

## Effect of Prefiltration on Scalability of 0.1- $\mu\text{m}$ Rated Membrane Filters

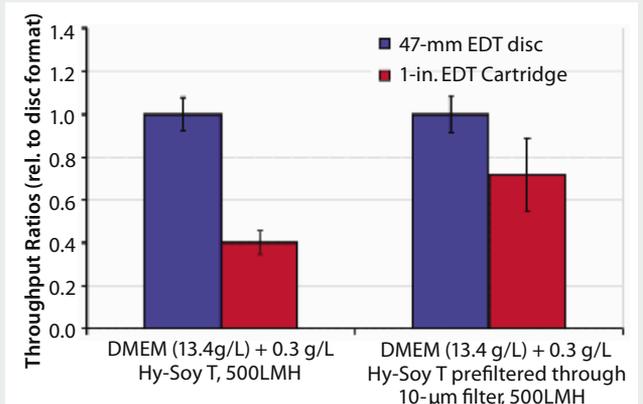
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The effect of prefiltration on the scalability of 0.1- $\mu\text{m}$  rated membrane filters is evaluated using a specific cell culture medium that showed reduced filtration throughput (in terms of  $\text{L}/\text{m}^2$ ) with pleated cartridges.

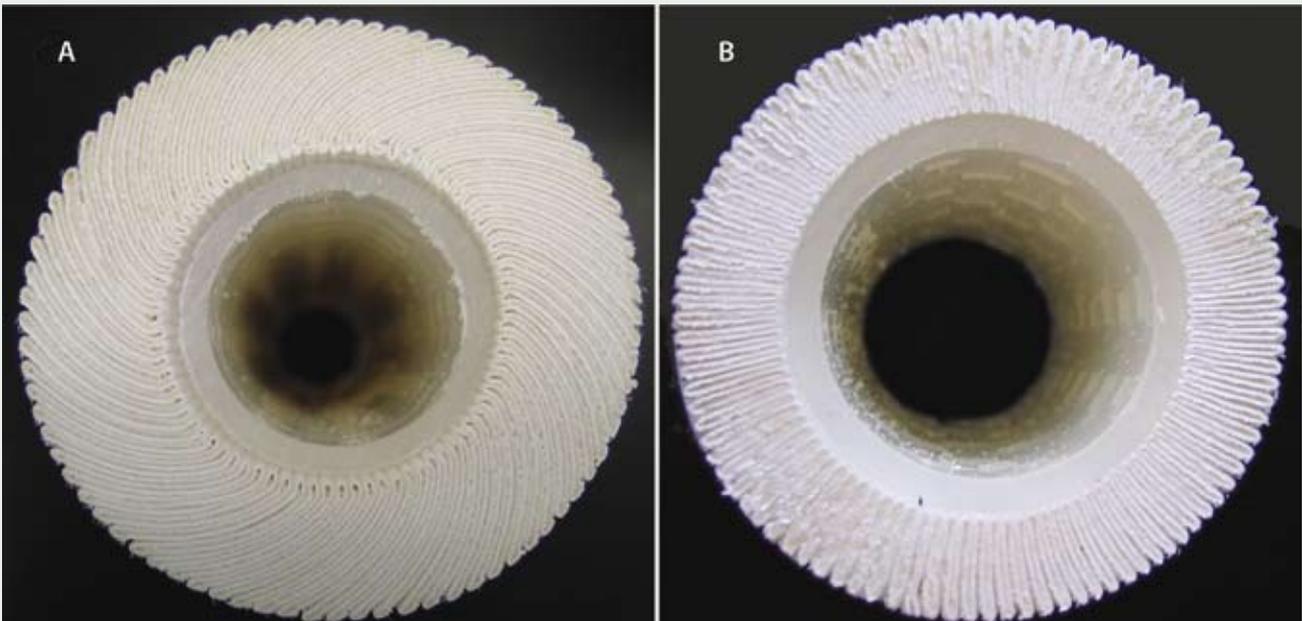
Biopharmaceutical process developers seek to size membrane filters more accurately to improve process economics. Understanding the scalability of filters from discs to pleated cartridges has thus become important. Contradictory claims on the scale-up between different filter configurations have been made in the literature (1, 2). Recently, we reported that 0.1- $\mu\text{m}$  rated Fluorodyne® EX grade EDT membrane filters showed good scalability from discs to pleated cartridges with a variety of cell culture media feeds (3). For some media additives, however, all 0.1- $\mu\text{m}$  rated membrane filters tested, including Fluorodyne EX grade EDT membrane, exhibited nonlinear scalability (throughput scaling factor  $< 1$ ). In this application note, we show that for such solutions, implementation of a coarse prefiltration step can improve the linearity of scalability and filter performance.



**Figure 2:** Throughput scaling factors for Fluorodyne EX EDT filters with and without 10- $\mu\text{m}$  prefiltration of a cell culture medium supplemented with Hy-Soy T. Use of the 10- $\mu\text{m}$  prefilter increased the throughput scaling factor by 80%. Error bars indicate standard deviation from multiple trials.



**Figure 1:** Different membrane pleating structures: (A) narrow-core laid over pleat design and (B) traditional fan pleat design with standard diameter core. The greater membrane packing density in narrow-core laid over pleat cartridge design enables more membrane area per 10" filter element.



## EXPERIMENTAL CONDITIONS

Two filter formats of 0.1- $\mu\text{m}$  rated Fluorodyne EX grade EDT filters were tested: a 47-mm disc (effective filtration area, efa = 11.1  $\text{cm}^2$ ) and a 1-in. pleated cartridge (efa = 950  $\text{cm}^2$ ) that is a 1:10 scale-down of a standard 10-in. pleated cartridge (efa = 9,500  $\text{cm}^2$ ) with the same Ultipleat<sup>®</sup> laid-over pleat and narrow core design (Figure 1). The challenge solution was a cell culture medium (DMEM) with 0.3 g/L Hy-Soy<sup>™</sup> T peptone additive (Sheffield Pharma). Hy-Soy T is a soy-derived hydrolysate that supports growth of mammalian cells in cell culture media. Filtration was performed at a constant flux of 500 L/m<sup>2</sup>/hr (LMH) using the well-mixed challenge solution prepared with and without prefiltration through a 10- $\mu\text{m}$  rated Pall HDC<sup>®</sup> II pleated polypropylene prefilter. Throughput scaling factors, defined as the ratio of the throughput of a filter to that of a 47-mm disc, were calculated. The absorbance of UV at 280 nm wavelength ( $A_{280}$ ) was used to measure concentrations of DMEM and DMEM with Hy-Soy T peptone.

## RESULTS

Figure 2 shows throughput scaling factors for the Fluorodyne EX grade EDT filters with and without 10- $\mu\text{m}$  prefiltration: 10- $\mu\text{m}$  prefiltration improves the throughput scaling factor by 80% (from 0.40 to 0.72) specifically resulting from removal of large particulates from the feed solution. Furthermore,  $A_{280}$  data indicate that a substantial fraction of Hy-Soy T peptone (~30% by absorbance) consists of particulates >10  $\mu\text{m}$  and an additional ~20% ranging of 0.1–10  $\mu\text{m}$  (Figure 3).

## CONCLUSIONS

As reported earlier (3), Fluorodyne EX grade EDT filters show good scalability from discs to pleated cartridges for many fluids. However, our prior study suggested that some media components influence scaling behavior, which was common to all 0.1- $\mu\text{m}$  rated pleated filters (3). This application note suggests that coarse prefiltration can improve scale-up for such solutions. General recommendations for 0.1- $\mu\text{m}$  filter scaling studies are

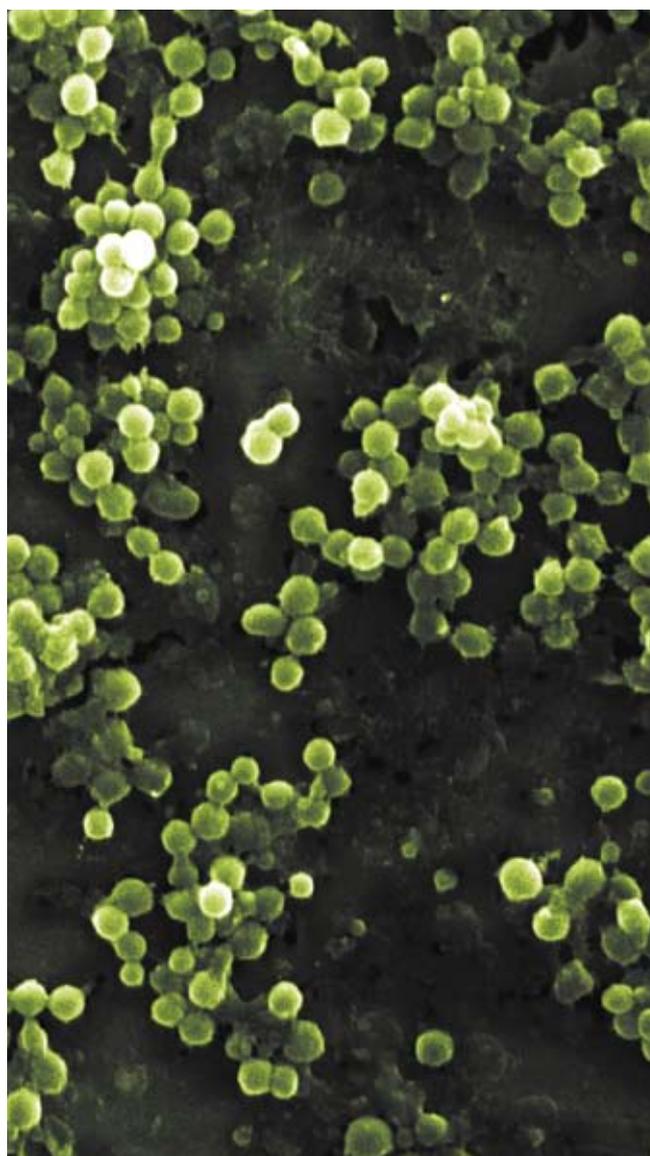
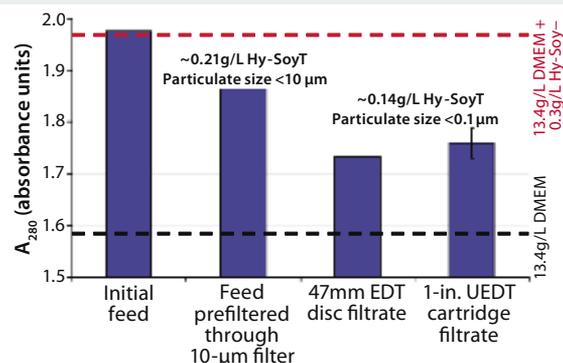
- 47-mm discs should be used for screening trials
- 1-in. cartridge elements should be used in filter sizing studies for more accurate scaling, and
- a prefiltration step should be implemented if a low throughput scaling factor is observed with 1-in. cartridge elements relative to a 47-mm disc. Prefiltration at  $\leq 10\mu\text{m}$  should be considered.

## REFERENCES

- 1 Giglia S, Yavorsky. Scaling from Discs to Pleated Devices. *PDA J. Pharmaceut. Sci. Technol.* 61(4) July–August 2007: 314–323.
- 2 Chandler M, Zydny A. High Throughput Screening for Membrane Process Development. *J. Membrane Sci.* 237, 2004: 181–188.
- 3 Evaluating the Scalability of 0.1- $\mu\text{m}$  Rated Membrane Filters. *BioPharm Int.* June 2009. 

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**Figure 3:**  $A_{280}$  values of (A) an initial feed containing 13.4 g/L DMEM with 0.3 g/L Hy-Soy T, (B) the same feed prefiltered through a 10- $\mu\text{m}$  filter, (C) the prefiltered solution following filtration through a 47mm EDT disc, and (D) through a 1" UEDT cartridge. The 10- $\mu\text{m}$  prefilter reduced the  $A_{280}$  difference between the initial feed containing 13.4 g/L DMEM with 0.3 g/L Hy-Soy T and 13.4 g/L DMEM by ~30%. Both the EDT disc and the UEDT cartridge reduced the  $A_{280}$  difference by an additional 20%.



SEM photomicrograph showing the mycoplasma *Acholeplasma laidlawii* (white spheres). Cells are rendered monodisperse using sonication before filter challenges.