Vmax™ Constant Pressure Test for Sizing Aseptic Filters

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This document describes how to perform a small-scale normal flow filtration study with Vmax™ filter sizing method to assess the performance of any feed solution on a membrane filter. We describe how to use the results of the small-scale study to predict the membrane filter area requirements for larger, production scale processes.

The Vmax™ filter sizing method assumes that size exclusion is the primary mechanism of particle retention and that decreases in flow during filtration are a consequence of gradual membrane pore blocking.

The Vmax™ filter sizing method is appropriate for sizing filters run under constant pressure using OptiScale® 25 filters.

A simplified tool can be used to size filters for non-plugging buffer streams*.

*Application Note - Simplified, efficient sizing of sterilizing-grade normal flow filters for buffer solutions.

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Technical Assistance

For more information or if you have any questions, please contact us:
MerckMillipore.com/asepticexperts

The filter proposals suggested in this protocol are based on data from a first evaluation trial and should be taken for indication only. In order to enable a stable and robust filter scaling, the feasibility data have to be confirmed by intermediate and larger scale filtration trials using representative feedstock and controlled process parameters such as temperature.

Material

1.1 Feed stream

Fresh and representative feed stream should be used for the small-scale study (concentration, density, temperature). One test with OptiScale® 25 devices requires approximately 150 – 250 mL.

The system should be cleaned using your standard decontamination procedure before Vmax™ testing. Note: some plastic tanks are not compatible with alcohols and an overnight static soak with 0.1 M NaOH solution can be considered as an alternative for sanitization.

1.2 Filtration devices

Filtration devices in OptiScale® 25 filter format (3.5cm²):

Membrane/Media	Pore size (µm)	Material
Durapore®	0.1	PVDF
	0.22	
Durapore® Multilayer	0.45/0.22	PVDF/PVDF
Durapore® Multimedia	0.2/0.22	MCE/ PVDF
	0.5/0.22	
	1.2/0.22	
	0.2/0.5/0.22	Three layers: MCE/MCE/PVDF
	0.5/0.2/0.22	
	1.2/0.2/0.22	
Durapore®	0.45	PVDF
	0.5/0.45	Bi-layer: MCE/ PVDF
Millipore Express® SHR	0.1	PES
Millipore Express® SHR-P	0.5/0.1	Bi-layer: PES/PES
Millipore Express® PHF	0.2	PES
Millipore Express® SHF	0.2	
Millipore Express® SHC	0.5/0.2	Bi-layer: PES/PES
Milligard® PES	1.2/0.8	Bi-layer: PES/PES
	1.2/0.45	
	1.2/0.2	
Lifegard®	1.0	BG
	2.0	
Milligard®	0.2	MCE
	0.5	
	1.2	
	0.5/0.2	Bi-layer: MCE/MCE
	1.2/0.5	
Polysep II®	1.0/0.2/0.1	Three layers: BG/ MCE/MCE
	1.0/0.2	
	1.0/0.5	
	1.0/1.2	
	2.0/1.2	

Where:
PVDF is PolyVinylidene Fluoride
MCE is Mixed Cellulose Esters
PES is PolyEther Sulfone
BG is Borosilicate Glass Microfiber

More information:

In order to select the most suitable device for your application, use the Filter Selection Guide or contact us.

1.3 Equipment

The following equipment will be required for the trials:

- A Vmax™ kit (Ref VIRUSVMAX). To double tank capacity or to perform two tests in parallel, two kits can be used.
- Three Luer lock valves (2-way)
- A stopwatch
- An equipment stand (Lab stand or retort stand)
- A balance (0.1 g accuracy)
- Beakers and bottles to collect filtrate and vent output during trials
- Personal protective equipment (PPE): safety glasses, gloves and lab coat.
- Printed copy of data collection sheet (page 8)

1.4 Bench space utilities

The following utilities will be required for the trials:

- Around 2 m linear bench space
- A source of compressed air (or nitrogen) with at least 1.5 bar / 22 psi outlet pressure
- Drain
- Electricity supply

Information and order:
MerckMillipore.com/vmaxtest

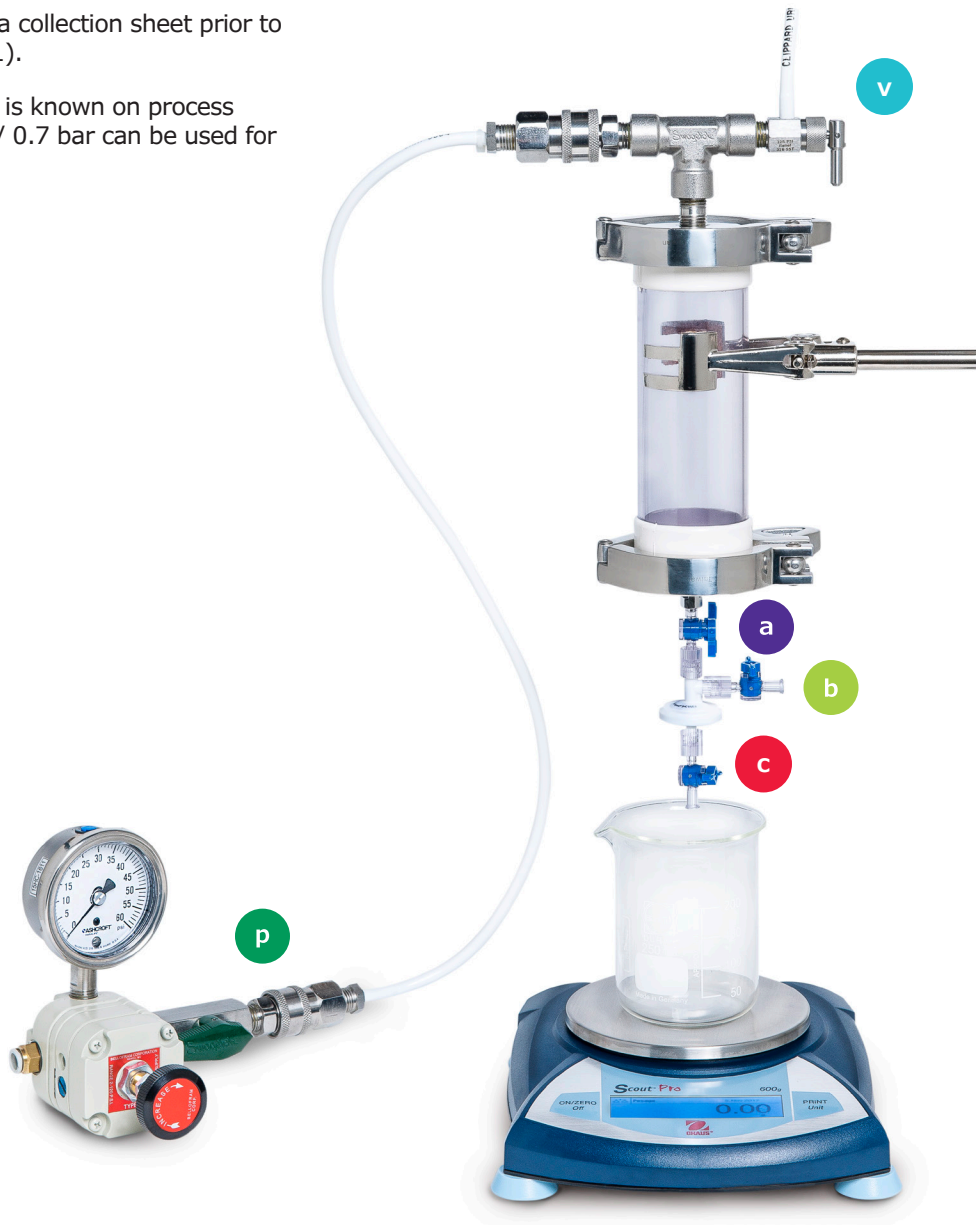
Test Method

The method below should be used in conjunction with the OptiScale® 25 Filter Capsule User Guide found in every OptiScale® filter box.

- Read this protocol from start to finish prior to the trials.
- Ensure that the equipment is clean before starting (cleaning procedure in Section 1.1).
- Prepare your data collection sheet prior to the trials (Table 1).
- If no information is known on process pressure, 10 psi / 0.7 bar can be used for Vmax™ test.

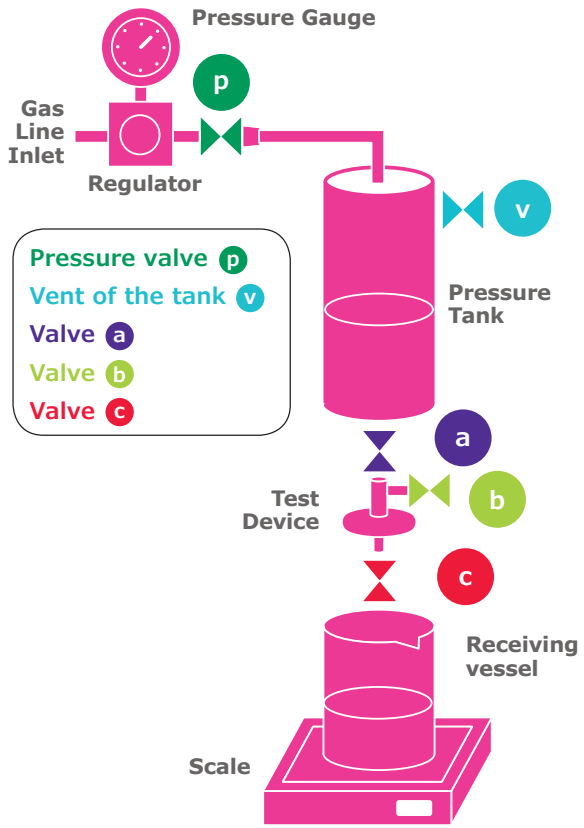
2.1 Equipment set up

- Connect the system to compressed air
- Check that all valves of the system are closed



2.2 Product Filtration

1. Introduce product in the pressure tank. Close the lid.
2. Set pressure regulator to 7 psi / 0.5 bars.
3. Slowly open the pressure valve (p).
4. Carefully vent filter by opening first the filter valve (a) and then carefully opening the vent valve (b). Once all air has been purged, close valve (b).
5. Set pressure regulator to a test pressure of 10 psi / 0.7 bar, or the process working pressure.
6. Open valve (c). Start the stopwatch when the first drop of product enters the receiving vessel. Use the Vmax™ data collection sheet (see page 8).
7. Monitor cumulative filtrate volume/weight every 1-2 minutes.
8. Stop the test when:
   - The process fluid has run out to almost 90-100% flux decay (few drops coming out of the filtration device)
   - OR when there is no product left
   - OR after 20-30 minutes
9. Close the valve (a). Stop the stopwatch.
10. Collect the filtrate and take a sample for analysis, if desired.
11. Remove the test device from the system and discard. At this step, another filter can be tested by repeating steps 3 to 8. Note: if there is enough product left for another test, there is no need to depressurize and empty/open the tank.
12. Close the pressure valve (p).
13. Open the vent of the pressurized tank (v).
14. Once all the pressure is released, open the lid.
15. Place a beaker or a bottle under the pressurized tank, open valve (a) and recover the product. Clean the equipment.



Watch our tutorial

MerckMillipore.com/viresolvepro

Table 1. Vmax™ Constant pressure test for aseptic filtration: data collection sheet

Product:		**Product:**	
Date:		Date:	
Test pressure (bar/psi):		Test pressure (bar/psi):	
Test Temperature:		Test Temperature:	
Filter:		Filter:	
Catalog number:		Catalog number:	
Lot number:		Lot number:	
Filtration area (cm^2):	**3.5**	Filtration area (cm^2):	**3.5**

RUN#			**RUN#**		
Time ( )	**Volume ( )**	**Comment ( )**	**Time ( )**	**Volume ( )**	**Comment ( )**

Stop when: the process fluid has run out to almost 90-100% flux decay (few drops coming out of the filtration device) OR when there is no product left OR after 20-30 minutes.

Data analysis and sizing

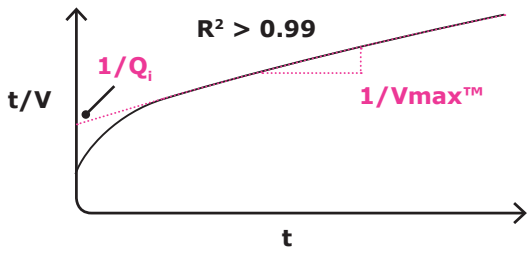
3.1 Experimental data analysis

Volume (V):	Liters (L)
Filtration area (A):	Square meters (m²)
Time (t):	Hours (h)

The units used in all calculations are:

To determine the filter sizing using Vmax™ method, the data are analyzed using a gradual pore plugging model as follows:

1. Enter the time (hours) and volume (in liters, assume density = 1) into a spreadsheet.
2. Plot t vs t/V.
3. Add a linear trendline to the data.
4. Using the trendline, determine slope, y-intercept and correlation coefficient (R^2).
   - If $R^2 > 0.99$, the Vmax™ method can be applied (i.e. gradual pore plugging is the main fouling mechanism).
   - If $R^2 < 0.99$, contact us (MerckMillipore.com/asepticexperts).
5. If $R^2 > 0.99$, divide 1 by the value of the slope. This is the Vmax™ value (maximum volume in liters that can be filtered through the test device used in this study).



6. Divide the Vmax™ value by the area (in m²) of the test device used in the study (OptiScale® 25 is 0.00035m²) to generate a Vmax™ value normalized for area, in L/m². This is the maximum volume in L that can be filtered through 1 m² of filter area.
7. Divide 1 by the y-intercept. This is the initial flow rate of the test device Q_i (in L/h).
8. Divide the initial flow rate Q_i by the area of the test device (in m²) to obtain the initial flux J_i (in L/m²/h or LMH):
   - $J_i = Q_i / 0.00035$
9. Calculate the minimum area (for a given batch size and process time) using the equations in the Sizing Calculation Section 3.2.

3.2 Sizing calculations

Either a specific **batch size**:

$$A_{min} = V_b/V_{max}$$

Or a **volume in a specific time**:

$$A_{min} = V_b/V_{max} + V_b/(J_i*t_b)$$

Or **volume with respect of a specific minimum filtrate flow rate**:

$$A_{min} = (V_b/V_{max})/(1-(Q_{min}/(J_i*A_{min}))^{0.5})$$

Where:
A_{min} is the minimum filtration area (m²)
V_b is the batch volume (L)
V_{max} is the maximum volume that can be filtered through 1 m² (L/m²)
J_i is the initial flux (L/m²/h)
t_b is the processing batch time (h)
Q_{min} is the minimum flow rate during the filtration (L/h)

The Vmax™ values from multiple tests can be used to compare the throughput of various filter media, the effects of process changes on filter performance, or to run batch to batch filterability measurements.

To size membrane filters, we recommend using the Vmax™ value calculated in Section 3.1. The Vmax™ value can be used with the equations described above to determine the minimum filtration area required to meet the process requirements. To allow for variability due to feed, and process conditions, a safety factor is typically included to define a required filtration area.

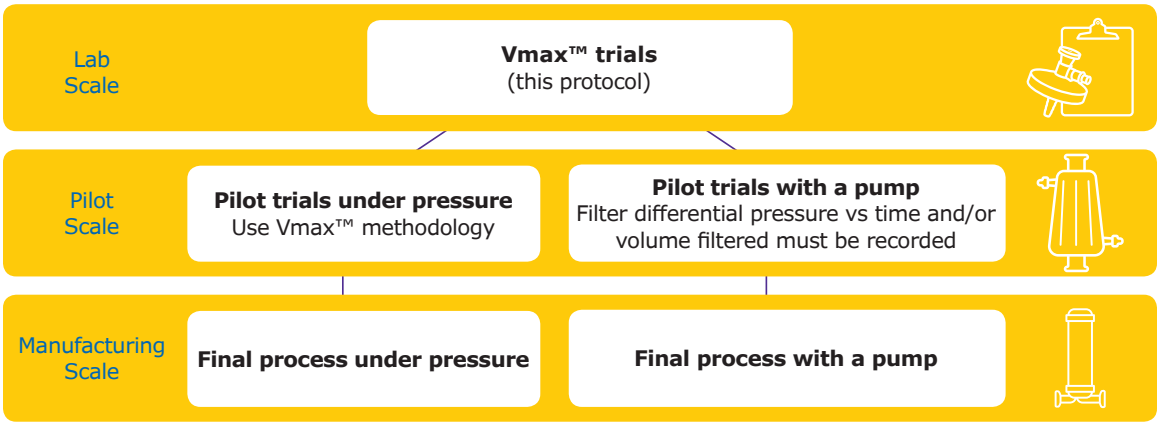
$$A = A_{min} * SF$$

Where:
A is the final process area (m²)
A_{min} is the minimum process area calculated (m²)
SF is the safety factor (Table 2)

Table 2. Typical range of safety factors

Application	Typical safety factor range	Initially recommended safety factor (without detailed information)
Sterile bulk	1.4-2.0	1.7
Sterile media	1.3-1.9	1.6
Clarification	1.3-1.9	1.6

The pilot trial should be a scaled-up version of the system recommended based on Vmax™ testing. When possible, the batch volumes, flow rates, temperatures, etc. should be simulated. The recommended scale-up strategy is as follows:



For more information on filter sizing, visit our website.

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