ExtenDATE™ Instructions for Use

View the ExtenDATE™ Sterility Testing System

USP <71> STERILITY TESTING TO EXTEND DATING OF BATCH-PREPARED COMPOUNDED STERILE PREPARATIONS

Definitions in accordance with USP <71> and <797>:

Batch:	Twenty or more items compounded in one, continous operation using the same lots of all components by the same compounder or compounding team.
Medium:	Microbiological growth-promotion solution used to test for the presence of viable microorganisms. USP <71> requires that all items be tested in two different media; one a broad spectrum medium for obligate and facultative aerobic organisms [usually Trypticase-Soy Broth (TSB) is used] and the other for obligate anaerobic organisms [the Valiteq System incorporates Alternative Fluid Thioglycolate (FTG)].
Aerobic:	Using an oxygen-dependent metabolic pathway.
Anaerobic:	Using an oxygen-free metabolic pathway.
Facultative:	An organism that can metabolize by both aerobic and anaerobic pathways, depending on environmental conditions.
Obligate:	An organism that can only metabolize by one or the other pathway.
Unit:	One final container from a batch.
Sample:	The portion of one final container tested per medium.

Complete Test:

(Consists of one sample in TSB and one sample in FTG to comply with the USP <71> requirements.)

In order to comply with USP <71> for batches of 100 CSPs or less, at least four units must be tested in each of the two media, for a total of 4 complete tests, or 8 individual tests.

Protocol for sterility testing based upon volume:

(The following chart* shows how many units must be tested based upon batch size.)

Number of items in the Batch:	Minimum number of items recommended to be tested:
Injectable preparations	
No more than 100 containers/articles	10% or four items, whichever is greater
More than 100 but less than 500 containers	10 containers

More than 500 containers	2% or 20 containers, whichever is less
Large-volume parenterals (LVPs)	2% or 10 containers, whichever is less
Ophthalmic and other non-injectable preparations	
No more than 200 containers	5% or two containers, whichever is greater
More than 200 containers	10 containers

(The following chart* shows the required sample size for each unit tested.)

Quantity Per Container:	Minimum Quantity to Be Used: (unless otherwise justified, authorized, and recorded.)
Liquids (other than antibiotics)	
Less than 1 mL	The whole contents of each container
1 to 40 mL	Half the contents of each container, but not less than 1 mL
Greater than 40 mL, but not greater than 100 mL	20 mL
Greater than 100 mL	10% of the contents of the container, but not less than 20 mL (note: 20 mL for 40 to 200 mL container)

*Chart derived from USP<71>.

Sterility Testing Procedure for 40 - 200 mL Containers:

1. For each Sterility Test to be performed, select 1 vial of ThioMS™ and 1 vial of SteriMS™. Fill in the Test ID on each label and enter in the Sterility Test Log.\
2. FOLLOW THIS PROCEDURE CAREFULLY TO ASSURE PROPER PRESSURE-EQUALIZED, ANAEROBIC CONDITIONS WITHIN THE ThioMS™ TEST VIAL. FAILURE TO FOLLOW THESE INSTRUCTIONS MAY ALLOW A VERY SMALL QUANTITY OF AIR TO ENTER THE ThioMS™ TEST VIAL, THEREBY DEFEATING THE COMPLETELY ANAEROBIC ENVIRONMENT NECESSARY TO ASSURE THE GROWTH OF THESE ORGANISMS, THUS PRODUCING A FALSE-NEGATIVE RESULT.

ThioMS™ PROCEDURE: In a stabilized, normal Room-Temperature testing environment (20-25 Degrees, C.; not a cold room), prepare and disinfect one ThioMS™ sample vial on a certified Class 5 critical work surface. Allow the alcohol to dry completely. Aseptically withdraw a 21mL test sample from the selected test CSP and eliminate ALL air within in the syringe, hub, and needle.

IMPORTANT: Accomplish this required total air-elimination by holding the syringe/needle unit vertically, needle-up. Carefully and aseptically tap the syringe lightly to dislodge all air bubbles from the interior to gather centrally at the very top needle-attachment point. Slowly and carefully depress the plunger to expunge all the air bubbles up through the needle, thereby completely filling the hub and needle with sample fluid as you slowly bring the remaining syringe volume to 20mL. Place a new, properly disinfected, empty sterile vial on the needle to capture all superfluous fluid, as necessary. Be certain the needle is, and remains, 100% filled with sample fluid.

Carefully invert and, using proper anti-coring technique, normally insert the needle into the upright ThioMS™ vial septum center. Pull back in increments on the plunger to draw the inert gas within the vial into the syringe. Release the plunger and allow the sample to flow into the vial. Repeat this cycle as necessary until the whole sample has been transferred. Set the plunger position at 19mL to produce very slight positive pressure within the test vial. This will assure that, as the needle is removed from the septum, no air is drawn into the vial in order to maintain its essential anaerobic environment. Tamper-seal the sample vial and incubate as directed.

3. Properly disinfect 1 vial of SteriMS™ and allow the alcohol to dry completely. Change to a new needle on the syringe. Withdraw another 20 mL sample from the same test CSP. (Because SteriMS™ is an aerobic culture, no air-elimination step is necessary; rather, air is required for proper incubation.) With the test vial upright on the aseptic work surface, and using appropriate anti-coring technique, insert the needle down, through the septum center, allowing its tip to remain above the fluid level. Pull back on the plunger in steps to exchange air from the test vial for the fluid in the syringe, thereby eliminating over-pressurization of the vial. Following complete transfer, set the plunger position at 19mL to assure very slight positive air pressurization of the test vial. Remove the needle from the test vial. Tamper-seal the sample vial and incubate as directed.

Incubation Instructions:

Enter the test procedure in the Sterility Monitoring Log and place the SteriMS in a stable 'room-temperature environment'(20 Degrees C. to 25 Degrees C.). No incubator is needed for normal room-temperature incubation, however, an adequately-sized, dedicated enclosed space is recommended. Placement of a small, portable, NIST-traceable temperature recording device (i.e., a "Tempscribe" or "Amprobe TR200 or TR300") into the incubation space is recommended to assure and verify that the specified incubation temperature has been achieved within this incubation space for the entire incubation period. The ThioMS culture should be incubated at 30 Degrees C. to 35 Degrees C. in a controlled incubator (See our IN-1 Economy Incubator). All temperature verifications should be entered on the Sterility Report.

INTERPRETATION OF RESULTS:

Periodically examine the sample(s) in accordance with the instructions on the enclosed sample log and make the appropriate result annotation on the Sterility Testing Log (i.e., "Pass" or "Fail," indicated by a prominent green "P" or red, circled "F," ball-point pen entry in the appropriate space.)

Complete clarity of the test solution indicates a negative test result *(PASS).* Turbidity (cloudiness) of the test medium, or any non-resoluble sedimentation present at any time during the incubation period constitutes a positive test result *(CONDITIONAL FAILURE)*, indicating a probable failure in the aseptic technique of the candidate. If any turbidity or non-resoluble sedimentation is detected, the test subject

should be immediately transferred to the microbiology laboratory, and a qualified microbiologist consulted to subculture the test solution.

FAILURE CONFIRMATION. If a positive subculture confirms microbiological contamination *(CONFIRMED FAILURE)*, the microbiologist should identify the organism(s), and render an opinion as to its/their likely or possible source(s), or route of introduction. This will assist the Sterile Products Preceptor in determining the likely source of contamination and the appropriate retraining, or other corrective action(s). Following completion of incubation, the negative test subject should be given to the microbiology laboratory for disposal, or disposed of in the normal manner of lawful drug product disposal.

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