, if there is no evidence of growth, the drug product complies with the USP <71> test for sterility. A "Sterile" result indicates that no contaminating microorganism is found in the sample examined under the conditions of the test.

If the drug product does not pass sterility, the drug product is considered "Not Sterile" and an OOS investigation will be initiated.

Please contact us (800) 393-1595 or info@arlok.com to request a quote.

Reference Documents:

United States Pharmacopeia <797>
FDA Current Good Manufacturing Practice — Interim Guidance for Human Drug Compounding Outsourcing Facilities