

Bubble point ratio determination for Vesphene® IIs (1:128)

Method using Durapore® 0.22 µm hydrophilic membrane and ultrapure water

The objective of these trials was to determine a recommended Bubble Point Ratio value for the Durapore® 0.22 µm hydrophilic membrane with Vesphene® IIs cleaner/disinfectant (1:128).

Background

Post use testing of sterilizing-grade membrane filters is a fundamental and regulatory requirement of sterility assurance. Bubble point testing is one of the recommended test procedures. Bubble point specifications are given for a standard wetting fluid, such as water for hydrophilic filters, or a type and concentration of alcohol for hydrophobic filters. However, it is not always possible or practical to test the filter with the standard fluid. If the filter is wet with a fluid other than the standard specified fluid, the minimum bubble point for the wetting fluid needs to be determined.

From controlled laboratory trials, Bubble Point Ratio (BPR) was determined between a reference fluid, test gas and product solution. The experimentally determined ratio are then used to calculate the bubble point limit for the Durapore® 0.22µm hydrophilic membrane. This scientific approach is derived from PDA technical report n°26. Calculated limits are valid for assessing the integrity of a filter used in a critical process.

Bubble point ratio between purified water and Vesphene® IIs solution was determined for 47 mm membrane discs at 22 ± 4 °C, using air as the test gas. As the bubble point phenomenon is independent from the nature of the gas, the determined ration is valid whatever the test gas used.

Materials

Durapore® 0.22 µm modified PVDF hydrophilic membrane, 47 mm discs

- (Catalogue No. GVWP04700)
- Bubble point specification with purified water = 50.0 psi
- Surface area = 13.8 cm²

Automatic filter integrity test instrument

- (Catalogue No. XEIT11000)
- Used to determine bubble point values.

Stainless steel holder

- (Catalogue No. XX4404700)
- Used to hold the 47 mm membrane discs.

Millipore Milli-Q® Ultrapure Water Purification System

- Used to produce purified water with ASTM Type I quality grade.

Vesphene® IIs cleaner/disinfectant

- The tested solution was Vesphene® IIs diluted to 1:128 (v/v) with purified water

Compressed air

Bubble Point Test Method

1. The membrane disc was thoroughly wetted with ultrapure water.
2. Thorough wetting ensured by filtration of 5 mL of water at ambient temperature.
3. The system was immediately connected to the Integrity tester; bubble point program initiated.
4. The bubble point measurement was repeated after membrane rewetting with an additional 5 mL of water.
5. The membrane disc was dried thoroughly for a minimum of 16 hours.
6. The membrane disc was reinstalled in the holder.
7. Membrane wetting ensured by filtering 5 mL of the Vesphene® Iise (1:128 (v/v)) test product.
8. The system was immediately connected to the Integrity tester; bubble point program initiated.
9. The bubble point measurement was repeated after membrane rewetting with 5 mL of fresh Vesphene® Iise (1:128) test product.
10. The bubble point measurement was repeated until a stable result was found (< 1.0 psi variation between 3 consecutive bubble point readings).

Results

The bubble point test results were obtained via a series of tests with 9 different Durapore® 47 mm membrane discs; 3 each for 3 different lots of Vesphene® Iise (1:128) test product. The highest stable values of the tests performed on each membrane disc are the bubble point. The results obtained with the Milli-Q ultrapure water agreed with the specifications of the filter device and confirmed the integrity of the different membranes tested.

Conclusion

Bubble Point Determination

The data from the Durapore® 47 mm membrane discs are used to determine the Bubble Point Ratio (BPR) between the test product and ultrapure water. The Bubble Point Ratio can be used to determine the minimum product bubble point value for Durapore® 0.22 µm hydrophilic membranes.

The average of all the theoretical calculations of BPR are used to determine the minimum BPR value:

$$\text{BPR} = \frac{\text{Product Bubble Point}}{\text{Water Bubble Point}} = \frac{33.6}{55.0} = 0.61$$

The minimum bubble point value of the Durapore® 0.22 µm hydrophilic membrane disc wetted with the Vesphene® Iise (1:128) solution will be:

$$\text{BP}_{\text{min}} = 50 \text{ psi} \times 0.61 = 30.5 \text{ psi}$$

Vesphene® Iise (1:128) solution can be used as a wetting agent to perform the Bubble Point Integrity Test. The recommended Minimum Product Bubble Point can be used as an initial specification until the validation process is completed. See discussion below.

Discussion

All Durapore® 0.22 µm hydrophilic membrane configurations (e.g. GVWP, KVGL, MPGL, MCGL, LAGL and CVGL) have the same Bubble Point Ratio (membrane consistency) when they are wetted with the same test product. All of this depends on the uniformity of product. Changes in formulation or concentrations of the components, especially those with surface activity and effects on surface tension, can affect the Bubble Point Ratio.

In PDA Technical Report No. 26, "Sterilizing Filtration of Liquids", it is suggested that a scale-down study is only the first part of product bubble point validation. The second part is obtaining additional ongoing product attribute data. We recommend that the end-user verify the lab generated minimum product bubble point with on-site verification or periodic process monitoring.

We have developed a technical guidance document (Lit. No AN1505EN00) for on-site bubble point ratio determination. This document is available upon request.

Remarks

Note that Water Bubble Point specifications for our membranes are based upon data we developed from testing using ultra-clean water under controlled testing conditions. Bubble point and diffusion testing on specific test products are based upon limited testing and may not be statistically representative of all test products. Variability in customer product, customer operating conditions, and environmental conditions may have some impact on the bubble point values. For these reasons, we do not guarantee that the results of these tests are statistically relevant beyond the scope of this report.

Bubble Point Data

Disc No.	Product Lot No.	Water Bubble Point	Product Bubble Point	Bubble Point Ratio
1	1	55.2	32.1	0.58
2	1	54.2	32	0.59
3	1	55.2	32.1	0.58
4	2	55.1	34.1	0.62
5	2	56.2	35.1	0.62
6	2	56.1	34.1	0.61
7	3	54.2	34.1	0.63
8	3	54.2	35.1	0.65
9	3	54.2	34.1	0.63
Overall Mean		55.0	33.6	0.61
Overall S. D.		0.8	1.3	0.02
Overall C.V.		1.5	3.9	3.3

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Merck KGaA
Frankfurter Strasse 250
64293 Darmstadt, Germany

