Installation Qualification Test Procedure For the Zeta Plus™ Encapsulated System

SAFETY INFORMATION

Read, understand, and follow all safety information contained in these instructions prior to installation and use of the Zeta Plus™ Encapsulated System. Retain these instructions for future reference.

Intended Use:

Zeta Plus Encapsulated System Model# 16EZA and 16EZB are intended for use in manufacturing of aqueous-based pharmaceutical (drug) products, including active pharmaceutical ingredients and vaccines.

Prohibited Use:

As a component in a medical device that is regulated by any agency, and/or globally exemplary agencies, including but not limited to: a) US Food and Drug Administration (FDA), b) European Medical Device Directive (MDD), c) Japan Pharmaceuticals and Medical Devices Agency (PMDA); Applications involving permanent implantation into the body; Life-sustaining medical applications; Applications requiring FDA Food Contact compliance without use restrictions.

EXPLANATION OF SIGNAL WORD CONSEQUENCES	
⚠ WARNING:	Indicates a potentially hazardous situation, which, if not avoided, could result in death or serious injury and/or property damage.
⚠ CAUTION:	Indicates a potentially hazardous situation which, if not avoided, may result in minor or moderate injury and/or property damage.
CAUTION:	Indicates a potentially hazardous situation, which, if not avoided, may result in property damage.

⚠ WARNING

To reduce the risk associated with crush or impact related injuries:

- **16EZA Holder can weigh up to 153 kg (337 lbs) and 16EZB holder can weigh up to 662kg (1460 lbs) when full of liquid. Take care** during movement of holder. **Do not** attempt to roll holder on inclines or to push into or roll over any objects in your path (doors, door thresholds, hoses, etc.) without adequate assistance when moving this holder;

- **Do not** attempt to move this holder if swivel casters are damaged;
- **Perform all required maintenance** on or before its scheduled date and always use specified replacement parts listed in the Installation and Operation Instructions.
- **Keep clear** of all moving parts and areas marked as pinch points.

To reduce the risk associated with chemical exposure due to system failure:

- **Do not** use with organic solvents.

To reduce the risk associated with burn or system burst related injuries:

- **Do not** use with or expose this product to hot liquids [> 40°C (>104°F)] or pressurized steam;
- **Do not** use this product for continuous service with compressed gases.

To reduce the risk associated with back strain:

- Wet capsule filters may weigh more than 9.1 kg (20 pounds) – use proper lifting procedures.

To reduce the risk associated with personal injury due to riding upon the holder:

- **Do not** use this product for personal transportation.

⚠ CAUTION

To reduce the risk associated with exposure to contaminants:

- **Always** use appropriate personal protective equipment (PPE) when installing or servicing the Zeta Plus Encapsulated System, or when changing capsule filters as per your Standard Operating Procedure;
- **Ensure** that all system pressure has been relieved prior to opening the system to atmosphere.

CAUTION

To reduce the risk associated with property damage due to product loss:

- **Do not** install where fluid pressure exceeds 3.4 bar (50 psig);
- **Ensure** a pressure release device with the pre-determined pressure limit set at 3.8 bar (55 psig) is installed upstream of the Zeta Plus Encapsulated System;
- **Do not** use with or expose this product to hot liquids [>40°C (> 104°F)] or pressurized steam;
- **Do not** use this product for continuous service with compressed gases;
- **Do not** use with organic solvents;
- **Do not** attempt to use capsules on other systems – they are designed for use on the Zeta Plus Encapsulated System only;
- **Use ONLY** Zeta Plus Encapsulated System capsule filters and manifolds with Model# 16EZA holder or Model# 16EZB.
- **Ensure** correct positioning of manifolds;
- **Do not** autoclave manifolds with clamps attached;
- **Do not** hang other items on this product;
- **Do not** attempt to use this product if damage has occurred to capsules;
- **Do not** modify the holder, capsules, manifolds, or any components;
- **Do not use** alkaline resistant* capsules or manifolds with standard capsules or manifolds.
- **Perform all required maintenance** on or before its scheduled date and always use specified replacement parts listed in Installation and Operation Instructions.

To reduce the risk associated with chemical exposure:

- The materials used in the construction of the Zeta Plus filters exhibit varying levels of chemical resistance depending on a number of factors including the solution, reagent concentration, temperature, pressure and exposure time. The lack of chemical compatibility may impact product safety by increasing the potential for capsule shell breach/failure under pressure or increasing the quantity of leachable materials into the final pharmaceutical product. Additionally, the filtration performance such as contaminant removal may be negatively impacted with exposure to specific chemicals and process conditions.
- 3M only tests a limited number of possible process fluids to design and characterize the product. The product is compatible with most aqueous solutions. The chemical compatibility of other solvents and process conditions must be determined through extensive capsule reliability and product extraction studies. In addition, the construction for each Zeta Plus product may vary in materials and relative fluid contact area of each material, therefore, the chemical compatibility must be assessed at each scale of operation. 3M may be able to support specific evaluations utilizing protocols offered through our Validation Service testing products.

To reduce the risk associated with property damage due to product contamination:

- Zeta Plus Encapsulated System capsule filters and the manifolds are designed for single use only. **Do not attempt to re-use.**

To reduce the risk associated with property damage to the holder:

- **Do not** use this device to carry other items.

Important Note: Always operate the filter system within the maximum differential pressure of 2.4 bar (35 psig).

CAUTION

To reduce the risk associated with property damage due to product loss:

- **Do not** install where fluid pressure exceeds 3.4 bar (50 psig).
- **Do not** use with or expose this product to hot liquids [>40°C (> 104°F)] or pressurized steam.

*Based on testing with 1M NaOH and 5% NaClO (Bleach).

Purpose

The purpose of this Installation Qualification (IQ) test is to determine if the Zeta Plus™ Capsules have been properly installed in the system holder 16EZA or 16EZB prior to operational use. This test detects failures such as those related to installation errors, defective or missing o-rings, rips or tears in the media that lead to gross leaks. The test procedure consists of two parts, a Hardware Qualification and a Capsule Qualification. The Capsule Qualification part of the test procedure is specifically intended for use with media grades 50, 60, 70, 90, and 120. This test can also be applied to dual layer EXT products if the qualifying media layer is 60, 90 or 120 tightness. This document defines the general procedure and the necessary equipment required to conduct the IQ Test. This test does not attempt to establish or define any correlation between the measured pressure drop during the test and the ability of the filter media to reduce or remove contaminants from the fluid being filtered.

General

The procedure can be applied when using 3M Purification Inc. part # E16E01A, E16R01A, E16E07A, E16ER07A, E16E11A, or E16R11A Capsules and Manifolds installed in either the 16EZA or the 16EZB Holders. This procedure can be used to test both the single stage and the two-stage filter assemblies. When testing a two-stage filter assembly, both stages can be tested simultaneously for the Hardware Qualification part of the test, but each stage must be tested independently for the Capsule Qualification part of the test. This document defines the general procedure and the necessary equipment required to determine if the Zeta Plus Capsules have been installed properly. This procedure does not attempt to establish or define any correlation between the measured pressure drop during the test and the ability of the filter media to reduce or remove contaminants from the fluid being filtered.

Equipment and Materials Required

- Stopwatch
- 0-5 psi Pressure Measuring Device with ± 0.25% full scale or better accuracy
- Clean dry regulated gas pressure source

Reagents

- Water or buffer solution

Procedure for Single Stage Usage Installation Qualification Test (Refer to Figures 1 and 2)

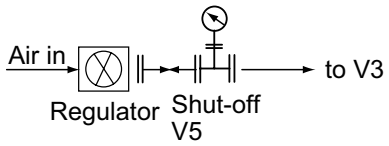

Figure 1 - Manual Test Assembly

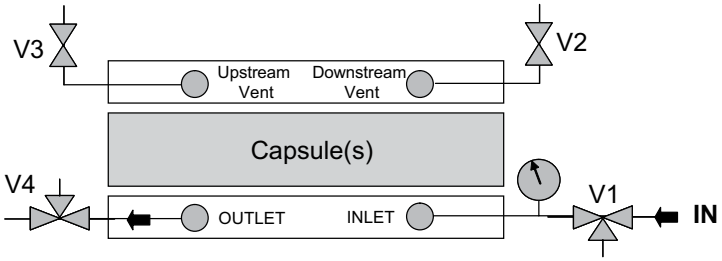

Figure 2 - Capsule and Manifold Assembly

Hardware Qualification Test

1. Install the Zeta Plus™ Capsules to be tested into the Holder.
   a. Follow Manual for "Zeta Plus™ Encapsulated System Model #16EZA Installation and Operation Instructions" Section II A when using the 16EZA Holder for testing.
   b. Follow Manual for "Zeta Plus Encapsulated System Model #16EZB Installation and Operation Instructions" Section II A when using the 16EZB for testing.
2. When the Capsules are installed in the holder and are still dry, close V1, V2, and V4.
3. Open V3 and V5.
4. Attach the manual test assembly (Figure 1) to V3 and V5.
5. Pressurize the filter housing to 207 mbar +/- 7 mar (3.00 psi +/- 0.1 psi).
6. Allow the pressure to stabilize for three (3) minutes with the air supply turned on.
7. Record the start pressure, close V5 and start the stopwatch.
8. After three (3) minutes record the pressure.
9. If the pressure decay is more than 5 mbar (0.07 psi) the system may be leaking. Identify the source of the leak and stop it. Possible sources of a leak include:
   a. external connections between the manifolds and isolation valves (V1-V4) and/or
   b. large capsule or manifold o-rings being damaged or absent.
10. Repeat steps 1-9 until the pressure decay recorded at the end of the three (3) minute test period is less than 5 mbar (0.07 psi), Proceed to the Capsule Qualification Test.

Capsule Qualification Test

1. Remove the manual test assembly shown in Figure 1 from V3.
2. Close V1, V2, and V4. Open V3.
3. Connect a filtered water source or buffer solution to V1.
4. Fill the capsules with liquid by slowly opening V1. When water or buffer solution emerges from V3, close V3 while simultaneously opening V2.
5. When water or buffer solution emerges from V2, close V2 while simultaneously opening V4.
6. Flow a volume of water or buffer solution through the filter ≥ 54 L/m^2 of media at the recommended flux of 210 LMH.
7. When the required volume of water or buffer solution has flowed through the capsules turn off the supply and close V1.
8. Leave V4 open, direct V1 to go to drain, and open V1.
9. Open V2 and V3. Allow the bulk of the fluid to gravity drain from the system. Leave the wetted capsule stack for 30- 60min before applying the Installation test.
10. Attach the manual test assembly to V3 (Figure 1) and open V5 to pressurize the capsule(s) to 100 mbar +/- 7 mbar (1.45 psi +/- 0.1 psi) using the manual test assembly (Figure 1).
11. After five (5) minutes inspect the drain lines V1 and V4 to determine if the bulk of water or buffer solution flow has stopped. If bulk water or buffer solution flow has not stopped, allow the housing to continue to drain until the water or buffer solution flow is reduced to a trickle. When bulk water or buffer solution flow stops close V1 and V2. V4 should remain open during the capsule qualification test.
12. Close V5, record the actual starting pressure, and start the stopwatch.

13. After three (3) minutes record the pressure.

14. If the pressure decay from the start pressure is ≤ 50 mbar (0.73 psi) the capsules have passed the qualification test.

15. If the pressure decay is > 50 mbar (0.73 psi), the filters may not have been fully wet out, there may be a defective or missing o-ring on one or more of the capsules, or the media inside the capsule may be damaged. The installation can be checked by removing the air supply and disconnecting the test assembly. Make sure the pressure on the system has been relieved. Inspect the manifolds and capsules to be sure that the small o-rings are present and undamaged. If all o-rings are present and undamaged the explanation for high pressure decay may be trapped air that prevented the filter media from full wet out.

16. Reinstall the capsules in the holder and repeat steps 1-15 as required. If inadequate wet out is the suspected problem, allow a trickle of flow through V2 and V3 during the wet out or flow at a higher rate 1.5 x.

Procedure for Two-Stage Usage Installation Qualification Test (Refer to Figures 3 and 4)

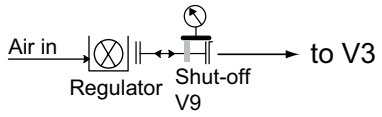

Figure 3 - Manual Test Assembly

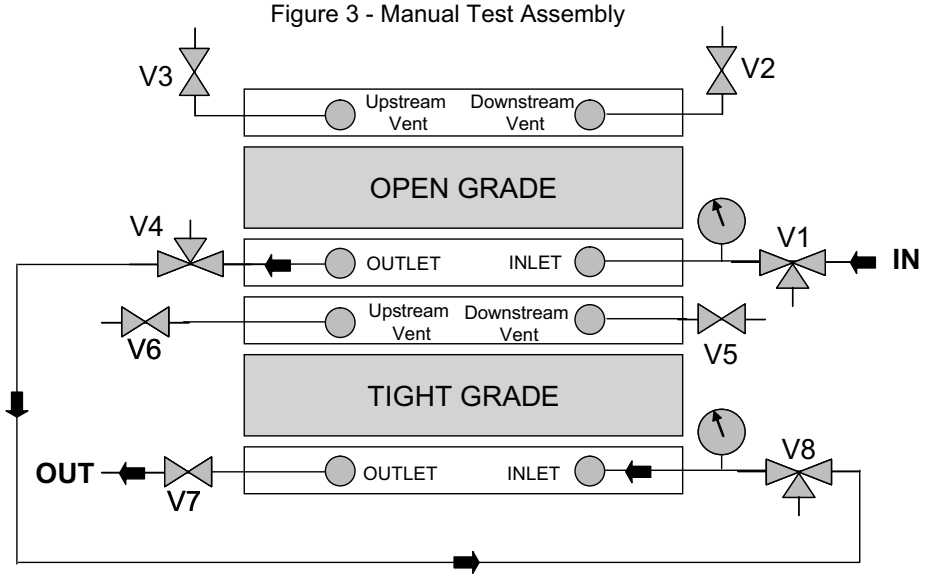

Figure 4 - Series Test Assembly

Hardware Qualification Test

1. Install the Zeta Plus™ capsules to be tested into the Holder.
   a. Follow Manual for "Zeta Plus Encapsulated System Model #16EZA Installation and Operation Instructions" Section II A when using the 16EZA Holder for testing.
   b. Follow Manual for "Zeta Plus Encapsulated System Model #16EZB Installation and Operation Instructions" Section II A when using the 16EZB for testing.

2. When the capsules are installed in the holder and are still dry, close V1, V2, V5, V6, and V7.

3. Open V3. V4 and V8 should be open to each other.

4. Attach the manual test assembly (Figure 3) to V3.

5. Open V9 and pressurize the filter housing to 207 mbar +/- 7 mbar (3.00 psi +/- 0.1 psi).

6. Allow the pressure to stabilize for three (3) minutes with the air supply turned on.

7. Record the start pressure, close V9, and start the stopwatch.

8. After three (3) minutes record the pressure.

9. If the pressure decay is more than 5 mbar (0.07 psi) the system may be leaking. Identify the source of the leak and stop it. Possible sources of a leak include:
   a. external connections between the manifolds and isolation valves (V1-V8) and/or
   b. large capsule or manifold o-rings being damaged or absent.

10. Repeat steps 1-9 until the pressure decay recorded at the end of the three (3) minute test period is less than 5 mbar (0.07 psi), Proceed to the Capsule Qualification Test.

Capsule Qualification Test

1. Turn off the air supply and remove the manual test assembly from V3.
   Note: Be sure to vent the pressure from the housing.

2. Close all valves (V1-V8).

3. Open all vent valves (V2, V3, V5, and V6).

4. Connect a filtered water source or buffer solution to V1. Open V1 slowly to begin fluid flow.

5. When the fluid exits V3, close V3.

6. When fluid exits V2, close V2, and simultaneously position V4 and V8 to direct the fluid to V8.

7. When fluid exits V6, close V6.

8. When fluid exits V5, close V5, and simultaneously open V7.

9. Flow a volume of water through the filter ≥ 54 L/m^2 of media at the recommended flux of 210 LMH.

10. When the required volume of water has flowed through the capsules turn off the water supply and close V1. Then close V7 to stop the flow.

11. Drain fluid from the system by turning V1, V4, V7, and V8 to the drain position. Then open V2, V3, V5, and V6. Leave the wetted capsule stack for 30- 60min before applying the Installation test.

12. After the bulk of the fluid has drained, close V2, V5, and V6.

13. Attach the manual test assembly (Figure 3) to V3 and pressurize the capsule stack to 100 mbar +/- 7 mbar (1.45 psi +/- 0.1 psi).

14. After five (5) minutes inspect the drain lines V1, V4, V7, and V8 to determine if the bulk of water flow has stopped. If bulk water flow has not stopped, allow the housing to continue to drain until the water flow is reduced to a trickle. When bulk water flow stops, the capsule qualification test can be conducted.

15. The capsule qualification test must be run on the two stages individually. If the first stage grade is too open (< 50 grade) to test, skip to step 23 and only test the tighter grade.

16. To test the first stage, close V1. V2 can be open and V4 can be open to drain.

17. Open V3 and attach the manual test assembly to it.

18. Open V9 and increase the air pressure to 100 mbar +/- 7 mbar (1.45 psi +/- 0.1 psi). When the system has stabilized, close V9, start the stopwatch, and record the actual starting pressure.

19. After three (3) minutes, record the pressure.

20. If the pressure decay from the start pressure is ≤ 50 mbar (0.73 psi), the first stage capsule(s) have passed the capsule qualification test.

21. If the pressure decay is > 50 mbar (0.73 psi), the filters may not have been fully wet out, there may be a defective or missing o-ring on one or more of the capsules, or the media inside the capsule may be damaged. The installation can be checked by removing the air supply and disconnecting the test assembly. Make sure the pressure on the system has been relieved. Inspect the manifolds and capsules to be sure that the small o-rings are present and undamaged. If all the o-rings are present and appear undamaged the problem may be trapped air that prevented the filters from fully wetting out.

22. Reinstall the first stage capsules and rewet and retest. **Note:** If inadequate wet out is the suspected problem, allow a trickle of flow through V2 and V3 during the wet out or flow at a higher rate.

23. To test the second stage, close V8. Open V5 and V7.

24. Attach the manual test assembly to V6. Open V6 and V9 and pressurize the capsule(s) to 100 mbar +/- 7 mbar (1.45 psi +/- 0.1 psi).

25. When the pressure is stabilized close V9, record the actual starting pressure and start the stopwatch.

26. After three (3) minutes record the pressure.

27. If the pressure decay from the start pressure is ≤ 50 mbar (0.73 psi) the capsules have passed the qualification test.

28. If the pressure decay is > 50 mbar (0.73 psi), the filters may not have been fully wet out, there may be a defective or missing o-ring on one or more of the capsules, or the media inside the capsule may be damaged. The installation can be checked by removing the air supply and disconnecting the test assembly. Make sure the pressure on the system has been relieved. Inspect the manifolds and capsules to be sure that the small o-rings are present and undamaged. If all the o-rings are present and appear undamaged the problem may be trapped air that prevented the filters from fully wetting out.

29. Reinstall the second stage capsules and rewet and retest. **Note:** If inadequate wet out is the suspected problem, allow a trickle of flow through V5 and V6 during the wet out or flow at a higher rate 1.5 x.

Product Selection and Use:
Many factors beyond 3M's control and uniquely within user's knowledge and control can affect the use and performance of a 3M product in a particular application. As a result, customer is solely responsible for evaluating the product and determining whether it is appropriate and suitable for customer's application, including conducting a workplace hazard assessment and reviewing all applicable regulations and standards (e.g., OSHA, ANSI, etc.). Failure to properly evaluate, select, and use a 3M product and appropriate safety products, or to meet all applicable safety regulations, may result in injury, sickness, death, and/or harm to property.

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