APPLICATION NOTE

Bubble Point Ratio Determination for Vesphene® IIse (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 IIse cleaner/ disinfectant, diluted 1:128 (v/v) and ultrapure water (ratio between product and water) at ambient temperature.

Materials

- **Durapore 0.22 µm modified PVDF hydrophilic membrane, 47 mm discs** (Catalogue No. GVWP04700)
  – Bubble point specification with ultrapure water = 50 psi
  – Surface area = 13.8 cm^2
- **Integritest® II automatic filter integrity test instrument** (Catalogue No. XEIT11000); used to measure bubble point values.
- **Stainless steel holder** (Catalogue No. XX4404700); used to hold the 47 mm membrane discs.
- **Stainless steel 1.5 in. sanitary tee fitting;** used between the Integritest II instrument and the 47 mm holder to provide expanded upstream volume.
- Millipore **Milli-Q® Ultrapure Water Purification System**; used to produce 18.2 megohm-cm water.

Bubble Point Test Method

1. The membrane disc was thoroughly wetted with ultrapure water.
2. Thorough wetting was ensured by filtration of 5 mL of water at ambient temperature.
3. The system was immediately connected to the Integritest II instrument and the 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. The membrane wetting was ensured by filtering 5 mL of the Vesphene IIse (1:128 (v/v)) test product.
8. The system was immediately connected to the Integritest II instrument and the 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 considered to be the bubble point. The results obtained with the Milli-Q ultrapure water were in agreement with the specifications of the filter device and confirm the integrity of the different membranes tested.

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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:

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

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

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

The product 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 0.22 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, of course, 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. Millipore recommends that the end-user verify the lab generated minimum product bubble point with on-site verification or periodic process monitoring.

There are several options for on-site verification including:

- Periodically monitoring the product Bubble Point Ratio by comparing pre-use water bubble points with post-use product bubble points. A Millipore protocol for on-site Bubble Point Ratio determination is available; request AN1505EN00.
- Periodically monitoring product surface tension and comparing to standard.
- Trending product bubble point results for consistency.
- End-user determined process specific testing.

Remarks

It should be noted that Water Bubble Point specifications for Millipore membranes are based upon data developed from extensive testing using ultra-clean water under controlled testing conditions.

Bubble point and diffusion testing on specific test product 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, Millipore does 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	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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