Application Note

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Sartopore Evo® – Embracing a PFAS-Free Future in Final Formulation and Filling

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Abstract

The final step in biopharmaceutical production, formulation and filling, requires sterile filtration of the active pharmaceutical ingredient and preservation of its formulation. Traditionally, membrane polymers made of per- and polyfluoroalkyl substances (PFAS), such as polyvinylidene fluoride (PVDF), have been preferred in this application due to their favorable adsorption properties for certain excipients such as polysorbate. However, concerns about the potential impact of PFAS chemicals and polymers on the environment and human health have resulted in proposals to restrict the use of these substances, highlighting the need for alternative solutions.

This study evaluated various polyethersulfone- (PES) and PVDF-based membrane filters, assessing their adsorption of Polysorbate 80, a commonly used excipient in monoclonal antibody formulations. The results highlight how advanced membrane surface modification can significantly reduce the adsorptive properties of a membrane polymer material. With its newly developed surface-modified PES membrane, Sartopore Evo® filters exhibited comparable low polysorbate adsorption to filters made of a PVDF membrane, making it an excellent alternative to PFAS polymer-based filters for biopharmaceutical final formulation and filling applications.

Introduction

Sterile filtration of the active pharmaceutical ingredient (API) is a critical process at the final formulation and filling stage of biopharmaceutical production. This step is crucial for ensuring product sterility and preserving the API's stability and functionality. Polyethersulfone (PES) membranes are well established in a broad range of filtration steps in up- and downstream biopharmaceutical processing. With their high flow rates and filter capacities, PES membrane filters support both time- and cost-efficient processing. However, for the late-stage sterile filtration processes of drug substances and drug products, PVDF membrane filters have been more commonly used due to their low adsorption of polysorbate.

The newly developed Sartopore Evo® filter combines the well-known excellent filtration performance of the Sartopore® 2 filter family with a newly developed surface modification for the PES membrane, resulting in significantly reduced adsorption of polysorbate, proteins, and other formulation additives. This application note describes the comparison of PES- and polyvinylidene fluoride (PVDF)-membrane filters, including the Sartopore Evo® filter, for their adsorption of polysorbate 80. For a comprehensive evaluation, PES- and PVDF-membrane filters from various manufacturers, in different sizes and formats (flat filter and pleated devices), were included in the study.

Materials and Methods

The filters analyzed for their polysorbate 80 adsorption properties are listed in Table 1. Each filter type was tested in two formats: flat filter disc screening devices and an effective filtration area (EFA) of 17 to 20 cm², typically used for filter screening trials, and a pilot-scale size in a pleated format and an EFA ranging from 200 to 900 cm².

Table 1: *Filter Types and Membrane Materials Analyzed for Their Polysorbate 80 Adsorption Properties*

Filter Type	Membrane Material
Sartopore® 2 0.45 | 0.2 µm	PES
Sartopore Evo® 0.8 | 0.2 µm	PES
Sartopore Evo® 0.2 µm	PES
Competitor 1 0.22 µm	PVDF
Competitor 1 0.5 | 0.2 µm	PES
Competitor 2 0.45 | 0.2 µm	PES
Competitor 2 0.2 | 0.2 µm	PVDF

All tests were conducted using a placebo solution that mimicked a common drug protein formulation but contained no API (Table 2). The concentration of polysorbate 80 at 0.1 mg/mL reflects common protein formulation conditions. Furthermore, this low concentration supports the detection of small changes in its concentration in the analyzed filtrate samples.

Table 2: *Composition of the Test Formulation (pH 6.0, Density 1.03 g/mL)*

Formulation Components	Concentration [mg/mL]
Sucrose	80
Polysorbate 80	0.1
L-Histidine hydrochloride monohydrate	1.096
L-histidine	0.741
Water for injection (WFI)	Ad 1 mL

Throughout the entire filtration process, 25 samples (fractionated sampling) of the filtrate were taken for each filter. The polysorbate 80 concentration of the samples was determined by HPLC analysis, which provided a comprehensive adsorption profile for each filter tested.

The total adsorption of each membrane material during the filtration process was calculated using the following formula:

Figure 1: *Formula Used to Calculate Polysorbate 80 Adsorption*

$$\Gamma = \frac{\sum_{n=1}^{c\sim 100\%} c \times V_n \times (1 - C_n)}{A}$$

A = Filter surface
c = Initial polysorbate concentration
V = Sample volume
C = Measured amount of polysorbates in the sample
Γ = Sum of all adsorption

Results

The polysorbate 80 adsorption properties of the tested filters varied significantly not only between the membranes made of the two different polymer materials tested (PVDF & PES) but also among filters made of the same membrane polymer material. This highlights that the adsorption properties are substantially influenced by the individual surface modifications of the base membrane polymer. Table 3 summarizes the polysorbate 80 adsorption results for the various tested filter types and formats.

Table 3: *Summary of Polysorbate 80 Adsorption Across Various Filter Types and Formats*

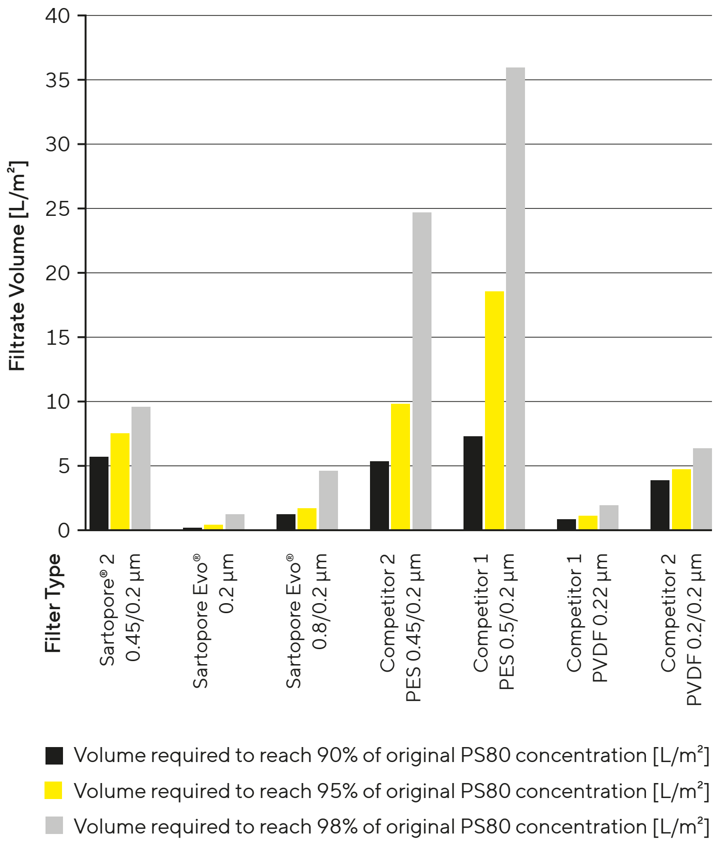
Filter Type	Material	Flat Filter Disc Screening Device [mg/m²]	Pilot-Scale Filter [mg/m²]
Sartopore® 2 0.45 | 0.2 µm	PES	291	146
Sartopore Evo® 0.8 | 0.2 µm	PES	63	66
Sartopore Evo® 0.2 µm	PES	37	36
Competitor 1 0.22 µm	PVDF	64	35
Competitor 1 0.5 | 0.2 µm	PES	363	453
Competitor 2 0.45 | 0.2 µm	PES	383	234
Competitor 2 0.2 | 0.2 µm	PVDF	147	191

Depending on the specific adsorption properties of each filter, a certain product volume is needed to recover the initial concentration of polysorbate 80 in the formulation. Figure 2 summarizes the filtrate volumes required to recover 90, 95, & 98% of the initial polysorbate 80 concentration for the pilot-scale (pleated devices) filters.

Due to their newly developed membrane surface modification, both Sartopore Evo® filter versions, the single and the double-layer filter, demonstrated exceptionally low polysorbate 80 adsorption. Consequently, the recovery of the initial polysorbate 80 concentration in the formulation was achieved after filtering very low product volumes. This is critical to assuring minimal product loss in commercial final formulation and filling operations.

This result was achieved regardless of whether the scale-up filters or the pilot-scale format was used, guaranteeing a smooth scale-up of the adsorption data generated in early filtration trials to pilot- and process-scale. The total adsorption was at 37 and 36 mg/m² membrane area for the Sartopore Evo® single-layer filter and 63 and 66 mg/m² membrane area for the Sartopore Evo® double-layer filter in the scale-up filter and pilot-scale formats, respectively (Table 3).

Figure 2: *Summary of the Product Volumes Required to Recover 90, 95, and 98% of the Initial Polysorbate 80 (PS80) Concentration in the Formulation (Pilot-Scale Filters)*

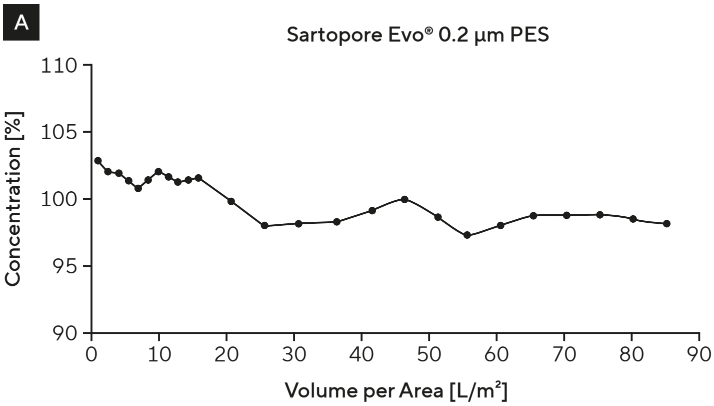


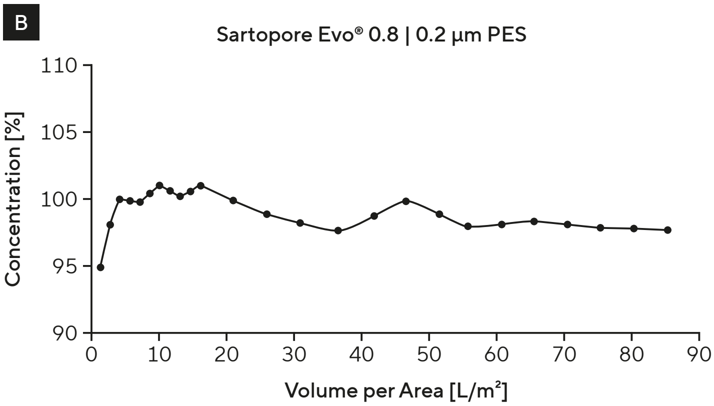
Only Competitor 1 (a PVDF single-layer filter) showed similar polysorbate 80 adsorption properties compared to the Sartopore Evo® filters, with a total polysorbate 80 adsorption of 64 and 35 mg/m² membrane area in the scale-up filter and pilot-scale formats, respectively (Table 3).

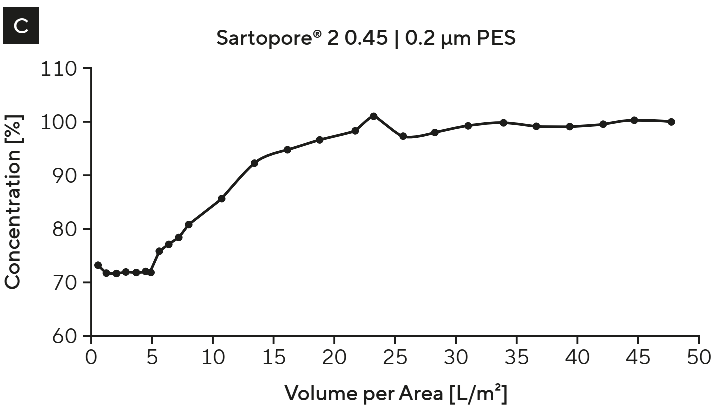
Polysorbate 80 adsorption, and consequently, the product volumes required to recover the initial concentration of polysorbate 80 in the formulation, were considerably higher in the other PES filters and the second PVDF filter, compared to the Sartopore Evo® filters.

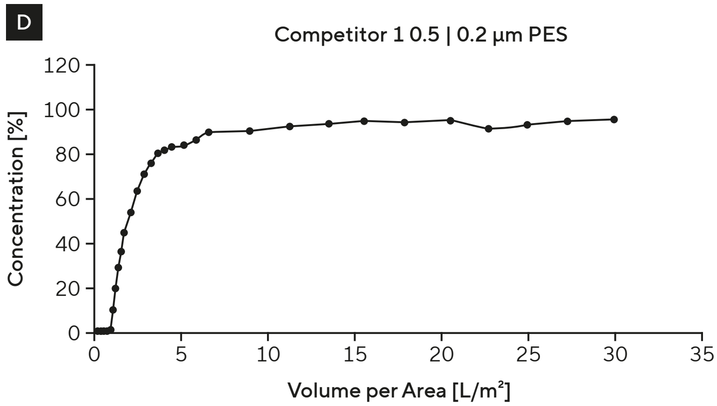
Figures 3 and 4 illustrate the specific adsorption profiles depicting the relationship between the relative concentration of polysorbate 80 in the filtrate (compared to 0.1 mg/mL in the starting solution) and the volume filtered per filter area (L/m²) for the individual scale-up and lab | pilot-scale filters. The more linear adsorption profiles of larger filter formats (Figure 4) can be attributed to their different volume-to-surface area ratios, which promote a more uniform flow distribution and improved contact between the filter medium and the solution.

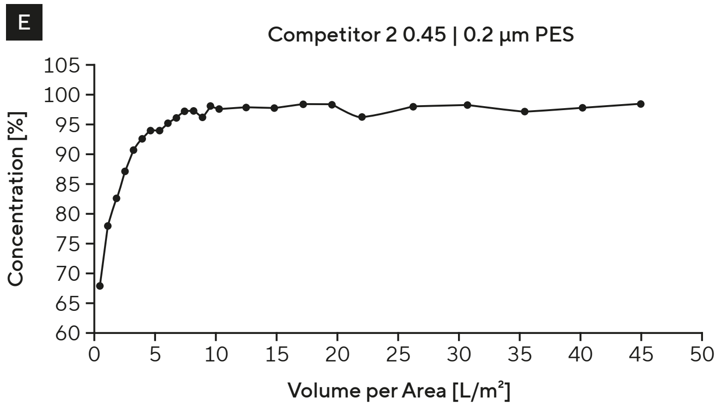
Figure 3: *Polysorbate 80 Adsorption Profiles for PES and PVDF Filter Membranes in Flat Filter Disc Screening Devices (17–20 cm²)*

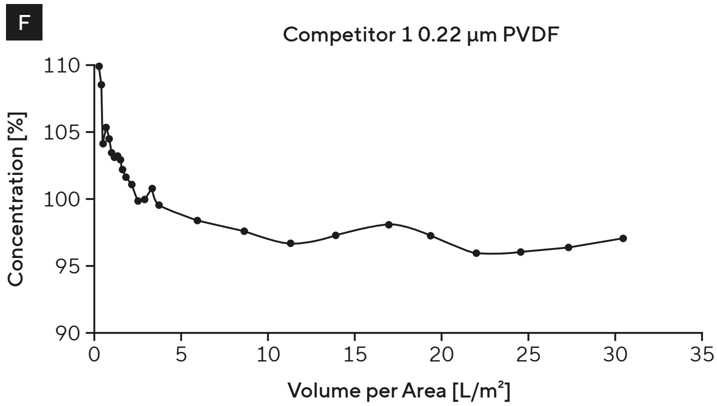


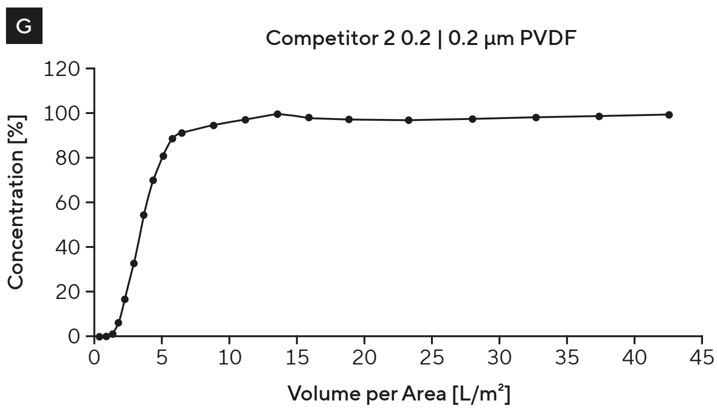






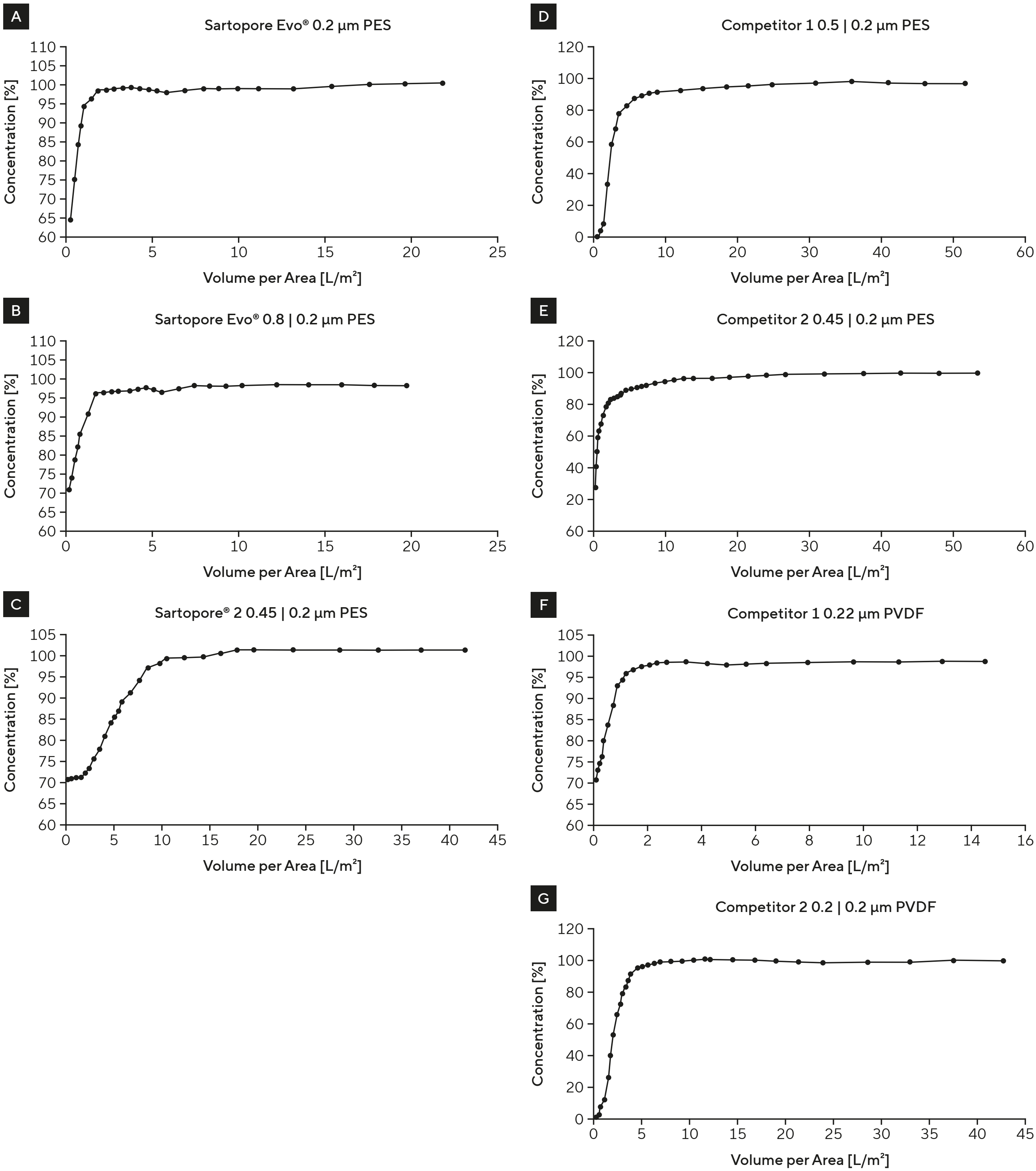






Note. (A–G) Individual membrane adsorption properties

Figure 4: *Polysorbate 80 Adsorption Profiles for PES and PVDF Filter Membranes in a Pleated Pilot-Scale Format (200–900 cm²)*



Note. (A–G) Individual membrane adsorption properties

Discussion

The potential ban of PFAS polymer-based membranes, such as PVDF, necessitates identifying alternative filter materials with minimal adsorptive properties for formulation and final filling in biopharmaceutical processes.

This comprehensive comparison of PES and PVDF filters revealed substantial differences in polysorbate 80 adsorption, highlighting the critical role of individual membrane surface modification over polymer class in determining a membrane's suitability for sterile filtration during final formulation and filling.

Notably, the Sartopore Evo® single- and double-layer PES filters exhibited low polysorbate adsorption, comparable to Competitor 1 PVDF 0.22 µm membrane filters. Consequently, a fast recovery of the initial polysorbate concentration in the filtered formulation is achieved, minimizing potential product loss in a commercial filling operation. In addition to low adsorptive properties, the consistent polysorbate 80 adsorptions between scale-up and lab- | pilot-scale formats support efficient scaling with Sartopore Evo® in biopharmaceutical production.

Conclusion

Sartopore Evo®, with its modified PES surface, combines excellent filtration capacity and flow rates with low polysorbate 80 adsorption. These properties position Sartopore Evo® as a competitive, PFAS-free alternative to PVDF-based membrane filters for reliable and efficient final sterile filtration of protein-based products.

While this application note focuses on Polysorbate 80 adsorption data, additional data is available for other excipients such as Polysorbate 20 and Poloxamer 188 as well as protein binding (e.g., monoclonal antibodies) in actual product formulations, confirming the general low binding properties of Sartopore Evo®.

References

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