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Application Note

# Integrity testing Durapore® and Millipore Express® Filters

## Test limits with common alcohol solutions

Integrity test values for hydrophilic Durapore® and Millipore Express® membrane filters wet with water are listed in filter documentation. However, in many bioprocessing applications sterilizing filters are wet with low surface tension fluids, such as alcohol solutions. These solutions are used for cleaning, flushing, and wetting during troubleshooting steps. The surface tension of an alcohol solution is lower than that of an aqueous product, and can improve filter wetting while negating the impact of surface active compounds, such as polysorbate, on the filter. For alcohol wetted filters, it is generally recommended to use nitrogen as the test gas for filter integrity testing.

The purpose of this document is to provide filter integrity test (FIT) limits for hydrophilic Durapore® and Millipore Express® membrane filters when wet with alcohol solutions.

### Methods

Diffusion and bubble point ratios were determined between a reference fluid, test gas and alcohol solutions in controlled laboratory studies.

Diffusion and bubble point ratios between purified water and various isopropyl alcohol (IPA) solutions were determined using 10-inch (25 cm) cartridge filters. All tests were performed at 22 ± 4 °C, using both air and nitrogen as the test gas.

The bubble point is independent of the filter size and identical with air and nitrogen, therefore only one ratio is reported.

These experimentally determined ratios were used to calculate the bubble point and diffusion limits for a particular filter size. This scientific approach is described in PDA Technical Report No 26[1].

These calculated limits can then be used for assessing the integrity of a filter used in a critical process.

**Why use filter integrity test ratios and calculations for diffusion?**

Given the extended portfolio of filter formats, sizes, and areas, it is most practical to share membrane specific invariant coefficients that can be used to calculate your specific FIT limits.

[1] PDA Technical Report No. 26 (TR26) Revised 2008, Sterilizing Filtration of Liquids.

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## Filters Containing Hydrophilic Durapore® Membranes

**Table 1** lists the experimentally determined bubble point and diffusion ratios between a reference fluid, test gas and alcohol for filters containing hydrophilic Durapore® 0.22 µm and 0.1 µm membrane.

Additional information on bubble point testing Durapore® filters with alcohol solutions is available in Application note AN1422EN00: Bubble point test method using Durapore® 0.22 µm hydrophilic membrane with 60/40 IPA.

**Table 1. Bubble point and diffusion ratios for filters containing Durapore® membrane.**

| Membrane | Wetting Fluid (v/v) | BPR[1] | Minimum Bubble Point[2] | Air DR[3] | Nitrogen DR |
|---|---|---|---|---|---|
| **Durapore® 0.22 µm** | IPA 70/30 | 0.370 | 1280 mbar (18.5 psi) | 0.930 @ 1.0 bar (15 psi) | 0.810 @ 1.0 bar (15 psi) |
| | IPA 60/40 | 0.388 | 1340 mbar (19.4 psi) | 0.580 @ 1.0 bar (15 psi) | 0.528 @ 1.0 bar (15 psi) |
| **Durapore® 0.1 µm** | IPA 70/30 | 0.390 | 1880 mbar (27.3 psi) | 0.913 @ 1.5 bar (22 psi) | 0.742 @ 1.5 bar (22 psi) |
| | IPA 60/40 | 0.400 | 1930 mbar (28.0 psi) | 0.516 @ 1.5 bar (22 psi) | 0.506 @ 1.5 bar (22 psi) |

[1] BPR: Bubble Point Ratio = Bubble point $_{\text{alcohol solution}}$/Bubble point $_{\text{water}}$

[2] Applicable for both air and nitrogen of all filter sizes

[3] DR: Diffusion Ratio = Diffusion $_{\text{alcohol solution @ test pressure}}$/ Diffusion $_{\text{water @ standard test pressure}}$

## Calculating Integrity Test Limits

The example below is for a 5-inch cartridge filter containing hydrophilic Durapore® 0.22 µm membrane.

**Product documentation lists:**

- The minimum air water bubble point is 3450 mbar (50.0 psi).
- The maximum diffusion limit is 6.6 mL/min with air at 2.8 bar (40 psi).

**Filter integrity test limits for each alcohol solution or filter size combination can be calculated as follows:**

- The minimum bubble point, or minimum limit for each alcohol solution is listed in **Table 1**.
- The diffusion limit for each alcohol solution is derived from diffusion specification listed in the product documentation multiplied by the air or nitrogen diffusion ratio for the new test fluid, listed in **Table 1**.
- Maximum diffusion limits should be rounded to the nearest tenth (e.g. 2.55 is rounded to 2.6 mL/min).

maximum **Diffusion** $_{\textbf{air}\ \text{IPA 60/40 @ 1.0 bar}}$ = maximum Diffusion $_{\textbf{air}\ \text{water @ 2.8 bar}}$ x air DR

= 6.6 mL/min x 0.580

= 3.8 mL/min @ 1.0 bar (15 psi)

maximum **Diffusion** $_{\textbf{nitrogen}\ \text{IPA 60/40 @ 1.0 bar}}$ = maximum Diffusion $_{\textbf{air}\ \text{water @ 2.8 bar}}$ x nitrogen DR

= 6.6 mL/min x 0.528

= 3.5 mL/min @ 1.0 bar (15 psi)

## Filters Containing Millipore Express® Membranes

Millipore Express® membrane filters have limited compatibility with organic solvents and can only be wetted with alcohol post-use for final integrity evaluations before the filter is discarded.

**Table 2** lists the experimentally determined bubble point and diffusion ratios between a reference fluid, test gas and alcohol for filters containing hydrophilic Millipore Express® SHF or SHC membranes.

**Table 2. Bubble point and diffusion ratios for filters containing Millipore Express® membranes.**

| Membrane | Wetting Fluid (v/v) | BPR[1] | Minimum Bubble Point[2] | Air DR[3] | Nitrogen DR |
|---|---|---|---|---|---|
| **Millipore Express® SHF (0.2 µm)** | IPA 70/30 | 0.321 | 1280 mbar (18.5 psi) | 0.818 @ 0.9 bar (13 psi) | 0.649 @ 0.9 bar (13 psi) |
| | IPA 60/40 | 0.347 | 1390 mbar (20.1 psi) | 0.476 @ 1.0 bar (15 psi) | 0.445 @ 1.0 bar (15 psi) |
| **Millipore Express® SHC (0.5/0.2 µm)** | IPA 70/30 | 0.321 | 1280 mbar (18.5 psi) | 0.729 @ 0.9 bar (13 psi) | 0.677 @ 0.9 bar (13 psi) |
| | IPA 60/40 | 0.348 | 1390 mbar (20.2 psi) | 0.491 @ 0.9 bar (13 psi) | 0.433 @ 0.9 bar (13 psi) |

[1] BPR: Bubble Point Ratio = Bubble point $_{\text{alcohol solution}}$/Bubble point $_{\text{water}}$

[2] Applicable for both air and nitrogen and all filter sizes

[3] DR: Diffusion Ratio = Diffusion $_{\text{alcohol solution @ test pressure}}$/ Diffusion $_{\text{water @ standard test pressure}}$

## Calculating Integrity Test Limits

The example below is for a 5-inch cartridge filter containing Millipore Express® SHC (0.5/0.2 µm) membrane.

**Product documentation lists:**

- The minimum air water bubble point is 4000 mbar (58.0 psi).
- The maximum diffusion limit is 13.3 mL/min with air at 2.8 bar (40 psi).

**Filter integrity test limits for each alcohol solution or filter size combination can be calculated as follows:**

- The minimum bubble point, or minimum limit for each alcohol solution is listed in **Table 2**.
- The diffusion limit for each alcohol solution is derived from diffusion specification listed in the product documentation multiplied by the air or nitrogen diffusion ratio for the new test fluid, listed in **Table 2**.
- Maximum diffusion limits should be rounded to the nearest tenth (e.g. 2.55 is rounded to 2.6 mL/min).

maximum **Diffusion** $_{\textbf{air}\ \text{IPA 60/40 @ 0.9 bar}}$ = maximum Diffusion $_{\textbf{air}\ \text{water @ 2.8 bar}}$ x air DR

= 13.3 mL/min x 0.491

= 6.5 mL/min @ 0.9 bar (13 psi)

maximum **Diffusion** $_{\textbf{nitrogen}\ \text{IPA 60/40 @ 0.9 bar}}$ = maximum Diffusion $_{\textbf{air}\ \text{water @ 2.8 bar}}$ x nitrogen DR

= 13.3 mL/min x 0.433

= 5.8 mL/min @ 0.9 bar (13 psi)

**Important**

Alcohol mixtures should be carefully handled due to their flammability.

It is recommended to use nitrogen for FIT with alcohol wetted filters.

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