Product recovery

Product recovery study for fill finish applications

Introduction

In aseptic biopharmaceutical manufacturing, the fill finish step involves transferring sterile drug products into final containers within an isolator or restricted-access barrier system (RABS). Pharmaceutical surge bags act as header bags, holding the drug product before it is fed into the filling manifold and then into containers through filling needles. Precision and reliability at this step are crucial, making surge bags essential for maximizing yields and ensuring sterility. However, challenges such as leakage and drainage inefficiencies can lead to significant product loss and operational inefficiencies. These issues can cause up to 10% product loss, resulting in millions of dollars in annual revenue losses for large-scale manufacturers [1]. Therefore, high-performance surge bags that help ensure maximum product recovery are critical.

Surge bags must be selected based on volume, material compatibility, and ability to maintain sterile conditions. Ideal surge bags should facilitate optimal flow, prevent overflows, and facilitate consistent delivery to the filling line. A simple drainage test can assess a bag's efficacy in draining and retaining liquid, ensuring it meets performance expectations.

Thermo Scientific™ Fill Finish surge bags are part of the Fill Finish Solution (Figure 1). They are engineered to address critical requirements like maximizing product recovery, and their performance is superior to that of alternative surge bags on the market. Here we describe how to assess product recovery with Fill Finish surge bags (Figure 2) in a drainage test. By focusing on product recovery as a key selection criterion, we demonstrate how adopting the Fill Finish Solution can significantly enhance process efficiency, reduce product loss, and support the overall success of the fill finish operation. Based on the results of the drainage test, we also highlight the economic advantages of Fill Finish surge bags for biopharmaceutical manufacturers seeking to optimize their fill finish processes.

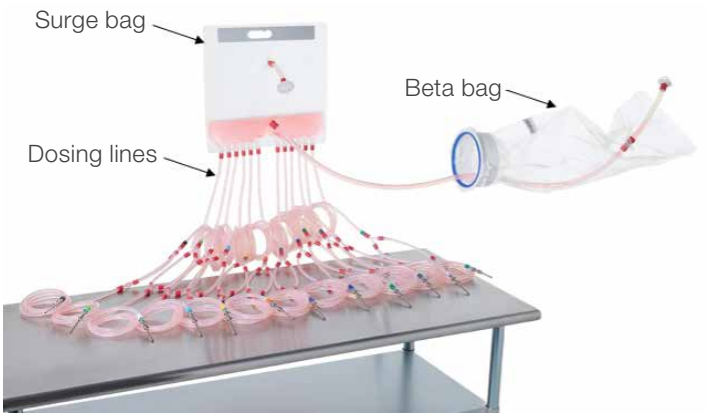

Figure 1. The Fill Finish Solution.

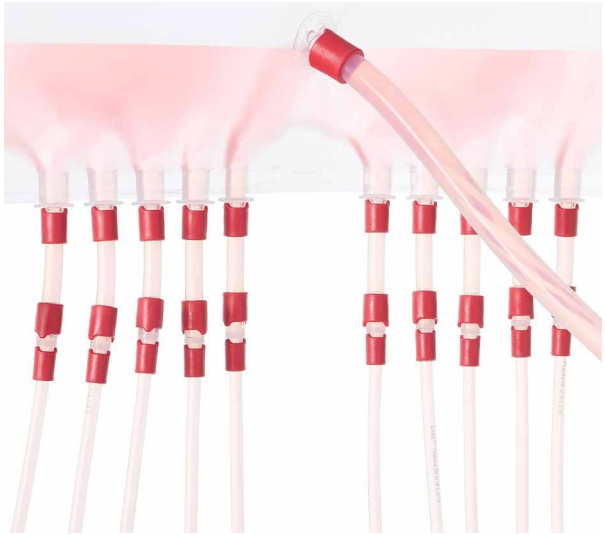

Figure 2. Fill Finish surge bags are designed to work with BioTitan Retention Devices to prevent leaks.

Fill Finish surge bags

Fill Finish surge bags are designed for the fill finish step in the production of vaccines, injection drugs, and cell and gene therapy products. Designed to maximize drug product recovery, Fill Finish surge bags feature Thermo Scientific™ BioTitan™ Retention Devices for tube connections. BioTitan devices are a novel replacement for traditional cable ties and provide a secure 360° seal around the tubing and fittings to reduce the risk of leaks and simplify the setup process. Fill Finish surge bags help ensure optimal drainage and undergo 100% helium testing for integrity assurance. Additionally, high-quality Thermo Scientific™ Aegis™ 5-14 and CX5-14 films are used in the construction of Fill Finish surge bags. They are thus durable and puncture-resistant, making them reliable choices for single-use applications.

Testing methods

Table 1 describes the characteristics of the Fill Finish surge bags tested for drainage efficiency, and outlines the methods used in the test.

The dosing line sets on each bag were closed using 3/16–3/8 in. snapper clamps (Part No. SV20031.04) and 1/2–3/4 in. snapper clamps (Part No. SV20031.05). The dry weight of each surge bag was measured using a Minebea Intec Midrics™ 2 scale prior to filling the bag with DI water to simulate product filling. After the weight was recorded, the bag was filled to approximately 75% of its capacity using a Masterflex™ I/P™ peristaltic pump (Model 77601-10). The ventilation and inlet line sets were closed off with snapper clamps before the filled surge bag was weighed again. To drain the surge bag, the clamps were removed from the ventilation, inlet, and dosing line sets, and the bag was hung over a container that would collect the water. Once drainage was complete and no substantial quantities of water were visible at the bottom of the bag, it was weighed again to determine the hold-up volume of water remaining. Product recovery was measured as the difference between the weight of the bag filled with water and the weight of the bag after it was drained, simulating the product recovered in the vials in the fill finish step.

Table 1. Testing matrix for Fill Finish surge bags.

Test	Bag description		Method
	Volume and configuration	**Number of dosing lines**	
1	1 L standard	2	1. The dry weight of the surge bag was recorded. 2. The surge bag was hung and filled with deionized (DI) water until the water level reached the bottom of the face port. 3. The inlet and dosing line sets were closed off with snapper clamps. 4. The filled surge bag was weighed, and the weight was recorded. 5. The filled surge bag was hung, and all liquid was drained from the bag by unclamping all ventilation, inlet, and dosing line sets. 6. Drainage was considered complete when liquid was no longer visible in the bottom of the bag. The inlet and dosing line sets were closed off, and the weight of the empty surge bag was recorded. 7. Steps 2–6 were repeated 10 times for each test.
2	2 L centered	2	
3	2 L offset	2	
4	5 L standard	8	
5	5 L wide	12	
6	5 L centered	2	
7	5 L offset	2	
8	10 L standard	12	

Results

Performance of Fill Finish surge bags

Fill Finish surge bags were tested to simulate a product being drained from the bags and recovered during the fill finish process. The drainage test demonstrated that only small hold-up volumes remained in the bags across all tested volumes and configurations (Figure 3). Due to the differences between the configurations of the bags (Table 1), marginal differences were observed between the hold-up volumes in the 2 L and 5 L surge bags. DI water drained effectively from the surge bags regardless of size or design, as none of the bags contained more than 2 mL of water after the test.

All tested Fill Finish surge bags enabled at least 99% product recovery regardless of size and configuration (Figure 4). The lowest recovery (99.76%) was obtained with the 1 L standard surge bag, while nearly 100% of the product was recovered with the 5 L centered surge bag.

Although small amounts of product remained in the bags after the drainage test, product recovery was sufficiently high that the hold-up volume in each bag was insignificant relative to the total bag volume. The surge bags also enabled consistent product recovery across all bag sizes and configurations.

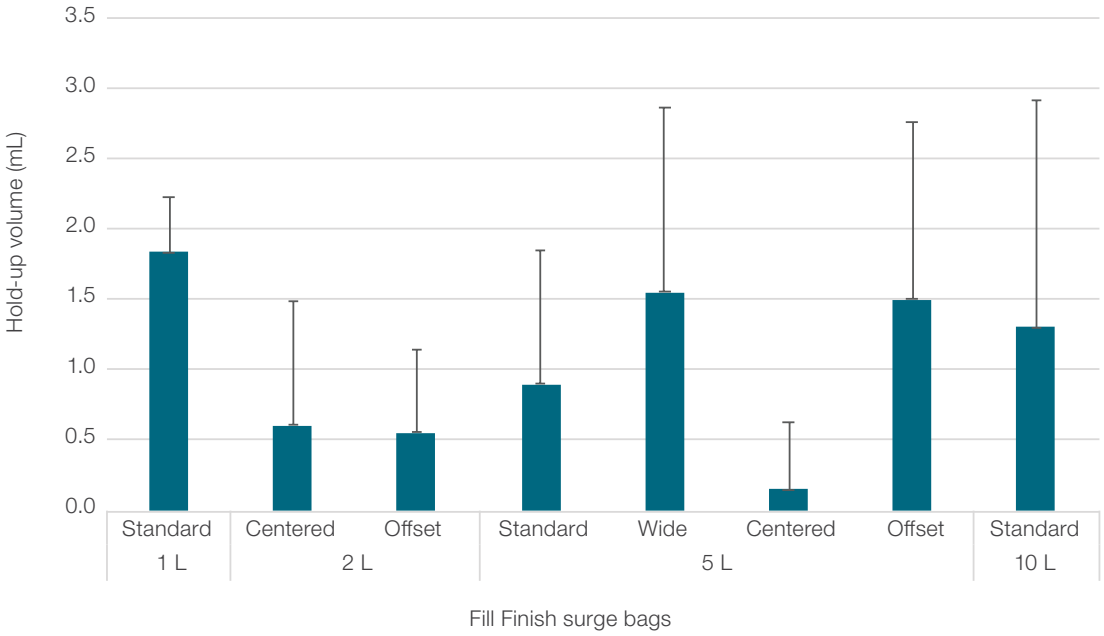

Figure 3. Hold-up volumes in Fill Finish surge bags. Each error bar represents one standard deviation.

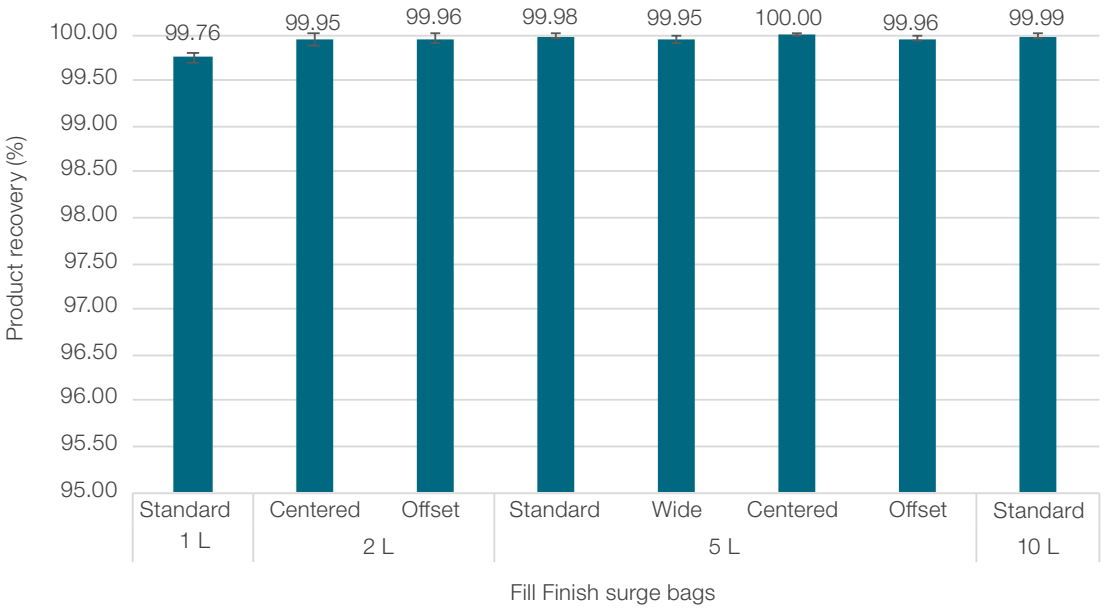

Figure 4. Product recovery from Fill Finish surge bags.

Economic benefits of product recovery with Fill Finish surge bags

As the final step before a product is sold, delivered to customers, and subsequently delivered to patients, product recovery during fill finish has significant economic implications for manufacturing operations and efficiency. For example, a 1% difference in recovery in monoclonal antibody (mAb) production may represent more than $30,000 for a contract manufacturing organization and $250,000 worth of product at the final sale price [1]. However, the industry currently averages only ~95% product recovery in fill finish operations due to the loss of product between surge bags and the final drug containers. This means that an increase in recovery from 95% to 99% in the fill finish process can be worth $1 million per production batch. Gene therapy materials are even more valuable, with doses worth hundreds of thousands or even millions of dollars. This equates to a monetary value of $750 to more than $25,000 for a milliliter of product [2]. While revenue from additional recovered product may not be fully realized due to industry demand, the manufacturing cost savings represent significant value. In an industry where every drop of product matters, consumables that recover even a few extra milliliters can make a significant economic difference.

Conclusion

Selecting a high-performance surge bag for the fill finish process is an important step towards process and manufacturing efficiency. In the drainage test described here, Fill Finish surge bags enabled at least 99% product recovery with insignificant product hold-up, regardless of bag size and configuration. Fill Finish surge bags are high-performing consumables that are available in 1 L, 2 L, 5 L, and 10 L formats. The high recoveries obtained with Fill Finish surge bags mean that manufacturers can maximize productivity during the final filling step. They can be confident that minimal amounts of product will be lost in filling components like beta bags, filling manifolds, tubing, and filling needles. With Fill Finish surge bags, manufacturers can aim to maximize recovery of their products during the filling step.

References

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