Millipore®
Preparation, Separation,
Filtration & Testing Products

Application Note

Sterile Filtration of Ophthalmic Solutions

Abstract

Liquid ophthalmic products include a wide variety of formulations for cleaning and storing contact lenses, eye washes, and drops, as well as many therapeutic treatments. All ophthalmic products must meet a number of requirements for safety and efficacy that include certification of sterility. Sterility is defined as the absence of viable microbial contamination which, if present in such formulations, could result in infections of the eye with possible serious consequences.

The preferred method to achieve sterility of ophthalmic preparations is sterile filtration. By this method, the finished preparation is passed through a sterilizing-grade membrane during fill of the final (presterilized) product container. The membrane filter in this application must not only meet established regulatory requirements for bacterial retention, but must also satisfy industry specifications for cleanliness (extractables, pyrogenicity), chemical compatibility, reliability, and process efficiency.

Introduction

Ophthalmic solutions of many types are packaged in multiple-dose containers, and a bacteriostatic preservative agent is generally added to reduce the risk of inadvertent bacterial contamination with repeat open-air exposure. Common preservatives used include benzalkonium chloride (BAK), paraben, potassium sorbate, chlorhexidine acetate, chloroscresol, and polyhexamine gluconate.

These preservatives will, to varying degrees, bind or be adsorbed onto many common membrane filter materials. The degree of adsorption depends on both the preservative and the chemical composition of the filter (membrane polymer, surface chemistry, support materials, etc.). The uptake of preservative by the filter is highest at the start of filtration and diminishes with time according to the volume of product processed relative to the membrane area.

To ensure the proper amount of preservative is maintained in the final product, some initial portion of the filtered product is typically discarded until the membrane filter is conditioned or saturated with the preservative. Therefore, to maximize production yields, sterilizing-grade filters must minimize membrane-specific adsorptive losses of these preservatives as well as maximize throughput per surface area.

Benefits

- Sterile filtration is a preferred method to achieve sterility of opthhalmic preparations
- Millipore Express® SHF filters provide sterilizing-grade performance with superior economy and efficiency
- Millipore Express® SHF membrane for high-flux, low inherent preservative binding
- Up to 2½ times the flow rate of competitive filters
- Lowest BAK binding of comparable test membranes

Millipore Express® SHF Filters for Superior Efficiency and Economy

Milipore Express® SHF filters are designed for cost-effective aseptic processing of aqueous based pharmaceuticals. They contain a patented, composite, asymetric polyethersulfone (PES) membrane that provides both high flux and sterility assurance.

Experimental Conditions and Results

The high flux of Millipore Express® SHF filters can mean substantial savings in sterile filtration costs for manufacturers of ophthalmic products. In a competitive comparison (Figure 1), Millipore Express® SHF filters achieved up to 2½ times the throughput of competitive filters.

In addition, a series of filtration tests were conducted to evaluate the preservative binding of various sterilizing-grade membranes. Eye wash product containing 0.01% Benzalkonium chloride (BAK) was chosen as a model test solution.

The test membranes were all 0.2 µm sterilizing-grade, and composed of either PES or polyvinylidene difluoride (PVDF). Aliquots of the filtered eye wash were collected at several incremental process volumes and analyzed for BAK content.

The test results (Figure 2) show that Millipore Express® SHF membrane demonstrated the lowest BAK binding. Of all filters tested, these filters had the highest levels of BAK in small volumes of filtrate, and were the first to reach a point of minimal BAK removal.

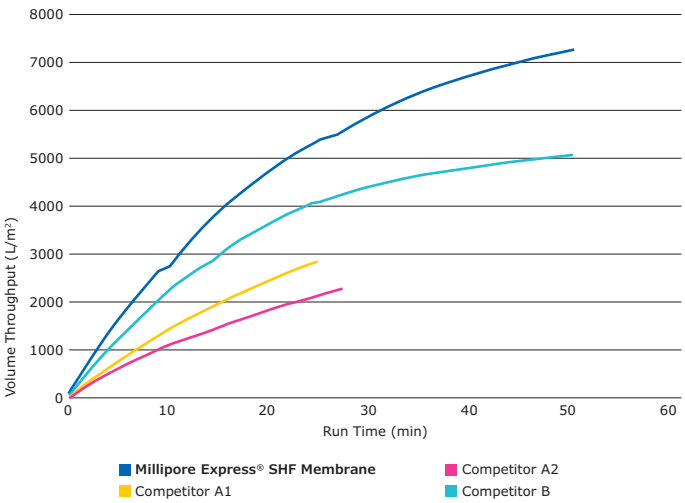

Figure 1. Contact Lens Solution Competitive Sterile Filtration Tests: 0.2 µm Membrane

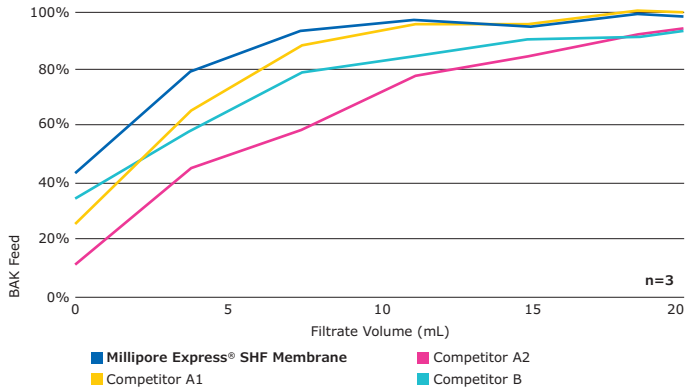

Figure 2. BAK Concentration in Filtrate of Millipore Express® SHF and Competitive Filters

Assuming a minimum performance requirement of 95% BAK passage, the nearest competitor would require more than 10% additional flush volume or lost product. For most other competitive membranes, product losses could be more than double that of Millipore Express® SHF membrane.

Conclusion

The combined benefits of low inherent preservative binding and high throughput per unit area make Millipore Express® SHF filters the ideal choice for the sterile filtration of ophthalmic solutions.

Merck KGaA
Frankfurter Strasse 250,
64293 Darmstadt, Germany

To Place an Order or Receive Technical Assistance

Please visit **MerckMillipore.com/contactPS**
For additional information, please visit **MerckMillipore.com**

AN1575EN00 Ver. 2.0
35681
05/2021