Flow rate and throughput of cell culture media and serum using Thermo Scientific Nalgene Rapid-Flow filters with 0.2 micron PES membranes

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Key Words
sterile filtration, media filtration, serum filtration, vacuum filter units, bottle top filters, Rapid-Flow™, PES membrane

Goal
The goal of this study was to compare the flow rate and throughput of Thermo Scientific Nalgene filter units, which utilize the Rapid-Flow support system, with filter devices from Corning and Millipore.

Abstract
Sterile filtration of liquids used in cell culture is a critical step in maintaining a contamination-free culture. Thermo Scientific Nalgene filter units and bottle top filters have the unique Rapid-Flow membrane support plate designed to increase the rate at which liquids can be filtered. The Rapid-Flow system provides more uniform membrane support and stability than does the radial spoke design used by other filter manufacturers. Here we test whether this design increases the rate at which liquids can be filtered and the maximum volume of filtered liquid, compared to competitors' filters. We find that the Rapid-Flow system offers significant performance advantages over similar size filters from other manufacturers.

Rapid-Flow provides faster flow rates and higher throughput.

Introduction
The first Nalgene vacuum filter was introduced in 1965, and since then filter units and bottle-top filters have become crucial tools in the sterile filtration of media in the laboratory. Such filtration is essential in maintaining contamination-free media, serum, and buffers for cells in culture. Since filtration takes time, advancements that increase the flow rate of liquid would be welcomed by cell culture researchers. Thermo Scientific Nalgene filter units and bottle top filters have the unique Rapid-Flow membrane support system. The Rapid-Flow system consists of a multi-column array that provides more uniform membrane support and stability than does the radial spoke design used by other filter manufacturers. Rapid-Flow is designed to allow increased flow rates and greater fluid throughput. Flow rate and throughput advantages of Rapid-flow have already been demonstrated in Nalgene 0.1 micron PES filters[1]. The purpose of this study is to compare the performance of Nalgene 0.2 micron PES Rapid-Flow filters with 0.2 micron PES filters from Corning and Millipore.

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Test Fluids

Cell Growth Media: DMEM + 10% FBS (fetal bovine serum), RPMI + 10% BGS (bovine growth serum). Both are typical cell growth media.

Serum: A mixture of 100% BGS (bovine growth serum) and 100% BCS (bovine calf serum) was used. 100% serum is a common component of cell growth media and also a severe filtration challenge.

Test Method

Flow Rate and Maximum Filtration Volume

The vacuum system was started and adjusted to full vacuum (27.4" Hg) in the 80L vacuum buffer and 25" Hg at the test stand. Testing did not begin until the vacuum buffer registered ≥ 25" Hg. The filter unit being tested was attached to a calibrated 2L glass receiver and to vacuum. Nalgene Rapid-Flow sterile filter units, Millipore Steritop-GP filter units, and Corning filter units were tested in random order. The filter units were filled to the top with test solution and the vacuum stopcock at the test stand was opened. Time points were taken every 200mL for DMEM + 10% FBS or RPMI 1640 + 10% BGS, and every 50mL for 100% serum until 2 Liters (L) of fluid had been filtered or clogging was reached (defined as less than 1 drop of fluid per second, or a flow rate such that the time to filter 100ml exceeded 2 min). Fluid was replenished as needed such that at least 200mL of test solution was in the filter unit at all times to prevent the filter unit from running dry. Six filters of each type were tested with RPMI and DMEM; three filters of each type were tested with 100% serum.

Data Analysis

Two-sample t-tests assuming unequal variances were used to determine the significance ($p<0.05$) of filter performance (flow rate and clogging volume) for DMEM + 10% FBS, RPMI 1640 + 10% BGS and 100% serum between a) 1000mL Nalgene Rapid-Flow filters and 1000mL Millipore Steritop-GP filters, and b) 500mL Nalgene Rapid-Flow filters and 500mL Corning filters.

Table 1. Filters Investigated

Description	Catalog #	Membrane Pore Size and Material	Membrane Diameter (mm)
Nalgene 1000mL Rapid-Flow Filter	567-0020	0.2µm PES	90
Millipore 1000mL Steritop-GP Filter	SCGPT10RE	0.22µm PES	70
Nalgene 500mL Filter	595-4520	0.2µm PES	75
Corning 500mL Filter	431097	0.22µm PES	63x63mm (square)

Table 2. Flow rate results

Description	Flow Rate with RPMI (mL/ttmin)	Flow Rate with DMEM (mL/min)	Flow Rate with BCS/ BGS (mL/min)	Maximum Volume of 100% Serum filtered
Nalgene 1000mL Rapid-Flow Filter	698.4	827.4	224.8	567
Millipore 1000mL Steritop-GP Filter	471.6*	626.8*	173.1	450
Nalgene 500mL Rapid-Flow Bottle Top Filter	508.7	618.1	180.6	367
Corning 500mL Filter	397.6*	508.7*	123.4*	267

*Nalgene Rapid-Flow filter is significantly faster ($p<0.05$).

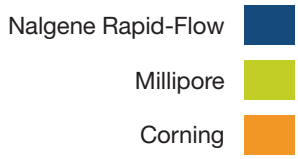


Figure 1. Flow Rate using RPMI + 10% BCS

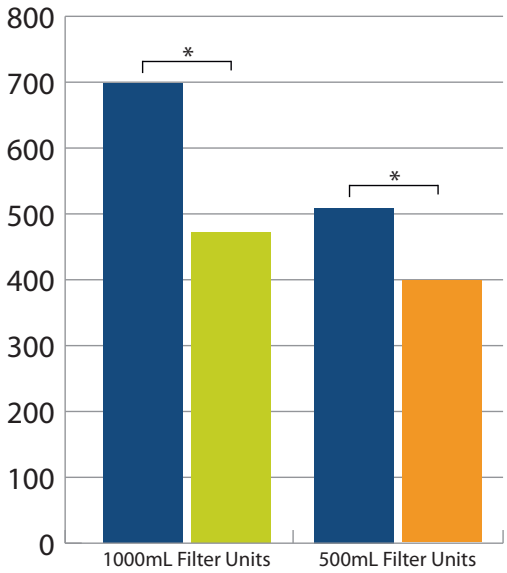


Figure 2. Flow Rate using DMEM + 10% FBS

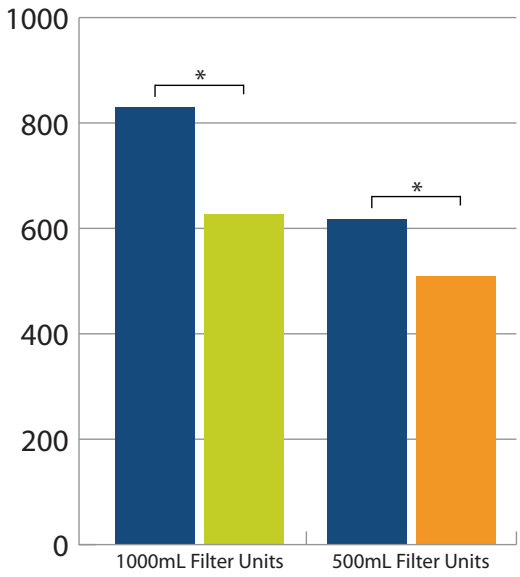


Figure 3. Flow Rate using 100% BCS/BGS

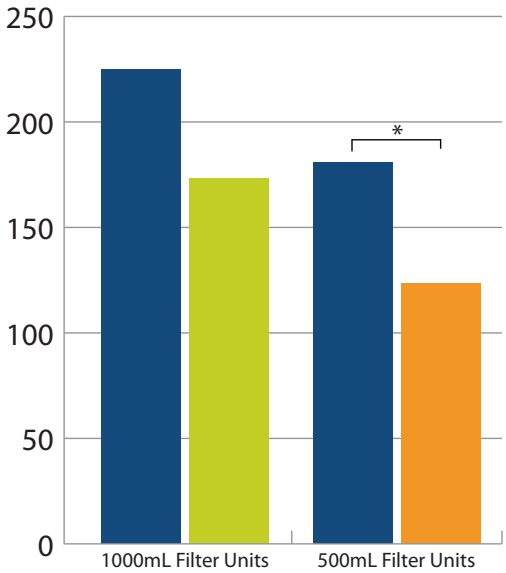
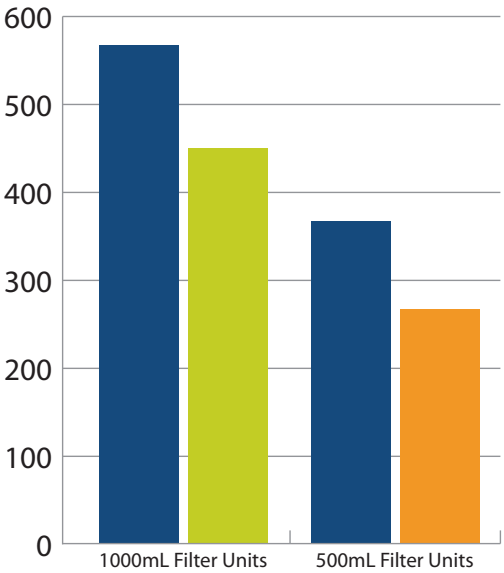


Figure 4. Maximum Volume filtered using 100% BCS/BGS



No significant differences were found.

*Nalgene Rapid-Flow filter units filter significantly faster than the others ($p<0.05$) – refers to all graphs.

Discussion

The improved performance of the new Rapid-Flow support plate was apparent when comparing filter performance under these media and serum conditions.

The 1000mL Rapid-Flow filters showed significantly faster flow rates over those from Millipore, with a 48% improvement for RPMI + serum and a 32% improvement for DMEM + serum. 1000mL Rapid-Flow filters showed a 30% higher average flow rate than 1000mL Millipore filters using 100% serum but were not significantly faster per t-test.

For 500mL filters, Nalgene Rapid-Flow filters showed statistically faster flow rates over Corning filters of 28% for RPMI + serum, 22% for DMEM + serum and 46% for 100% serum.

While the filters used for this study are designed to filter 1000mL or 500mL of liquid, all were capable of filtering more than 2000mL of media plus serum without clogging. 100% serum, however, was a more challenging fluid for all filters tested, with throughputs of 600mL or less. Although the Rapid-Flow filters filtered more serum on average than did the other filters, there were no statistically significant differences seen in volume of serum filtered between the 500mL filters or the 1000mL filters tested.

Contamination is the enemy of anyone maintaining cell cultures. While close attention to sterile technique can reduce the chance of introducing contamination, it is critical to ensure that the materials used to maintain the culture are sterile at the outset. Final filtration in the laboratory is an easy and effective way to remove microbial and particulate contamination from any liquids that will come in contact with the cells in culture. Conventional filter units are designed with membrane support plates that contain ribs that radiate from the center. When vacuum is applied to filters with this design, the spacing of the ribs allows distortion of the membrane resulting in a reduction of fluid flow. To overcome this effect Nalgene Rapid-Flow filters contain a multi-column array that provides more uniform and less restrictive support to the membrane; this unique design permits higher flow rates and throughput. Rapid-Flow offers increased rates of flow in 1000mL units when filtering media + serum compared to filter units offered by Millipore. In 500mL units, the Nalgene Rapid-Flow filters offer increased flow rates compared to Corning filters for media + serum and for pure serum. The new design may also offer improvements in the maximum volume filtered when filtering 100% serum.

Conclusion

Rapid-Flow 1000mL filters flowed significantly faster than Millipore filters with media + serum and were equivalent with 100% serum.

Rapid-Flow 500mL filters flowed significantly faster than Corning filters with both media + serum and 100% serum.

Neither 500mL nor 1000mL filters showed significant differences in throughput for media + serum or 100% serum.

References

[1]Flow rate and throughput of Thermo Scientific Nalgene 0.1 micron Rapid-Flow PES filter units with cell culture media. Application note #ANLSPFILT01PES, 2012.

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