

**SINGLE  
USE  
SUPPORT.**

PIONEERING BIOPHARMA



# Automated aseptic filling

Better filling through flexibility and precision





## Automated filling: The way to go

Still more than half of CDMOs and biopharmaceutical manufacturers use manual filling to dispense drug substances into primary packaging, such as single-use bags and bottles.<sup>1</sup> Nevertheless, manual handling comes with a higher potential risk of “human error” than automated filling. With 8 out of 10 cases of process deviations in pharmaceutical manufacturing environments, human error is the biggest cause of operational errors.<sup>2</sup>

Since the implementation of Annex 1, the importance of automated filling in establishing an aseptically closed system during the filling process has increased even more, as has the risk of contamination.

### Which of these terms best describes the process at your site for drug substance filling?

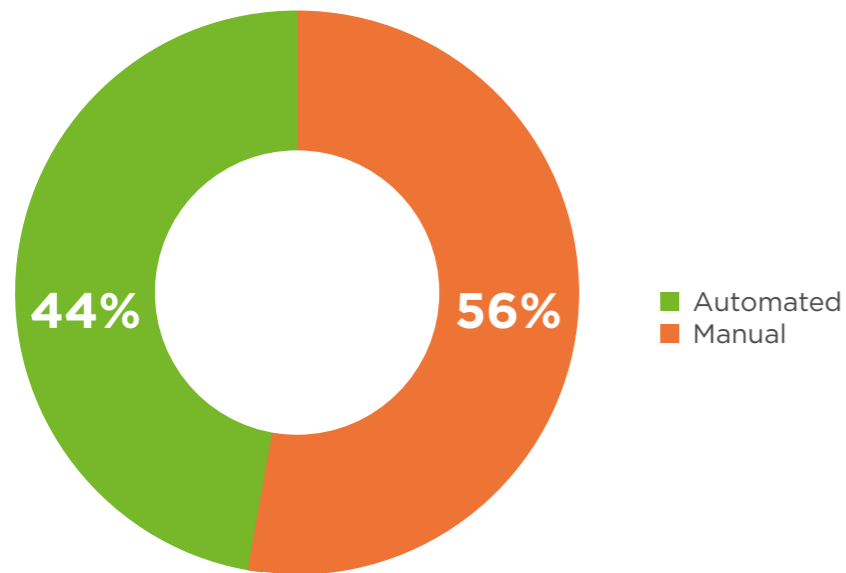


Figure 1: Automated vs. manual process at drug substance filling<sup>1</sup>

Automated filling systems help CDMOs and manufacturers to reach the next level in drug substance management. There is an overall trend within the biopharmaceutical industry to start automation initiatives for fluid management - for good reason: Automated fluid transfer systems help to reduce both contamination risks and the risk of human errors.

RoSS.FILL is Single Use Support’s automated filling platform for drug substances. With its modular design it can be used for dispensing of small volumes to bulk drug substances into different sizes of single-use bags and bottles. RoSS.FILL outshines other filling solutions with regards to precision, scalability, flexibility, speed, its process upgrade options and its process integration.

## ACCURACY

At low filling volumes, the need for accuracy becomes critical. Ensuring high filling accuracy minimizes manufacturing errors and supports compliance when dispensing drug substances into single-use containers.

The RoSS.FILL system from Single Use Support is an automated, aseptic filling system that accurately dispenses active pharmaceutical ingredients into primary packaging, such as single-use bags and bottles. A variety of modular filling racks are available to meet customer requirements regarding single-use container size and batch quantity.

RoSS.FILL can dispense small volumes, ranging from 1 mL to 1000 mL, into single-use bioprocess containers and bottles. Depending on whether gravimetric or flow filling technology is used, highly precise aliquoting can be achieved.

- **Gravimetric filling** with integrated load cell scales ensures weighing accuracy within  $\pm 2$  g.
- **Filling with a flow sensor** enables accuracy of down to  $\pm 1$  mL.

The unprecedented accuracy with which low-volume single-use systems can be filled gives operators better control.



Figure 2: RoSS.FILL enables filling for small volumes with highest accuracy



## SCALABILITY

One big challenge is scaling fluid management according to manufacturing needs. The RoSS.FILL system opens doors to scale-up or scale-out in terms of both number of bags and size of bags. For example, it can fill 100 single-use bags at 50 mL each or 20 single-use bags at 20 L each per module, making it suitable for small volumes of cell therapies, viral vectors, mAbs, and other early-phase studies as well as for commercialized bulk drug substance. It is even possible to attach one or more additional filling modules to the control unit, which allows operators to aliquot and filter 400 L or more of drug substance in one batch run.



Figure 3: Unlimited scalability for aseptic filling from laboratory to commercial production

### RoSS.FILL Lab Scale | 1 mL to 1000 mL

Fully automated aseptic filling of up to 12 small single-use bags for clinical studies and cell & gene therapies.

### RoSS.FILL CGT | 1 mL to 1000 mL

Fully automated aseptic filling of up to 72 small single-use bags for clinical studies and cell & gene therapies.

### RoSS.FILL Bottle | up to 10 L per bottle

Fully automated aseptic filling of single-use bottles of up to 10L.

### RoSS.FILL Bag | up to 20 L per bag

Fully automated bulk drug substance handling with 20 individual weighing scales.

### RoSS.FILL Base | up to 1000 L per container

Fully automated system for aseptic filling for large volumes into 3D single-use bags and other bulky containers.

## FLEXIBILITY

Aseptic filling processes vary from one manufacturing facility to another. Multi-product facilities in particular benefit from modular systems like RoSS.FILL. These systems allow manufacturers and CDMOs to adapt to custom requirements, setups, and volumes with one platform.

**Modular:** The RoSS.FILL control unit, which houses GMP-ready software, is always the centerpiece. Its modular design allows different filling modules to be attached to it, making it easily and quickly configurable for different processes. Both single-use bags and bottles can be filled, and several modules can be attached to further increase process efficiency.

**Vendor-agnostic:** Facing incompatibilities based on the primary container used, is a challenge. Bag-independent solutions that help streamline the fluid management process, regardless of the size and type of single-use bag or bottle that needs to be filled. Single Use Support follows its vendor-independent path and provides solutions for all different scenarios.



Figure 4: Modularity enables hybrid filling with (A) RoSS.FILL Bottle and (B) RoSS.FILL Bag



## PROCESS UPGRADE OPTIONS

The filling process may include additional steps beyond aliquotation into single-use containers. For example filtration, PUPSIT, homogenization, draining or other temperature-controlled preconditioning of cells during fluid transfers. Modular designs make it easy to add extra process steps.

### Filtration

Single-use filters can be integrated in the process flow of liquid transfer during the sterile dispensing into single-use systems. This option simplifies the complexities of bulk filtration and the associated PUPSIT requirements recommended by GMP Annex 1. With its modular fluid management solutions, Single Use Support literally filters complex demands that need to be considered into practical and effective solutions.

### Automated stepper & sealer valve

Advanced sealer and stepper pinch valves can be integrated into the RoSS.FILL platform filling modules. With a variable fluid control to accelerate the throughput for fast filling, and simple aseptic decoupling of single-use bags, these valves offer two functions that significantly enhance the fluid management process. Both functionalities are fully automated and integrated in the process step of aseptic filling and filtration to considerably advance process efficiency.

## SPEED

Automated filling significantly reduces the time required compared with manual handling. If fast operation is a priority, the automated filling platform RoSS.FILL can handle tens or hundreds of liters with the highest throughput. The RoSS.FILL Bag can dispense over 100 L of bulk drug substance into 10 L single-use bags in less than 60 minutes. This process can be accelerated further with parallel filling.

The RoSS.FILL CGT filling system is specifically designed for smaller volumes. The platform provides filling for dozens of small bags and enables the aliquotation of up to 36 L per hour with highest accuracy. An efficient filling process helps manufacturers secure timely business continuity while maintaining product stability. Furthermore, a fast automated filling process saves resources and reduces the risk of operational errors caused by manual filling.

### More than 3 times faster filling

A case study of a biopharmaceutical manufacturer producing live-attenuated vaccines demonstrated that automated filling is up to 70 % faster than manual handling when filling bottles of varying sizes. The case study looked not only at actual filling duration, but also at preparation and documentation, which is not required when filling with automated systems meeting 21 CFR Part 11-relevant standards.



Figure 5: Automated stepper and sealer valve enables integrated aseptic decoupling of single-use assemblies



## PART OF END-TO-END PROCESS

Breaking free from silo thinking and streamlining the manufacturing environment is increasingly important. The risk of product loss diminishes when compatible and bag-independent platform systems cover the entire ecosystem from drug substance to drug product site.

This is already reflected in the flexible, end-to-end process solutions provided by Single Use Support. These solutions allow for seamless filling, freezing, storing, shipping, thawing, and draining. This approach ensures controlled transportation while preventing incompatibilities and damage.

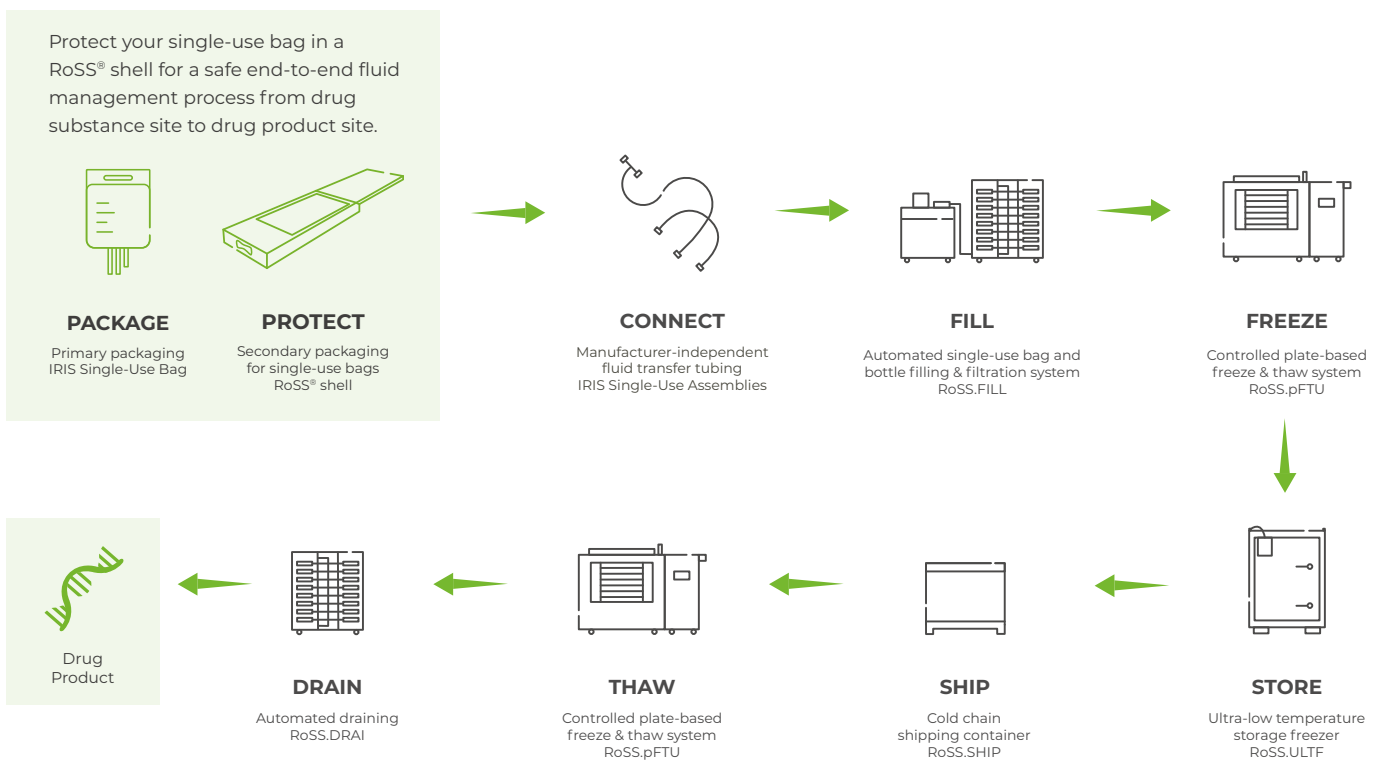


Figure 6: End-to-End process for single-use bags in biopharmaceutical manufacturing

## References

1. Aspen Alert Survey: Which of these terms describe best the process at your site for drug substance filling? April 2022, available at: <https://www.aspenalert.com/asq-787-2022-0401-which-of-these-terms-best-describes-the-process-at-your-site-for-drug-substance-filling>
2. Lowe, M.: Avoiding Human Error in Pharmaceutical Manufacturing, 2022, available at: <https://www.worldpharmatoday.com/articles/avoiding-human-error-in-pharmaceutical-manufacturing/>