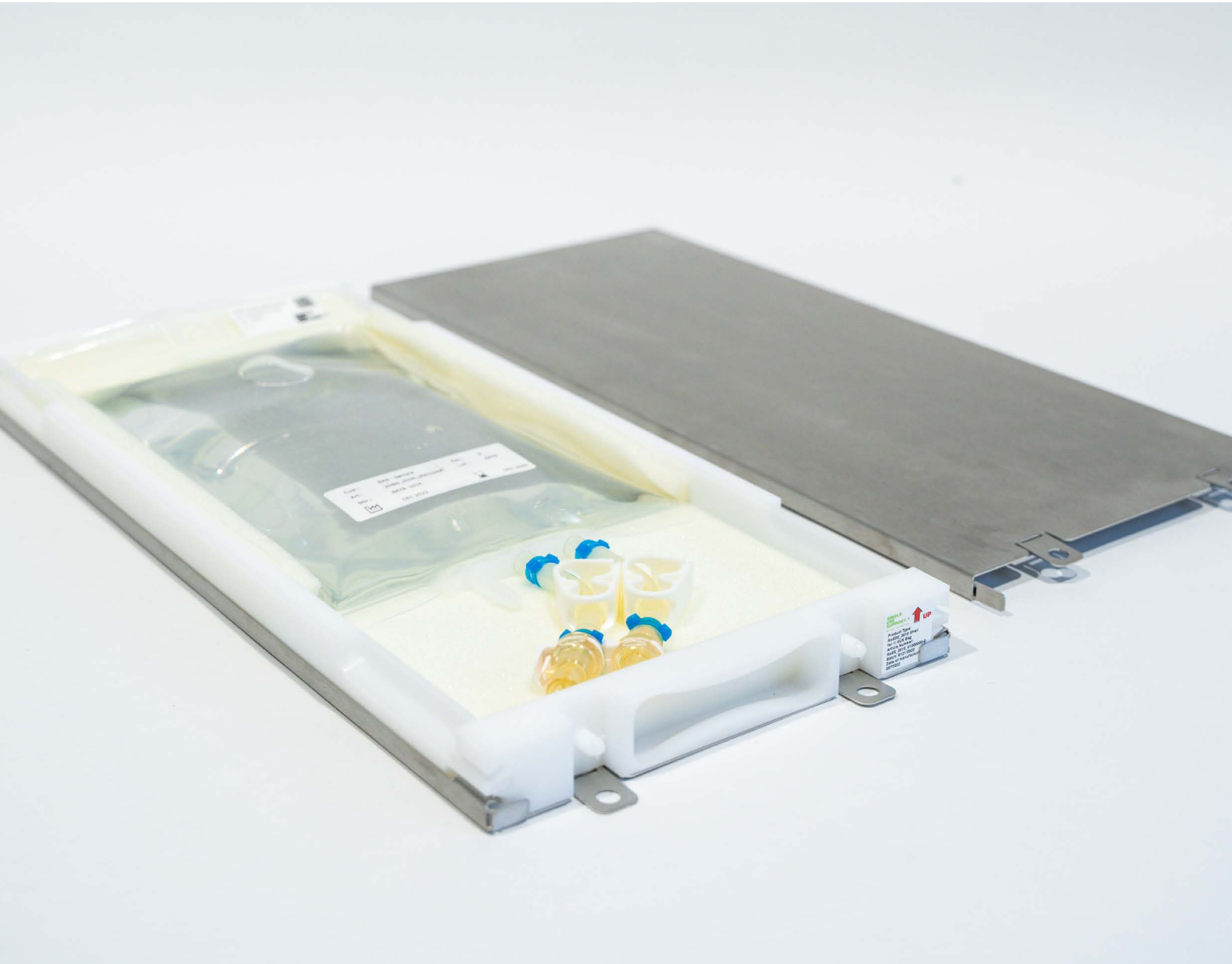
SINGLE USE SUPPORT.

PIONEERING BIOPHARMA

RoSS® shell: Robust storage and shipping

The secondary packaging for every single-use bag



ONE FOR ALL: THE ROSS® SHELL

The RoSS® shell offers a **robust & safe protection for bioprocess containers** of any size and vendor **during freezing, transportation, storage & thawing**.

With more than 300,000+ RoSS® shells sold worldwide, the RoSS® shell provides a tamper-evident system with minimized risk of contamination. The perfect composition for **robust storage & shipping for all 2D single-use bags**.

THE SETUP FOR BAG PROTECTION

The RoSS® shell is composed of a stainless-steel top and bottom lid, a robust plastic frame and 3D foam inlays (see figure 1). These components provide unparalleled advantages in the handling of liquids in single-use bags. The composition of elements that embed the bioprocess containers is simple, easy to recycle, validated for use in cleanroom environment, and it offers significant cost-efficiency and process flexibility.

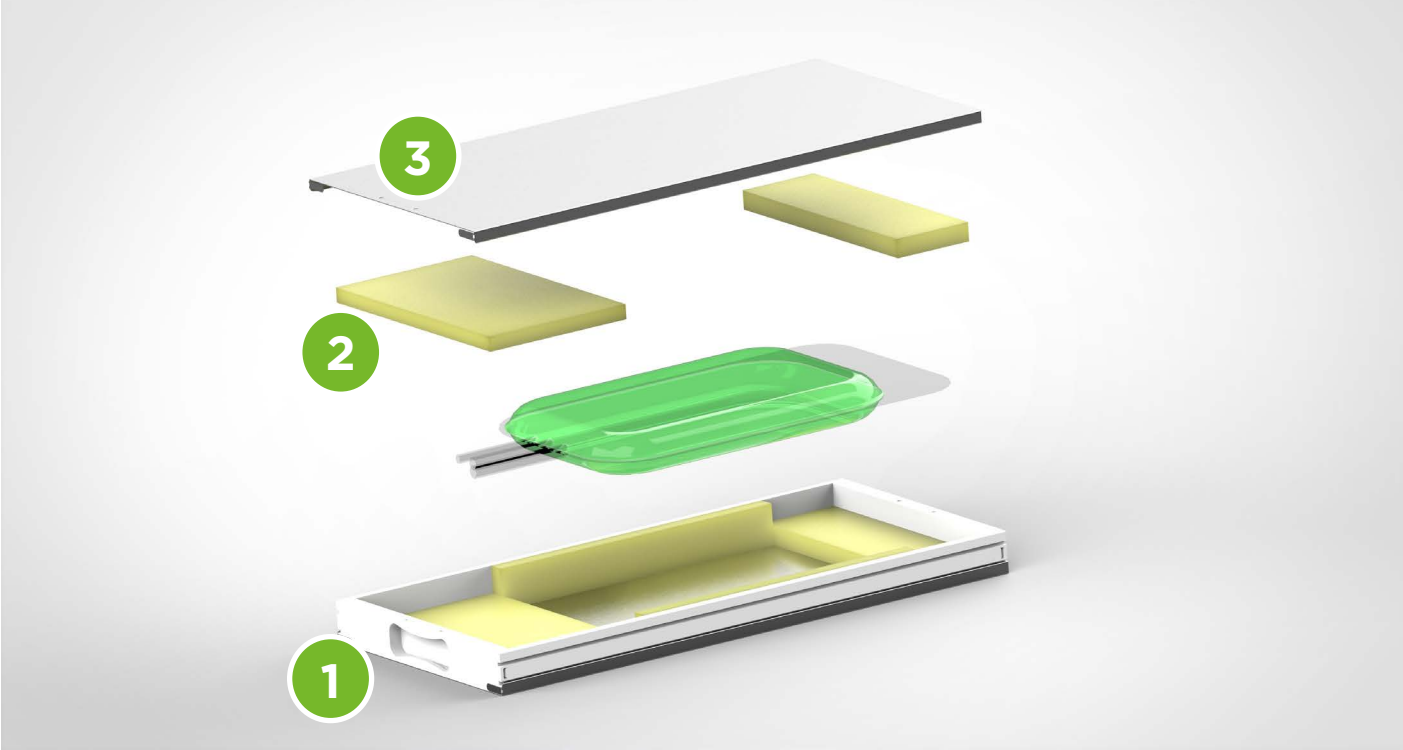


Figure 1: Components of RoSS® shell

1	PE frame	**Provides robustness**
2	3D foam inlays	**Ensures immobilization**
3	Stainless-steel lids	**Enables plate freezing**

VALIDATED ROBUSTNESS

All types of RoSS® shells manufactured by Single Use Support are subjected to rigorous testing and validation to ensure their robustness. The aim of the tests is to simulate real-life handling under standardized conditions, thereby verifying the shells protective ability in cryogenic conditions. **Drop tests** but also **bioburden validation test** in cleanroom environments[1] are performed to optimize handling of single-use bags.

Figure 2: Single Use Support's in-house production of RoSS® shells

As a result, the RoSS® shell has been proven to reduce bag rupture down to 0 %[2]. The robustness of this secondary packaging helps to protect frozen single-use bags when frozen down to -80 °C. Its equivalent for smaller bags, RoSS.KSET, is validated down to -196 °C.

FULL IMMOBILIZATION OF SINGLE-USE BAGS

While the outer shell is constructed from durable stainless steel and robust plastic elements, the interior is lined with specialized foam inlays that provide additional stabilization.

The 3D foam offers a protective enclosure for the single-use bag and its assemblies. But it also absorbs the bag's/liquid's expanding energy caused by the density drop during freezing. At sub-zero temperatures, when the bag is already frozen, the foam hardens. The bag is fully immobilized in the hardened foam setup, making it safe to handle during storage and shipping.

Figure 3: 3D foam insert ensuring complete immobilization of the single-use bag during freezing, ultra-cold storage and shipping

ENABLING PLATE FREEZING

The RoSS® shell enables plate-based freezing of single-use bags which is an advanced method for cooling biologics.

The stainless-steel lid serves as the sole barrier between the bag and the cooling medium, facilitating efficient heat transfer. This **direct cold exposure between the cooling plates and the single-use bag** accelerates the freezing process, resulting in homogeneous freezing with controlled ice front growth from the bottom and top preventing the effects of cryoconcentration.

Figure 4: Frozen RoSS® shells in Single Use Support's plate freezer RoSS.pFTU Large Scale

ONE SHELL TO ADVANCE COLD CHAIN MANAGEMENT

Manufacturers and CDMOs can greatly benefit from using a robust secondary packaging: Robustness, full immobilization of the single-use bag and the option to perform plate-based freezing are prerequisites to equip the pharmaceutical industry to handle liquids more effectively.

The RoSS® shell provides unprecedented advantages for biomanufacturers, such as

- **Minimized product loss**
- **Maximized product viability**
- **Free choice of type of single-use bag**
- **Limitless scalability**
- **Integration in end-to-end process**

Figure 5: RoSS® shells significantly reduce product loss when handling single-use bags in biopharmaceutical processes

MINIMIZED PRODUCT LOSS

One of the biggest challenges faced by biotech companies is the high product loss rate, ranging from 0.5 % to 5 %, when handling with single-use bags.[2] This loss rate is dependent on various factors, including the sensitivity of the bag at sub-zero temperatures, the type of bag used, the protection of the bag during the cold chain process, the freezing-thawing and storage process and the shipper/shipping route.

By implementing the RoSS® shell as a robust secondary packaging solution in manufacturing and logistics suites, the risk of leakage and breakage can be reduced significantly. In fact, a case study demonstrated that it reduced product loss to 0 %. The results showed that minimizing product loss from 2.5 % to 0 % can result in savings of approximately $ 700,000 per batch.[2]

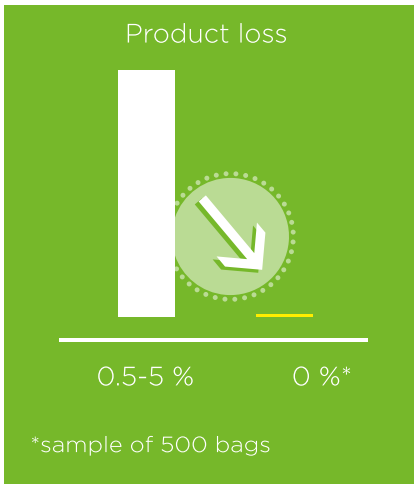


Figure 6: Case study results demonstrate that the RoSS® shell reduced product loss to 0%

MAXIMIZED PRODUCT STABILITY

The RoSS® shell is the enabler for advanced plate-based freezing of single-use bags with direct cold exposure between the cooling plates and the single-use bag. This allows for accelerated freezing and controlled ice front growth from the bottom and top, ultimately providing homogenous freezing results that are game-changing for the industry.

The enhanced level of control over freezing and direct surface contact maximizes the survival of cells, proteins and other APIs. The freezing rate for each product is adjusted based on its characteristics. Cells can now be frozen at a recommended freezing rate of -1 °C to -4 °C/min leading to maximum cell survival after cold chain storage and shipping.[3] This level of control over the freezing process can be applied to any API.

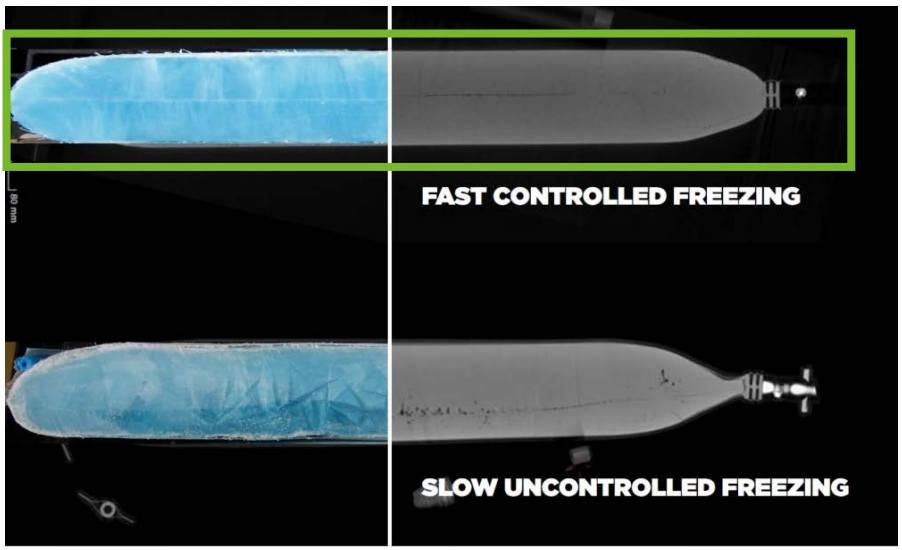


Figure 7: Results of controlled and uncontrolled freezing of single-use bags

Visualization of cryoconcentration by using Naphthol Blue Black as color agent. The intense blue coloration shows a high concentration of dissolved solutions. The bags frozen in the plate freezer exhibit a homogenous tinge with a white line running through the center. The bag frozen in the static freezer exhibits higher concentration levels in the lower areas.

VENDOR-AGNOSTIC PROTECTION

Various single-use bags are utilized for transferring liquids during bioprocessing. These bags vary in their film, form, structure ports and other features, and are selected based on the content's behavior. It is important to consider that when choosing a single-use bioprocess container; CDMOs may become limited to a specific ecosystem of solutions, which may restrict access to other solution providers.

Figure 8: The RoSS® shell is suitable for all available single-use bags, including Labtainer® from ThermoFisher, Mobius® from Merck/Millipore, Allegro™ bags and more. Allegro™ is a registered trademark of Cytiva.

The RoSS® shell provides a solution to the inflexibility of specific 2D bioprocess containers from certain manufacturers and sizes. **It can be used with all available 2D bioprocess containers**, making it a vendor-independent protective shell that unifies the cold chain logistics process.

By using bag-independent process solutions, CDMOs can reduce their costs for cold chain logistics utilizing single-use bags by up to 60 % and significantly improve fluid and cold chain storage and shipping processes.[4]

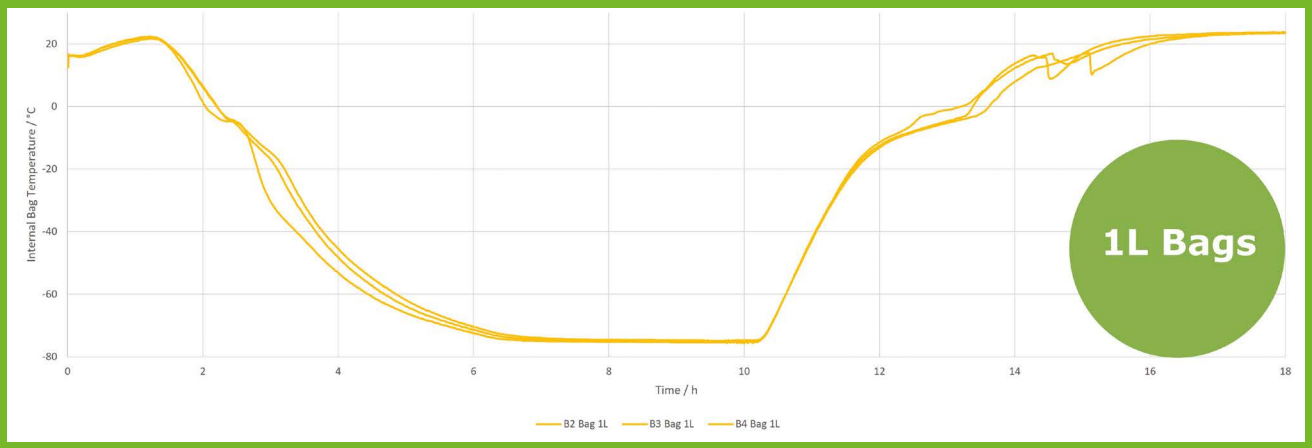
LIMITLESS SCALABILITY

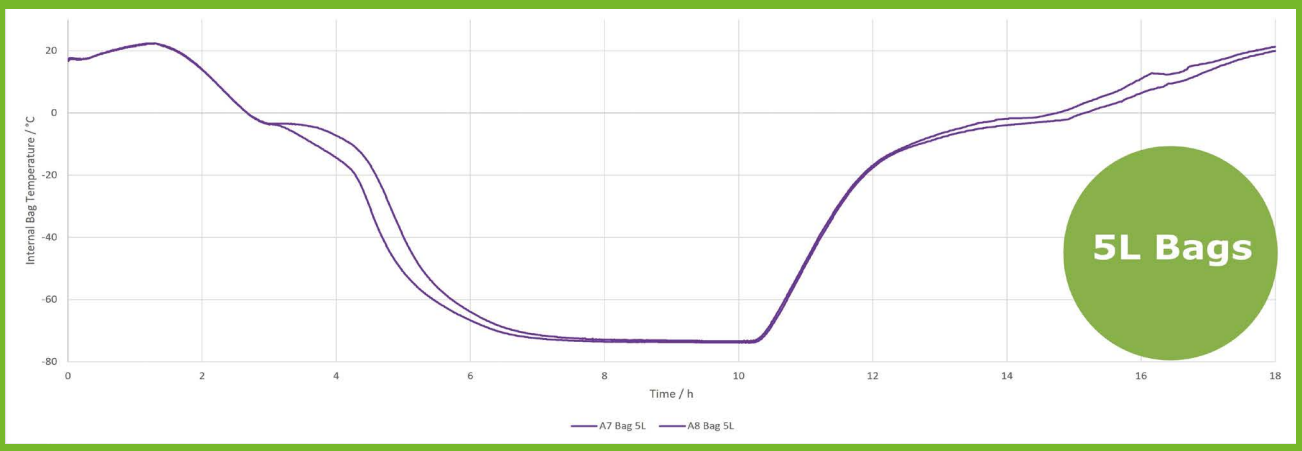
In biomanufacturing, the volumes handled can range from 1 mL to 1000 L+ per batch. The RoSS® shell is available 2D single-use bags up to 50 L. For bags of 250 mL and below, the RoSS.KSET is the appropriate solution as protective shell.

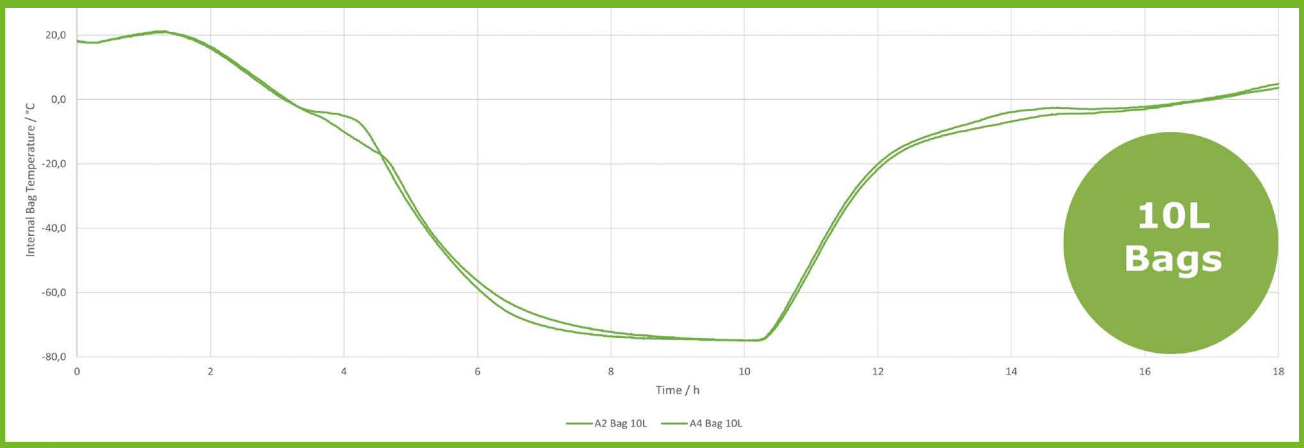
Scale-up and scale-out are both approaches to increase manufacturing volumes throughout commercialization. Scale-out involves increasing the quantity of same-sized single-use bags, while scale-up involves changing to larger single-use bags.

When scaling up production, one of the biggest challenges in freezing is ensuring consistent and reproducible stress on proteins (biopharmaceutical molecules) across all scales, filling volumes and loading scenarios. Single Use Support addresses this challenge by standardizing the ice front growth speed for all possible scenarios, regardless of the filling volume, bag type or freezing platform size[5].

Figure 9: The RoSS® shell is available in sizes up to 50L







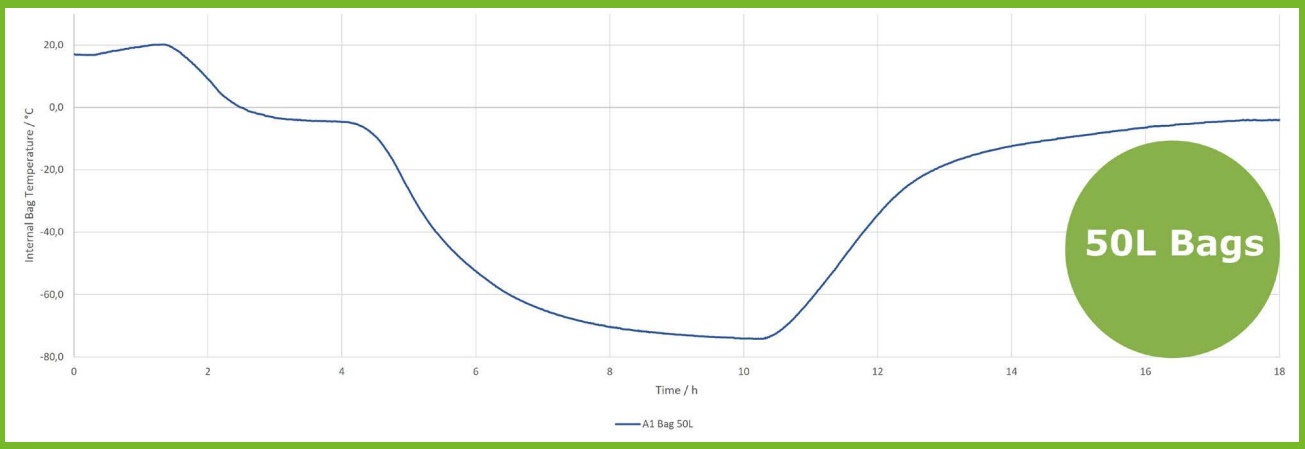


Figure 10: Scalable freezing with single-use bags from 1 L to 50 L

INTEGRATION IN END-TO-END PROCESS

Siloed platform systems were identified as the biggest cost drivers. Limited process flexibility, inhibited process flows, and slowed speed-to-market are all results from the lack of compatibility of single-use bags and the lack of interconnectedness among different platform systems from multiple suppliers.

With RoSS technologies around biologics liquid transfer, the customer is free to choose from any of the platform solutions that can be embedded in an end-to-end process covering aseptic fluid management and cold chain logistics in an automated manner.

Single Use Support's end-to-end process is inclusive of all types and sizes of single-use containers, unifying the bioprocess containers and standardizing the process steps in biomanufacturing throughout aseptic aliquoting, controlled freezing and thawing, ultra-cold storage and shipping.

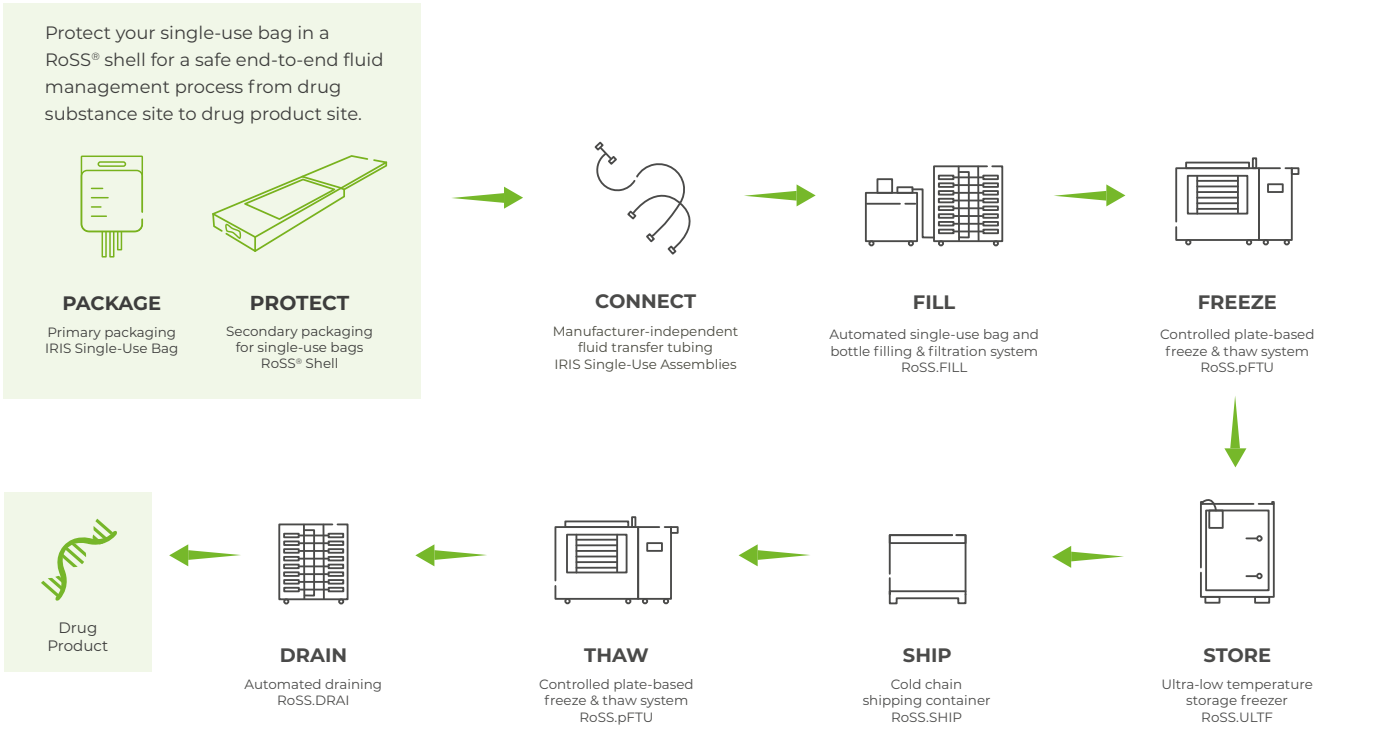


Figure 11: Single Use Support's fluid and cold chain management process for single-use bags

References

1. *Single Use Support: Case Study Bioburden Testing of RoSS. 2022.*
2. *Single Use Support: Case Study Reducing Product Loss, Cost-Efficiency. 2022.*
3. *Brandmayr P.: Optimization of the freezing process with a liquid nitrogen freezer to increase cell viability of a mammalian cell line. 2023.*
4. *Single Use Support: Case Study Reducing Product Loss, Bag-Independence. 2022.*
5. *Single Use Support.: Controlled freezing becomes a reality: Impact of ice front growth speed on scalability of freezing protein solutions. 2022.*