



Application Note

Mycoplasma Retention Testing for 0.1 μm Sterilizing-Grade Filters

SERVICE PROCESS DESCRIPTION

Retention testing is required to validate retention of sterilizing-grade membrane filters with specific pharmaceutical preparations. Millipore's Validation Sciences Laboratories conduct testing on a lab-scale using scaled-down processing conditions such as batch volume and flow rate. After preliminary studies with the candidate process fluid, a test protocol is submitted to the client. Millipore and the client sign the project specific test protocol prior to the start of testing. A standard report summarizing testing data is submitted to the client after completion of testing, and a copy of the raw data is provided with the final report.

TEST PROCEDURE

In addition to generating product and project specific *Brevundimonas diminuta* retention data, *Acholeplasma laidlawii* is commonly used to provide supplemental mycoplasma clearance data for 0.1 μm sterilizing-grade filters where mycoplasma is a bioburden organism. Although there is no current industry standard for testing or rating filters for mycoplasma clearance, we know that an ideal bacterial challenge suspension contains small, mono-dispersed cells which present a rigorous challenge to the test filter. We also know that cultivation medium, incubation conditions, and challenge suspension preparation can have a significant effect on *A. laidlawii* cell size and degree of aggregation. In the absence of standard, industry-wide methods, Millipore developed growth media and a cultivation method which reproducibly results in high *A. laidlawii* cell concentrations with a consistently small cell size. Millipore's validated *A. laidlawii* challenge test was modeled after the ASTM® F838-05 Standard Test for Determining Bacterial Retention of Membrane Filters Utilized

for Liquid Filtration method and is used for characterization of membrane filters during development and for manufacturing lot release.

Testing with worst-case, scale-down client processing conditions is used to determine the ability of a 0.1 μm sterilizing-grade filter to retain a minimum challenge of 10^7 cells of *A. laidlawii* per cm^2 of filter area. One lot of finished drug product or process fluid is evaluated using three lots of Millipore sterilizing-grade, 47-mm membrane discs. Test membranes will have pre-use, water-wet integrity test values at or near the stated minimum specification. Size controls are run with each test to prove that the test organism is the appropriate size.

WHEN TO PERFORM BACTERIAL RETENTION TESTING

- Filtration is the sole method of sterilization of a pharmaceutical drug or intermediate, and there is no subsequent terminal sterilization
- There is a sterilizing claim on a filter when sterility would not otherwise be required
- There has been a major change to a previously validated filtration process
- There is a claim of bioburden reduction for a filter which would otherwise not require validation

WHAT YOU NEED TO KNOW TO BEGIN...

- How much process fluid is available for testing and when?
- Is there an MSDS for the process fluid?
- Is this a controlled drug? If so, what classification and code?
- All process fluid incompatibilities
- Can small batches of unpreserved process fluid be made?
- Information on any pre-use filter flush
- Exact filter catalog number, number of filters, in parallel or in series
- Maximum batch volume
- Flow control parameter: flow rate or pressure. If pressure, how is that measured, upstream or differential across the filter?
- Filter/fluid contact time
- Filtration time
- Filtration dynamic, intermittent or continuous
- Bioburden, identification and concentration or total amount

This information will be put into the questionnaire by the client to begin the request process.

Regulatory Compliance

Bacterial retention testing for pharmaceutical preparations is a critical step in filter validation required by all regulatory bodies worldwide. The U.S. Food and Drug Administration's Guidance on Sterile Drug Products Produced by Aseptic Processing recommends that microbial retention testing be conducted using the candidate pharmaceutical preparation under simulated pharmaceutical processing conditions to validate sterilizing-grade membrane filter performance. PDA's Technical Report 26 further outlines parameters to be considered and modeled during the testing process. Further, it is important to test with relevant bioburden isolates if demonstrated to be smaller than the standard retention test organism, *B. diminuta*. Mycoplasma species are smaller than *B. diminuta*. Millipore's testing is performed in compliance with these guidelines.

ORDERING INFORMATION

Description	Catalogue No.
Standard Mycoplasma Retention Testing	VSERVMYCO

Related Tests

- Bacterial Retention Testing for Validation of Sterilizing-Grade Membrane or Quantification of Bioburden Reduction
- Extractables Analysis
- Drug Product-Based Integrity Testing

HOW TO REQUEST MICROBIAL RETENTION TESTING

To request microbial retention testing or to get information on other validation services offered by Millipore, call your Millipore Applications Specialist or the Millipore office nearest you (Millipore Support) or for instructions on locating and using our secure on-line request process.

In the U.S. and Canada, call toll-free
1-800-MILLIPORE (1-800-645-5476)

Outside of North America contact your local office. To find the office nearest you: www.millipore.com/offices



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