

Bubble Point Test Method Using Durapore® 0.45 µm Hydrophilic Membrane with 70/30 IPA

The objective of these trials was to determine a recommended Bubble Point Ratio value for the Durapore® 0.45 µm hydrophilic membrane wetted with 70/30 IPA

Background

Post use testing of 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 alcohol solution. The experimentally determined ratios are then used to calculate the bubble point limit for the Durapore® 0.45µm 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.

BPR between purified water and IPA 70/30 solution was determined for 47 mm membrane discs at 22 ± 4 °C, using nitrogen as the test gas. As the bubble point phenomenon is independent from the nature of the gas, the determined ratio is valid whatever the test gas used.

Important safety note: The use of alcohol mixture creates safety concerns due to its flammable nature. It is therefore advisable to use Nitrogen for filter integrity tests with alcohol wetted filters. Consult your local EHS department for alcohol mixture utilization and safety measures on your premises.

Materials

Durapore® 0.45 µm modified PVDF hydrophilic membrane, 47 mm discs

- (Catalogue No. HVMP 047 00)
- Bubble point specification with purified water = 28 psig
- Surface area = 13.8 cm²

Automatic filter integrity test instrument

- (Catalogue No. XEIT 110 00); used to determine bubble point values.

Stainless steel holder

- (Catalogue No. XX44 047 00); used to hold the 47 mm membrane discs.

Millipore Milli-Q® Synthesis A-10™ Water Purification System

- Used to produce purified water with ASTM Type 1 quality grade

70/30 IPA

- Isopropyl alcohol/purified water 70/30 mixture (v/v)

Nitrogen

Bubble Point Test Method

1. The membrane disc was thoroughly wetted with Milli-Q water.
2. Thorough wetting ensured by filtration of 105 mL of Milli-Q 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 fresh Milli-Q water.
5. The bubble point measurement was repeated until a stable result was found (≤ 1.0 psig variation between 3 consecutive bubble point readings).
6. The membrane disc was dried thoroughly for a minimum of 2 hours.
7. The membrane disc was reinstalled in the holder.
8. Membrane wetting ensured by filtering 5 mL of the 70/30 IPA test product.
9. The system was immediately connected to the integrity tester; bubble point program initiated.
10. The bubble point measurement was repeated after membrane rewetting with 5 mL of fresh 70/30 IPA test product.
11. The bubble point measurement was repeated until a stable result was found (≤ 1.0 psig variation between 3 consecutive bubble point readings).
12. Steps 1–11 were repeated for discs 2–9.

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 lab scale compositions of 70/30 IPA test product. The highest stable values of the tests performed on each membrane disc are the bubble point. The results obtained with Milli-Q 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 Milli-Q water and 70/30 IPA. The Bubble Point Ratio can be used to determine the minimum product bubble point value for Durapore® 0.45µm hydrophilic membrane. The average of all the theoretical calculations of BPR are used to determine the minimum BPR value.

$$\text{BPR} = \frac{\text{(70/30 IPA Bubble Point)}}{\text{(Milli-Q Water Bubble Point)}} = \frac{12.8}{34.0} = 0.38$$

The minimum bubble point value of the Durapore® 0.45µm hydrophilic membrane disc wetted with 70/30 IPA will be:

$$\text{BP}_{\text{min}} = 28.0 \text{ psig} \times 0.38 = 10.6 \text{ psig}$$

The product (70/30 IPA) can be used as a wetting agent to perform the Bubble Point Integrity Test and 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® 0.45µm hydrophilic membrane configurations (e.g. LAHL, KPHL and CVHL) 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 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 of the 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.	Membrane Lot No.	Milli-Q® Water Bubble Point	70/30 IPA Bubble Point	BPR 70/30 IPA
1	R4EM58113	35.2	13.1	0.37
2	R4EM58113	35.1	13.1	0.37
3	R4EM58113	35.2	13.1	0.37
4	R7NM43964	33.1	13.1	0.4
5	R7NM43964	34.1	13.1	0.38
6	R7NM43964	34.1	13.1	0.38
7	R1BN88995	33.1	12.1	0.37
8	R1BN88995	33.1	12.1	0.37
9	R1BN88995	33.1	12.1	0.37
Overall Avg.		34.0	12.8	0.38
Overall S.D.		1	0.5	0.01
Overall C.V.		2.9	3.9	2.6

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