



Life Sciences

Application Note

USTR 805 Rev K

Steam Sterilization of Pall® Filter Assemblies

Utilizing Replaceable Filter Cartridges

Table of Contents

1. Important Recommendations	1
1.1 Installation Prior to SIP	1
1.2 Integrity Testing	1
1.3 Procedure for Water-wetting prior to Steam Sterilization.....	1
1.4 Control of Steam Sterilization	1
1.5 Direction of Steam Flow	2
1.6 Steam for Sterilization	2
1.7 Flushing of Process System.....	2
1.8 Air for System Pressurization	2
2. In-Situ Steam Sterilization Procedures.....	3
2.1 In-Situ Steam Sterilization of a Dry Filter Assembly	3
2.1.1 Configuration	3
2.1.2 Procedure	3
2.2 In-Situ Steam Sterilization of a Wet Filter Assembly	4
2.2.1 Configuration	4
2.2.2 Procedure	5
2.3 In-situ Steam Sterilization of a Hydrophobic Filter Assembly	6
2.3.1 Configuration	6
2.3.2 Forward Direction	6
2.3.3 Reverse Direction	8
3. Guidelines for Simultaneous Steam Sterilization of Filter Assemblies and Downstream Process Equipment	10
3.1 Filter Sizing and Steam Supply.....	10
3.2 Differential Pressure.....	10
3.2.1 Hydrophilic Filters	10
3.2.2 Hydrophobic Filters.....	10
3.3 Monitoring of Temperature and Pressure	10
3.4 Air Entrapment	11
3.5 Condensate Drainage	11
3.6 Rapid Cooling.....	11
3.7 Factors Affecting Filter Life.....	11
4. Guidelines for Sterilizing Filter Assemblies by Autoclaving.....	12
4.1 Assembly	12
4.2 Integrity Testing	12
4.3 Wrapping of Open Ports.....	12

4.4 Downstream Vessels..... 12

4.5 Autoclaving of Filter Assemblies..... 12

 4.5.1 Non-Vacuum Autoclave Sterilization.....13

 4.5.2 Vacuum Autoclave Sterilization13

4.6 Autoclave Cycle Control..... 13

5. Scientific and Laboratory Services 14

List of Figures

Figure 1: Recommended Filter Installation In-Situ Steam Sterilization of a Dry Filter Assembly3

Figure 2: Recommended Filter Installation for In-Situ Steam Sterilization of Filter Assembly.....5

Figure 3: Recommended Filter Installation for In Situ Steam Sterilization of Filter Assembly in the Forward Direction6

Figure 4: Recommended Filter Installation for In Situ Steam Sterilization of Filter Assembly in the Reverse Direction.....8

1. Important Recommendations

This section includes important procedures and guidelines; it should be reviewed carefully before implementing steam sterilization protocols.

This publication describes important procedures to be adopted before implementing autoclave or steam-in-place (SIP) steam sterilization protocols for Pall® filter assemblies. It cannot account for specific features of individual systems. Should you have difficulty in applying these recommendations, or if you have any questions concerning steam sterilization, please contact your nearest Pall office.



Please note that the procedure and validation of sterilizing non-sterile Pall filters and capsules is the responsibility of the user.

1.1 Installation Prior to SIP

The filter assembly should be installed so that condensate from the steam supply cannot accumulate in the housing, and so the open end of the filter cartridge is oriented downwards.

It is preferable for all sterile filling operations that the pipework downstream of the filter assembly be kept as short as possible. Critical pipe lengths are shown in the procedural diagrams.

1.2 Integrity Testing

Critical filters should be integrity-tested after steam sterilization before product is introduced to the filter. An additional test after filtration is also recommended.

The recommended method for verifying the integrity of the filters is the Forward Flow Test for hydrophilic filters and either the Water Intrusion Test or the Forward Flow Test for hydrophobic filters. Bubble point values can also be provided. Pall provides automated test equipment for this purpose. Please contact your nearest Pall office or distributor for details.

1.3 Procedure for Water-wetting prior to Steam Sterilization

The following filters must be water-wetted prior to steam sterilization. Other filters may be autoclaved or steamed wet or dry.

- **Pall Supor® Filters⁽¹⁾**
Flush with 0.2 µm filtered water at a rate of 4 L/min for at least 10 minutes.
- **Pall Ultipor® DV50 Filters⁽¹⁾**
Flush with 0.2 µm filtered water at a rate of 1 L/min for at least 10 minutes.
- **Pall Pegasus™ LV6 Virus Filter**
Pall Pegasus LV6 virus filters are supplied water-wet. They can be steam sterilized as supplied.

1.4 Control of Steam Sterilization

Steam used for sterilization must be saturated and free from condensation. Superheated steam must not be used.



Warning: Pall Supor, Pall Ultipor VF DV50, and Pall Pegasus LV6 virus filter membranes must be water-wet prior to steam sterilization and sterilized as detailed in Section 2.2: In-Situ Steam Sterilization of a Wet Filter Assembly on page 4.

Introduction of steam into the system should be in such a way as to prevent trapping of air. Air pockets can inhibit steam flow and produce regions where inadequate sterilizing conditions are achieved. This requires special attention where steam is introduced from more than one position.

Adequate means for condensate drainage should be employed to ensure that any condensate that forms is removed from the system and not allowed to collect. Condensate will wet hydrophilic filter assemblies, increase differential pressures across hydrophilic and hydrophobic filters, and reduce steam flow.

1. Values per 254 mm (10 in.) module.

It is important to consider:

- Steam supply
- System to be steamed (adequate drainage)
- Pipe orientation
- Pipe insulation

Steam and air pressure should be regulated carefully to avoid over-pressurization that can damage filter cartridges. Accurate and calibrated pressure gauges are important. Differential pressure should be kept to a minimum, and should not exceed 300 mbard (4.3 psid).⁽²⁾ At the completion of steam sterilization, air should be introduced to replace the steam; compensation for steam collapse is important to prevent the formation of a vacuum that may cause filter damage, leakage via pressure seals, or vessel collapse.

The maximum allowable steam sterilization temperature for a specific filter type is given in the appropriate Pall publications. In addition, maximum accumulated steam sterilization times are also specified and should not be exceeded. Please note that capsule filters can be autoclaved, but should not be sterilized by in-situ steaming (except Pall Novasip™ filters — see separate procedures).



Warning: Pall Pegasus LV6 virus filters must not be dried or allowed to dry out after steam sterilization.

1.5 Direction of Steam Flow

Filter cartridges are intended to be steam sterilized either by autoclaving or in-situ by steam flow in the normal forward (out to in) flow direction. Pall Emflon® PFR, CPFR, PFA and Emflon II hydrophobic filter cartridges can be steam sterilized in the reverse flow direction; however particular care should be taken when reverse-steaming small filter assemblies. Insufficient control of condensate loading in the steam may cause blinding at the filter core when the steam reaches the filter membrane. Such blinding results in excessive differential pressures across the filter and filter damage. It is strongly recommended that such a reverse-steaming procedure be adopted only if operational circumstances make it impossible to introduce steam in the forward flow direction.

1.6 Steam for Sterilization

The steam should be free of particulate matter such as rust and pipe scale that will be removed by the filter to be sterilized and shorten its life. Pall PSS® porous stainless steel filters are suitable for the filtration of steam and appropriate assemblies may be selected from Pall.

1.7 Flushing of Process System

It is strongly recommended that the process filter assembly and associated downstream equipment be flushed after steam sterilization to remove any residues originating from the steam and to remove trace amounts of filter extractables remaining after sterilization.

1.8 Air for System Pressurization

Conditions leading to steam collapse such as rapid cooling must be avoided. Application of compressed air or nitrogen can help to overcome this risk. If the filter assembly and associated system is pressurized after sterilization, the air or nitrogen should be free of oil, water and particulates.

2. See product specifications for maximum steam conditions and differential pressure variations.

2. In-Situ Steam Sterilization Procedures

2.1 In-Situ Steam Sterilization of a Dry Filter Assembly

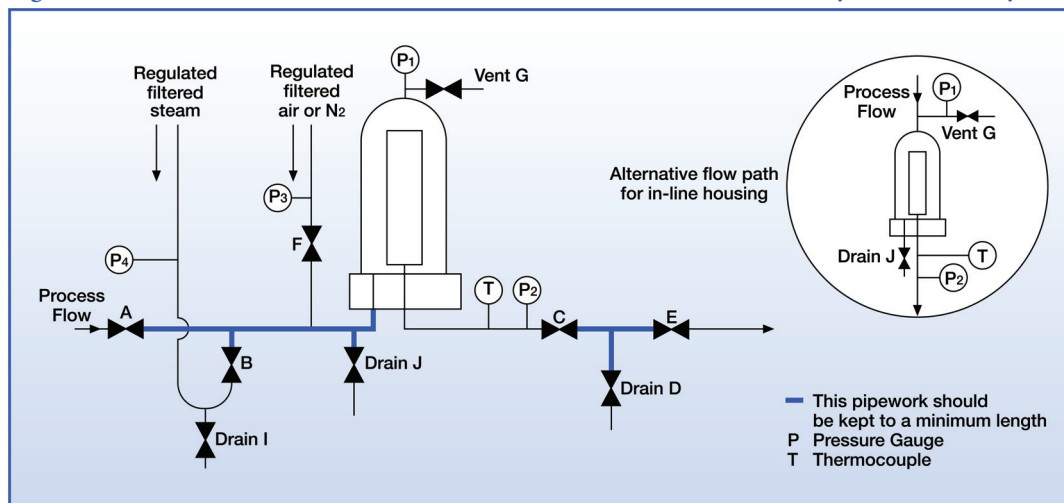
2.1.1 Configuration

A recommended filter installation is presented in Figure 1. Pressure gauges that can be read with accuracy over the range 0 – 3 barg (0 – 43.5 psig) must be installed to monitor steam pressure and differential pressure across the filter assembly during the sterilization cycle. To ensure effective sterilization, steam temperature (measured at position T) in the assembly should be held at a minimum of 121 °C — about 1 barg (15 psig) — saturated steam for the minimum time validated by the user as necessary to achieve system sterilization.



Caution: Pall Supor filter membranes, Ultipor VF DV50, and Pegasus LV6 virus filter membranes must be water-wet prior to steam sterilization, and sterilized by Section 2.2: In-Situ Steam Sterilization of a Wet Filter Assembly on page 4. All other materials can be steam sterilized wet or dry.

Figure 1: Recommended Filter Installation In-Situ Steam Sterilization of a Dry Filter Assembly



2.1.2 Procedure

1. Ensure that all valves are closed.
2. Fully open valve C.
3. Fully open the condensate drain trap or valve I, housing drain valve J, and housing vent valve G.
4. Preset the steam pressure (P4) to 300 mbarg (4.3 psig) above the steam pressure required at the filter assembly.
5. After condensate has been expelled from I, partially close valve I (if necessary).
6. Slowly open steam valve B to admit steam to system.
7. After condensate has been expelled from J, partially close valve J.
8. When steam flow is evident:
 - (a) Partially close vent valve G.
 - (b) Ensure that the pressure at P2 remains within 300 mbard (4.3 psid)⁽³⁾ of the pressure at P1.
9. Partially open drain valve D to drain condensate.
10. Permit steam to flow through the system until steam pressure is stabilized.
11. Adjust the regulated steam supply until the validated temperature is achieved at position T.
12. Monitor the temperature at T for the necessary sterilization time.
13. Ensure that the pressure at P2 remains within 300 mbard (4.3 psid)⁽³⁾ of the pressure at P1.
14. When sterilization is complete:⁽⁴⁾
 - (a) Close drain valves D, J, and I and vent valve G.
 - (b) Close steam valve B.

3. See product specifications for maximum steam conditions and differential pressure variations.

4. Step 14 may vary when ballasting with Air or Nitrogen.

- (c) Allow the assembly to cool to ambient temperature or process-fluid temperature.
- (d) Open valve G to compensate for any differential between the pressure within the assembly and ambient pressure.

The filter assembly is now ready for use.

Ballasting with Air or Nitrogen

Air ballasting may be used after steam sterilization in order to avoid wetting out the membrane. Instead of Step 14:

- (a) Preset the pressure (P3) of regulated air or N₂ at 200 mbarg (2.9 psig) above steam pressure (P4).
- (b) Close drain valves D, J, and I and vent valve G.
- (c) Close steam valve B.
- (d) Immediately introduce pre-regulated air or N₂ through valve F.
- (e) To assist cooling, steam may be flushed from the assembly by carefully opening vent valve G and drain valve J.
- (f) Allow the assembly to cool to ambient temperature or process-fluid temperature.
- (g) Close valves G and J after flushing.
- (h) Close the air or nitrogen valve F.
- (i) Relieve the gas pressure in the filter assembly via vent valve G.



The filter assembly is now ready for use.

2.2 In-Situ Steam Sterilization of a Wet Filter Assembly

2.2.1 Configuration

This procedure applies to filter assemblies where the following conditions may be encountered:

- (i) Difficulty in obtaining steam flow through a water-wetted filter, due to an inability to safely exceed the bubble point of the filter membrane without damaging the filter.
- (ii) Where difficulties are experienced in draining condensate.
- (iii) Difficulty in obtaining positive gas pressure downstream of the sterilized filter assembly, where required to replace steam during cooling.

A recommended filter installation is presented in [Figure 2](#).



A Pall Emflon PFR filter should be installed to maintain sterility of the downstream section if post-sterilization pressurization with air is required to break the vacuum. Pall will be pleased to advise on the sizing of this assembly to meet specific requirements.

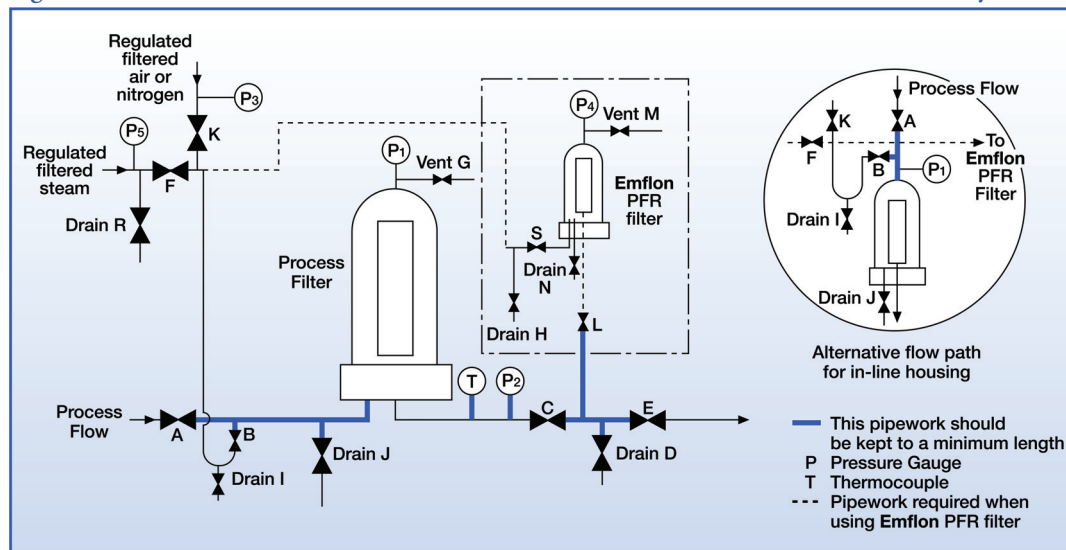
INSTRUCTIONS IN SQUARE BRACKETS [] REFER TO THIS DOWNSTREAM EMFLON PFR FILTER ASSEMBLY.

Pressure gauges which can be read with accuracy over the range 0 – 3 barg (0 – 43.5 psig) must be installed to monitor steam pressure and differential pressure across the filter assembly during the sterilization cycle. To ensure effective sterilization, steam temperature (measured at position T) in the assembly should be held at a minimum of 121 °C — about 1 barg (15 psig) — saturated steam, for the minimum time validated by the user as necessary to achieve system sterilization.



Caution: Pall Pegasus LV6 virus filters must not be dried or allowed to dry out after steam sterilization.

Figure 2: Recommended Filter Installation for In-Situ Steam Sterilization of Filter Assembly



The filter assembly shown within the chain dotted square will apply if post-sterilization pressurization is required.

Pall Supor filter membranes, Ultipor VF DV50 and Pegasus LV6 virus filter membranes must be water-wet prior to steam sterilization and sterilized as in [Section 2.2: In-Situ Steam Sterilization of a Wet Filter Assembly on page 4](#). All other filters can be steam-sterilized wet or dry.

2.2.2 Procedure

1. Ensure that all valves are closed.
2. Fully open valve C.
3. Fully open the condensate drain trap or valve I, housing drain valve J, and housing vent valve G.
4. [Fully open drain H, housing drain N, and vent valve M].
5. Preset the steam pressure (P5) to 300 mbarg (4.3 psig) above the steam pressure required at the filter assemblies. Partially open drain valve R to remove condensate.
6. Slowly open steam valve F.
7. When condensate has been expelled, partially close valves I [and H].
8. [Slowly open valve S.
9. When condensate has been expelled from housing drain valve N, partially close valve N.
10. When steam flow is evident from housing vent M, partially close vent M].
11. Slowly open valve B. Ensure that the differential pressure ($P_1 - P_2$) does not exceed 300 mbard (4.3 psid).⁽⁵⁾
12. When condensate has been expelled, partially close drain valve J.
13. Slowly open drain valve D.
14. Purge steam via vent valve G.
This allows steam to flow vigorously across the face of the process filter to heat the filter membrane.
15. Partially close vent valve G. Ensure that the differential pressure ($P_1 - P_2$) does not exceed 300 mbard (4.3 psid).⁽⁵⁾
16. [When thermocouple T indicates the validated steam temperature, slowly open valve L. Ensure that the differential pressure ($P_4 - P_2$) does not exceed 300 mbard (4.3 psid).⁽⁵⁾].
17. Partially close drain valve D.
18. Perform air ballasting after steam sterilization:
 - (a) Set the pressure (P3) of regulated air or N₂ at 200 mbarg (2.9 psig) above steam pressure (P5).
 - (b) When the validated sterilization period is complete, close drain valves D, J, I [N and H].
 - (c) Close vent valve G [and M].
 - (d) Close steam valve F, and immediately open air or N₂ valve K.

5. See product specifications for maximum steam conditions and differential pressure variations.

- (e) To assist cooling, steam may be flushed from the assembly by carefully opening vent valve G [and M]. Close valve G [and M] after flushing. Allow the entire assembly to cool at pressure to ambient or process temperature.
- (f) Close air or nitrogen valve K and valves B [L and S].
- (g) Relieve gas pressure via vent valves G [and M].

The filter assembly is now ready for use.

Where Positive Gas Pressure is Required

Where positive gas pressure downstream of the process filter is required at all times:

1. Complete steps 1 – 15.
2. Introduce process fluid at a pressure greater than P2.
3. Vent the assembly via vent valve G.

2.3 In-situ Steam Sterilization of a Hydrophobic Filter Assembly

2.3.1 Configuration

Hydrophobic filters can be safely steam-sterilized in both the forward and reverse flow directions.

Steam sterilization of hydrophobic filters in the reverse flow direction requires more careful control than in the forward flow direction (see [Section 2.3.3: Reverse Direction on page 8](#)).



Caution: If the filter assembly has been integrity tested using the Forward Flow test (or other non destructive test procedure) that requires wetting of the filter membrane with mixtures of water and organic solvents prior to steam sterilization, all traces of the solvent must be removed by flushing with water. It is essential to ensure that the filter cartridge is fully dried prior to initiating steam flow. Failure to do so may result in damage to the filter.

Recommended filter installations are presented in Figures 3 and 4. Pressure gauges that can be read with accuracy over the range 0 – 3 barg (0 – 43.5 psig) must be installed to monitor steam pressure and differential pressure across the filter assembly during the sterilization cycle.

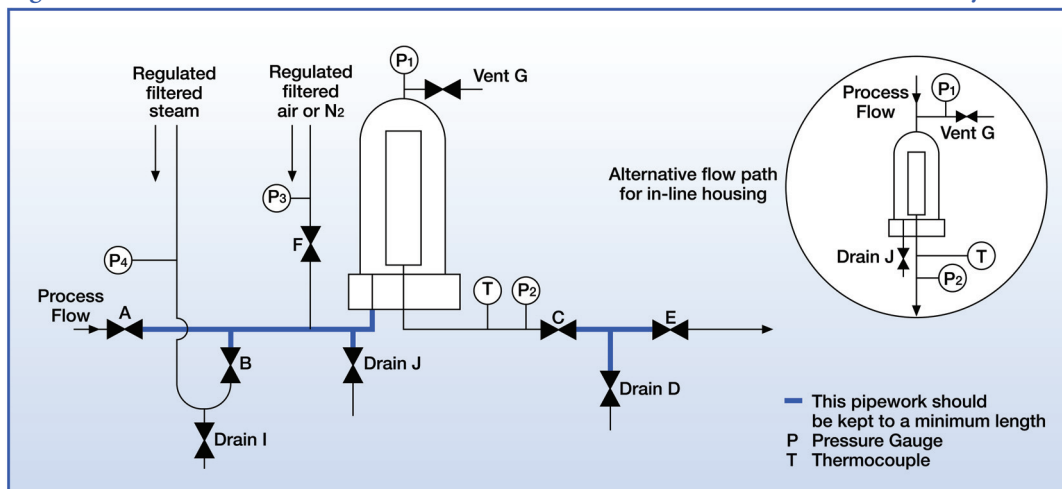
A recommended filter installation is presented in [Figure 2: Recommended Filter Installation for In-Situ Steam Sterilization of Filter Assembly](#).



To ensure effective sterilization, steam temperature (measured at position T) in the assembly should be held at a minimum of 121 °C — about 1 barg (15 psig) — saturated steam, for the minimum time validated by the user as necessary to achieve system sterilization.

2.3.2 Forward Direction

Figure 3: Recommended Filter Installation for In Situ Steam Sterilization of Filter Assembly in the Forward Direction



1. Ensure that all valves are closed.
2. Fully open valve C.
3. Fully open the condensate drain trap or valve I, housing drain valve J and housing vent valve G.
4. Preset the steam pressure (P4) to 300 mbarg (4.3 psig)⁽⁶⁾ above the steam pressure required at the filter assembly.
5. After condensate has been expelled from I, partially close valve I (if necessary).
Note: If the assembly being sterilized is a Pall Junior-style or similarly-sized small filter assembly fitted as a sterile vent on a vessel, it is particularly important to ensure that the housing is maintained completely free of condensate throughout the sterilization procedure. Failure to ensure this may lead to collapse of steam at the end of sterilization causing damage to the vessel and filter cartridge.
6. Slowly open steam valve B to admit steam to system.
7. After condensate has been expelled from J, partially close valve J.
8. Partially close vent valve G when steam flow is evident.
Note: Ensure that the pressure at P2 remains within 300 mbard (4.3 psid) of the pressure at P1.
9. Partially open drain valve D to drain condensate.
10. Permit steam to flow through the system until steam pressure is stabilized.
11. Adjust the regulated steam supply until the validated temperature is achieved at position T.
12. Monitor the temperature at T for the necessary sterilization time.
Note: Ensure that the pressure at P2 remains within 300 mbard (4.3 psid)⁽⁶⁾ of pressure at P1. It is recommended that steam sterilization is followed by air ballasting as detailed in the following section.
13. Preset the pressure (P3) of regulated air or N₂ at 200 mbarg (2.9 psig) above the steam pressure (P4).
14. When sterilization is complete:⁽⁷⁾
 - (a) Close drain valves D, J, and I and vent valve G.
 - (b) Close steam valve B.
 - (c) Allow the assembly to cool to ambient temperature or process-fluid temperature.
 - (d) Open valve G to compensate for any differential between the pressure within the assembly and ambient pressure.

The filter assembly is now ready for use.

Ballasting with Air or Nitrogen

Air ballasting may be used after steam sterilization in order to avoid wetting out the membrane. Instead of Step 14:

- (a) Preset the pressure (P3) of regulated air or N₂ at 200 mbarg (2.9 psig) above steam pressure (P4).
- (b) Close drain valves D, J, and I and vent valve G.
- (c) Close steam valve B.
- (d) Immediately introduce pre-regulated air or N₂ through valve F.
- (e) To assist cooling, steam may be flushed from the assembly by carefully opening vent valve G and drain valve J.
- (f) Allow the assembly to cool to ambient temperature or process-fluid temperature.
- (g) Close valves G and J after flushing.
- (h) Close the air or nitrogen valve E.
- (i) Relieve the gas pressure in the filter assembly via vent valve G.

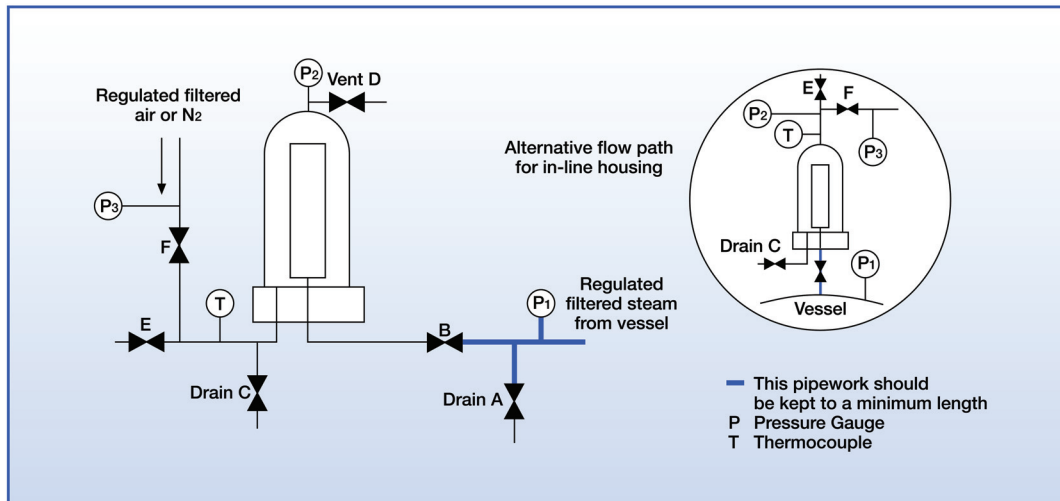
The filter assembly is now ready for use.



6. See product specifications for maximum steam conditions and differential pressure variations.
7. Step 14 may vary when ballasting with Air or Nitrogen.

2.3.3 Reverse Direction

Figure 4: Recommended Filter Installation for In Situ Steam Sterilization of Filter Assembly in the Reverse Direction



1. Ensure that all valves are closed.
2. Fully open the condensate drain trap or valve A and housing drain valve C.
3. Slowly open valve B.
Note: Ensure that pressure at P2 remains within 200 mbard (2.9 psid)⁽⁸⁾ of pressure at P1.
4. Allow condensate to drain from housing drain valve C.
5. When steam flow is evident from valve C, partially close valve C.
6. Partially open vent valve D and E.
Note: Ensure that the differential pressure (P2 – P1) does not exceed 200 mbard (2.9 psid).⁽⁸⁾
7. Permit steam to flow through the system until the steam pressure is stabilized.
8. Adjust the regulated steam supply until the validated temperature is achieved at position T.
9. Monitor the temperature at T for the necessary sterilization time.
Note: Ensure that the pressure at P2 remains within 200 mbard (2.9 psig) of the pressure at P1. It is recommended that steam sterilization be followed by air ballasting.
10. When sterilization is complete:⁽⁹⁾
 - (a) Close valve E, drain valve A, housing drain valve C, and vent valve D.
 - (b) Close the vessel steam supply valve (not shown) and immediately introduce pre-regulated air or N₂ through valve F.
 - (c) Allow the assembly to cool to ambient temperature or process-fluid temperature.
 - (d) Open valve D to compensate for any differential between the pressure within the assembly and ambient pressure.

The filter assembly is now ready for use.

8. See product specifications for maximum steam conditions and differential pressure variations.
9. Step 10 may vary when ballasting with Air or Nitrogen.

Ballasting with Air or Nitrogen

Air ballasting may be used after steam sterilization in order to avoid wetting out the membrane and to replace steam pressure in the sterile vessel and to prevent vessel collapse.

Instead of Step 10, when sterilization is complete:



- (a) Preset the pressure (P3) of regulated air or N₂ at 200 mbarg (2.9 psig) above steam pressure (P1).
- (b) Close valve E, drain valve A, housing drain valve C, and vent valve D.
- (c) Close the vessel steam supply valve (not shown) and immediately introduce pre-regulated air or N₂ through valve F.
- (d) To assist cooling, steam may be flushed from the assembly by carefully opening drain valve C and vent valve D.
- (e) Close drain valves E, J, and I and vent valve G.
- (f) Close steam valve B.
- (g) Immediately introduce pre-regulated air or N₂ through valve F.
- (h) Allow the assembly to cool to ambient temperature or process-fluid temperature.
- (i) Close the air or nitrogen valve F.
- (j) Close valves C and D.

The filter assembly is now ready for use.

3. Guidelines for Simultaneous Steam Sterilization of Filter Assemblies and Downstream Process Equipment



It is the responsibility of the user to validate the effectiveness and safety of the procedures used to steam sterilize process equipment and filter assemblies. The following guidelines are intended only to highlight some aspects of such procedures that require special attention. For further assistance or information, please contact Pall Scientific and Laboratory Services.

3.1 Filter Sizing and Steam Supply

Process filter assemblies should be sized appropriately for product filtration, with gas or air flow, to permit adequate steam flow to effectively sterilize the downstream equipment. Failure to take account of steam flow requirements may result in filter damage, caused by high differential pressures at elevated temperatures, and possible non-sterility of downstream equipment.

3.2 Differential Pressure

3.2.1 Hydrophilic Filters

During steam sterilization of downstream equipment, differential pressure across hydrophilic filter assemblies must not exceed 300 mbard (4.3 psid)⁽¹⁰⁾ in the forward direction ([Section 2.2: In-Situ Steam Sterilization of a Wet Filter Assembly on page 4](#)). If the filter membrane is wet at the start of such procedures, steam flow will be restricted, and special attention must be given to provision of an adequate steam supply to the downstream equipment.



Caution: Steam sterilization of downstream equipment through hydrophilic filter assemblies by steam flow in the reverse direction may lead to filter damage and is not recommended.

3.2.2 Hydrophobic Filters

During steam sterilization of downstream equipment, differential pressure across hydrophobic filter assemblies must not exceed 300 mbard (4.3 psid) in the forward direction (See [Section 2.3.2: Forward Direction on page 6](#)). If the filter assembly has been integrity tested using a procedure requiring wetting of the filter membrane prior to steam sterilization, it is essential to ensure that the filter cartridge is fully dried prior to initiating steam flow ([Section 2.3: In-situ Steam Sterilization of a Hydrophobic Filter Assembly on page 6](#)).



Caution: It is acceptable to steam sterilize hydrophobic filter assemblies in the reverse direction either by direct supply of steam or with steam supplied from process equipment ([Section 2.4.3: Procedure 2: Reverse Direction on page 8](#)). Do not, however, sterilize process equipment using steam supplied through a hydrophobic filter assembly in the reverse flow direction.

3.3 Monitoring of Temperature and Pressure

It is important to monitor temperature and pressure in downstream equipment to ensure that:-

- (i) Validated sterilizing conditions have been achieved
- (ii) Excessive differential pressures are not experienced across filter assemblies
- (iii) A sudden fall in pressure due to steam collapse does not compromise downstream equipment



Caution: Where vessels in the downstream systems are unable to withstand negative pressure without collapse, appropriate safety devices must be fitted.

10. See product specifications for maximum steam conditions and differential pressure variations.

3.4 Air Entrapment

It is important to ensure that valve sequences do not lead to entrapment of air pockets in the process equipment, as sterility may be compromised.

3.5 Condensate Drainage

Adequate means for condensate drainage should be employed to ensure steam is free from condensate. Condensate will wet hydrophilic filter assemblies, increase differential pressures across hydrophilic and hydrophobic filters and reduce steam flow. Provision should be made for drainage of condensate from process equipment following steam sterilization where such condensate is undesirable for operational reasons.

3.6 Rapid Cooling

For operational reasons it may be considered necessary to cool process equipment rapidly following steam sterilization. Rapid cooling of disposable filter cartridges by initiating liquid flow is not recommended and may cause filter damage. In addition it may lead to acceleration of steam collapse (See [Section 3.3: Monitoring of Temperature and Pressure on page 10](#)). If cooling is required, air ballasting should be performed out using a flow of compressed air (or other suitable gas) as detailed in [Section 2.1: In-Situ Steam Sterilization of a Dry Filter Assembly on page 3](#), [Section 2.2: In-Situ Steam Sterilization of a Wet Filter Assembly on page 4](#), and [Section 2.3: In-situ Steam Sterilization of a Hydrophobic Filter Assembly on page 6](#).

3.7 Factors Affecting Filter Life

Steam Exposure

In applications where filter cartridges are re-used and thus repeatedly steam sterilized, a record of steam exposure should be maintained. Where extended exposure times are required to sterilize downstream equipment, similar exposure of the filter cartridge to steam may exceed the filter's recommended maximum steam life. In such circumstances separate sterilization of filters and downstream equipment is recommended.

Air Cooling

Air cooling of process equipment may involve extended periods of air flow. Air raised to elevated temperatures during such cooling should not be permitted to flow through replaceable filter assemblies for extended periods, as this may reduce filter life. Where cooling of process equipment necessitates long periods of air flow, filter assemblies should be cooled in a separate procedure.

4. Guidelines for Sterilizing Filter Assemblies by Autoclaving



The autoclave cycle must ensure that the filter and associated items are sterilized and must be validated accordingly. Cycles should be qualified based on whether the filter is autoclaved wet or dry.

Pall Supor filter membranes, Ultipor VF DV50 and Pegasus LV6 virus filter membranes must be water-wet prior to autoclaving. All other materials can be autoclaved wet or dry.

4.1 Assembly

It is essential to ensure adequate purging of air and steam penetration during the autoclave cycle. Failure to ensure adequate steam penetration due to air entrapment may result in an inability to sterilize the assembly.

Where possible, the housing head and bowl of the filter assembly may be separated to achieve this. However, under no circumstances should the filter cartridge support the head, or the bowl be allowed to rest against the filter cartridge.

For Sealkleen™ filter assemblies the head and bowl must be clamped together, but vent valves left fully open. Separation of a Sealkleen assembly may compromise sterility.

Where it is not possible to separate the head and bowl of the filter assembly, for example with disposable filter assemblies such as Kleenpak™ filters, it is essential that vent and drain valves are opened fully.

When autoclaving wet filters, it is recommended that the housing (or capsule) is drained prior to autoclaving.

4.2 Integrity Testing

In instances where integrity testing has been carried out using alcohol based wetting fluids, it is essential to ensure that all alcohol has been removed from the filter assembly prior to autoclaving. Failure to remove all alcohol may result in filter damage. Residual alcohol may be removed by flushing of the filter assembly with water or compressed air.

4.3 Wrapping of Open Ports

In order to maintain sterility following autoclaving, the outlet connection from the assembly should be covered by an appropriate steam porous covering. This covering should not be tightly sealed or taped to the filter assembly, otherwise adequate steam penetration may not occur.

4.4 Downstream Vessels

It may be necessary to autoclave filter assemblies attached to downstream vessels. In these instances the autoclave cycle must be validated to ensure the cycle parameters can achieve sterility of the vessels used.

4.5 Autoclaving of Filter Assemblies

When filter assemblies are loaded into the autoclave, it is important to ensure that all openings on the assembly (covered or uncovered) remain clear of water laying in the autoclave chamber.

Failure to observe this precaution may result in filter damage or inability to sterilize the assembly.

Important considerations when autoclaving such vessels include:

- (i) The volume of the vessel
- (ii) Length of connecting tubing
- (iii) Presence of moisture in the vessel
- (iv) Adequate support for the filter assembly to ensure tubing does not become kinked or occluded during autoclaving

Where vessels are fitted with a hydrophilic filter the vessel must also be fitted with a hydrophobic vent filter. Failure to do so may result in steam collapse in the vessel, and possible damage to the filter and vessel.

Where vessels are fitted with a hydrophobic filter, it is important that the filter is of sufficient size to allow replacement of steam during cooling. In addition the hydrophobic filter must be positioned in such a way to avoid accumulation of condensate on either side of the membrane.

4.5.1 Non-Vacuum Autoclave Sterilization

1. With a cartridge installed in the filter head, loosely cover the outlet connection (e.g., bowl or hose adaptor) with an approved steam-porous covering. The covering should not be tightly sealed or tightly taped.

This step is extremely important in order to ensure that air can flow from the inside of the filter cartridge and any attached process equipment, and allow steam penetration. This is necessary for proper sterilization.

2. It is recommended that the filter head and bowl be separated during autoclaving to facilitate the purging of air. Longer cycle times may result if the assembly is closed. Under no circumstances should the filter cartridge support the head or should the bowl rest against the filter cartridge.

When a downstream vessel is connected to the filter outlet during the autoclave cycle, the receiver volume must not exceed 25 liters nor must the connection tubing be longer than 1.5 m (5 ft) unless the receiver vessel has been charged with a small amount of water to facilitate sterilization.

The vessel should be fitted with a hydrophobic vent filter. Any attached hose clamp or valves should be left open. For larger vessels, autoclave the filter and vessel separately and aseptically connect.

3. Carry out autoclave sterilization at a temperature of 125 °C for not less than one hour. Use a low exhaust cycle.

The autoclave cycle must ensure that the filter assembly and any connected process equipment are maintained at sterilizing temperature for this time.

4. Complete the assembly of the filter and install it in the system using aseptic techniques

4.5.2 Vacuum Autoclave Sterilization

The internal absolute pressure within the autoclave must be drawn down to at least 60 – 80 mbara (0.9 – 1.2 psia). A system purge of two (2) vacuum cycles is suggested to remove the non-condensable gases that may interfere with sterilization.

Vacuum autoclave sterilization of cartridges and assemblies may be carried out using one of the time/temperature relationship as outlines in [Step 2](#).

1. With a cartridge installed in the filter head, loosely cover the outlet connection (e.g., bowl or hose adaptor) with an approved steam-porous covering. Covering should not be tightly sealed or tightly taped.

This step is extremely important in order to ensure that air can flow from the inside of the filter cartridge and any attached process equipment, and allow steam penetration. This is necessary for proper sterilization.

When a downstream receiver is connected to the filter outlet during the autoclave cycle, the receiver volume must not exceed 25 liters nor must the connection tubing be longer than 1.5 m (5 ft) unless the receiver vessel has been charged with a small amount of water to facilitate sterilization.

The receiver should be fitted with a hydrophobic vent filter. Any attached hose clamp or valves should be left open. For larger receivers, autoclave the filter and receiver separately and aseptically connect.

2. Carry out autoclave sterilization using an exhaust cycle temperature of:
 - (i) 121 °C for at least 30 minutes at temperature, or
 - (ii) 125 °C for at least 30 minutes at temperature

The autoclave cycle must ensure that the filter assembly and any connected process equipment are maintained at sterilizing temperature for the time given above.

3. Complete assembly of the filter and install it in the system using aseptic techniques

4.6 Autoclave Cycle Control

At the end of sterilization it is important to use a slow exhaust cycle.

Rapid removal of steam, particularly under the influence of a vacuum pump, may result in filter damage if steam is not readily removed from both sides of the filter membrane.

Air cooling of the autoclave chamber may involve extended periods of air flow. Air at elevated temperature during cooling may reduce life of disposable filter cartridges or assemblies.

5. Scientific and Laboratory Services

Pall provides a full laboratory and field technical service to assist in the application and evaluation of Pall filter products. If you have technical questions please do not hesitate to use this customer service, available through your local sales office.

Index

A

air	
compressed for pressurization	2
cooling autoclave chamber	13
elevated temperature, at	13
entrapment	11
pressure	2
purging	12
air ballasting	9
dry filter assembly	4
hydrophobic filter assembly	
forward direction	7
reverse direction	9
wet filter assembly	5
air entrapment	12
alcohol removal	12
autoclave sterilization	
assembly openings clear of water in chamber	12
cycle control	13
downstream vessels	12
end of	13
guidelines	12
loading filter assemblies	12
non-vacuum	13
vacuum	13
validation requirements	12
automated test equipment	1

B

ballasting with air or nitrogen	9
dry filter assembly	4
hydrophobic filter assembly	
forward direction	7
reverse direction	9
wet filter assembly	5
blinding, filter core	2

C

compressed air, for pressurization	2
condensate	
accumulation	13
drainage	1, 11
cooling, rapid	11
covering, steam porous for sterility after autoclaving	12
covering, vacuum autoclave sterilization	13

D

differential pressure	1–3, 10
gauges	3
hydrophilic filters	10
hydrophobic filters	10
monitoring	3–4
direction of steam flow	2
downstream	
monitoring pressure	10
monitoring temperature	10
process equipment	10
receivers	12
vessel autoclaving	12
vessel, length and volume	13
drainage	
adequate	1–2, 11
condensate, difficulties	4
wet filter assembly	12
dry filter assembly	
in situ steam sterilization	3
recommended filter installation	3
steam temperature	3

E

Emflon CPFR filter cartridges	2
Emflon II filter cartridges	2
Emflon PFA filter cartridges	2
Emflon PFR filter cartridges	2
extractables	2

F

filter core, blinding	2
filter life	
air cooling	11
steam exposure	11
filter sizing	10
flushing	
alcohol removal with water or compressed air	12
process system	2
Forward Flow Test	1

G

gauges, pressure accuracy	3
---------------------------	---

H

hydrophilic filters.....	1
differential pressure.....	10
Forward Flow Test.....	1
Pegasus LV6.....	5, 12
recommended filter installation.....	3–4, 6
Supor.....	5, 12
Ultipor VF DV50.....	5, 12
hydrophobic filter cartridges	
Emflon CPFR.....	2
Emflon II.....	2
Emflon PFA.....	2
Emflon PFR.....	2
hydrophobic filters.....	6
differential pressure.....	10
Emflon CPFR.....	2
Emflon II.....	2
Emflon PFA.....	2
Emflon PFR.....	2
Forward Flow Test.....	1
positioning to avoid condensate.....	13
recommended filter installation.....	6
removing solvent.....	6
reverse flow steam sterilization.....	6
steam sterilization, reverse flow.....	2
vent, when required.....	12–13
Water Intrusion Test.....	1

I

in-situ steam sterilization	
hydrophobic filters.....	6
installation.....	1
insulation.....	2
integrity testing.....	1

K

Kleenpak capsules.....	12
------------------------	----

M

monitoring	
differential pressure.....	4
pressure, downstream.....	10
temperature, downstream.....	10

N

nitrogen	
for pressurization.....	2
nitrogen ballasting.....	9
dry filter assembly.....	4
hydrophobic filter assembly	
forward direction.....	7
reverse direction.....	9
wet filter assembly.....	5
non-vacuum autoclave sterilization.....	13

P

particulates, in steam.....	2
Pegasus LV6 filters.....	5, 12
pipe insulation.....	2
pipe orientation.....	2
ports, wrapping.....	12
pressure	
air.....	2
differential.....	2
steam.....	2
vacuum autoclave sterilization.....	13
pressure gauge	
accuracy.....	3
process equipment, downstream.....	10
PSS porous stainless steel filters.....	2
purging air.....	12

R

rapid cooling, avoiding.....	2, 11
receivers, downstream.....	12
recommended filter installation	
dry filter assembly.....	3
hydrophilic filters.....	3–4, 6
hydrophobic filters.....	6
wet filter assembly.....	6
Supor filter membranes, Ultipor VF DV50 and Pegasus LV6 virus filters.....	4
removing solvent.....	6

S

Scientific and Laboratory Services.....	14
Sealkleen filter assemblies.....	12
services, scientific and laboratory.....	14
sizing.....	10
wet filter assembly.....	4, 6
slow exhaust cycle.....	13
solvent, removing.....	6
stainless steel filters, porous.....	2
steam	
filtration of.....	2
flow, direction.....	2
introducing.....	1
particulates.....	2
pressure.....	2
pressure gauges.....	3
quality.....	2
rapid removal.....	13
superheated, not used.....	1
supply.....	2
steam porous covering	
sterility after autoclaving.....	12
vacuum autoclave sterilization.....	13
steam sterilization	
filter assemblies, downstream process equipment.....	10
forward flow.....	2
in-situ.....	6
maximum accumulated times.....	2
maximum allowable temperature.....	2
normal flow.....	2
reverse flow.....	2
water-wetting, before.....	1
steam supply.....	10
sterility after autoclaving, steam porous covering.....	12
superheated steam, not used.....	1
Supor filters.....	5, 12
system pressurization, air.....	2

T

temperature, maximum allowable.....	2
test equipment.....	1

U

Ultipor VF DV50 filters.....	5, 12
------------------------------	-------

V

vacuum autoclave sterilization	
exhaust cycle temperature.....	13
steam porous covering.....	13
sterilization.....	13
vent filters, when required.....	12–13

W

Water Intrusion Test.....	1
water-wetting	
before steam sterilization.....	1
Pegasus LV6 filter membranes.....	12
procedure.....	1
steam sterilization temperature.....	2
Supor filter membranes.....	12
Ultipor VF DV50 filter membranes.....	12
wet filter assembly	
drainage.....	12
recommended filter installation.....	4, 6
sizing.....	4, 6
WIT	
<i>See</i> Water Intrusion Test	
wrapping open port.....	12



New York — USA
+1 800 717 7255 toll free
+1 516 484 5400 telephone
+1 516 801 9548 fax
biotech@pall.com e-mail

Portsmouth — Europe
+44 (0)23 9230 3303 telephone
+44 (0)23 9230 2506 fax
BioPharmUK@europe.pall.com e-mail

Filtration. Separation. Solution.SM

Visit us on the web at www.pall.com/biopharmaceutical

Pall Corporation has offices throughout the world in locations including: Argentina, Australia, Austria, Belgium, Brazil, Canada, China, France, Germany, India, Indonesia, Ireland, Italy, Japan, Korea, Malaysia, Mexico, the Netherlands, New Zealand, Norway, Poland, Puerto Rico, Russia, Singapore, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, the United Kingdom, the United States, and Venezuela.
Distributors are located throughout the world.

All data, specifications and information contained in this publication are based on information we believe reliable and represent values in effect at the time of printing. Pall Corporation reserves the right to make changes without prior notice.

PALL, Pall, Emflon, Kleenpak, Novasip, Pegasus, PSS, Sealkleen, Supor, and Ultipor are trademarks of Pall Corporation.
Filtration.Separation.Solution. is a service mark of Pall Corporation.

Part Numbers quoted above are protected by the Copyright of Pall Corporation.
® indicates a trademark registered in the USA.
© 2008, Pall Corporation USTR 805 Rev K