Single Use Systems for PUPSIT

Pre-Use Post-Sterilization Integrity Testing

DATASHEET

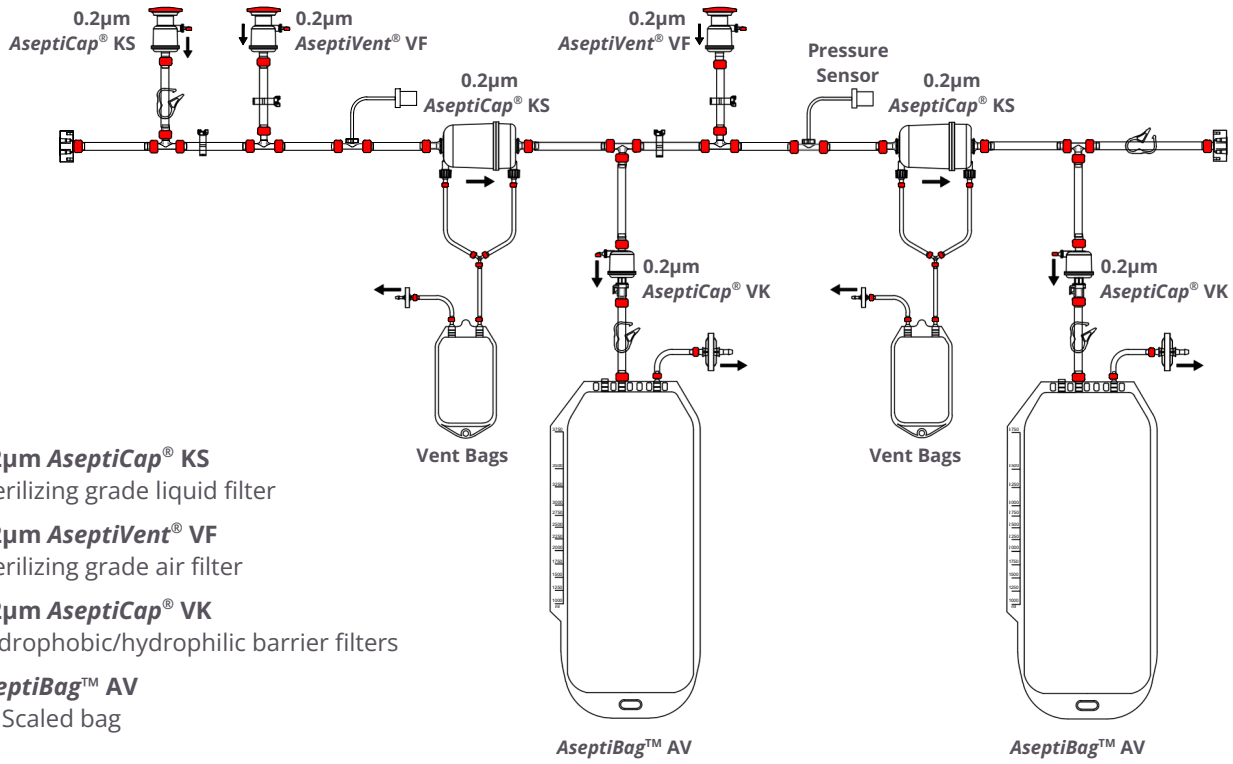
Manufacture of sterile drug products using sterilizing filters mandates that the drug product is filtered through an integral filter, failing which passage of microbial contamination is an eventuality that poses a high risk to the patient. Regulatory bodies such as US Food and Drug Administration (USFDA) and European Medicines Agency (EMA) make it mandatory to carry out post filtration integrity testing of the filter. However, some regulatory bodies such as EMA (Annexure 1) insist on pre-use/ post sterilization integrity testing (PUPSIT). PUPSIT has become more relevant as in some cases, due to filter clogging, the post use bubble point may be significantly higher, thereby concealing pre-use integrity failure.

PUPSIT (pre-use post-sterilization integrity testing) is therefore a much desired process step to ensure that the filter is integral before use.

Adhering to this regulatory requirement for PUPSIT, makes the filtration and filling process more challenging and the single use systems more complex.

During PUPSIT, the process owner faces several challenges such as wetting the filters, performing the integrity test, minimizing product loss, maximizing product recovery, maintaining sterility on the downstream side of the filter, leakages due to high pressure (> 4 bar) and, in specific cases, preventing product dilution and ensuring proper filter drying.

Typical PUPSIT Assembly



- **0.2µm *AseptiCap*® KS**
  Sterilizing grade liquid filter
- **0.2µm *AseptiVent*® VF**
  Sterilizing grade air filter
- **0.2µm *AseptiCap*® VK**
  Hydrophobic/hydrophilic barrier filters
- ***AseptiBag*™ AV**
  2D Scaled bag

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MDI provides a customized single use systems for aseptic filtration single use PUPSIT designed to overcome these challenges by addressing all PUPSIT requirements, ensuring process reliability, regulatory compliance, and providing maximum efficiency.

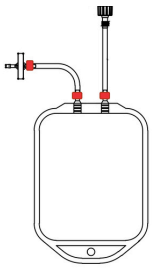
AseptiCap® VK barrier filters: Handling of large flush volumes during filter wetting

Although vented flush bags downstream of sterilizing filters ensure wetting fluid drainage and test gas venting without exposure to the environment, large sterilizing filters may require large volumes of wetting fluid and handling large capacity flush bags may pose a risk to operator safety. *AseptiCap*® VK hydrophobic/hydrophilic barrier filters mitigate such risks by easy handling of large flush volumes without microbial ingress from the environment.

Drain/ Vent Bags: Adequate filter wetting

Drain bags are used to collect the wetting fluid (usually WFI) that is flushed through the filter to fully wet the membrane before integrity testing. After the filter has been properly wetted, the fluid needs to be carefully drained while preventing any spillage of wetting fluid into the sterile environment. These also help manage large flush volumes effectively during hydrophilic filter wetting.

Vent bags are installed on the filter vents to ensure removal of entrapped air. Vent bags allow proper venting without risk of contamination.



AseptiBag™ AV: PUPSIT with drug product as wetting fluid

In case of drug product immiscible/incompatible with the recommended wetting fluids, the assembly needs to be completely dry before introducing the drug product (DP). Blow drying incompatible wetting fluids requires very high pressures and is not practically feasible in single use systems, thereby necessitating PUPSIT with the drug product as wetting fluid.

However, this can be prohibitively expensive in case of high value drug products. MDI *AseptiBag*™ AV 2D scaled bags can help minimize such costs by ensuring accurate DP volumes for filter wetting.

PresFlo™ Platinum Cured Silicone (PCS) high pressure tubing: Mitigating risk of leakages

Use of MDI *PresFlo*™ Platinum Cured Silicone (PCS) high pressure tubing along with Oetiker clamps ensure secure connections and prevent leakages.

Pressure Sensors for monitoring

Pressure sensors are used to continuously monitor the pressure applied during the pre-use integrity test. It ensures that the applied pressure remains within the validated limits. It helps to detect any unusual pressure drop or sudden fluctuation, which may indicate leakage, or improper filter wetting. These sensors enhance process control, making the PUPSIT more reliable.

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Clean Room Manufacturing

PUPSIT assemblies are manufactured in clean rooms certified by external agencies and monitored in-house for viable and non viable particles. Employee hygiene, change rooms, gowning and de-gowning procedures and continuous monitoring of the areas is an essential part of these facilities. These facilities have been designed for unidirectional work flow with appropriate change rooms for personnel and air locks for material movement.

Quality Management Systems

PUPSIT assemblies are well designed products with in-built quality assurance. ISO-9001:2015 Certified Quality Management System, careful selection of raw materials, validated production processes and testing procedures based on international standards and guidelines such as CFR, PDA, and ASTM, ensures manufacture of consistently high quality assemblies.

Regulatory Compliance

PUPSIT assemblies are deeply characterized and validated to meet international regulatory requirements with regards to bioburden, endotoxins, particulate matter and extractables.

Customization

MDI PUPSIT single use assemblies can be customized to suit user requirements in terms of filters, high pressure tubing, connectors, tube fittings, bags, transfer tubes, tube clamps, and vent filters.

Product Realization Flow Chart

User Specified PUPSIT Single Use Assemblies Design Specifications
User process requirements such as filters, high pressure tubing, connectors, tube fittings, bags, transfer tubes, tube clamps, vent filters etc. are established

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Technical Feasibility
Based on the above information and available components a technical feasibility of the Assemblies are done and an initial drawing of same is submitted for user approval

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Design approval
- User approval of bag assemblies drawing
- Changes to finalize drawing, if required

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Finalized PUPSIT Single Use Assemblies

PUPSIT Stand

For Pre-Use Post-Sterilization Integrity Testing

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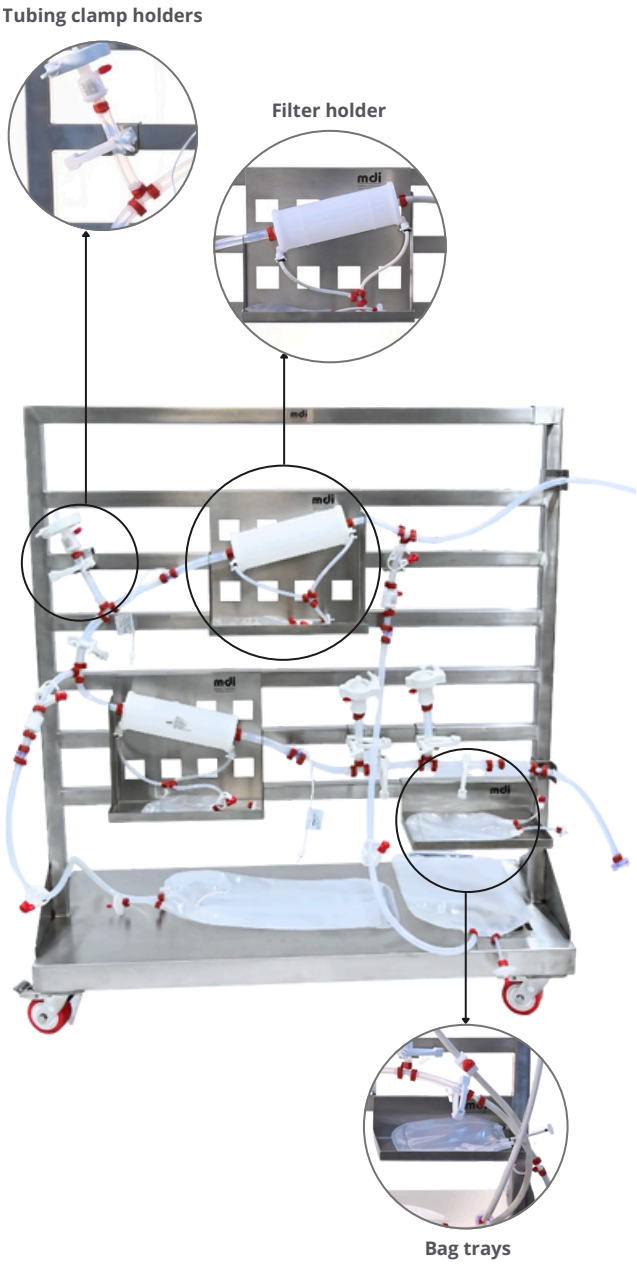
PUPSIT Stand

The PUPSIT (Pre-Use Post Sterilization Integrity Test) Assembly Stand is designed to securely hold and support PUPSIT single use assemblies during integrity testing and aseptic filtration. The PUPSIT stand, constructed entirely from high quality 316L stainless steel, ensures maximum cleanliness and compatibility with ISO Class 5 (Class A) cleanroom.



Advantages

Process Support

It provides stability and support for PUPSIT assemblies during

- Pre-use integrity testing
- Aseptic filtration
- Post-use integrity testing

Cleanroom operations

Easy to clean and disinfect SS 316L construction, suitable for ISO Class 5 (Class A) cleanrooms

Risk Mitigation

- Minimizes risk of disconnection or damage to PUPSIT single use systems
- Equipped with lockable wheels for stability and grip

Custom Design

Customized design and accessories such as filter holders, bag trays and tubing clamp holders for custom PUPSIT Single Use Systems

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