Application Note

Zebragard[™] Membrane Barrier Filter: A Critical Element for Ensuring Sterility in Fill & Finish Applications

Introduction

Bioprocessing fill and finish applications are subject to extensive sterility regulations. A number of regulatory guidelines recommend that critical sterilizing filters for aseptic processing be flushed, pre-conditioned, integrity tested, and dried prior to product filtration.

Several methods have been developed for conducting pre-use, post sterilization integrity testing (PUPSIT) without breaching system sterility. Such methods include the use of a flush bag, holding tank, catch-can/flush bottle, or a filter arrangement downstream of the sterilizing filter to create a sterile boundary.

Zebragard[™] filters feature the dual characteristics of sterilizing grade 0.2 µm hydrophilic SteriLUX[®] and hydrophobic Steridyne[®] PVDF membranes. As such, they deliver effective passage of both air/gas and liquid solutions for a simple yet robust and versatile approach to PUPSIT.

Zebragard[™] filters are designed for seamless implementation in autoclaved or irradiated systems and feature widely adopted pleated membrane technology to deliver faster recovery of air flow after filter wetting.

Optimizing Bioprocess Operations

Prior to product filtration, biopharma manufacturers must perform system sterilization, confirm critical filter integrity, and dry the system. Inefficient filter wetting is a frequent cause of integrity test failures and requires large volumes of wetting fluid to rewet and retest. Rigid sterile boundaries, such as flush bags and catch cans, may limit the flushing volume available to the system and can lead to integral filters being discarded for improper wetting. This can be mitigated using downstream filter(s), which allow passage of unlimited volumes of particle-free water and air.

Zebragard[™] filters allow for the simplest operational protocol by combining the wetting properties of the proven hydrophilic SteriLUX[®] and hydrophobic Steridyne[®] membranes to allow for the passage of liquid and air in a single component. **Figure 1** depicts the various sterile boundary methods.



Sterile Boundary Designs



Figure 1: Of the common sterile boundary methods used in aseptic processing, Zebragard[™] offers the simplest design and allows for seamless system wetting and drying without volume constraints.

Pleated Membrane Technology

Zebragard[™] filters feature pleated membrane technology to allow rapid air flow recovery at low pressure differentials after filter wetting.

High air flow recovery at low pressures affords a higher level of accuracy when integrity testing critical filters by reducing air flow hinderance in the system caused by a wetted barrier filter. After integrity testing, rapid airflow recovery will lead to faster filter drying time for a decrease in process time without product dilution. **Table 1** details Zebragard[™] filters' typical air flow rate recovery times as they compare with alternative barrier filter solutions.

Air Flow Recovery Intervals	Zebragard [™] Filter	Alternative Barrier Filter
Air flow rate recovery time to 30% (minutes)	< 5	> 15
Air flow rate recovery time to 50% (minutes)	< 7	> 25

Table 1: Air flow rate recovering time for Zebragard[™] filters and alternate barrier filters on the market. Air flow rate recovery time is defined as the typical time required to reach a percentage of the dry filter's air flow rate.



Operation Considerations

Sterilization of Filtration System

Sterilization is a critical step in aseptic manufacturing processes for the removal of microorganisms in a system. Zebragard[™] filters may be irradiated between 25 to 40 kGy once. Alternatively, Zebragard[™] filters can be sterilized via autoclave at 121 °C for 60 minutes or 125 °C for at least 45 minutes. Capsule filters should not be inline steam sterilized. Do not Autoclave irradiated capsules.

System Flushing and Filter Wetting

System flushing ensures critical filters are completely wet for integrity testing and extractable residues are minimized. The implementation of Zebragard[™] filters in a system allow for direct flushing through a sterile boundary to drain. The use of an alternate wetting medium other than water for injection (WFI) should be verified before use. Alternate wetting medium may affect the filter's breathability and increase the pressure drop across the system.

Zebragard[™] Filters Facilitate PUPSIT

PUPSIT is performed on the product filter by either diffusion or bubble point determination. Membrane barrier filters are self-venting and allow for passage of air during integrity testing without the need to manipulate the filtration assembly. Since membrane barrier filters are downstream of the critical filters, it is imperative that they do not induce levels of back pressure that may affect integrity test results. Given Zebragard[™] filters' pleated membrane configuration, breathability is rapidly recovered after filter wetting even at low pressures, which diminishes back pressure and increases accuracy in integrity readings. This holds true even in the worst-case scenario, where the Zebragard[™] filter is fully wet with WFI. **Figure 2** showcases a sample PUPSIT assembly featuring Meissner components.



Figure 2: Redundant filtration PUPSIT assembly featuring Zebragard[™] PVDF membrane barrier filter.

- 1. Zebragard[™] allows passage of liquids and gases while maintaining system sterility.
- 2. TepoFlex[®] biocontainer allows evacuation of air within the fluid path while maintaining a closed system.
- 3. Single-Use Gauge Tee (SGT) allows for noninvasive pressure monitoring.
- 4. M-Sil[™] is a braid reinforced tubing engineered to withstand high pressures.
- 5. UltraClamp[™] polyketone (PK) sanitary clamp.
- 6. Vent filters allow passage of gases while maintaining system sterility.
- 7. Sterilizing product filter.

Drying of Filtration System

To avoid product dilution or product contact with wetting liquid, systems may be blown down or dried prior to product filtration. Zebragard[™] filters are designed to achieve rapid drying times via their bifunctional nature. The interconnected hydrophilic media will dry as air is passed through the hydrophobic membrane. This is a unique feature only found in Zebragard[™] products.

Integrity Testing Zebragard[™] filters

ZebragardTM filters can be integrity tested offline with 60% IPA/40% water with bubble point \geq 18 psi (1.24 bar). Alternatively, filters can be integrity tested offline with 70% IPA/30% Iwater with bubble point \geq 17 psi (1.17 bar).

Compatibility with Meissner's Automated Integrity Tester: AccuFlux[®]

Zebragard[™] filters are compatible with automated integrity testers including Meissner's AccuFlux[®] system. Integrity testing of sterilizing filters on a PUPSIT assembly or integrity testing of Zebragard[™] filters offline both can be carried out with AccuFlux[®], which contains pre-installed testing parameters for both cases. AccuFlux[®] can facilitate and streamline the integrity testing of Zebragard[™] filters and assemblies through:

- Barcode scanning to recognize filter type and upload parameters.
- Rapid automated integrity testing.
- Data storage 21 CFR Part II compliant to meet strict documentation requirements.

Learn How Zebragard[™] Can Help You

Zebragard[™] filters allow for fewer components, fewer connections, and simpler operational protocols for final fill and finish applications. The filter construct follows the established and proven platform for both SteriLUX[®] and Steridyne[®] membranes in a single, robust and highperformance product. For additional information about SepraPor[®] ultrafiltration membranes, please visit <u>www.</u> <u>meissner.com/zebragard</u>.



www.meissner.com