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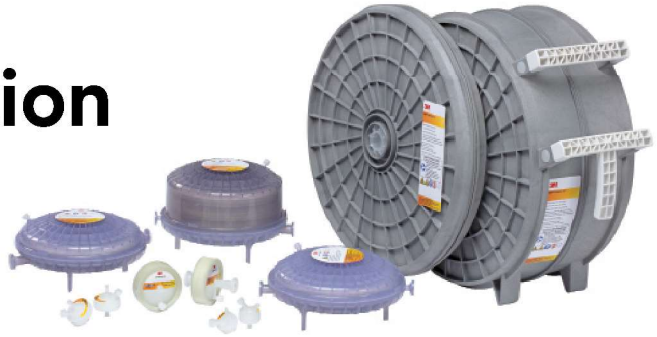
3M Separation and Purification Sciences Division

Installation Qualification Technical Brief



3M™ Polisher ST Series Capsules

Safety Information

Read and follow all safety information contained in these instructions and the instructions provided with the original filtration system, prior to installation and use. Retain for future reference.

Intended Use:

3M™ Polisher ST single-use filter products are intended for use in biopharmaceutical processing applications of aqueous based pharmaceuticals (drugs) and vaccines in accordance with the product instructions and specifications, and cGMP requirements, where applicable.

Since there are many factors that can affect a product's use, the customer and user remain responsible for determining whether the 3M product is suitable and appropriate for the user's specific application, including user conducting an appropriate risk assessment and evaluating the 3M product in user's application.

Restrictions On Use:

3M advises against the use of these 3M products in any application other than the stated intended use(s), since other applications have not been evaluated by 3M and may result in an unsafe or unintended condition. Do not use in any manner whereby the 3M product, or any leachable from the 3M product, may become part of or remains in a medical device that is regulated by any agency, and/or globally exemplary agencies, including but not limited to: a) FDA, b) European Medical Device Directive (MDD), c) Japan Pharmaceuticals and Medical Devices Agency (PMDA) or in applications involving permanent implantation into the body; Life-sustaining medical applications; Applications requiring food contact compliance.

Explanation of Signal Word Consequences	
⚠ **WARNING:**	Indicates a hazardous situation which, if not avoided, could result in serious injury or death.
⚠ **CAUTION:**	Indicates a hazardous situation which, if not avoided, could result in minor or moderate injury and/or property damage.
NOTICE:	Indicates a situation which, if not avoided, could result in property damage.

Explanation of Safety and Related Symbols	
	WARNING: Explosion hazard
	Single use
	Wear PPE
	Storage conditions
	Heavy Parts

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1. Introduction

Herein are described orthogonal a) pre-use installation verification and b) post-use installation validation tests recommended to reduce the risk of undetected viral clearance loss during the use of 3M™ Polisher ST capsules.

The pre-use installation verification is a non-destructive test that is useful in identifying larger capsule defects that might occur, for example, during shipment. The pre-use installation verification is conveniently performed during the required preconditioning flush. Performance of this test reduces the risk that a damaged capsule is used to process product-containing fluid.

The post-use installation validation test is a **destructive** bubble point test[1] that is useful in detecting smaller mechanical defects in the media or seals within the capsule. Post-use bubble point test values correlate closely with measured viral clearance in 3M™ Polisher ST capsules.[2] Performance of this test helps reduce the risk of undetected viral clearance loss prior to further downstream processing due to mechanical damage of the capsule which may have occurred either before or during processing.

Notice:
The post-use bubble point test MAY NOT be used as a pre-use test. The bubble point test is destructive, in that wetting and air pressurization of 3M™ Polisher ST capsules prior to use may introduce air bubbles between media layers within the capsules that cannot be reliably removed, resulting in decreased performance of the capsules during use.

⚠ WARNING

To reduce the risk of injury from possible end user exposure associated with a) biological contamination and b) degradation products released from the purification media; and To reduce the risk of product loss associated with a) chemical release from purification media, and b) nullification of Supplier's USP <87> and <88> Class VI compliance of filter capsule components:

- Use the installation procedure specified in Operation Instructions.
- The capsule must be subjected to a preconditioning flush prior to use. Use the procedure specified in Operation Instructions.
- The minimum required preconditioning flush volume is 54 L/m^2.
- After pre-use NaOH sanitization, flush the capsule with aqueous buffer until the pH of the effluent is within ±0.5 pH units from the pH of the buffer.
- Capsules are designed for single use only. Do not reuse.
- Do not store under conditions outside of the recommended storage temperature range (0-30°C).
- Do not use past the expiration date.
- Do not use with organic solvents or flammable liquids.
- Use only with aqueous based process fluids in the pH range of 5 to 9.
- Use only alkaline resistant manifold sets.
- Do not use with or expose to hot liquids >40°C.
- Perform all required maintenance on or before its scheduled date and always use specified replacement parts in the Service & Maintenance Details.
- Do not use on unleveled surfaces.
- Do not gamma or ethylene oxide sterilize.
- Do not steam-in-place sterilize.
- Only expose the capsule to 1 sterilization or 1 sanitization cycle prior to use.
- Do not autoclave and base sanitize the same capsule prior to use.
- During pre-use autoclave sterilization do not exceed a temperature of 121°C or a duration longer than 30 minutes for capsules BC1-BC340 and BC2300, and 40 minutes for BC1020 and BC16000.
- Do not use with or expose to process liquids until capsule temperature is <40°C.
- Only use NaOH as sanitizing chemical and do not exceed 1 M NaOH concentration or 60 minute duration for sanitization.
- Use only 3M™ Encapsulated System Holders.

⚠ WARNING

To reduce the risks associated with chemical exposure, impact, crush, tipping hazards, property damage from product loss, bypass or cross contamination due to pressure barrier failure, connector failure, purification media or capsule failure:

- Use the installation procedure specified in Operation Instructions.
- Follow the installation and operation manual and inspect the o-rings.
- Hardware Qualification testing is recommended prior to use.
- Wear Personal Protective Equipment (PPE) to prevent chemical contact upon a chemical splash.
- The capsule must be subjected to a preconditioning flush prior to use. Use the procedure specified in Operation Instructions.
- After pre-use NaOH sanitization, flush the capsule with aqueous buffer until the pH of the effluent is within ±0.5 pH units from the pH of the buffer.
- Capsules are designed for single use only. Do not reuse.
- Do not modify or alter the capsules, manifolds, and holders.
- Do not put capsule into service if any damage is observed.
- Do not install where fluid pressure exceeds 3.4 bar (50 psig.) for BC1 and BC4, BC2300, and BC16000, 2.8 bar (40 psig.) for BC25, and 3.1 bar (45psig.) for BC170, BC340, and BC1020 capsules.
- Do not use in organic solvent based processing.
- Use only with aqueous based process fluids in the pH range of 5 to 9.
- Use only alkaline resistant manifold sets.
- Do not use with or expose to hot liquids >40°C.
- Perform all required maintenance on or before its scheduled date and always use specified replacement parts in the Service & Maintenance Details.
- Do not use on unleveled surfaces.
- Do not use for more than 8 hours.
- Do not use for continuous service with compressed gasses. Use of compressed gas is permissible for post-use bubble point testing and blow-down purposes only. Limit post-use bubble point test and blow-down gas pressures to less than 1.4 bar (20 psig) and temperature less than 25°C for no longer than 30 minutes.
- Do not hang other items on the capsule.
- Do not gamma or ethylene oxide sterilize.
- Do not steam-in-place sterilize.
- Only expose the capsule to 1 sterilization or 1 sanitization cycle prior to use.
- Do not autoclave and base sanitize the same capsule prior to use.
- During pre-use autoclave sterilization do not exceed a temperature of 121°C or a duration longer than 30 minutes for capsules BC1-BC340 and BC2300, and 40 minutes for BC1020 and BC16000.
- Only use NaOH as sanitizing chemical and do not exceed 1 M NaOH concentration or 60 minute duration for sanitization.
- Do not pressurize the capsule more than 0.3 bar (5 psig) during introduction of NaOH solution and static soak during sanitization.
- Do not wipe the exterior of the capsule with an aqueous solution having an ethyl and/or isopropyl alcohol concentration greater than 70%.
- Do not use with or expose to pressurized steam or sanitizing chemicals other than NaOH.
- Use only 3M™ Manifolds and 3M™ Encapsulated System Holders.

⚠ CAUTION

To reduce the risks associated with chemical exposure due to pressure barrier failure, connector failure, purification media or capsule failure from use of disinfectants within the product:

- Use up to 1 M NaOH for pre-use and post-use sanitization and up to 5% NaClO (bleach) for post-use sanitization.
- Do not expose the capsule to NaOH for more than 60 minutes during sanitization.
- Use only alkaline resistant manifold sets.
- Do not pressurize to more than 0.3 bar (5 psig) during introduction of NaOH solution and static soak during sanitization.
- Wear personal protective equipment (PPE) to prevent contact upon a chemical splash.
- Use only 3M™ Manifolds and 3M™ Encapsulated System Holders.

CAUTION

To reduce the risk of burn or exposure injuries associated with autoclave sterilization.
- Wear personal protective equipment (PPE) to handle hot capsules.

WARNING

To reduce the risk of fluid exposure:
- Evaluate the risk of your process liquids and determine an appropriate protocol to dispose of spent capsules and all other waste.
- Dispose of capsules and all other waste in accordance with federal, state, and local regulations or your local country's laws and regulations.
- The protective caps on the capsule connections are designed for the protection of the capsule and packaging. The protective caps are not intended to contain process liquids during the disposal of used capsules.

2. Materials and Equipment

Pre-use Installation Verification
The following equipment is recommended to conduct the filter wet-out, the required preconditioning flush, the pre-use installation verification test, and (if required) re-wetting of the capsule media in the case of performing a repeat post-use installation validation test:

BC1, BC4, and BC25 Capsules
- GE Health Care Life Sciences ÄKTA chromatography system, or similar

BC25, BC170, BC340, BC1020, BC2300, and BC16000 Capsules
- Peristaltic pump system:
  - Peristaltic pump, e.g., Masterflex® L/S® pump drive, or similar;
  - Peristaltic pump head, e.g., Masterflex® L/S® Easy-Load® II Pump Head, or similar;
  - Peristaltic pump tubing

Post-use Installation Validation
3M recommends the use of an automated Sartorius Sartocheck® 4 Plus Filter Tester, or similar unit, for performance of the post-use bubble point test. The instructions herein pertain specifically to the Sartocheck® 4 Plus instrument. A different automated bubble point test instrument may be used, or the bubble point pressure may be measured manually according to the current revision of the appropriate ASTM method.[1] The test should be set up to provide a "Pass" if the measured bubble point pressure of the capsule is greater than or equal to 900 mbar and a "Fail" if the measured bubble point pressure is less than 900 mbar. **At no time should the applied inlet gas pressure be allowed to exceed 1,400 mbar.** Additional information on the basis for the post-use bubble point test pass/fail criteria and the correlation of the criteria with viral clearance is provided in a companion technical brief.[2]

Equipment recommended to conduct the post-use installation validation bubble point test:

- Sartorius Sartocheck® 4 Plus Filter Tester available from Sartorius Stedim Biotech

Notice:
The operating instructions provided by the manufacturer of any equipment used must be followed and, where required, validated.

3. Safety Requirements

- Read and follow all safety requirements in the 3M™ Polisher ST Installation and Operation Instruction manual for the capsule being used.
- Review and follow all manufacturer safety requirements for any equipment used.
- At a minimum, wear safety eyewear, lab coat, and gloves when performing the procedures described herein. Wear any additional protective equipment appropriate to your work location and to the fluid contained within the capsule.
- To prevent an explosion hazard, never pressurize the capsule with a gas pressure greater than 1,400 mbar.

4. Required Preconditioning Flush and Pre-Use Installation Verification Procedure

4.1. Follow the Required Preconditioning Flush Instructions in Section 2 of the Installation and Operation Instructions for the 3M™ Polisher ST capsule being used.

4.2. While performing the required preconditioning flush, monitor the pressure upstream of the capsule. This can be done using a pressure transducer positioned upstream of the capsule or positioned on the capsule vent.

4.3. The differential pressure at the end of the preconditioning flush must be equal to or greater than 3.0 psid when conducting the preconditioning flush at the recommended flow rate of 600 liters/m^2/hr (LMH).

4.4. If the differential pressure at the end of the preconditioning flush is less than 3.0 psid, do not use the capsule to process fluid. Obtain a different 3M™ Polisher ST capsule, repeat steps 4.1-4.4, and contact your 3M Sales Representative or Application Engineer.

5. Post-Use Installation Validation Procedure

5.1. Gravity drain or blow down the capsule to remove excess fluid from the capsule headspace. **If blowing the capsule down, do not exceed an inlet air pressure of 500 mbar.** (Blowing down the capsule with an inlet air pressure greater than 500 mbar risks introduction of air into the media, which can result in a bubble point test error or a false test "Fail" of an integral capsule.)

5.2. Connect the outlet tubing of the Sartocheck® 4 Plus Filter Tester to the inlet of the capsule for BC1-BC1020 sizes. For BC2300 and BC16000 capsules attach to the Inlet Vent on the top manifold.

5.3. Ensure the vent cap is closed.

5.4. Set the test parameters in the Sartocheck® 4 software as specified in Tables 1 and 2, using "Page Down" to step through each successive page of parameters and pressing "Enter" to save each setting.

5.5. Tap "Start" to begin test.

5.6. As soon as the instrument begins applying air pressure to the capsule, check the capsule inlet connection, vent, and tubing for air leaks. If desired, inlet and vent air leaks can be detected by immersing the capsule in water and looking for air bubbles at the connections.

5.7. If there is an air leak, stop the test, fix the connection, and restart the test.

Note: Upon application of air pressure, fluid may initially flow from the capsule outlet. This is normal as the fluid previously retained in the filter media is forced out when air pressure is applied to the capsule.

Table 1. Sartocheck® 4 Plus Test Parameters for Post-Use Installation Validation

Screen/Parameter	Value
Program test: Select test method	
Filter test method	Customer-specific Bubble Point test
Test parameters – Default settings	
Ext. pressure sensor	No
Ext. valves	No
Test parameters – Standard/Non-Standard	
Pressure unit	mbar
Pressure level	50 mbar
Limits	Not active
Test parameters – Customer-specific Bubble Point	
Start factor	0.9
Prestabilization	180 sec
Stability by phase	6 sec
Phase test	12 sec
A1 criterion	Varies by capsule; see Table 2
A2 criterion	Varies by capsule; see Table 2
Test parameters – Bubble point test	
Minimum BP	900 mbar
Maximum BP	1,400 mbar
Net volume	Measuring

5.8. Upon completion of the test, obtain test print out.

5.9. Record test result data from the Sartocheck® 4 Plus print out. Typically, the instrument will display "Pass" or "Fail" at the conclusion of the test.

5.10. **PASS.** A "Pass" result indicates the capsule has a bubble point pressure greater than or equal to 900 mbar and is deemed acceptable.

5.11. **FAIL.** A "Fail" result indicates the capsule has a bubble point pressure less than 900 mbar. Repeat the bubble point test as described in steps 5.13-5.18, below. If, after repeating the test, the result remains a "Fail," then the capsule is not deemed to be integral and the viral clearance performance results may be compromised. Contact your 3M Sales Representative or Application Engineer for additional support as required.

5.12. **"Test cancelled" (9141 error).** Occasionally, the Sartocheck® 4 Plus may provide this test result along with the following message: "*The diffusion from the third or higher bubble point pressure increment exceeds the limit.*" This error may result from a leaking inlet connection or vent cap or, more rarely, from incomplete wetting of the filter media. Repeat the bubble point test as described in steps 5.13-5.18, below, paying special attention to possible air leaks in the tubing, inlet connection, or vent cap. If, upon repeating the test, a test error still occurs, contact your 3M Sales Representative or Application Engineer for additional support.

Table 2. Sartocheck® 4 Plus Bubble Point Test Parameters that Vary by Capsule

Parameter	Units	Capsule							
		BC1	BC4	BC25	BC170	BC340	BC1020	B2300	BC16000
A1 criterion	ml/min	0.2	0.2	0.2	3	3	9	5	40
A2 criterion	ml/min	0.6	0.6	1.5	20	20	60	100	400

Repeating the post-use bubble point test:

5.13. Detach the capsule inlet from the Sartocheck® 4 Plus and open the capsule vent.

5.14. Attach the capsule inlet to tubing connected to a peristaltic pump.

5.15. Fill the upstream capsule volume, using a buffer or salt solution having a **conductivity greater than or equal to 2.5 mS/cm**, at a flow rate up to that specified in Table 3. Once all air has been removed from the upstream capsule volume, close the vent cap.

5.16. Continue pumping the fluid through the capsule, at the flow rate specified in Table 3, until a permeate volume greater than that specified in Table 3 has been collected.

5.17. Disconnect the capsule and gravity drain the capsule headspace. **Do not blow down the capsule with air pressure.**

5.18. Repeat steps 5.2-5.12.

Table 3. Parameters for Capsule Re-Wetting to Repeat the Post-Use Test

Parameter	Units	Capsule							
		BC1	BC4	BC25	BC170	BC340	BC1020	BC2300	BC16000
Flow Rate	ml/min	1	4	27	170	340	1,020	2,300	6,000
Volume	ml	2.5	10	68	425	850	2,550	5,750	40,000

References

1. ASTM Standard F316 – 03 (2011), Standard test methods for pore size characteristics of membrane filters by bubble point and mean flow pore test, ASTM International, West Conshohocken, PA, 2011.

2. 3M™ Polisher ST Post-Use Installation Validation Technical Brief, https://multimedia.3m.com/mws/media/1878778O/3m-polisher-st-post-validation-tech-brief.pdf.

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