Vmax™ Constant Pressure Test

Protocol

Notice

Contents

Introduction

Constant pressure testing is used to size sterilizing grade and prefiltration (membrane-based) filters. The Vmax™ method predicts the capacity of filters using constant pressure testing, based on the gradual pore plugging model. This method, unlike traditional flow decay methods, allows prediction of filter lifetimes (volumetric loading capacities, Vmax™ method) without having to actually run the filter until it is completely plugged.

Gradual pore plugging occurs when colloids or suspended matter collect on the sides of filter pores to gradually block them off, until a state of total occlusion is eventually reached. This gradual blocking of the pores occurs in a distinct geometric pattern.

In a Vmax™ test, the time and volume collected up to that time are recorded at regular intervals. The data is then plotted as time/volume versus time. If the data plot as a straight line, this indicates the filter is plugging by the gradual pore plugging model and the formulas of the Vmax™ method can be applied to predict filter life. If the data do not plot as a straight line, this indicates the filter is plugging by some other model, such as cake formation. In these cases, the Vmax™ method should not be used and a traditional flow decay method, in which the filter is actually run until completely plugged, should be used.

Sterilizing grade filters and prefilters are typically run at a constant pressure of 5 to 10 psi (for process intermediates). Final bulks and fill solutions are generally run at higher pressures, 20 to 30 psi. A typical Vmax™ test will take 30 minutes to perform. This protocol will outline the methods and equipment used to perform a Vmax™ sizing study.

Study Objectives

The objectives of a Vmax™ constant pressure study are to determine the sterilizing grade filters and membrane-based prefilters capacity and provide sizing for sterilizing grade filters and membrane-based prefilters for a given unit operation.

Required Materials

Feed Stream

The feed stream used in the study should represent the actual process (temperature, concentration, density, etc.). Feed and filtrate (post-testing) samples should be taken and tested for product recovery.

Equipment

- Vmax™ set up (see Figure 1 below and Appendix I for details and catalog numbers)
- Bench space
- Stopwatch
- Thermometer
- Beakers
- Suitable vessels (1 or 2 L bottles) to collect filtrate and vent output during trials
- Appropriate personal protective equipment
- OptiScale®-25, 47mm disc and Optiscale® capsule devices see Appendix I.

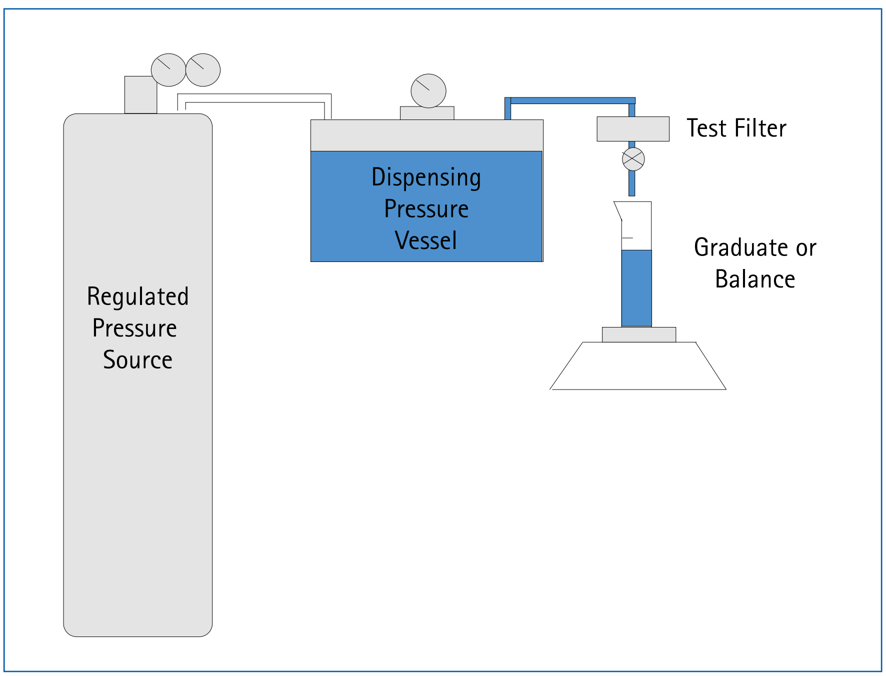

Figure 1: Vmax™ Constant Pressure Test Set-up.

Required Utilities

- Pressure supply (maximum of 30psi)
- Drain
- Electricity supply

Methods

Vmax™ tests are conducted under constant pressure. The test pressure is dictated by filter type, process step and the manufacturing set up (i.e. pressure drops, piping sizes, etc.). The maximum expected pressure at large scale should be used as the test pressure in scale down Vmax™ studies. The goal of a Vmax™ test is to monitor flow decay as a function of time and to determine the maximum volume that can be filtered through a test device. This information can then be used to determine sizing for a given scale up batch size and process time.

Test Method

Step	Description	Completed
1	Ensure that all of the equipment is thoroughly clean.	
2	Assemble the equipment as shown in Figure 1 with the equipment listed in Appendix 1.	
3	If using a 47mm disc holder, place a layer of Base 30 support material on the down-stream side of the holder.	
4	Use the filter forceps to place the membrane test filter on top of the support material (Millipore Express® filters must be installed shiny side down).	
5	Connect the holder or device to the pressure gauge (XXPXLGAGE). This will allow visibility of the pressure directly upstream of the test device to ensure accurate testing. Place a valve downstream of the pressure gauge (to allow manipulation of the pressure if necessary, to achieve the desired test pressure, without releasing test fluid).	
6	Place a piece of tubing downstream of the device or holder and clamp the end.	
7	Fully open the vent – for Optiscale®-25 devices, place a valve on the vent (place tubing on the vent using a luer fitting and direct tubing into a reservoir for easier venting).	
8	Pour the test fluid into the 5L pressure vessel (or other pressure container) and close the lid.	
9	With the pressure regulator, set the pressure to 5 to 10 psi for prefilters, 10 to 30 psi for final filters. **Note:** Pressure settings outside these guidelines may be necessary for trials with viscous fluids, limited feed volumes, or to more closely mimic actual process conditions. Pressure settings must be compatible with the tubing.	
10	Open the pressure vessel inlet valve.	
11	Slowly open the pressure vessel outlet valve. Monitor pressure gauge just upstream of the test device. Ensure that it is at the desired test pressure.	
12	Ensure that the vent valve on the test device is open and that the downstream of the test device is closed.	
13	Slowly open the valve just below the pressure gauge and fully vent the device.	
14	After venting, open the downstream of the test device (usually by removing the hemostat on the tubing that is attached to the outlet), close the valve on the vent, and begin recording filtrate volume (at 0.5 to 1.0 minute increments).	
15	Stop the test when the process fluid has run out, to at least 30% flux decay and/or for 30 minutes (to ensure adequate loading is achieved).	
16	Close the outlet valve to the pressure vessel.	
17	Open the filter holder vent valve.	
18	Remove the test device or filter holder from the pressure vessel and remove the filter from the holder.	
19	To test another filter using the same feed material, place the new device downstream of the pressure gauge or clean the filter holder and carefully place the new membrane to be tested in the holder. Proceed from step 5 above.	
20	When testing is complete or another process fluid must be tested, close the inlet to the pressure vessel and bleed/vent the air from the vessel. Proceed from step1 above.	

Vmax™ Equations for Data Analysis

The following equations are applicable to filters which fouling follows the gradual pore plugging model. In the gradual pore plugging model, flow decay follows the equation:

$$Q=Qi(1-kV/2)2$$

where: Q = flow rate (L/min.)

Qi = initial flow rate (L/min.)

k = constant (from Hagen Poiseuille relationship)

V = Volume filtered (L)

At infinite time, Q = 0, and the following equation results:

Maximum volume filtered = Vmax™ = (k/2)-1

When time/volume vs. time is plotted and a straight line results, it follows the equation:

$$t/v = At + B$$

where: t = time

v = volume filtered up to that time

A = slope

B = y-intercept

Solving for V gives the following equation:

$$V = t/At + B \quad = \quad 1/(A +(B/t))$$

Letting time go to infinity, B/t becomes zero and:

V = Vmax™ = 1/A

Therefore, the inverse of the slope of the plot of t/v vs. t equals the maximum volume which can be filtered by the test filter.

B is the y-intercept, or the value of t/v when time is zero.

1/B has the dimensions volume per time, a flow rate.

Therefore, the inverse of the y-intercept is the flowrate through the test filter at zero time, or the initial flowrate.

Rearranging equation 1 with Vmax™ = 2/k results in the equation:

$$Q/Qi = (1 – V/Vmax)2$$

This equation can be used to determine the percentage of the Vmax™ value which has been used when the flow rate has dropped to a percentage of the initial flow rate.

Sizing Method

Step	Description
1	Enter the time (minutes) and volume (assume density = 1, unless value is known, and divide by 1,000 to obtain volume in L) into a spreadsheet.
2	Plot t vs. t/V.
3	Add a linear trend line to the data.
4	Using the trend line, determine slope, y-intercept and correlation coefficient (r^2).
5	If $r^2 > 0.99$, the Vmax™ model can be applied (i.e. gradual pore plugging is the main fouling mechanism).
6	If $r^2 < 0.99$, determine if there are any outliers in the dataset and, if so, eliminate them and replot the data and add the linear trend line. If this does not change the correlation coefficient, another fouling model should be used (contact Technical Service for additional help). The Vmax™ model can be used to generate approximate sizing, but additional data analysis should be done for accurate sizing.
7	If $r^2 > 0.99$, divide 1 by the slope. This is the Vmax™ value (maximum volume in liters that can be filtered through the test device used in this study).
8	Divide the Vmax™ value by the area (in m^2) of the test device used in the study.
9	Divide 1 by the y-intercept. This is the initial flow rate of the test device.
10	Divide the initial flow rate by the area of the test device to obtain the initial flux (Qi).
11	Calculate the minimum area (for a given batch size and process time) using the equations in Vmax™ Equations for Data Analysis.

Refer to Application Note AN1512EN00 for additional information.

Sizing Calculations

Use the following equation when only the batch size (VB) is given (no process time, tB): $A_{\min} = \dfrac{V_B}{V_{\max}}$

Use the following equation when batch size, process time and initial flow rate (Ji) are given:

$$A_{\min} = \frac{V_B}{V_{\max}} + \frac{V_B}{J_i \times t_B}$$

Use the following equation when minimum flow rate (Qi) is given: $1 - \sqrt{\dfrac{Q_{\min}}{J_i \times A_{\min}}} = \dfrac{V_B}{V_{\max} \times A_{\min}}$

Note Solve iteratively for A_{min} using this equation. Use the equation in Vmax™ Equations for Data Analysis for the first 'guess' at A_{min}

All of the above equations can be used to calculate the minimum area. Add additional safety factors to account for feed, device and test variability. The safety factor is based on the value of a failed batch (at that process step) versus cost. For example, a safety factor of 1.1 to 1.3 is typically used for buffer sterile filtration versus a typically used 1.4 to 2.0 for final bulk sterile filtration.

Ordering Information

Equipment

Description	Catalog Number
5 Liter pressure vessel	XX6700P05
Pressure gauge 0-100 psi	YY1301015
1/4" NPT quick release nipple and coupling	XX6700030
Vent relief valve	XX6700024
3/4" Gaskets 4/pack	XX42T1901
3/4" Clamps 4/pack	XX42T1900
1/4" NPTM 2" Hex nipple	XX6700125
Pressure gauge 0-30psi 1/8" NPT	XXPXLGAGE
Forceps	XX6200006P

Description	Suggested Vendor	Vendor Catalog Number
Plug 1/4" OD 10/pack	Cole Palmer	C-34006-73
Valve, 1/4" OD x 1/4" NPTM PP	Cole Palmer	C-07391-00
Valve, 1/4" OD x 1/4" OD	Cole Palmer	C-07391-04
Pipe Adapter 1/4" OD x 1/4" NPTM 10/pack	Cole Palmer	C-34006-03
Bushing 1/4" NPTM x 1/8" NPTF	Cole Palmer	A-08539-89
Fitting luer x 3/4 TC	Cole-Parmer	A-31200-50
Bellofram regulator	Pilgrim Instruments	960-015-00
2-way valve Luer-Lok™ 100/pack	Value Plastic	VP455980
1/8" NPTF Luer-Lok™100/pack	Value Plastic	18FTLL-1
1/4" NPTM Luer-Lok™100/pack	Value Plastic	14MTLL-1

Devices

Membrane				Catalog Number
Membrane	Description	Material	Pore Size (mm)	
47mm Disc				
N/A	Base 30 Support Material	Polypropylene	N/A	SH1J806H5
Milligard®	RW Prefilter	Mixed Cellulose Esters	0.2	RW0304700
Milligard®	RW03 Prefilter - Low Binding	Mixed Cellulose Esters	0.2	SH1M211H2
Milligard®	RW06 Prefilter - Low Binding	Mixed Cellulose Esters	0.5	SH1M212H2
Milligard®	RW19 Prefilter - Low Binding	Mixed Cellulose Esters	1.2	SH1M213H2
Polygard® CN	Prefilter	Polypropylene	0.3	SH1B947J1
Polygard® CN	Prefilter	Polypropylene	0.6	SH1B948J1
Polygard® CN	Prefilter	Polypropylene	1.2	SH1B949J1
Polygard® CN	Prefilter	Polypropylene	30	SH1B950J1
Polygard® CN	Prefilter	Polypropylene	5	SH1B951J1
Polygard® CN	Prefilter	Polypropylene	10	SH1B952J1
Polygard® CN	Prefilter	Polypropylene	30	SH1B953J1
Durapore®	0.65 Durapore® Membrane	PVDF	0.65	DVPP04700
Durapore®	0.22 Durapore® Membrane	PVDF	0.22	GVWP04700
Durapore®	0.45 Durapore® Membrane	PVDF	0.45	HVHP04700
Durapore®	0.10 Durapore® Membrane	PVDF	0.1	VVLP04700
Durapore®	0.22 Charged Durapore® Membrane	PVDF	0.22	CCGL04725
Durapore®	0.22 Phobic Durapore® Mem-brane	PVDF	0.22	GVHP04700
Fluoropore™	0.2 Fluoropore™ FG Membrane	PTFE	0.2	FGLP04700
Millipore Express®	Millipore Express® SHR Mem-brane w/Prefilter (0.5/0.1)	PES	0.5/0.1	HVEP04710
Millipore Express®	Millipore Express® SHC (0.5/0.2) Membrane	PES	0.5/0.2	HGEP04710
Millipore Express®	Millipore Express® SHF (0.2) Membrane	PES	0.2	GEPP04725

Membrane				Catalog Number
Membrane	Description	Material	Pore Size (mm)	
OptiScale®-25 Devices				
Durapore®	Multilayer	PVDF	0.45/0.22	SHGLA25NB6
Durapore®	Prefilter	PVDF	0.45	SPHLA25NB6
Durapore®	Durapore® Membrane w/ Prefilter	PVDF	0.45	SVHLA25NB6
Durapore®	Durapore® 0.22 Membrane	PVDF	0.22	SVGLA25NB6
Durapore®	Durapore® 0.10 Membrane	PVDF	0.10	SVVLA25NB6
Durapore®	Multimedia	PVDF	0.2/0.22	SV03A25NB6
Durapore®	Multimedia	PVDF	0.5/0.22	SV06A25NB6
Durapore®	Multimedia	PVDF	1.0/0.22	SV19A25NB6
Durapore®	Multimedia	PVDF	1.0/0.5/0.22	SVSCA25NB6
Durapore®	Multimedia	PVDF	0.5/0.2/0.22	SVSSA25NB6
Durapore®	Multimedia	PVDF	1.0/0.2/0.22	SVSXA25NB6
Millipore Express®	SHC	PES	0.50/0.20	SHGEA25NB6
Millipore Express®	SHF	PES	0.20	SGEPA25NB6
Millipore Express®	SHR	PES	0.10	SVEPA25NB6
Millipore Express®	SHR w/Prefilter	PES	0.5/0.10	SHVEA25NB6
Millipore Express®	HPF Prefilter	PES	0.5/0.30	SHPSA25NB6
Optiscale® Prefilter Device				
Polysep™ II	Prefilter	glass fiber (prefilter), mixed cellulose ester (filter)	1.0/0.2/0.1	SGW1A47HH3
Polysep™ II	Prefilter	glass fiber (prefilter), mixed cellulose ester (filter)	2.0/0.1	SGW9A47HH3
Polysep™ II	Prefilter	glass fiber (prefilter), mixed cellulose ester (filter)	1.0/0.2	SGW3A47HH3
Polysep™ II	Prefilter	glass fiber (prefilter), mixed cellulose ester (filter)	1.0/0.5	SGW6A46HH3
Polygard® CN	Prefilter	polypropylene	0.3	SN03A47HH3
Polygard® CN	Prefilter	polypropylene	0.6	SN06A47HH3
Polygard® CN	Prefilter	polypropylene	1.2	SN12A47HH3
Polygard® CN	Prefilter	polypropylene	10.0	SN1HA47HH3
Polygard® CN	Prefilter	polypropylene	2.5	SN25A47HH3
Polygard® CN	Prefilter	polypropylene	30.0	SN3HA47HH3
Polygard® CN	Prefilter	polypropylene	5.0	SN50A47HH3
Lifegard™	Prefilter	glass fiber	1.0	SP15A47HH3
Lifegard™	Prefilter	glass fiber	2.0	SP20A47HH3
Milligard®	Prefilter	mixed cellulose esters	0.2	SW03A47HH3
Milligard®	Prefilter	mixed cellulose esters	0.5	SW06A47HH3
Milligard®	Prefilter	mixed cellulose esters	1.2	SW19A47HH3
Milligard®	Prefilter	mixed cellulose esters	1.2/0.5	SWSCA47HH3
Milligard®	Prefilter	mixed cellulose esters	0.5/0.2	SWSSA47HH3
Durapore®	0.45	PVDF	0.45	SVHLA47FH3

Membrane				Catalog Number
Membrane	Description	Material	Pore Size (mm)	
Optiscale® Sterile Filter Device				
Durapore®	0.22	PVDF	0.22	SVGLA47HH3
Durapore®	0.1	PVDF	0.1	SVVLA47FH3
Durapore®	0.45/0.22	PVDF	0.45/0.22	SHGLA47FH3
Durapore®	Multimedia	mixed cellulose esters (prefilter) PVDF (filter)	0.2/0.22	SV03A47HH3
Durapore®	Multimedia	mixed cellulose esters (prefilter) PVDF (filter)	0.5/0.2/0.22	SVSSA47HH3
Durapore®	Multimedia	mixed cellulose esters (prefilter) PVDF (filter)	1.2/0.2/0.22	SVSXA47HH3
Durapore®	Multimedia	mixed cellulose esters (prefilter) PVDF (filter)	0.5/0.22	SV06A47HH3
Durapore®	Multimedia	mixed cellulose esters (prefilter) PVDF (filter)	1.2/0.5/0.22	SVSCA47HH3
Durapore®	Multimedia	mixed cellulose esters (prefilter) PVDF (filter)	1.2/0.22	SV19A47HH3
Millipore Express®	SHF	PES	0.2	SGEPA47FH3
Millipore Express®	SHC	PES	0.5/0.2	SHGEA47FH3
Millipore Express®	SHR with Prefilter	PES	0.5/0.1	SHVEA47FH3
Millipore Express®	SHR	PES	0.1	SVEPA47HH3

HH refers to hosebarb connections (on top and bottom of the device), if you would like ¾ in. sanitary connections use HH or hose barb to ¾ in. sanitary use FH.

For additional information refer to the Durapore® Filters Datasheet, DS8932EN00, the Millipore Express® SHC Filters Datasheet, DS1428EN00 or the Millipore Express® SHR Filters Datasheet, DS0105EN00.

Technical Assistance

For more information, contact the office nearest you or visit the Technical Service page at www.emdmillipore.com/techservice. Worldwide contact information is available at www.emdmillipore.com/offices.