



Celsius[®] CFT

The Controlled-Rate
Freeze & Thaw Platform
Technology



Simplifying Progress

SARTORIUS

Celsius® CFT – A Well-Controlled, Scalable Freeze & Thaw Platform for Drug Substance Transfers in cGMP Manufacturing

Celsius® FT100 System ▾



The Celsius® CFT technology is a controlled-rate freezing and thawing system designed to minimize cryoconcentration in biopharmaceutical products. This robust and reliable platform ensures the bulk drug substance is well protected from start to finish, and gives flexibility by processing up to 100 L of solution in single-use Celsius® Paks. A qualified shipping solution is offered as part of the Celsius® CFT platform.

8.3 L and 16.6 L Celsius® Pak >



Maximum Product Security

- Celsius® Paks are secured in structural frames for robust handling – even at low temperatures – as proven through extensive functional qualification.
- Control of the entire process logistics from filling to dispensing, including frozen transport, to easily manage large frozen volume.
- Fast, reproducible thermal cycling preserves product stability and mitigates the major adverse effects of large scale freezing and thawing of biologics.

Process Flexibility

- Decouple process steps to provide higher manufacturing flexibility.
- Increase capacities: extend product shelf-life, stockpiling and enable batch processing, easy transfer between DS & DP sites, facilitate management of multi-product facilities.
- Optimize overall process time with fast freeze and thaw processes (5 hours to freeze 100 L of product down to -60°C, everytime).

Process Reproducibility & Reliability

- Total integration with monitoring of freeze & thaw process critical quality attributes.
- Process control with CFR21 Part.11 & cGMP compliant system for production-scale equipment.
- Reproducible freeze and thaw cycles from Celsius® Pak to Celsius® Pak, from production batch to another production batch and from Celsius® F-T module to another Celsius® F-T module.

Scalable From 30 mL to 100 L

- Celsius® CFT is the only fully scalable single-use technology for freeze and thaw on the market.
- Allows R&D & Process Development activities to explore & properly designed future production-scale processes.
- Celsius® S³, the scale-down system, reproduces the freeze & thaw rates observed at large scale and is an unique tool to run stability studies & formulation development.

Product Security to Maximize the Product Safety

Robustness of the Celsius® Pak at low temperature (down to -80°C)

Because Celsius® CFT is mainly used in the highly critical application of long-term storage of the Bulk Drug Substance (BDS) and its frozen transfer or shipment to the drug product manufacturing site, an extensive functional qualification has been ran to guarantee the robustness of the Celsius® Pak under real-process conditions.

Over 100 freeze & thaw cycles using the Celsius® CFT equipment were performed to assess the design performances.

The results are summarized in the Validation Guide for Celsius® bags (section 6) including connection, freeze & thaw (real and extreme conditions), liquid | frozen robustness and shipping tests.

Manage large scale freeze & thaw processes with optimized logistics

Celsius® CFT provides safe and easy-to-use solution through a series of accessories designed to minimize manual handling of Celsius® Pak and to mitigate the associated risks.

This gives to the end-users the possibility to build an industrial process from filling and freezing to shipping, thawing and dispensing.

Fast freeze & thaw processes to minimize bulk-scale freeze concentration and preserve product stability

The adverse effects of slow freezing and thawing rates and its related cryoconcentration phenomenon on biologics (proteins, mAbs and cells) have been well described in the industry resulting to product loss (activity | recovery).

Please contact your local FMT Application Specialist to get access to the relevant literature highlighting the benefits of the Celsius® CFT to maintain product quality with concrete studies.

Product Security

- Controlled-rate Freezing and Thawing to defeat cryo-concentration, minimize product variation and prevent from product degradation
- Proven bag (same film, bag construction and quality as Flexboy®)
- 100% Leak test on bag and immediate connections
- Robust protective frames to hold securely frozen DS stored in bags with protection over tubing | connectors
- Over 150 000 Celsius® Paks sold with proven performances in commercial drug manufacturing processes
- Complete integrated platform from filling through draining
- Filled Celsius® Paks are never carried or directly handled throughout lifecycle

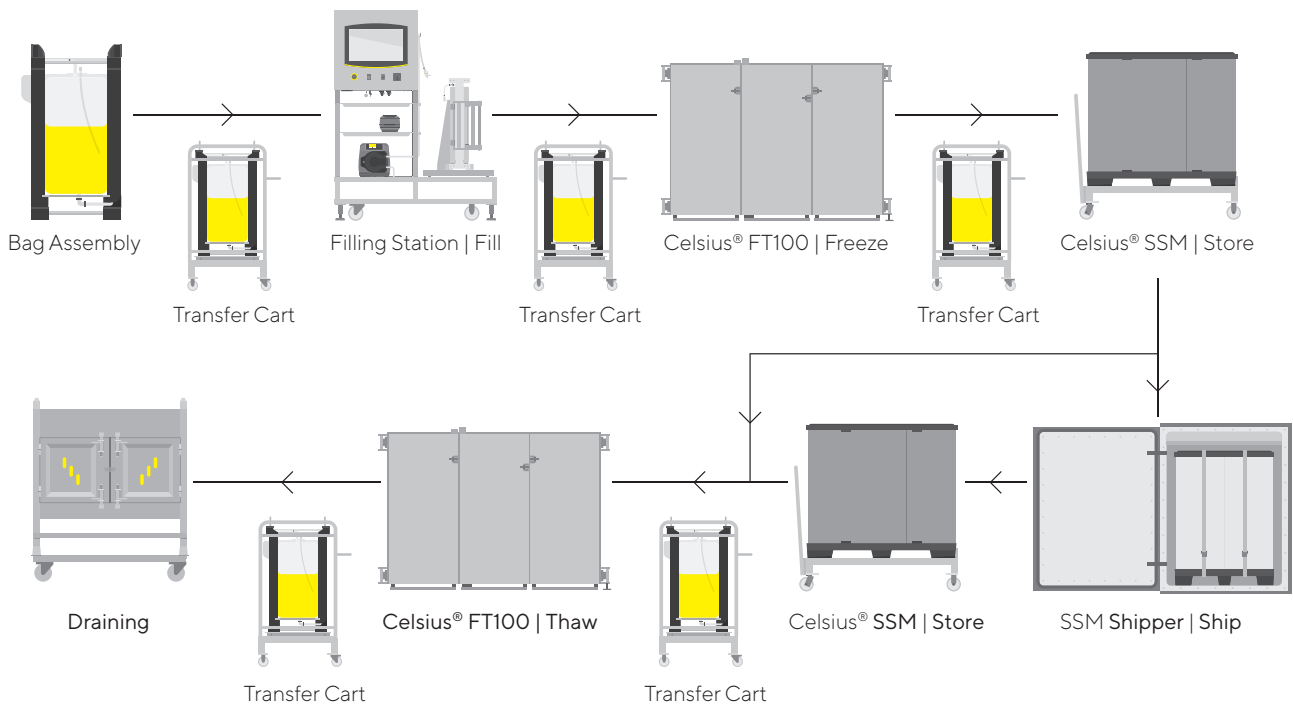
“Slow freezing rates can result in cryoconcentration. This can further lead to pH shifts and phase separation among those components resulting in protein structural damage.”

Puri & Al., BioProcess International 13(1), January 2015

“Controlled-rate technologies such as Celsius® CFT prove to be much more efficient than the conventional uncontrolled-rate methods ... and also show minimal to negligible cryoconcentration.”

PDA J Pharm Sci and Tech 2010, 64 290-298

Complete Logistics for Celsius® Paks



Process Reproducibility and Reliability for Consistent Operations, Worldwide

Reproducibility & monitoring of the CQAs: Integration of the Freeze & Thaw process step into GMP operation

The entire automatic freeze, thaw and hold operations are processed through the Control Cabinet. Connected to the Temperature Control Unit and the Celsius® F-T module, the critical parameters of the different process steps are commanded, monitored and stored in an automatic manner with minimal operator intervention.

Celsius® FT100 System

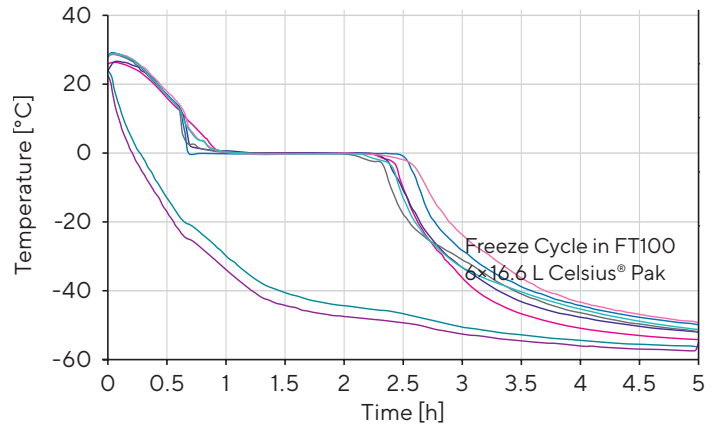
TCU

Control Cabinet

F-T Module



Inside to the freezing chamber of the Celsius® F-T module, the Celsius® Pak will be hold between two heat transfer plates for bi-directional and maximized heat transfer performances. Controlled-rate freezing and thawing will take place independently from different process conditions providing highly reproducible operation. Well defined, freezing and thawing processes in Celsius® CFT will be characterized at the most critical point inside to the Celsius® Pak, the last point to freeze.



Process Reproducibility and Reliability

- Celsius® CFT is the only fully integrated platform (Hardware & Bags) available on the market to transfer frozen DS worldwide coming from the same supplier
- Accountable platform from design to supply, performances and service
- More than 70 Production systems installed worldwide
- Excellent reproducibility from bag to bag, batch to batch and from unit to unit with strong process control for cGMP manufacturing
- Pre-qualified shippers (mechanical and thermal) with up to 100 L of BDS for International shipment

1 L and 2 L Celsius® Pak ▾

HMI panel touch screen ▾



Process Flexibility to Create Opportunity to Improve and Expand Manufacturing Networks

Improve the overall manufacturing process efficiency

Besides the benefits on product stability linked to long-term frozen storage & shipment, Celsius® CFT will actively participate in maximizing productivity and flexibility of the manufacturing process. Celsius® CFT will decrease overall

production costs by facilitating Drug Substance & Drug Product decoupling (one-way logistics possible) and by enabling batch processing.

Risk of microbial contamination is also mitigated as Celsius® CFT will make possible large scale freeze and thaw operation an aseptic process.

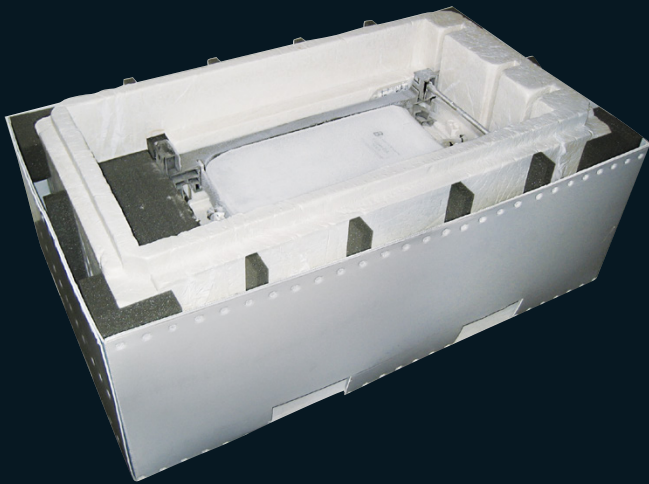


Celsius® SSM Shipper

The Celsius® SSM shipper is a reusable shipper and allows shipment of multiple frozen Celsius® Pak to remote location.

The SSM Shipper is qualified according to the ASTM D4169 Assurance Level 1 and the ISTA 7D extreme summer temperature profile.

[Celsius® SSM Shipper >](#)



Celsius® Single-Unit Shipper

The Celsius® Shipper is a single-use shipper and allows shipment of individual frozen Celsius® Pak to remote locations.

The shipper is qualified according to the ASTM D4169 Assurance Level 1 and extreme summer temperature profile.

[< Celsius® Single-Unit Shipper](#)

- Passed ASTM D4169 AL1 Shipping Test
- Passed ISTA7D Shipping Test
- Full Control of Process Logistics –
Optimized Accessories from Fill to Drain
- Safe and Robust Handling –
Qualified Shippers and Shipping Methods



Process Flexibility

- Extends Shelf- Life
- De-couple process steps, stockpile, and stop bioprocessing clock
- Improve production management and create opportunity

The fundamental purpose for Celsius® success:

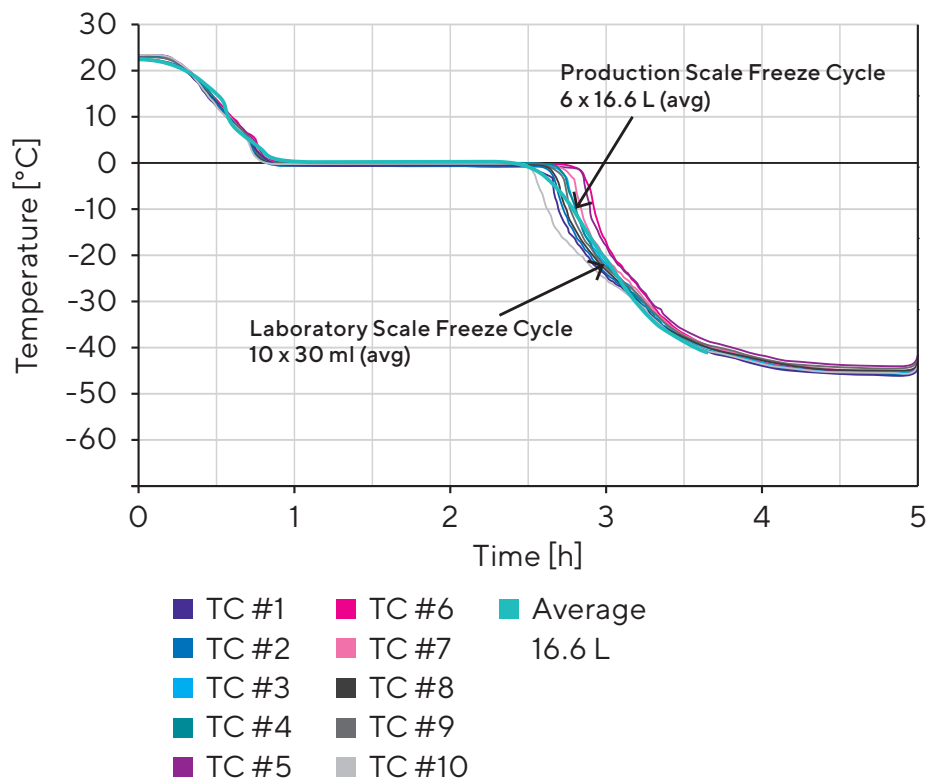
- Efficient Process
- Transfers using the same system with same performances worldwide
- Leverage prior developments with benchtop data and production scale-up

Scalability With 30 mL to Create a 100 L Process

Celsius® S³ Laboratory-Scale System, the Ideal Tool to Explore Production-Scale Freeze & Thaw Operations

When selecting scale-down freeze thaw model, different parameters such as the material of construction of the container and its interaction | compatibility with the Drug Substance or the storage temperature must be based on the most representative solution to be used at large process scale. Freeze & thaw rates are known to affect product stability and cannot be scalable if using uncontrolled-rate freeze & thaw system.

Celsius® CFT is the only single-use technology on the market which provides full scalability from laboratory to commercial production scale. Risk of microbial contamination is also mitigated as Celsius® CFT will make possible large scale freeze and thaw operation an aseptic process.



Scalability

- Benchtop System for quick, low-cost feasibility with 30 mL product to verify compatibility to Celsius® CFT F&T cycles
- Celsius® Pak Range from 1 L to 16.6 L
- F-T Module is Modular (FT33 for development, add modules for clinical | commercial mfg, up to 100 L per cycle)
- Same Film: scale-up from Celsius® FFT to CFT platforms




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Specifications subject to change without notice.

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Publication No.: SPT1511-e | Order No.: 85037-557-39 | Status: 03 | 29 | 2023