



## Application Note

# Bacterial Retention Testing for Validation of Sterilizing-Grade Membrane or Quantification of Bioburden Reduction

Bacterial retention testing is required to validate retention of Millipore sterilizing-grade membrane filters with specific process fluids at the chosen filtration conditions. Millipore's Validation Sciences Laboratories conduct testing at lab scale using scaled-down processing conditions. First, a standard test protocol is submitted to the client. Then, project specific parameters are determined by scaling down by filter area. Millipore will perform preliminary studies to determine the best test method for your process fluid and process conditions. These will require process fluid samples and may include viability, flush, flow or recovery studies. 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 at the completion of testing.

Millipore's Specialists are committed to performing testing at validation labs in the U.S., Europe, India and Japan. Millipore welcomes and encourages cGMP audits at our worldwide laboratory facilities. Let the experts with years of filtration and process optimization experience save you time and resources.

- Determine the correct testing for your process
- Recommend process parameters to be mimicked or scaled down
- Provide test protocols, reports and customized test systems when necessary
- Maintain raw data files
- Ensure confidentiality

## REGULATORY COMPLIANCE

Bacterial retention testing for process fluids is a critical step in filter validation required by all regulatory bodies worldwide. The United States Food and Drug Administration Guidance on Sterile Drug Products Produced by Aseptic Processing recommends that microbial retention testing be conducted using the candidate pharmaceutical preparation under simulated processing conditions; this validates sterilizing-grade filter performance. PDA's Technical Report 26 further outlines parameters to be considered and modeled during the testing process. Millipore's testing is performed in compliance with these guidelines.

## TEST PROCEDURE

Testing is conducted using worst-case client processing conditions to determine the ability of a sterilizing-grade filter to retain a minimum challenge of  $10^7$  cells of *Brevundimonas diminuta* (*B. diminuta*) per  $\text{cm}^2$  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. All test membranes will have pre-use, water-wet integrity test values at or near the stated or manufacturing minimum specification. Size controls are run with each test to prove that the test organism is the appropriate size. Although *B. diminuta* is the industry standard, a thorough evaluation of bulk or pre-filtration bioburden should be conducted by the client prior to requesting this test.

## WHEN TO PERFORM BACTERIAL RETENTION TESTING

- Filtration is the sole method of sterilization of a pharmaceutical drug or intermediate, there is no subsequent terminal sterilization, and sterilization is required.
- There is a sterilizing claim on a filter when sterility would not otherwise be required.
- There has been a major change to a validated process such as an increase in flow rate, pressure, batch volume or change in filter.
- There is a claim or requirement for bioburden reduction for a filter which would otherwise not require validation.

## WHAT YOU NEED TO KNOW TO BEGIN

- How much candidate test solution is available for testing, and when?
- Is there an MSDS for the candidate test solution?
- Is this a controlled drug? If so, what classification and code?
- Product incompatibilities.
- May small batches of unpreserved candidate test solution be prepared?
- Pre-use flush information.
- Exact filter catalogue number, number of filters, in parallel or in series.
- Batch size.
- Flow control parameter, flow rate or pressure. If pressure, how is that measured, upstream or differential across the filter?
- Filter/fluid contact time.
- Fluid filtration time.
- Filtration dynamic, intermittent or continuous.
- Bioburden, identification and concentration.



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## ORDERING INFORMATION

The scope of your project will be determined by process parameters such as time, temperature, pressure, flow rate, test organism, number of uses etc. A catalog number will then be assigned accordingly.

To request microbial retention testing or to get information on other validation services, call your Millipore Applications Specialist or the Millipore office nearest you.

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

In Europe call: **+33 (0) 390 469898**

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