Pharmsteri™ PES and PTFE Cartridge Filters

Installation and Use Manual

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1. INTRODUCTION

Please follow the instructions when using Pharmsteri™ cartridge filters. It is very important to strictly operate according to this manual. It is proposed that the instructions in this manual are included in users' standard operation manual. If any step is not applicable in actual operation, please contact Entegris.

This manual is applicable to Pharmsteri family including Pharmsteri PES cartridge filters, Pharmsteri PTFE cartridge filters, Pharmsteri AHC PES liquid cartridge filters, and Pharmsteri APFS PES liquid cartridge filters.

Entegris assumes no responsibility if any harm or loss occurs due to operations without following this manual.

1.1 MATERIALS OF CONSTRUCTION

Pharmsteri PES and PTFE cartridge filters are constructed from polypropylene components and either a PES or PTFE membrane. The filters are developed for sterilizing filtration in the pharmaceutical industry.

COMPONENT	MATERIAL
Membrane	Polyethersulfone (PES) or Polytetrafluoroethylene (PTFE)
O-rings	Silicone
Reinforced code 0, 5, 6, or 7 connector	Polypropylene (PP)
Others	Polypropylene (PP)

1.2 NET CONTENT AND PRODUCT WEIGHT

Each filter is double bagged with a certificate of quality (COQ) in an inner box, then put in an outer carton before shipment.

Cartridge filter length	Standard package	Dimensions	Weight
5"	40 pieces/ carton	62.5 cm L x 39.5 cm D x 23.5 H (24.6" L x 15.6" D x 9.3" H)	12.6 kg (27.8 lb)
10"	24 pieces/ carton	62.5 cm L x 39.5 cm D x 23.5 H (24.6" L x 15.6" D x 9.3" H)	12.3 kg (27.1 lb)
20"	15 pieces/ carton	62.5 cm L x 39.5 cm D x 23.5 H (24.6" L x 15.6" D x 9.3" H)	13.5 kg (29.8 lb)
30"	15 pieces/ carton	87.5 cm L x 40.0 cm D x 20.0 cm H (34.4" L x 15.7" D x 7.9" H)	18.4 kg (40.6 lb)
40"	15 pieces/ carton	112.5 cm L x 40.0 cm D x 24.0 cm H (44.3" L x 15.7" D x 7.9"H)	23.5 kg (51.8 lb)

2. ACCEPTANCE

Please check product's specifications and material number after receiving. Besides material number, each product has its own lot number as shown in Figure 1.

The tracking number can be found on the cartridge filter's fin, end cap, or cage body near the end cap.

G	Year	Month	SAP lot number	-17
G: Hangzhou	1: 2021 2: 2022 3: 2023 4: 2024 5: 2025 6: 2026 7: 2027 8: 2028 9: 2029	A: January B: February C: March D: April E: May H: June J: July K: August M: September N: October P: November S: December	Last 6 numbers of the work order	Sequence number of the cartridge filter in the batch

Example: *G2A471270-17 = 17th cartridge of lot 471270 in January 2022.*

Figure 1. Annotation for lot number.

3. STORAGE

1. Store the filters in a cool dry area away from the sun, rain, or heat.
2. To keep cartridge filters in good condition, do not store them with toxic, corrosive, volatile, or pungent materials.
3. Handle filters gently during shipment and unpack only when ready to use.

4. INSTALLATION

4.1 PREPARATION BEFORE INSTALLATION

To ensure the cartridge filter is suitable for fluid prior to installation, follow these instructions.

1. Purge or rinse equipment and pipes before installing filters to remove particles or welding slag.
2. Make sure the cartridge filter package is in good condition before use.
3. Unpack carefully to prevent damaging the filter.
4. To keep the filter free from contamination, we suggest wearing dust-free gloves when unpacking and installing the filter.

4.2 INSTALLATION PROCEDURE

4.2.1 Single Open Ended Cartridge Filters

1. Visually inspect that the O-rings are undamaged and properly placed in grooves.
2. Verify that the sealing surface of the filter housing is clean and undamaged.
3. We strongly recommend that the cartridge filter adapter be immersed into an appropriate liquid to lubricate the O-rings and make installation easier.

   In most cases, satisfactory lubrication can be achieved with the same rinsing liquid used after installation.

   Attention: Low boiling point liquids (e.g., ethanol or isopropanol) should not be used as installation lubricants because high vapor pressure may damage O-rings or the adapter if the cartridge filter is steam sterilized or used under temperature higher than the lubricant's boiling point.
4. Gently insert the cartridge to the correct position.
5. For a filter with bayonet lock, rotate the filter clockwise after inserting until the bayonet locks into position.
6. If necessary, secure a positioning plate or spring on the end of the cartridge filter.

4.2.2 Double Open Ended Cartridge Filters with Gaskets

1. Visually inspect that the gaskets are not damaged and properly placed at the ends of the filter.
2. Verify that the sealing surface and filter housing nut are clean and undamaged.
3. Slide the cartridge filter to the proper position through the rod and secure with a sealing nut.

5. FLUSHING AND WETTING

5.1 PURPOSE

1. Flushing can fully wet a cartridge filter more easily and the integrity test results will be more accurate with a fully wetted cartridge filter.
2. Flushing can also clean cartridge filters.

5.2 METHODS

5.2.1 Parameters for Hydrophilic Membrane Cartridge Filters

1. Prepare components: filter housing, pressure gauges, combined connectors, clean gas source, pump, tank, pipes etc, Figure 2.
2. Set up a flushing and wetting system.
3. Close V1 and V3.
4. Open V2, V4, and the vent valve.
5. Turn on the pump and regulate V4.
6. Close the vent valve when the wetting fluid flows from the vent valve.
7. Start flushing and wetting.
8. Fully open V4, flush for 5 – 10 seconds.
9. Then adjust V4 until the pressure gauge shows the pressure is P1 = 3 ± 0.5 bar, keep flushing for 10 to 15 minutes. (Alternative solution: Adjust V4 until the pressure gauge shows the pressure is 1.5 to 2.0 bar, keep flushing for 20 minutes.)

   NOTE: Purified water or water for injection (WFI) is recommended to flush hydrophilic membrane cartridge filters.

5.2.2 Parameters for Hydrophobic Membrane Cartridge Filters

1. Soak hydrophobic membrane cartridge filters in a 95% ethyl alcohol aqueous solution before flushing.
2. Flush and wet the cartridge filters according to step 5.2.1.

6. INTEGRITY TEST

6.1 OVERVIEW

Integrity tests should be performed when the cartridge filter is designed to remove bacteria.

1. Perform integrity tests on the sterilized cartridge filters following methods approved by pharmacopoeia or pharmaceutical production validation guidelines before sterilization, after sterilization, and after use.
2. The integrity test before sterilization verifies filter integrity, pore size, and installation.
3. The integrity test after sterilization can tell if the cartridge filter is integral or not. The downstream of the filter should keep sterile in performing integrity test after sterilization.
4. The integrity test after use can tell if the cartridge filter is damaged during operation.

Filter components are shown in Figure 2.

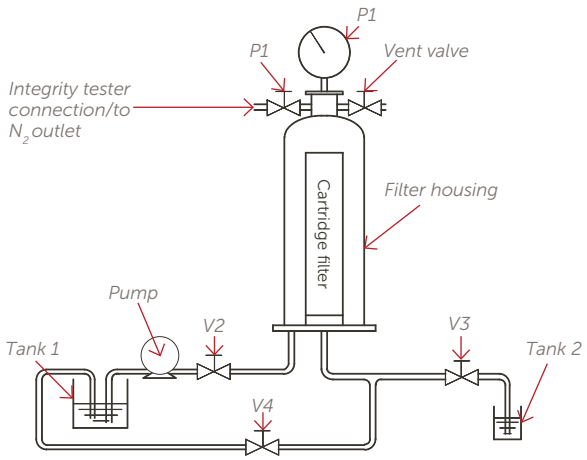

Figure 2. Flushing and wetting system.

6.2 BUBBLE POINT TEST

6.2.1 Using Automation Equipment

1. Turn off the pump.
2. Close V2 and V3. Open V4.
3. Connect equipment gas tube to N_2 outlet.
4. Open V1.
5. Conduct bubble point test with the full-automatic integrity tester.

6.2.2 Using Manual Equipment

1. Turn off the pump. Close V2.
2. Connect equipment gas tube to N_2 outlet.
3. Regulate V1 and increase the pressure P1 evenly within 1.5 minutes to a set value.
4. The set value is 80% of standard bubble point pressure.
5. Close V4 and open V3.
6. Increase the pressure P1 at a rate of 1 bar/min until continuous bubbles appear in tank 2.
7. Now, P1 pressure is the real bubble point pressure. After measurement, close V1 and slowly open the vent valve.
8. Close the vent valve after the gas is exhausted.
9. End test with recording data.

A fully wetted cartridge filter is necessary. If the integrity test result does not meet the requirement, please rewet the cartridge filter according to instruction 5.2, and then repeat the integrity test.

1. Maintain the temperature at 23° – 25°C (73° – 77°F) during bubble point testing.
2. In the bubble point test, if P1 reaches 4 bar before bubbles continuously appear in tank 2, stop the test to prevent damaging the cartridge filter. And the bubble point test should be regarded as passed.
3. The bubble point test result may be lower if pressure increases too rapidly as gas flow will impact and damage liquid film on membrane.
4. It is not necessary to keep increasing pressure after bubbles continuously show in tank 2. Continuing to increase pressure may damage membrane or cartridge filter structure.
5. If lots of bubbles continuously show soon after pressurizing, two causes should be considered. First, the cartridge filter may not be fully wetted and not be sealed properly at the adapter. Rewetting and reinstalling after checking the seal material may help. Second, the cartridge filter's structure is damaged after use and the filter should be discarded.

7. STERILIZATION

Unless marked on label, all of Entegris' cartridge filters, and membrane components are shipped unsterilized.

Both steam-in-place (SIP) sterilization and autoclave sterilization can be used to sterilize Pharmsteri PES and PTFE cartridge filters.

7.1 STEAM-IN-PLACE STERILIZATION

7.1.1 Standard Operating Procedure for Liquid Cartridge Filters

1. A common SIP system for liquid cartridge filters is shown in Figure 3.

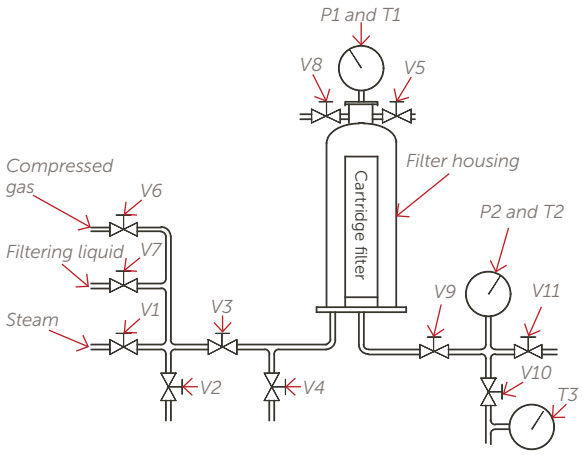

Figure 3. Steam-in-place system for liquid cartridge filters.

2. Make sure all valves are closed.
3. Check that the steam supply and compressed gas pressures are set to the required values. It is recommended that the steam pressure be set between 1.5 and 2 bar.
4. Open V1 and V2 and purge the steam line until condensate is completely removed.
5. Fully open V4 and V5 to drain condensate water from the filter.
6. Slowly open V3 to progressively introduce steam and heat up the filter.
7. Partially close V2, V4, and V5, so that a wisp of steam and a continuous drip of water can be seen exiting.
8. Respectively open V9 and V10 to establish a steady flow of steam and allow condensate drainage and air removal from the housing.

   NOTE: It is very important to control the pressure P1 and P2 to keep ΔP (P1-P2) below 350 mbar.

9. Ensure all air and condensate are effectively removed by keeping the V2, V4, V5, and V10 open and a wisp of steam and a continuous drip of water can be seen exiting.
10. When the downstream temperature of the filter, as measured by the pressure thermometer T2, reaches over 121.1°C (250°F) start the timer. (Ensure the temperature at the pressure thermometer T1 does not exceed 128°C [262°F]). Sterilization time should be at least 30 minutes or longer. During the sterilization phase both pressure and temperature should be recorded regularly.

11. After completing the sterilization cycle, close the steam supply V1 and slowly open V6 to introduce compressed gas into the system.

    NOTE: Make sure that the system remains under positive pressure (P1>P2>0) and ΔP (P1-P2) across the filter does not exceed 350 mbar.

12. After all steam is exhausted from system by compressed gas, close V2 and V4 and increase the flow of gas through the system. Maintain the gas flow to cool down the system until the temperature gauge T3 indicates approximately 30°C (86°F).

13. When it is not in use, close V10, V9, and V5, and keep V6 and V3 open to maintain a positive pressure into the sterile filter system. Make sure that P1 does not exceed 2 bar.

7.1.2 Standard Operating Procedure for a Sterile Tank Equipped with a Vent Filter

A common SIP system for a vent filter is shown in Figure 4.

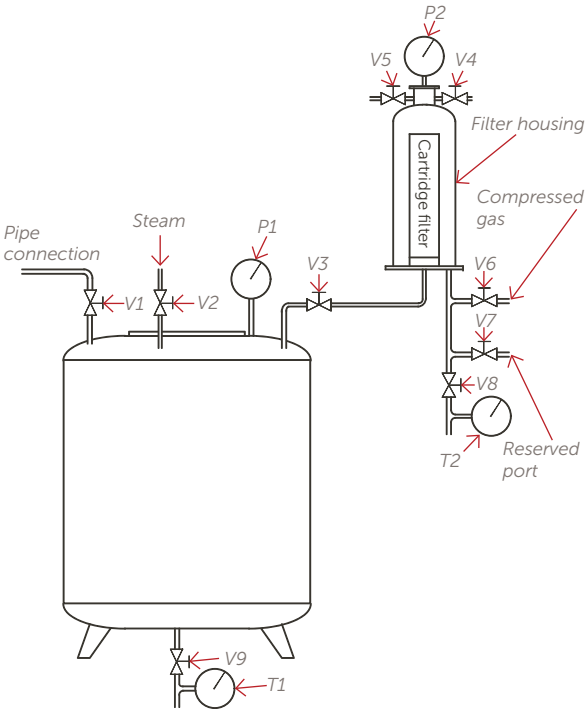

Figure 4. Steam-in-place system for vent filters.

1. Make sure all valves are closed.
2. Check that the steam supply and compressed gas pressures are set up at the required values.
3. Respectively open V1, V2, and V9 to introduce steam to the system and to exhaust air from the system.
4. Partially close V1 and V9 to build tank pressure to at least 0.5 bar and wait for the temperature gauge T1 to indicate more than 100°C (212°F).
5. Slowly open V3 to introduce steam to the vent filter, and then open V5 and V8 to eatablish a steady flow of steam and allow for condensate drainage and air removal from the filter housing.

   NOTE: It is very important to control the pressure P1 and P2 to keep ΔP (P1-P2) below 100 mbar. For reverse direction SIP, the configuration of 226 (code 7) is recommended.

6. Ensure all air and condensate are effectively removed by keeping the V1, V5, V8, and V9 open and a wisp of steam and a continuous drip of water can be seen exiting.
7. When the temperature throughout the system reaches over 121.1°C (250°F), as measured by the temperature gauges T1 and T2, start the timer. Sterilization time should be at least 30 minutes or longer. During the sterilization phase both pressure and temperature should be recorded regularly.
8. At completion of the sterilization cycle, close the steam supply V2 and slowly open V6 to introduce compressed gas into the system.

   NOTE: Make sure that the system remains under a positive pressure (P2>P1>0) and keeps ΔP (P2-P1) on the filter does not exceed 350 mbar.

9. Allow for steam to exhaust from all valves and close V5 and V8 to increase the flow of compressed gas through the system. Maintain the gas flow to cool down the system until the temperature gauge T1 indicates approximately 40°C (104°F).
10. Close V1 and V9, and keep V6 and V3 open to maintain a positive pressure into the sterile filter system when the sterilization is done and system is not in use.

7.1.3 Steam

1. Dry, saturated steam is necessary.
2. Overheated steam is not allowed.
3. Steam must be clean and free of particles.
4. Strictly control steam temperature and pressure.
5. Strictly control the differential pressure across cartridge filters.

7.2 AUTOCLAVING

Sterilize for 30 minutes at 121°C (250°F).

1. Do not put stress on cartridge filters.
2. Air inside autoclave should be exhausted at the initial stage of sterilization.
3. Orient filter components properly so that condensate water can flow out easily.
4. Strictly control the differential pressure across cartridge filters in cooling stage.
5 To avoid potential oxidative destruction by hot air, remove cartridge filters once sterilization is finished.

8. PRODUCTION OPERATION

After sterilization, the cartridge filter can be used for aseptic filtration with passed integrity test, refer to instruction 5 and 6.

8.1 LIQUID FILTRATION DEVICE

1 For aseptic filtration, cartridge filter components and all components downstream should be presterilized. It is recommended that filtration and sterilization be carried out under a controlled environment.
2. At the beginning of filtering, open the vent valve allowing liquid to flow into the filter slowly so that gas inside the filter housing could be exhausted from the vent valve. Once the liquid flows from vent valve, close the vent valve.
3. Slowly regulate the valve. Gradually increase the flow rate or pressure to a desired value and avoid impacting the cartridge filter with a sudden high flow. The filtration pressure should not exceed the maximum operating pressure written in the product specification data sheet. The filtration pressure is recommended to be less than 2 bar in a terminal sterile filtration.
4 To prevent cartridge deformation, the cartridge filter should not be used under reverse pressure conditions.
5. After filtration, it is recommended to push the liquid out of the filter.

8.2 GAS DEVICE

For gas systems that may contain liquid or condensate, install filter so it can drain liquid and condensate easily.

9. CLEANING AFTER USE

9.1 PURPOSE

Thoroughly cleaning cartridge filters after use can reduce the physical blockage of the membrane and preserve filter integrity as well.

9.2 SUGGESTIONS

1. Soak the cartridge filter for two hours with 1% sodium hydroxide solution 30° – 60°C (86° – 140°F) and rinse it with pure water.

   NOTE: This is not recommended for the mixed cellulose membrane cartridge filter.

2. Soak the cartridge filter in 0.5% hydrochloric acid solution for 10 minutes and rinse it with pure water.

   NOTE: This is not recommended for the nylon membrane cartridge filter.

9.3 NOTES

1. To prevent deformation, the cartridge filter should not be washed backwards.
2. Take precautions to avoid filter damage by other objects when cleaning.
3. The cartridge filter should be cleaned with high quality water.
4. It is recommended that the cleaning temperature is 30° – 60°C (86° – 140°F) and the soaking time is 30 – 60 minutes.
5. Cleaning agents should be thoroughly washed after soaking.
6. Contact Entegris if other cleaning agents or methods are needed.

10. PRESERVATION

10.1 PRESERVATION IN DRY

10.1.1 Applicable Scenario

Preservation time ≥3 days.

10.1.2 Method

1. The cartridge filter should have been thoroughly cleaned.
2. Sterilize the cartridge filter (if necessary).
3. Push out the residual water contained in the cartridge filter core with clean aseptic compressed air or nitrogen. The air pressure is controlled at about 70% of the bubble point pressure of the cartridge filter.
4. Put the cartridge filter into a clean circulating hot air oven and dry for 24 hours under 60 ± 5°C (140°F).
5. If the cartridge filter is still wet, continue drying at 50°C (122°F) until totally dry.
6. Cool the cartridge filter to room temperature, then pack it with a clean polyethylene bag and store it in a proper place.

10.2 PRESERVATION IN WET

10.2.1 Applicable Scenario

Preservation time <3 days.

10.2.2 Method

1. The cartridge filter should have been thoroughly cleaned.
2. Soaking

   Method 1: Soak in injection water (preservation time <24 hours);

   Method 2: Soak in 1 – 1.5% alkali solution (preservation time ≤3 days, applicable for PES, PTFE, PP cartridge filter).

10.3 NOTES

1. To prevent membrane damage, keep cartridge filters away from sharp objects.
2. To prevent bacteria growth, do not pack wet cartridge filters in plastic bags.
3. Drying temperature of the cartridge filter should not exceed 65°C (149°F).
4. Drying times may differ between ovens.
5. It is recommended that pharmaceutical manufacturers should do cleaning validation of residual soaking reagents after wet preservation to make sure the cartridge filters are safe to be used in process again.

11. REPLACEMENT

Pharmaceutical manufacturer should follow GMP requirements for replacing cartridge filters.

Entegris recommends replacing a cartridge filter once any of the following situation occurs:

1. The cartridge filter fails integrity test.
2. The differential pressure in normal operation is above 2 bar.
3. The flow rate cannot meet production requirements.
4. The cartridge filter is beyond its verified lifetime.

12. FIRST AID

1. **Ingestion:** These devices are not likely to be hazardous by ingestion. Consult a physician if necessary.
2. **Eyes:** Because of the size and solid nature of these devices they are not expected to present an eye injury hazard.
3. **Inhalation:** These devices do not present an inhalation hazard because of the non-volatile nature of the polymeric component materials.
4. **Skin:** These devices are not likely to be hazardous by skin contact but cleansing the skin is advisable.

13. HAZARD IDENTIFICATION

1. **Appearance:** Porous white membrane encased in a solid polymer (plastic) housing with silicon O-rings on end cap subassembly.
2. **Health Hazard:** Under normal operating temperature and pressure conditions, these devices do not present a health hazard.
3. **Physical Hazard:** Under normal operating temperature and pressure conditions, these devices do not present a physical hazard. If removed from its housing, the membrane and nonwoven fabric are considered a combustible solid.

14. WARNING

To reduce the risk associated with choking, do not allow children under three years of age to have access to small parts during the installation of this product.

15. WARRANTY AND CLAIMS

Entegris warrants that all products are manufactured in accordance with their specifications and quality standards. A certificate of quality will also be issued by quality upon lot release and attached to product package. Date of manufacture of all products is indicated on label and the shelf-life claim validated.

To ensure the capsule filter is not damaged during transportation, carefully check that the product packaging corrugated cartons are not damaged.

16. EPA INFORMATION

PRODUCED BY:

Hangzhou Anow Filtration and Materials Co., Ltd.
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EPA Est. No.: 97725-CHN-002

Hangzhou Anow Filtration and Materials Co., Ltd. is a subsidiary of Entegris, Inc.

17. SERVICES

Entegris provides a variety of technical services including filter selection, system design, process verification, and more. Contact us to learn more.

LIMITED WARRANTY

Entegris' products are subject to the Entegris, Inc. General Limited Warranty. To view and print this information, visit entegris.com and select the Legal & Trademark Notices link in the footer. Entegris does not warrant any failure in the case of customers using unapproved foreign components.

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