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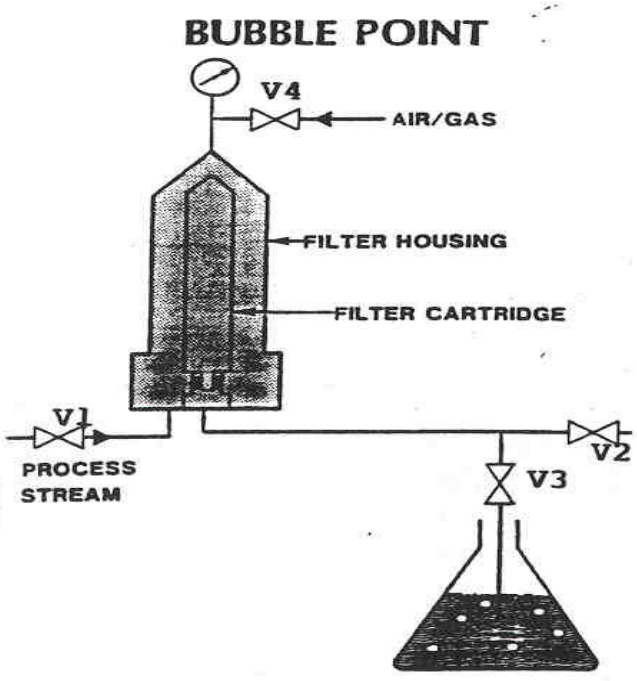
MANUAL
INTEGRITY TESTING PROCEDURES

Disclaimer: These procedures do not address the regulatory issues associated with manual integrity testing. The vast majority of pharmaceutical manufacturers use automated integrity test instruments such as the Palltronic® Flowstar, for effective batch record keeping.

1- BUBBLE POINT PROCEDURE

Pall membrane filters are validated for bacterial, removal efficiency (i.e. Titre Reduction or 'T_R') using the Forward Flow test. For critical applications the Bubble Point test is not recommended. Please consult Pall's SLS Department prior to selecting any integrity test.

Test is to be performed at ambient temperature (20°C +/- 5°C):



a) Filter(s) must be fully wet prior to performing test. This is achieved by flushing the assembly with ambient temperature water at approximately equal the normal process flow for ten minutes. The housing must be bled of air during the wetting period to ensure the entire length of the filter is completely wet. Failure to do so will result in false bubble point failure. Also, apply a small amount (approximately 5psi) of backpressure during the wetting stage by closing V2 slightly.

b) Completely drain the housing either by I) gravity or II) closing V1 and applying 10 psi of air pressure from V4.

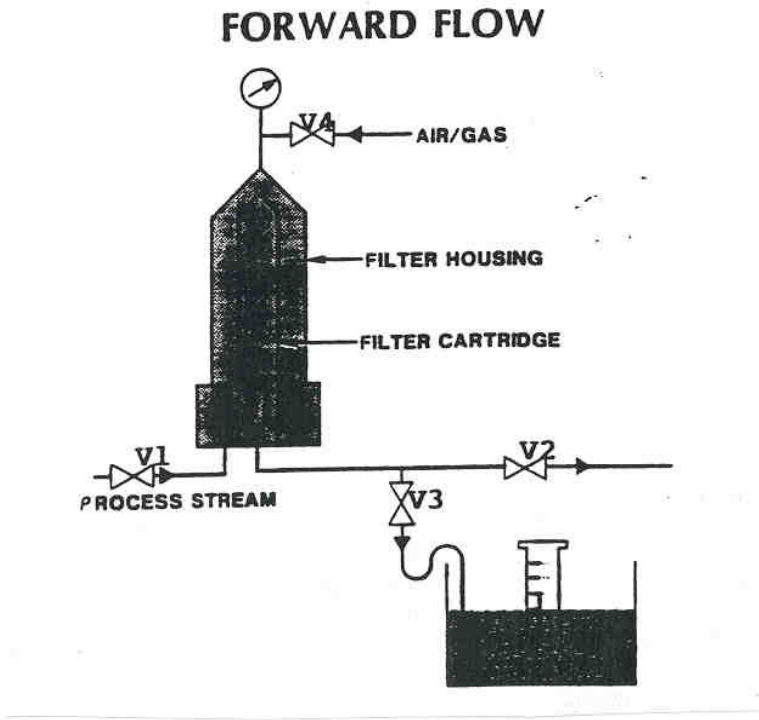
c) Close V1 and V2. Open V3. V3 should be connected via tubing to a reservoir (beaker, bucket, etc.) filled with water.

d) Slowly increase air pressure to upstream side of housing using V4 (or air pressure regulator). Carefully watch the submerged tube in the bucket and watch for a continuous stream of bubbles.

e) When a continuous stream of bubbles is seen, immediately read the pressure gauge on the upstream side of the housing. This pressure is the bubble point.

2- FORWARD FLOW (DIFFUSIONAL FLOW) TEST PROCEDURE

Test is to be performed at ambient temperature (20°C +/- 5°C):



a) Filter(s) must be fully wet prior to performing test. This is achieved by flushing the assembly with ambient temperature water at approximately equal the normal process flow for ten minutes. The housing must be bled of air during the wetting period to ensure the entire length of the filter is completely wet. Failure to do so will result in a false integrity test failure.

b) Completely drain the housing either by I) gravity or II) closing V1 and applying 10 psi of air pressure from V4.

c) Close V1 and V2. Open V3. V3 should be connected via tubing to a reservoir (beaker, bucket, etc.) filled with water.

NB: If system has been sterilized, special care must be taken to ensure that contamination does not enter the system via V3. In the case of a sterilized system, V3 should not be opened until 80% of the test pressure is reached.

d) Open V4 and bring upstream pressure to the required test pressure.

e) Wait 5 minutes for system to stabilize. This stabilization period is very important in performing a correct integrity test. Bubbles will be seen exiting from the tubing in the reservoir full of water. This is the diffusive or "Forward" Flow and must be quantitatively measured.

f) Submerge a graduated cylinder in the reservoir and allow all air to escape from it. Invert the cylinder while submerged.

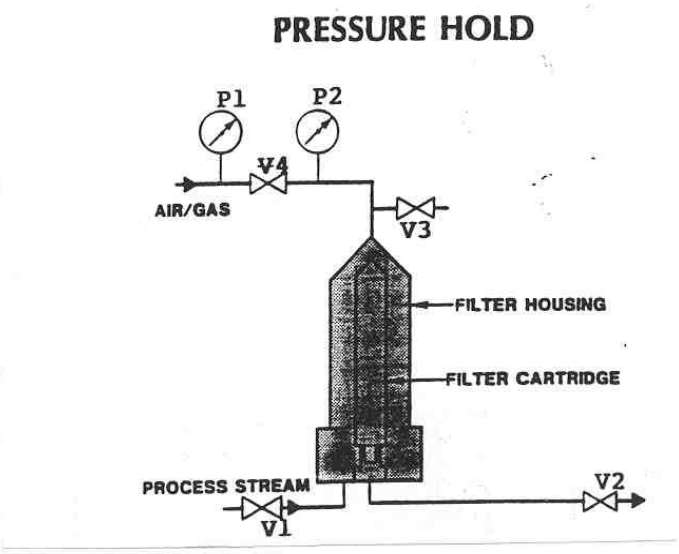
g) The volume of air escaping from the tubing is then measured. Place the tubing in the inverted graduated cylinder for a period of one minute. Measure the volume of air in the graduated cylinder after one minute. This is the Forward Flow. Check this value against the maximum allowable forward flow per Pall's literature or consult pall's Scientific and Laboratory Services (SLS) Department.

A more accurate measurement of Forward Flow is achieved when the volume of air is measured for two minutes, then divide by two; or for three minutes and divided by three, etc.

Please consult Pall's Scientific and Laboratory Services (SLS) Department with any questions.

3- FORWARD FLOW PRESSURE HOLD TEST PROCEDURE

Test is to be performed at ambient temperature (20°C ± 5°C):



(a) Filter(s) must be fully wet prior to performing test. This is achieved by flushing the assembly with ambient temperature water at approximately equal the normal process flow for ten minutes. The housing must be bled of air during the wetting period to ensure the entire length of the filter is completely wet. Failure to do so will result in false integrity test failures. Also, apply a small amount (approximately 5psi) of backpressure during the wetting stage by closing V2 slightly. **There is usually no need to drain the housing when performing the Pressure Hold test. Please consult Pall's Scientific and Laboratory Services (SLS) Department with any questions.**

(b) Close V1. Open V2. Apply air from V4 until P2 reads the appropriate test pressure.

(c) Allow the system to stabilize for five minutes. This stabilization period is very important in performing a correct integrity test.

(d) Close V4. Wait ten minutes.

(e) Read P2. Subtract this value from the test pressure to get the net pressure decay (DeltaP) over the ten minutes period. Compare this value with the maximum allowable DeltaP per Pall's specifications. **Since the Pressure Hold test measures pressure decay, air escaping from fittings, valves, etc. will also result in a pressure decay. Ensure that all upstream fittings, valves and housing seals are leak-free prior to performing a Pressure Hold Test.**