SINGLE USE SUPPORT.

PIONEERING BIOPHARMA

Controlled blast freezing of drug substances

Maintaining product quality throughout freeze-thaw cycles using bulk-packaged solutions

Why controlled freezing is a blast

The freezing of drug substances is a critical step in the manufacturing process - especially for high-value products like monoclonal antibodies (mAbs), antibody-drug conjugates (ADCs), and other biologics. These substances are highly sensitive to temperature fluctuations, and improper freezing can compromise their stability and potency as well as overall quality. That's why precision matters.

With single-use bags, bottles, and larger bulk packaging, different types of primary packaging are used for freezing applications that support cold chain processes in both upstream and downstream bioprocessing. The varying geometry of containers can lead to specific limitations during manufacturing, such as uneven temperature distribution, risk of cryoconcentration, and limited scalability. Manufacturers need solutions that not only preserve product stability and integrity but also meet strict regulatory and operational requirements while ensuring cost-efficiency in manufacturing facilities.

One of the greatest challenges is mastering the freezing process, independent of the single-use container used. Ensuring consistent, scalable, and repeatable temperature profiles helps safeguard the molecular structure of biologics and supports GMP readiness. As the industry moves toward more flexible and sustainable production environments, advanced freezing technology for single-use bags and bottles is becoming increasingly important.

Although blast freezers have long been part of the solution, innovations are now redefining what's possible. Next-generation systems like RoSS.BLST are setting new standards – they feature better temperature control, greater process flexibility, and smarter designs with modular configurations.

Figure 1: Human-machine interface of RoSS.BLST for controlled blast freezing

CONTROLLED | BLAST FREEZING PERFORMANCE

Maintaining consistent and controlled freezing conditions is crucial to preserving the stability of sensitive biopharmaceutical products. Thanks to their improved thermal convection, airflow-based systems can better manage temperature gradients than static freezers, which is particularly important for ensuring protein stability and overall product quality.[1]

RoSS.BLST features a controlled high-volume airflow system down to -80 °C that delivers up to 1,800 m^3/h, and performs a complete **air circulation every 2.5 seconds** to ensure even temperature distribution throughout the chamber. This enables gradual and uniform freezing to -70 °C during an **idle freezing cycle of two hours**. The cooling rate can be adjusted based on research findings recommending an optimal freezing rate of –0.1 °C to –0.5 °C per minute for larger bottles (≥1 L) to minimize cryoconcentration and preserve protein integrity.[2] Thanks to its higher efficiency and improved freezing performance, the RoSS.BLST ensures optimal product integrity for biologics during freeze-thaw cycles (see Figure 2).[3]

Median freezing cycle with 168 bottles

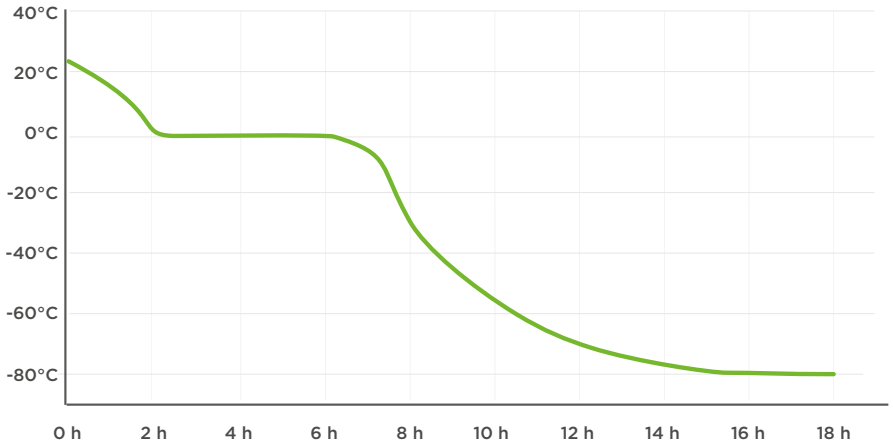

Figure 2: Exemplary controlled-rate freeze run of 168 2 L bottles down to -80°C with RoSS.BLST

Visualization of heat transfer and airflow patterns shows that high-performance forced-air distribution enables consistent temperature control and uniform freezing. Single Use Support's blast freezer RoSS.BLST controls the rate of cooling by employing smart air distribution, as shown in Figure 3.

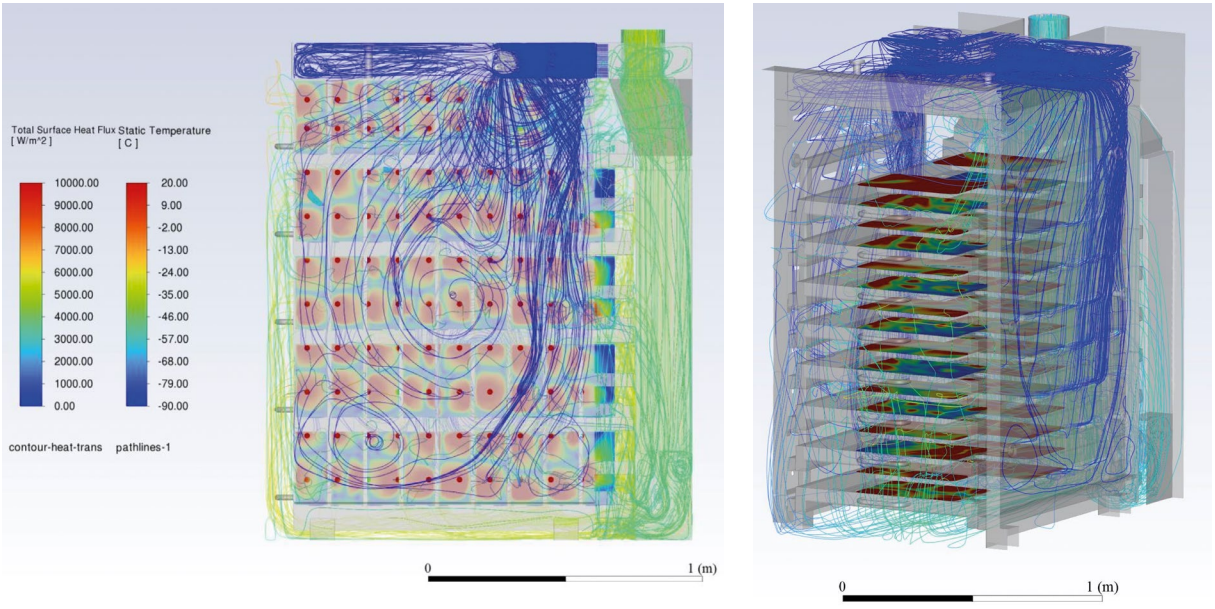

Figure 3: Visualization of heat transfer and airflow patterns when using RoSS.BLST for temperature control , showing the high-performance forced-air distribution when used with single-use bottles (left) and bags (right).

MULTIFUNCTIONAL | FREEZE, THAW, SHAKE

Beyond freezing, RoSS.BLST also supports a range of functions that enhance process control and operational flexibility. Both freezing and thawing can be carried out at controlled rates, which is particularly important for maintaining the stability of temperature-sensitive biologics.[2]

During thawing, integrated shaking is available and often preferred, as it facilitates uniform temperature distribution throughout the container. This is critical for preventing localized hot or cold spots that can lead to uneven reconstitution, protein aggregation, or phase separation. Shaking also helps minimize the formation of concentration gradients, especially in high-viscosity or freeze-concentrated solutions.[3] Together, controlled thawing and active agitation reduce the risk of denaturation and ensure consistent product quality across the entire batch.

The system is designed to meet qualification and validation requirements in line with GMP, FDA, and EU Annex 1 standards. This supports regulatory compliance across different markets and simplifies documentation during tech transfer or scale-up. It can also be integrated into Manufacturing Execution Systems (MES) and Enterprise Resource Planning (ERP) platforms, allowing for automated data logging and process control.

COMPACT | LOW FOOTPRINT PER LITER

Space is often limited and costly in manufacturing facilities. This makes space utilization a key consideration in biopharmaceutical production.

With this in mind, RoSS.BLST is designed to offer an exceptional balance between footprint and loading capacity. With its small footprint, the system fits comfortably into compact environments while still providing a generous chamber volume. It can hold up to 192 bottles with 2 L filling volumes each, maximizing output without the need for additional space.

This ratio of chamber volume to overall footprint ensures up to **30% more space-efficient** freezing than comparable blast freezing systems and allows for efficient use of available space. Additionally, the system's design incorporates the temperature control unit into the main housing, eliminating the need for separate installations and simplifying layout planning. For multi-product facilities using different single-use containers or for facilities aiming to optimize spatial efficiency without having to compromise batch size, this configuration offers a practical solution.

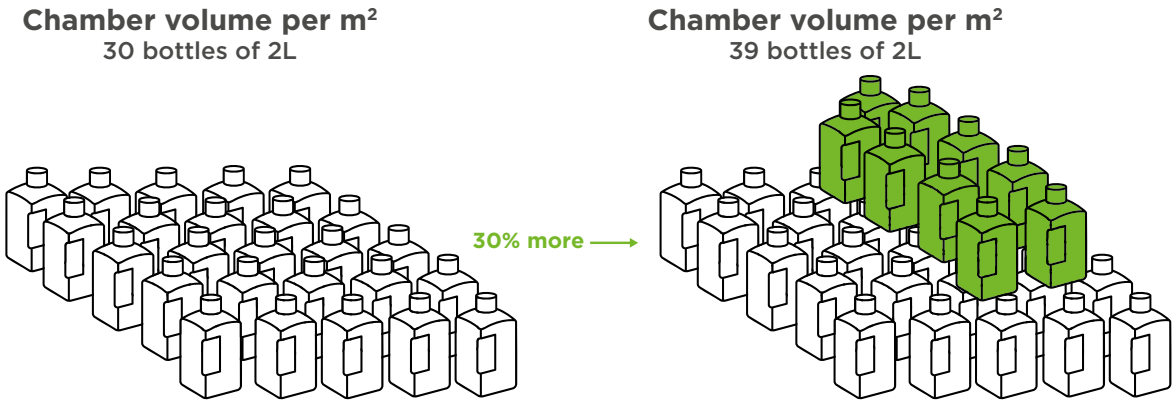

Figure 4: 30% more space-efficient blast freezing with RoSS.BLST

SUSTAINABLE | NATURAL REFRIGERANTS

Refrigeration systems in pharmaceutical environments are increasingly expected to meet sustainability standards without compromising safety or performance. RoSS.BLST operates with the natural refrigerants propane (R290) and ethane (R170). Their low volume of <500 g helps reduce environmental impact while maintaining system integrity. Thanks to the low refrigerant charge, the blast freezer can be placed in standard rooms without the need for additional safety or cleanroom-grade measures.

The blast freezer's hermetically sealed construction complies with EN378 and ISO5149 standards. It is equipped with gas detection systems that provide an added layer of protection in case of refrigerant leakage while also supporting operational safety. This approach allows for more installation flexibility in manufacturing facilities and aligns with current environmental and safety regulations.

Another promising approach is the use of cold compressed air as a cooling medium. This feature helps achieve a global warming potential of zero and will soon be available in Single Use Support's freezers. These initiatives align with the industry's broader trend toward minimizing the ecological footprint of temperature-controlled processes.

Figure 5: Controlled bottle freezing in RoSS.BLST

FLEXIBLE | MODULAR INTERIOR

Biopharmaceutical multi-product facilities are well aware that efficiently and effectively handling a variety of packaging formats can be highly challenging.

RoSS.BLST is designed to accommodate a wide variety of bulky primary packaging, ranging from standard bottles to larger 2D or 3D single-use bioprocess containers. The blast freezer has a modular shelving system, with adjustable shelves to fit different containers of varying sizes. This enables a single unit to handle multiple products and workflows, providing the flexibility required for CDMOs, where switching between formats is a routine part of operations.

The interior can be reconfigured to accommodate different production volumes or packaging requirements without additional equipment. The modular design can be adapted to different container types and batch sizes, helping to streamline processes. This simplifies planning and improves the overall utilization of available resources.

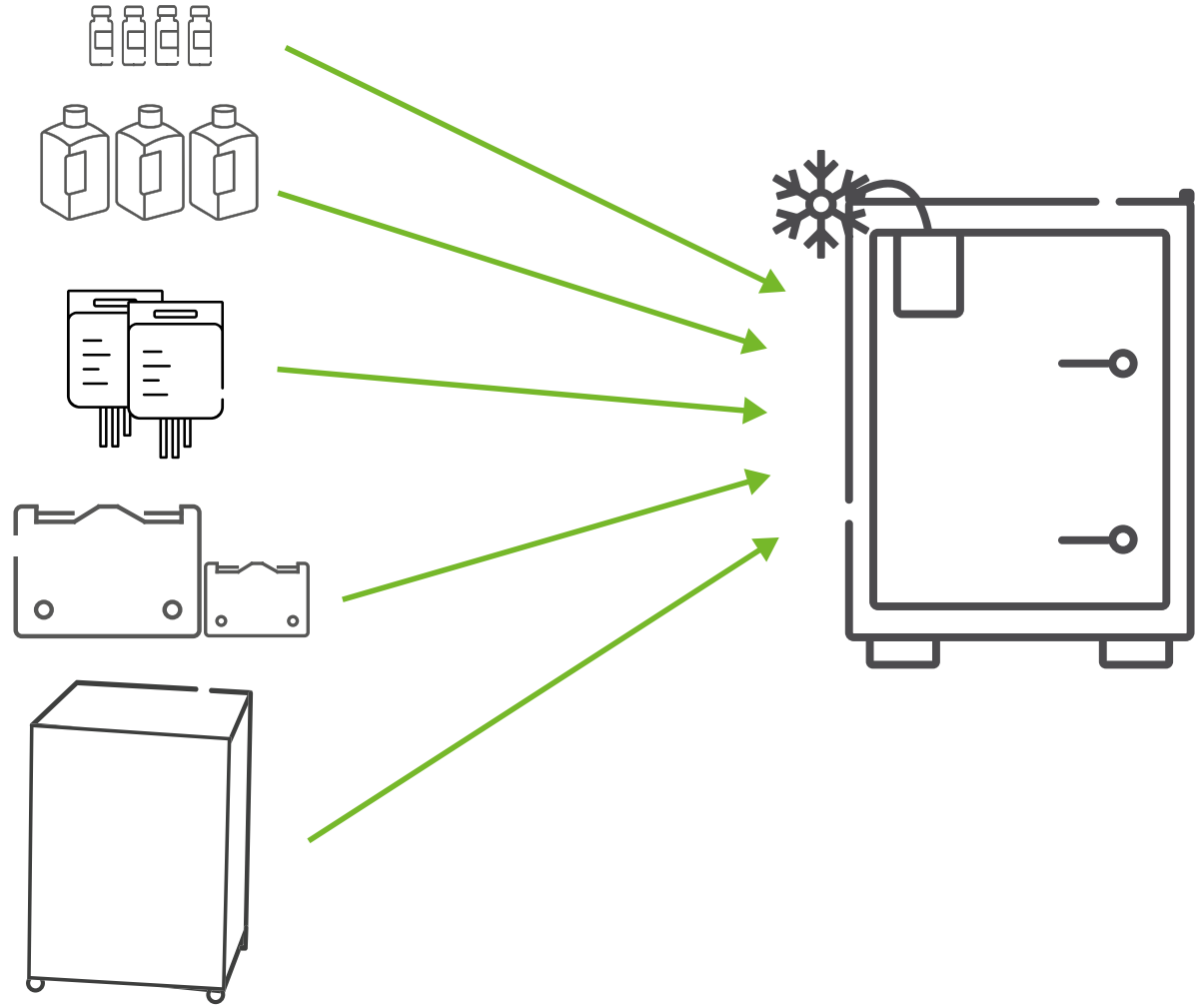

Figure 6: Modular interior design for single-use bottles and other primary packaging

From bottlenecks to breakthroughs

While blast freezers are well-established in biopharmaceutical manufacturing, challenges remain – especially in efficiently and consistently filling and freezing single-use bottles without compromising product integrity.

RoSS.BLST is designed to address these shortcomings. It is more than just another blast freezer, as it combines high-performance freezing with modular design features that support compatibility, scalability, and automation for a variety of primary packaging formats.

Developed by Single Use Support, this blast freezer is part of a modular, end-to-end solution for handling single-use bags and bottles that connects the entire fluid and cold chain management workflow. Crucially, this system also incorporates sterile and protective single-use consumables that maximize product safety, integrity, and regulatory compliance at every step. As part of this system, Bottle RoSS provides a robust secondary packaging solution that protects tubing and the assemblies on bottle caps from damage during cold chain handling. Similarly, the RoSS® shell accommodates 2D single-use bioprocess containers of all types and sizes to considerably reduce product loss. The design of both allow for secure handling during automated freezing workflows and facilitate standardization and safety during cold storage and transport.

Manufacturers can gain enhanced control, increased throughput, and superior product quality with an advanced blast freezer that addresses existing gaps and transforms bottlenecks into opportunities.

Figure 7: Robust secondary packaging for bottle tubing with Bottle RoSS

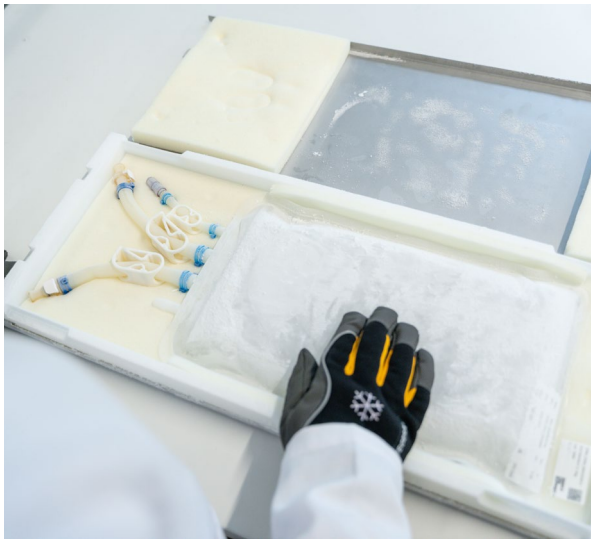

Figure 8: The RoSS® shell for robust storage & shipping of 2D single-use bioprocess containers.

REFERENCES

1. Minatovicz B et al. 2020: Freeze-concentration of solutes during bulk freezing and its impact on protein stability

2. Minatovicz B et al. : Large-Scale Freeze-Thaw of Protein Solutions: Study of the Relative Contributions of Freeze-Concentration and Ice Surface Area on Stability of Lactate Dehydrogenase - Journal of Pharmaceutical Sciences

3. Single Use Support, 2025: data on file

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