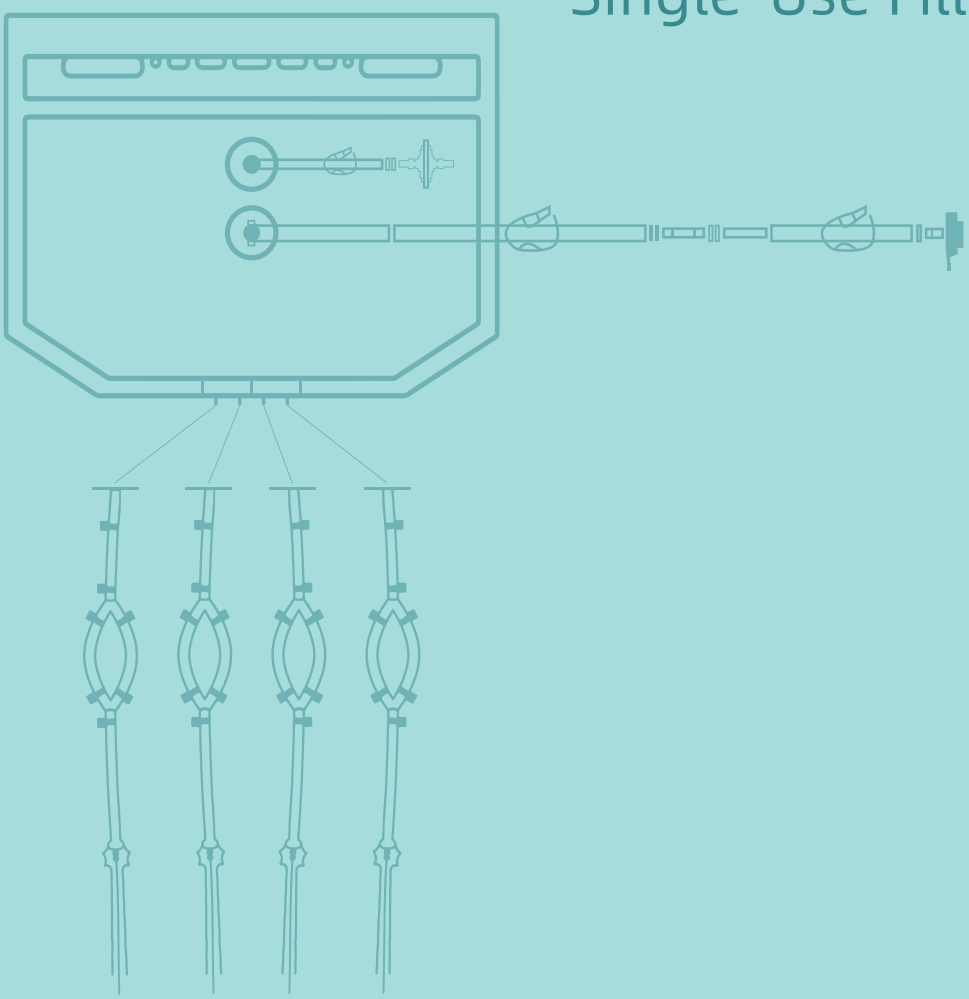
BIO-LINK

BioHub®

Single-Use Filling System

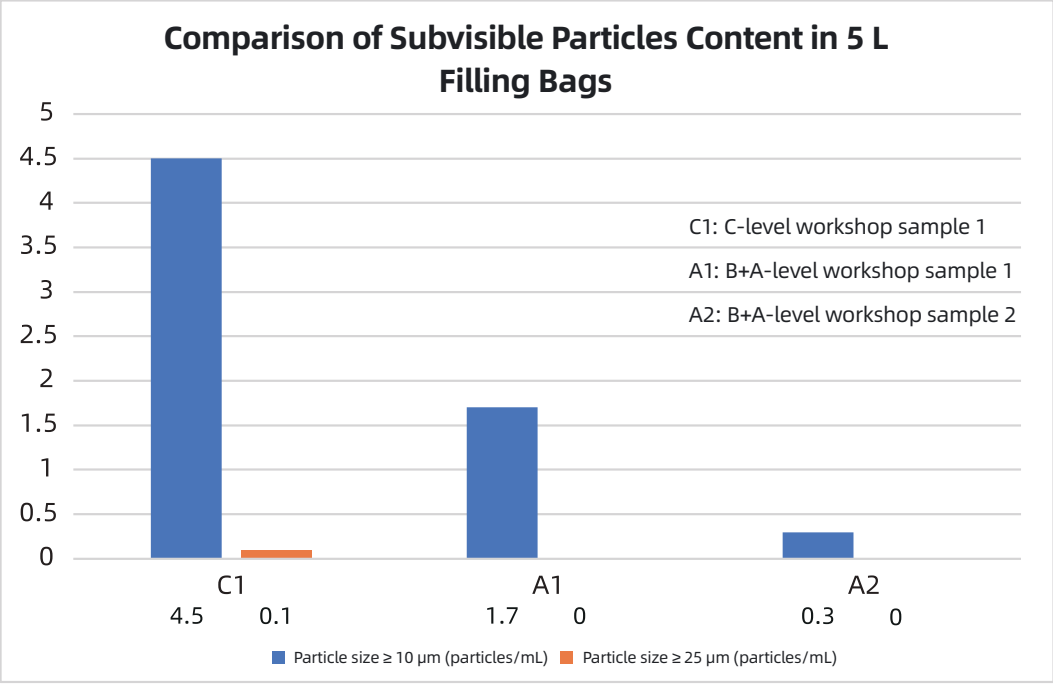


BioHub® Single-Use Filling System is a pre-sterilized, ready-to-use solution that consists of single-use mixing bag, sterile storage bag, filling bag, single-use capsule filter, filling tubing, single-use aseptic connector, disconnector and single-use filling needle. BioLink is committed to minimizing customer risks by offering top quality consumables, services and support.

- **Subvisible Particles:**

Subvisible particles are tiny, water-insoluble particles with a typical size of 2 μm - 50 μm. Subvisible particles in pharmaceutical injections in quantities exceeding certain limits may pose risks to patients, potentially even life-threatening in severe cases. Therefore, it is necessary to strictly control the subvisible particles in single-use sterile filling bags that may come into contact with injections.

BioLink controls the level of subvisible particles in products from the source by establishing B+A-level workshop, ensuring a controlled production environment. Processes such as film cutting, welding, assembly are all conducted in B+A cleanrooms, reducing the impact of environment on product subvisible particles. The tubing, connectors and filling needles and other components are pre-flushed to ensure high cleanliness, eliminating visible foreign matter and reducing particle levels.



- **Sterility Assurance:**

To ensure product sterility, BioLink follows the guidelines of ISO 11137:2013 for single-use sterile filling bags, applying the VDmax[25] (radiation sterilization) method (i.e. possible SAL of 10^{-6} in the case of product sterilization with the given minimum dose of 25 kGy). BioLink provides the field distribution verification (PQ) of radiation dose by combining the packaging and loading methods of the product and selecting the packing density limit with the help of an irradiator of the commissioned radiation processor. Verification results indicate that the product was successfully radiated at a required dose of 25 kGy ~ 40 kGy when placed on the radiation pallets. Moreover, BioLink provides the quarterly validation of effective radiation to ensure the stable radiation measurement.

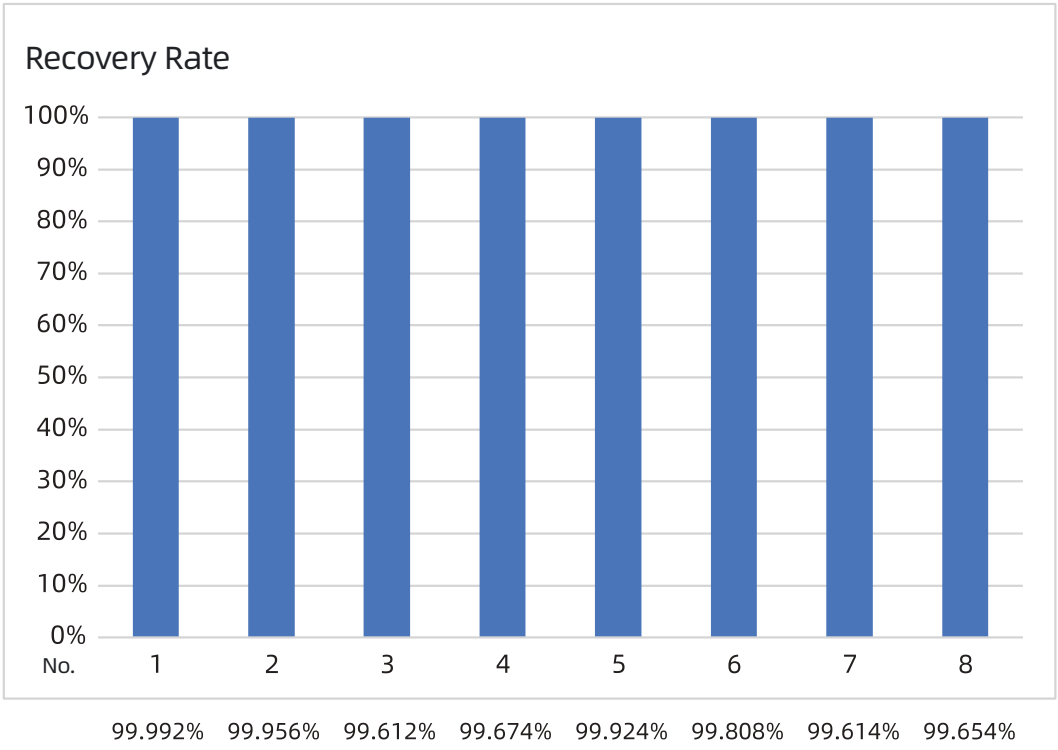
The regulatory agencies worldwide recommend performing pre-use integrity tests on filters and post-use integrity test on sterilizing-grade filters when applying aseptic process. Successful filter integrity tests with the combined inherent sterility and antibacterium of the system constitute a key link of filter verification, smooth processing and product quality.

- **Flexible Adaptability:**

BioHub® single-use filling bag is superior in flexibility to ensure its adaptation to different scenarios and use requirements. In addition, it secures the minimum costs of cleaning verification, the accelerated interbatch switch and the reduced risks of interbatch-based product cross-contamination.

- **High Recovery Rate:**

The design of BioHub® single-use filling bags with boat-shaped connectors prevents expensive drug product from remaining in the bag. We tested the recovery rate of eight different designs of filling bags (with 2-12 filling lines) by filling each bag with 5 liters of purified water and then measuring the weight of the residual liquid using gravity. Test results showed that the recovery rate was greater than 99.5% in all cases.

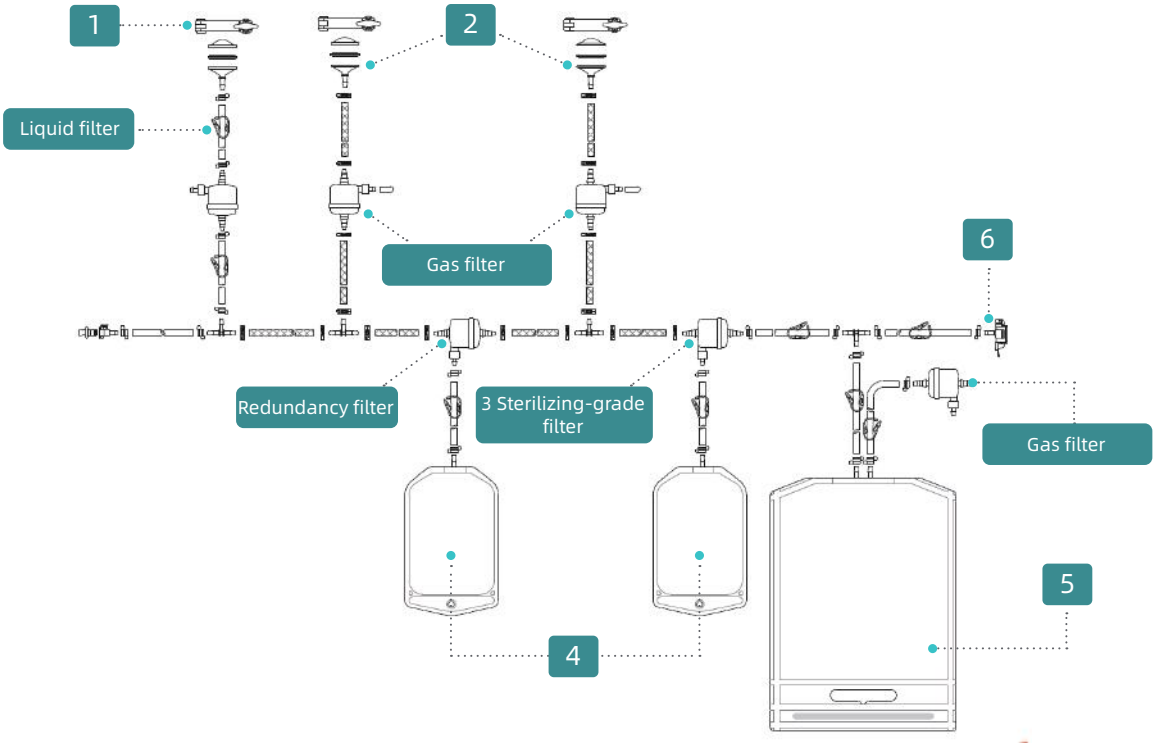


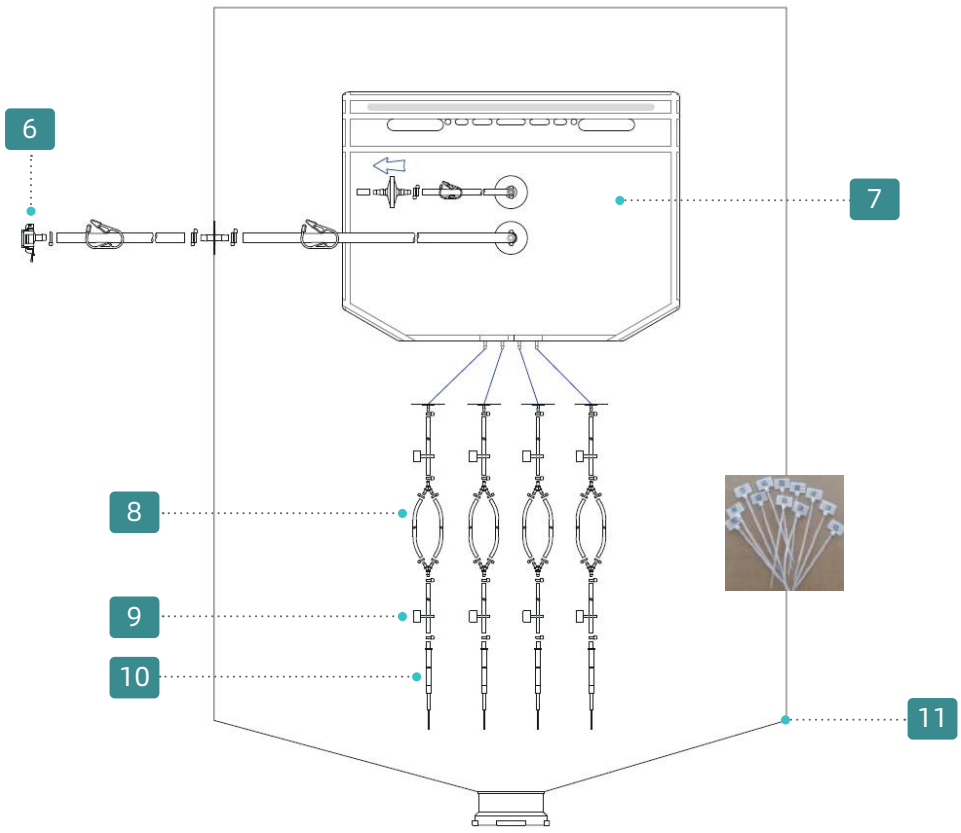
- **Quality Assurance:**
  - BioLink quality system complies with both ISO 9001 and ISO 13485 standards
  - Quarterly validation of sterility verification and dose effectiveness
  - Subvisible particles (refer to the Chinese Pharmacopoeia <0903> (USP <788>))
  - Endotoxins (refer to the Chinese Pharmacopoeia <1143> (USP <85>))
  - USP <87> Cytotoxicity test
  - USP <88> Class VI systemic acute toxicity test, intradermal irritation test and intramuscular implantation test
  - ISO 10993-4 In-vitro hemolysis test

- **Features and Strengths:**
  - Low residuals
  - Rigorous control of subvisible particles during production
  - Pre-sterilization and 100% integrity test (including β bags)
  - Reliable filling accuracy
  - Lower upfront capital investment and cross-contamination risks

Single-Use Filling Solution

BioLink offers overall single-use filling solutions to meet multiple filling volumes and use scenarios from R&D to production phases.

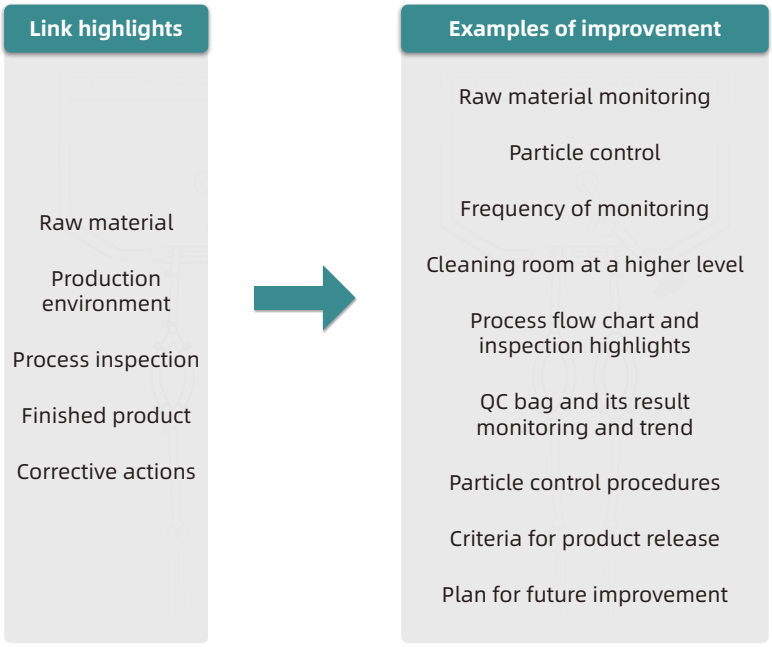




No.	Description
1	Wetting filter with water or buffer for pre-use integrity test.
2	Connected to integrity tester for pre-use integrity test.
3	Sterilizing-grade filter for filtration drug product.
4	Used for collecting gases in exhaust filter.
5	Used for collecting liquids and gases for pre-use integrity test.
6	Aseptic connector to ensure the sterile process of connection and injection delivery.
7	Buffer bags available in the volume from 250 mL to 20 L.
8	Filling pump tubes with different specifications offered by multiple suppliers to ensure the filling accuracy and effective matching with filling pump.
9	Possible design of multiple (up to 12) filling tubes depending on the use requirements. The tubes are marked with numbered zip ties for quick and convenient identification.
10	Multiple filling needles available in different forms.
11	Based on the specifications of the filling machine, the need for β bags and their specifications can be selected accordingly.

Quality Control

An overall approach is applied in quality control of filling bags for the single-use components. We are in a position to provide the phased risk assessment of raw material procurement and assembly manufacturing statement and its continuous monitoring, correction, control and improvement.



Custom Services

According to the customer's effective use, BioLink provides the well-matched tailored services for each filling system including its consumables, hardware and verification. Please feel free to contact your local point of sales and the technical support center for any request.

www.biolink.com

About BioLink

BioLink is a group of technology-driven businesses that provide process solutions in the life sciences industry. The company focuses on the development and production of the key processing equipment and consumables used in the manufacturing process of recombinant protein drugs, vaccines, antibodies, cell therapies, gene therapies, and other biological products. BioLink's portfolio of offerings covers the entire upstream and downstream bioprocess such as cell culture, single-use mixing and storage, chromatography, filtration (ultrafiltration/diafiltration, clarification, and virus removal), and hydration products, as well as process development services. BioLink is committed to providing customers with high-quality, innovative products and solutions and strives to build an efficient, safe and competitive biopharmaceutical supply chain eco-system.

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