



Life Sciences

Application Note

USD2121a

Meeting Regulatory Requirements for Vent Filtration on Water For Injection (WFI) Tanks

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1. Introduction

Water systems for the production, storage and distribution of purified water or WFI remain critical points in pharmaceutical production plants. A key concern of regulatory authorities is the installed vent filter on high purity water-holding tanks. This document provides Pall's technical recommendations to meet current regulatory requirements and to ensure:

- ▶ Sterile protection of the tank utilizing Emflon® HTPFR or PFR vent filters
- ▶ Built-in drainage utilizing Pall Advanta™ liquid and gas filter housings
- ▶ Prevention of condensate utilizing Pall Advanta housing trace heaters
- ▶ Reliable water intrusion testing utilizing the Palltronic® AquaWIT filter integrity test system

2. Regulatory Guidelines

The FDA's Guide to Inspections of High Purity Water Systems (1993)*, recommends regular filter testing and prevention of condensate formation in vent filters on high purity water-holding tanks.

The guide states: *"VII. HOLDING TANK - In hot systems, temperature is usually maintained by applying heat to a jacketed holding tank or by placing a heat exchanger in the line prior to an insulated holding tank. The one component of the holding tank that generates the most discussion is the vent filter. It is expected that there be some program for integrity testing this filter to assure that it is intact. Typically, filters are now jacketed to prevent condensate or water from blocking the hydrophobic vent filter. If this occurs (the vent filter becomes blocked), possibly either the filter will rupture or the tank will collapse. There are methods for integrity testing of vent filters in place. It is expected, therefore, that the vent filter be located in a position on the holding tank where it is readily accessible..."*

In a similar manner, the European GMP Guide calls for regular testing of vent filters used in applications such as vents on water tanks. Additionally, the ASME Bioprocessing equipment guide (ASME BPE 2012) defines how equipment must be designed and installed to be classed as hygienic. Chapter SD-5.2.1 states that "...the filter housing shall be designed to allow for complete venting and draining. Liquid tee-type filter housings should be installed vertically, and vent type in-line filter housings should be installed vertically with the condensate/drain port directed downward". Furthermore it states: "Vent filters for hot process services should be heat traced or steam jacketed".

* <http://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074905.htm> accessed 5th October 2012

Figure 1A and Figure 1B show recommended arrangements for single/dual vent filter installations on hot WFI tanks.

Figure 1: System A

Vent filter installation for hot WFI tanks. A single installation without continuous use of the WFI tank during Water Intrusion Testing (WIT) of the vent filters

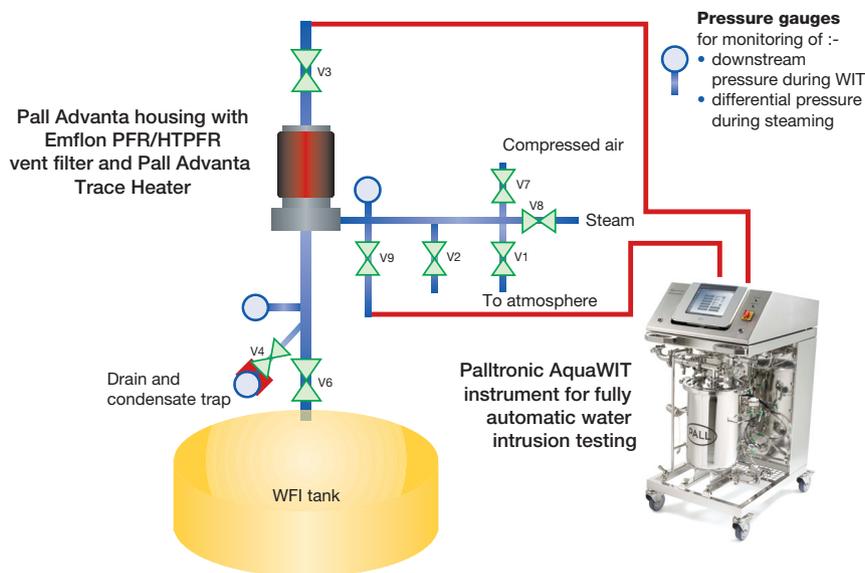
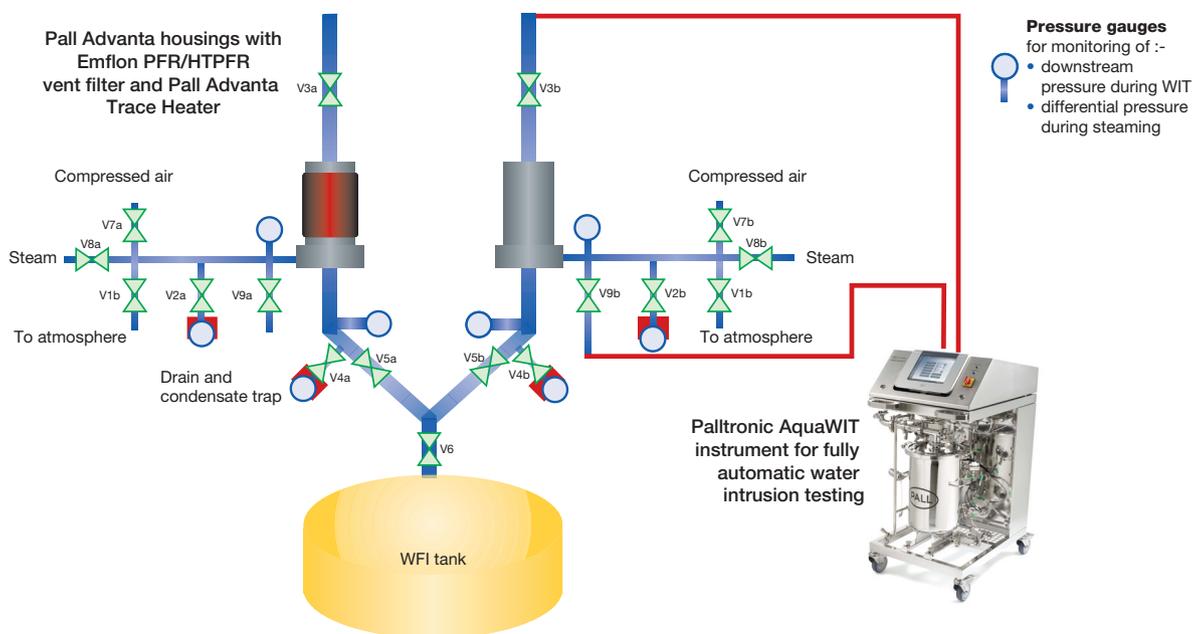


Figure 1: System B

Vent filter installation for hot WFI tanks. A double installation is recommended to allow continuous use of the WFI tank and Water Intrusion Testing (WIT) of the vent filters



3. Brief Description of System Operation

A dual system will operate with both or either of the vent filters in operation, and allows continuous operation of the WFI tank. A single system has only one vent filter in operation and therefore does not allow continuous operation of the WFI tank during steam sterilization and testing. An example of how a system might be operated is detailed below:

3.1 Steam Sterilization Of Filter Assemblies

This procedure is the same for System A or B, either of which can be steamed whilst the other is in operation. For a single system, the procedure described below can be used with slight modifications (without V5). System B only is described.

Normal Operation (see below) with Palltronic AquaWIT system disconnected from V3B and V9B:

- ▶ V6, V5A, V5B, V1A and V1B open
- ▶ Heat tracing on filter system to be steamed switched off (cool-down may take several hours)
- ▶ Close V5B and V1B
- ▶ Open V8B and V2B until steam emits, open V3B and V4B
- ▶ Partially close V4B, V3B and V2B
- ▶ Leave system to steam for required period
- ▶ The valves V1, V3 and V9 can also be remotely controlled from the Palltronic AquaWIT system to fully automate the test procedure

On Completion of Steaming:

- ▶ Close V4B, V3B, V2B, V8B and open V7B with a pressure of >200 mbar (2.9 psi) over steam pressure
- ▶ To purge steam out of system, open V2B, V3B and V4B
- ▶ System can then be left to dry and cool down by closing V2B, V3B and V4B

On Completion of Cooling/Drying:

- ▶ Remove air - close V7B, open V2B and V3B. Close V3B and V2B

3.2 Water Intrusion Test (WIT)

Heat tracing on filter system switched off (cool-down may take several hours).

This procedure is a general one, allowing use of the Palltronic AquaWIT filter integrity test system. At this point all valves on System B are closed.

- ▶ Connect Palltronic AquaWIT filter integrity test system to V9B and V3B. Open V9B and V3B. Conduct test.
- ▶ Filling and automatic testing is by V9B and V3B

On Completion of Test:

- ▶ Drain and dry system (via V9B and V3B). Close V3B and V9B
- ▶ If system required for use switch heat tracing ON and open V1B and V5B

3.3 System A and B in Operation

- ▶ V6, V5A, V5B, V1A and V1B open
- ▶ All other valves closed
- ▶ Heat tracing on both housings or on housing in operation switched ON at tank temperature plus 5°C
- ▶ System A or B can be isolated by closing V5A or V5B respectively
- ▶ The valves V1, V3 and V9 can also be remotely controlled from the Palltronic AquaWIT system to fully automate the test procedure

For full details of system operation, contact your local Pall office.

Table 1
Features and Benefits of Components

Features of Emflon HTPFR/PFR Filter Cartridges	Benefits
Water Intrusion Testable	Improved handling, reproducible in situ integrity test using water, alcohol not required
Proprietary Pall-manufactured polytetrafluoroethylene membrane	Provides secure supply source, optimum performance under Pall manufacturing and quality control
High-area, hydrophobic filter	Economical: high air flow allows use of smaller filtration systems reducing installation and operational costs
Liquid challenge validation with <i>Brevundimonas diminuta</i> (ATCC19146) at $>10^7$ cfu/cm ² effective filtration area per modified ASTM 838-05 standard	Resistant to condensate: provides sterile air under dry or humid conditions. Meets sterilizing grade filter requirements under Guidance for Industry Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice (September 2004)
Aerosol retention: validated with <i>Brevundimonas diminuta</i> , <i>Bacillus subtilis</i> spores, phages and sodium chloride particles in aerosol	Virus Safety and Efficiency: removing microorganisms, spores and phages during intended air filtration or vent use mitigates risk of virus contamination from aerosol sources. Sodium chloride particle challenge demonstrates high aerosol particle removal efficiency - filters rated at 0.003 µm in gas
Multi-cycle sterilization: autoclave and in situ steam challenged in both forward and reverse direction	Robust construction, enhanced steaming resistance
Oxidation-resistant materials of construction (Emflon HTPFR)	High-temperature and oxygen-resistant, demonstrates long service life even at elevated temperatures in oxygen aeration applications and ozonated water tanks
Laser-etched part/serial number and 2D matrix (Emflon HTPFR)	Ease Of Use and traceability – product information can be easily read or scanned with barcode readers (e.g. Palltronic barcode reader)
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Features of Pall Advanta AVL housings	Benefits
Large (1 ½ inch) bottom inlet	Condensate generated between tank and filter housing can easily drain back to tank
Sanitary valves with non-rotating outlet	Allows improved handling
Vent and drain connection on non-sterile side	Enables in-line water intrusion test without the risk of microbial contamination of the sterile side
Vent and drain connection with 'Stäubli' quick coupling	Easy connection to Palltronic AquaWIT filter integrity test system, therefore providing easy, fast and safe performance of a water intrusion test with hydraulic bridge

Features of Pall Advanta electrical trace heaters

Designed for use with Pall Advanta housings: pre-formed pull-over sleeve and silicone insulation

Temperature operating range between room temperature and 140°C with a resolution of 0.1°C and a cut-out temperature of 150°C ± 5°C, controlled by a PT100 sensor

Separate control unit with available cable extensions between control unit and jacket heater

Integrated silicone insulation limit surface temperatures to typically < 70°C

Benefits of Pall Advanta electrical trace heaters

In contrast to steam jackets, no investment cost for valves, pressure regulators or piping. Easy handling and changeout of filter elements, as no steam supply pipes must be dismantled

Avoids condensate formation on hydrophobic vent filters. High level of operational safety, as temperatures can be controlled precisely

Ability to position control unit independent of installation location allows flexible operation and integration into central control facilities

Reduces energy consumption

Features of Palltronic AquaWIT IV Filter Integrity Test System

Fully automated test preparation and integrity test cycle for hydrophobic filters

Fully automated filter wetting and testing sequence for hydrophilic filters

Automated control of the key parameters that influence Water Intrusion Test results

Designed for use in GMP environments subject to controls on Electronic Records and Signatures (21 CFR Part 11)

Sanitary design with removable internal water tank

Benefits

Saves operator time, delivers a fully-controlled test sequence

Enables accurate, reliable testing of sterile liquid filters

Ensures reproducible test results

Assures and protects the safety of paperless test records

Simple to clean, enables trouble-free maintenance

Product webpages, specifications and ordering information for all products shown is available at www.pall.com

4. Summary

Condensate blinding of high-flow sterile filters such as Emflon HTPFR or Emflon PFR can be avoided by using Pall Advanta housings together with the Pall Advanta trace heater, and is simple to deploy. The Palltronic AquaWIT filter integrity test system can be used to automatically perform water intrusion tests on tank vent filters, to assure that these critical filters still have sterilizing capability during long-term operation, or after steam sterilization.

5. Further Reading

- ▶ *Steam Sterilization of Pall Filter Assemblies*, Pall publication USTR805
- ▶ *The Pall Water Intrusion Test for Integrity Testing Sterile Gas Filters*, Pall publication USD1603
- ▶ *Czermak and Catapano: Automated Integrity Testing of Hydrophobic Filters Based on Water Intrusion Measurements: Comparative Analysis of a Refilling Continuous-Flow and a Pressure Decay Batch Device*, accessible at <http://www.pall.com/main/Biopharmaceuticals/Literature-Library-Details.page?id=20120224152153>
- ▶ *Jaenchen et al: Studies on The Theoretical Basis Of The Water Intrusion Test (WIT)*, accessible at www.pall.com/wit



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