WHITE PAPER

EFFECTIVE LOW VOLUME FILTER WETTING FOR INTEGRITY TESTING

PROPOR sterilizing grade filters

Parker

LUCY ANGUS

Lucy Angus is a Technical Support Scientist at Parker Bioscience Filtration, United Kingdom. Lucy is focused on providing technical support to assist customers in the application and optimization of filtration products. Lucy is an active member of Parker's PUPSIT optimization team.

1. INTRODUCTION

Efficient filter wetting for integrity testing is critical to achieving a first-time pass. In single-use systems, this may be even more important if there is a limited amount of wetting fluid or capacity for fluid waste. One method of ensuring the filter is fully wet is a pressure hold and this study explores the required pressure and hold time to efficiently wet Parker's range of sterilizing grade PROPOR filters.

The latest revision of EU GMP Annex 1, Manufacture of Sterile Medicinal Products, means Pre-Use, Post Sterilization Integrity Testing (PUPSIT) is a default expectation. For many manufacturers, this has meant introducing a new step at the start of their process.

Filter wetting is a key component of getting this step right to avoid delays to processing time and unnecessary wastage of filters and single-use systems due to false fails.

It is equally important to avoid false fails in the post-use test that will result in time-consuming and costly investigations, as well as a delay to product release.

The object of wetting is to ensure the pore structure of the filter membrane is fully wetted to prevent gas flow through dry areas that may impact the integrity test outcome, i.e. false failures.

Wetting is typically performed with water, a preconditioning buffer or product.

Typically filter vendors provide integrity test parameters based on water wetting. For other fluids, parameters are determined through correlation to the water wet values, using methods described in ISO 13408 part 2 or PDA Technical report 26.

Parker's PROPOR range of sterilizing grade filters

2. TEST METHOD

A full factorial experiment was conducted to determine the optimum pressure and time to effectively wet a sterilizing grade filter with water. Optimum settings were used with a model biological fluid to determine if the results were transferable.

Parker PROPOR HC 0.2 micron polyethersulfone (PES) sterilizing grade filters were selected for testing as these filters represent a worst case incorporating two layers of membrane that must be wet.

To perform the wetting trial 10 inch PROPOR HC filter cartridges were placed in a stainless steel housing. A valve on the outlet of the housing was closed and the housing filled with water using a SciLog FilterTec™ peristaltic pump. The housing upstream vent valve was opened until all the air was vented from the housing.

The SciLog FilterTec™ was set to produce a pressure of 0.5 barg for 1 minute. The system was depressurized, and the downstream valve opened. A Porecheck 4 automated integrity tester (AIT) was connected, and a diffusional flow integrity test performed using PROPOR HC test parameter: 2.8 barg test pressure and a maximum diffusional flow 18mL/min.

After integrity testing, the filter was dried in an oven until it returned to its dry weight.

Tests were repeated in a full factorial design of experiment, using the factors and levels detailed in Table 1.

To determine if the optimum results would be effective with a biological fluid, a model fluid was produced with 10g/L protein solution in deionized water

Factors	Levels
Time (mins)	1, 3, 5, 7, 10
Pressure (barg)	0.5, 1, 2

Table 1: Experiment factor and levels

3. RESULTS

An increase of both pressure and time caused a reduction in the filter diffusional flow results, indicating improved wetting effectiveness.

The wetting times and pressures are shown in Table 2, with the diffusional flow results.

A pressure of 1 barg and a time between 3 and 5 minutes significantly reduced diffusion. Increasing the pressure or time further was less impactful.

The simulated biological fluid wetting trail was conducted with a time of 3 minutes and pressures of 1 and 2 barg, as shown in Table 3.

The higher pressure trial yielded a better result, however, both results were significantly lower than the diffusional flow limit, indicating the effectiveness of the method.

Time (min)	Pressure (barg)	DF limit (ml/min)	DF result (ml/min)	Pass/ Fail
1	0.5	18	24.5	Fail
1	1	18	17.6	Pass
1	2	18	9.8	Pass
3	0.5	18	20.6	Fail
3	1	18	8.8	Pass
3	2	18	9.8	Pass
5	0.5	18	17.6	Pass
5	1	18	5.8	Pass
5	2	18	5.8	Pass
7	0.5	18	8.8	Pass
7	1	18	6.8	Pass
7	2	18	7.8	Pass
10	0.5	18	9.8	Pass
10	1	18	8.8	Pass
10	2	18	9.8	Pass

Table 2: Water wetting experiments

Time (min)	Pressure (barg)	DF limit (ml/min)	DF result (ml/min)	Pass/ Fail
3	1	28.8	15.7	Pass
3	2	28.8	9.8	Pass

Table 3: Simulated biological fluid wetting experiments

4. CONCLUSION

The pressure hold method of wetting out the Parker PROPOR range of polyethersulfone membrane filters has been shown as an effective means of achieving a fully wet filter with a low volume of fluid.

A hold pressure between 1 and 2 barg and a time of 3 to 5 minutes were observed to effectively wet filters in water and a simulated biological fluid. Increasing the pressure and time further is likely to have diminishing results but this should be evaluated in the sterilizing filtration validation process.

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