

# Novel Single-Use Systems Allow Faster Powder Transfer and Higher Recovery Rates

Ronald Szewczyk, Douglas Durney and William Ayrey

### ABSTRACT

Single use powder containment practices are still in their infancy but keeping your product from cross contamination and reducing airborne particulates is important. Understanding how more modern bag designs can increase safety and speed is a concern to the industry. We looked at the ease of fill along with dispensing times and product loss. ILC Dover’s EZ-Biopac shows a 71 % decrease in filling times when measured against an industry standard 2D bag. Due to the non-static film we saw an almost 20% reduction in powder discharge times. In addition, it demonstrates a 33.3% improvement in powder recovery showing reduced waste. Choosing the proper containment system can have a significant impact on plant productivity and profitability.

### INTRODUCTION

#### Issues of powder handling

For many years, media and buffer ingredients used in powder form were transferred from stock containers using open scoops, weighed and mixed in buckets or open-top bags, and then carried in and dumped from those buckets or open-top bags directly into production vessels—based on the premise that sterility wasn’t required at that early stage of manufacturing. While much of this process was often carried out in a separate room from the production line to contain airborne contaminants, final transfer to the production line still had to occur.

In recent years, manufacturers have recognized that, while sterility may not be an issue, worker exposure to airborne particulates, and the potential for cross-contamination when changing the line over to different products are.

Consequently, biopharmaceutical manufacturers have started to implement single-use systems for powder transfer. Unfortunately, many early systems were simply adapted from liquid-handling systems already in use at the time, and converted to handle powders. These systems often have shortcomings inherent in the genesis of their designs.

#### The keys to efficient powder transfer and containment

The most efficient powder containment and transfer equipment will exhibit a number of specific characteristics, including:

- A design developed specifically to handle powders
  - Fast filling
  - Easy, complete sealing
  - Fast, clean dispensing
  - Complete product recovery (i.e., no powder left in the container)
  - Self-supporting containers to promote easy handling and distribution
- Just as important as the system’s performance characteristics are the attributes of the system supplier.
- Are they responsive and adaptable to all of your manufacturing processes and procedures?
  - Do they have the necessary regulatory approvals for their equipment and containment materials?
  - Are they supported by a long history of service to the industry and a dedication to strong customer support?
  - Do they offer expert consultation during system development?

#### Evaluating potential systems

The simplest approach to evaluating powder containment and transfer systems is to proceed step-by-step through the criteria listed above for determining system applicability and efficiency.

#### Genesis of the design

The first question to ask any supplier is whether or not their powder-handling system was specifically designed for that application, or if it was, in fact, adapted from an existing liquid-handling system.

While powders and liquids do behave similarly under some conditions, their flow and handling characteristics are not the same. Differences arise in required dispensing volumes, flow rates, and the most efficient cross-sectional area of the filling and dispensing openings, among others.

Static build-up in the containment material also plays a different role in powder handling than in liquid handling.

ILC Dover’s EZ BioPac® system, for instance, was designed by its DoverPac® Containment Systems engineers from scratch, specifically for powder handling in the biopharmaceutical industry. Their focus, from the beginning, was to get the usability of the system just right. Furthermore, the EZ BioPac® system is a true 3-dimensional design, allowing for enhanced flow and control of the powder, unlike its 2-dimensional competitors.

### METHODS

To measure its specific performance, ILC Dover tested a typical competitive 2D transfer bag (Figure 2) versus the EZ BioPac® system (Figure 3).

The test procedure required filling each bag to approximately 5.25 kg, then adjusting the final weight to a consistent endpoint value of 5.0 kg. This replicates typical fill practice where the exact amount isn’t reached initially and adjustments must be made to fine-tune the final weight. Finally, we measured speed of powder discharge and looked for any powder that remained in the bag.

We ran three independent trials.

#### Test procedure

EZ BioPac Test Procedure Activity: Lay out bag & clamp on table. Start time when bag is picked up. 1) Install onto fixture 2) Pour ~ 5.25 kg powder into bag - remove .25 kg 3) Close bag - stop timer

2D Transfer Bag Test Procedure Activity: Lay out bag & clamp on table. Start time when bag is picked up. 1) Install Bag 2) Pour ~ 5.25 kg powder into bag - remove .25 kg 3) Remove Bag-install Cap 4)Wipe down bag & fixture - stop timer

EZ BioPac Discharge Test Procedure Activity: Lay out bag & clamp on table. Start time when bag is picked up. 1)Install bag 2) Unfasten tie closures 3)Discharge using gravity. 2D Transfer Bag Discharge Test Procedure Activity: Lay out bag (clamp installed) on table. Start when bag is picked up. 1) Remove clamp & cap 2)connect 3) Remove Weeloc 4)Discharge 5) Fasten Weeloc

After the powder was done exiting the bag we measured how much powder was left in the bag.



Figure 1: Containment and transfer systems should be easy to fill and fast to dispense.

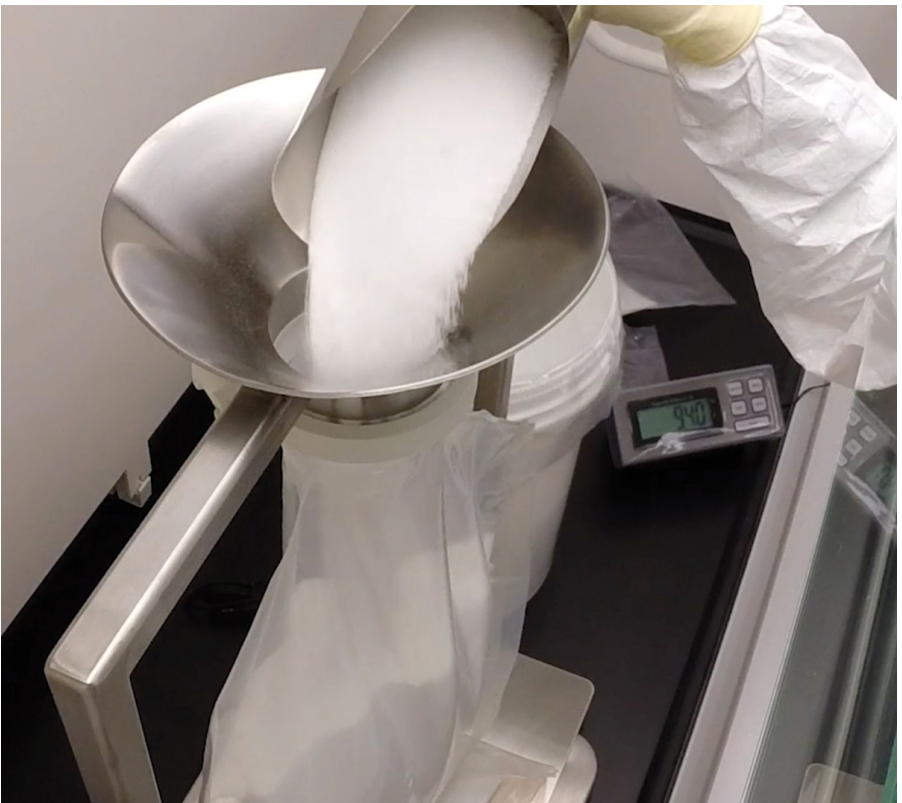


Figure 2: The narrow opening used with many liquid-derived containers can make them difficult to fill.



Figure 3: Wide openings and protective outer skirt make ILC Dover’s EZ BioPac® containers easy to fill, easy to seal cleanly and easy to handle during transport.

### RESULTS

#### Fill time

EZ BioPac was able to be filled 71.1% faster than a industry standard 2D bag (Figure 4). EZ BioPac® yielded 18.6% faster total discharge time, , averaged over three independent trials (Figure 5). In addition there was 33.3% less product remaining in the bag at the end of the trial (Figure 6).

#### Filling ease

The narrow openings in many of the packs derived from liquid-handling systems can make filling slow and difficult while increasing the risk of spillage, which can lead to contamination of the pack surfaces as well as wasted raw materials. In addition, even during careful filling, particles hitting the funnel’s hard surface can bounce out of the funnel, contaminating the bag and its support stand.

ILC Dover has designed its EZ BioPac® vessels with a large-diameter, open-funnel top for easier and quicker filling. The pack fits into a light, nonmetallic frame that holds the top open, so the need for a separate funnel is eliminated, along with the need to clean it.

By reducing uncontrolled powder handling, the EZ BioPac® system lessens the amount of powder that disperses into the air, thereby lowering the risk of cross-contamination and perhaps reducing cleaning frequency. Lower powder dispersal also serves to reduce staff exposure to inhaled particulates, while reducing ignition risk.

#### Fill adjustment

The large fill opening of the EZ BioPac® bag also reduces the chance of overfilling and makes it easier to fine-tune the weight of product. If the operator overshoots the target weight, he or she has only to reach in and easily scoop out the overage until the weight is exact.

With narrow-neck bags, fine-tuning the final weight is awkward, requiring use of a narrow ladle and cumbersome manipulation of the filled bag.

Figure 4: Filling Trials—Time to Fill to 5.0 kg

|                        |                   | EZ BioPac®                  | 2D Transfer Bag             |
|------------------------|-------------------|-----------------------------|-----------------------------|
| ILC Dover Filling Test | Test Media        | Process Fill Time (min:sec) | Process Fill Time (min:sec) |
| Trial 1                | Magnesium Sulfate | 2:03.91                     | 3:09.21                     |
| Trial 2                | Magnesium Sulfate | 1:54.66                     | 3:01.06                     |
| Trial 3                | Magnesium Sulfate | 1:37.07                     | 3:24.13                     |

#### Fill speed

The larger opening and design of the fill opening and skirt proved to offer filling performance superior to other, narrower opening designs. The EZ-Biopac bag’s design allows for much more rapid filling and adjustment of powder amount.

#### Contamination potential

During filling, many types of single-use bags can become contaminated on the outside surface when product is spilled or overflows, or when it simply settles out from the surrounding air. The separate support stand can also become contaminated during bag removal. Both the bag and stand, therefore, require wipe-down after filling, to avoid cross-contamination.

To avoid this requirement, ILC Dover’s EZ BioPac® system includes a protective outer skirt (Figure 3) that folds down to completely cover the outside of the bag and the support stand during filling. After filling, this skirt is simply turned up to its original position and sealed, locking any powder residue on its interior surface.

The potential for surface contamination is thereby drastically reduced and sealing and handling are much easier and cleaner.

#### Sealing speed and simplicity

The EZ BioPac® is simple to seal by either of two methods. The first requires only making a V-fold in the bag’s upper neck and then clamping the fold tightly closed with attached cable ties. The second (shown) uses ILC Dover’s proprietary, robust crimping system, which allows quick, one-person sealing under virtually any conditions.

Competitive bags require placing a cap over the opening, then holding it in place while putting a split-ring clamp in position over the cap and tightening it in place. The cap can easily slip out of position during this process, requiring repeated attempts to properly align the cap and clamp before the clamp can be tightened to seal the bag.

#### Discharge ease and speed

Just as filling containment packs must be done as accurately and repeatably as possible, discharging them must provide for complete powder transfer to the mixing vessels.

While the bags in many systems must be discharged through the same narrow neck used for filling, the EZ BioPac® system’s bags feature a discharge outlet completely separate from the fill inlet. With this configuration, the discharge flow path remains clean and untouched by powder until transfer is initiated. Again, comparison trials show the superiority of this design approach.

ILC Dover tested its EZ BioPac bag versus a competitive 2D transfer bag in head-to-head time trials.

Figure 5: Discharge Trials—Time to Discharge 5.0 kg

|                          |               | EZ BioPac®                     | 2D Transfer Bag                |
|--------------------------|---------------|--------------------------------|--------------------------------|
| ILC Dover Discharge Test | Test Material | Test discharge rate, [min:sec] | Test discharge rate, [min:sec] |
| Trial 1                  | Flour         | 1:49.0                         | 1:45.0                         |
| Trial 2                  | Flour         | 1:51.81                        | 2:03.07                        |
| Trial 3                  | Flour         | 1:21.42                        | 2:10.70                        |

#### The cost of static and bag geometry

The two primary sources of incomplete discharge and product waste for many 2D single-use bags are bag geometry and the static that can build up on the film. The 2D bag’s pinch seams create narrow channels where powder can become trapped, while static can cause particles to cling to the inside of the bag’s surface, regardless of the degree of shaking or agitation of the bag.

To counter this problem, the EZ BioPac® 3D containment packs provide a round, smooth discharge path and are fabricated from ILC Dover’s proprietary ArmorFlex® 114 antistatic film, which meets FDA, USP and EU regulatory compliance standards. With little or no static charge, the EZ BioPac releases its contents much more completely, reducing ingredient waste and making batch-to-batch product more consistent.

Figure 6: Discharge Trials—Retention

|                         |               | EZ BioPac    | 2D Transfer Bag |
|-------------------------|---------------|--------------|-----------------|
| ILC Dover Recovery Test | Test Material | Retention, g | Retention, g    |
| Trial 1                 | Flour         | 2            | 3               |
| Trial 2                 | Flour         | 2            | 2               |
| Trial 3                 | Flour         | 2            | 3               |

Comparative testing demonstrates a 33.3% improvement in recovery rates offered by the EZ BioPac™ bag geometry, when measured against a 2D bag made from ILC’s own ArmorFlex 114.

#### Ergonomic design

Some manufacturing processes require large quantities of buffer and media, readily available in a number of locations. Because the filled EZ BioPac® 3D containment pack is self-supporting, it can be filled in a central location, then moved easily and staged in appropriate locations, as required by the process.

Standard sizes are available in a range from 1 liter to 100 liters, and custom sizes are available. They include built in handles or lifting loops, depending on the size, and are made from heavy-gauge materials to support the weight of product with which they’re filled.

#### CONCLUSION

Handling any powder disperses fine particles into the air. While the ingredients used in media and buffer preparation are typically benign and stable, long-term exposure can cause harm. With even the most stable of compounds, a fine powder ‘haze’ in the air can also create some risk of ignition. In addition, airborne particles eventually settle out onto surfaces, posing a risk of cross-contamination and requiring cleaning.

Solutions such as the EZ BioPac® system from ILC Dover® lessens the amount of powder that disperses into the air substantially, thereby lowering the risk of cross-contamination. Reducing the amount of contamination, in turn, reduces the time needed for changeover, lowers staff costs, and frees staff to work on more vital jobs, which all contribute to profitability.

#### A look at the future

While media and buffer materials have been notorious contributors to airborne particulates and contamination in the past, they don’t have to be. With careful evaluation and system specification, new, dedicated powder transfer systems like EZ BioPac® can help eliminate those issues in closed processes and provide a rapid single-use solution that will reduce contamination and safety issues. This can have a significant impact on plant productivity and profitability.

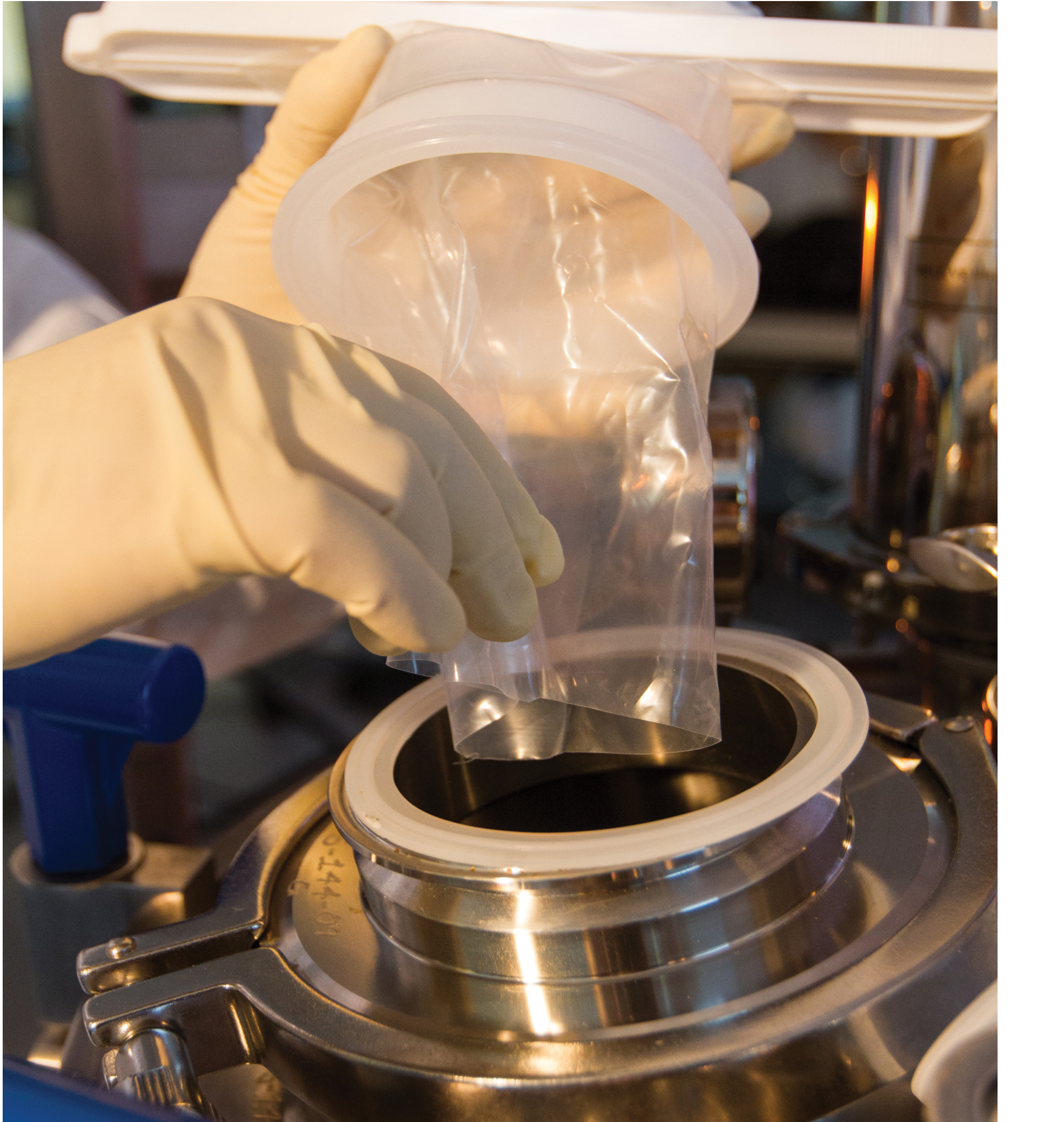


Figure 7: EZ BioPac® bag includes separate discharge opening to increase discharge speed and reduce contamination.