Celsius® Pre-Designed Solutions for Freeze & Thaw

Robust, Complete and Scalable Solutions for Frozen Storage and Shipment

Simplifying Progress

SARTORIUS

Celsius® pre-designed solutions

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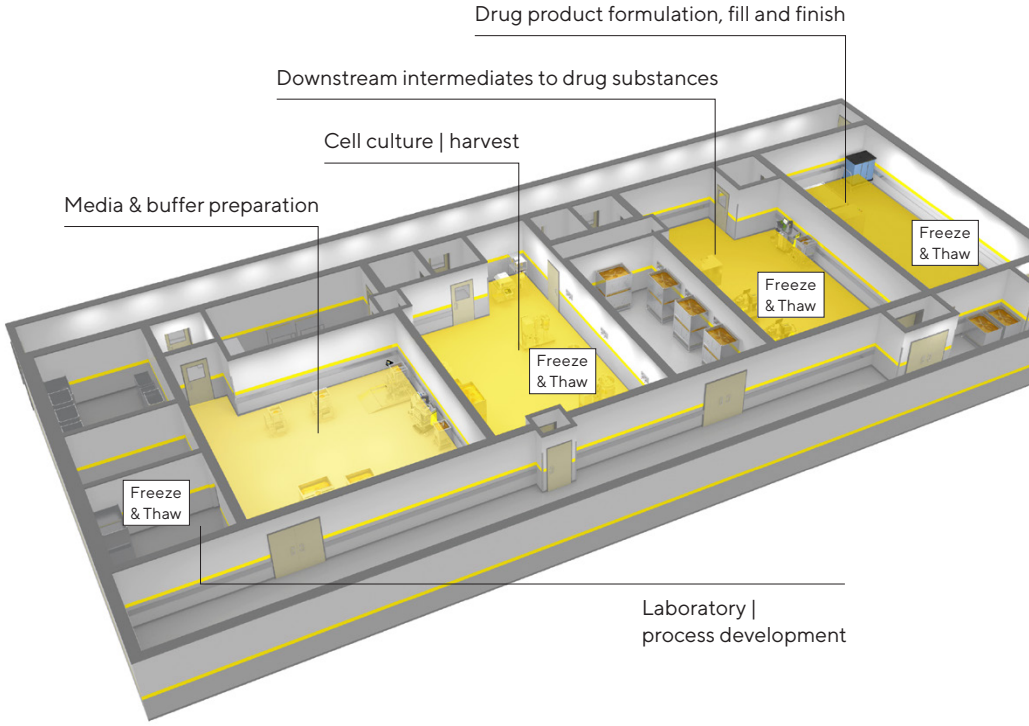
Celsius® pre-designed solutions

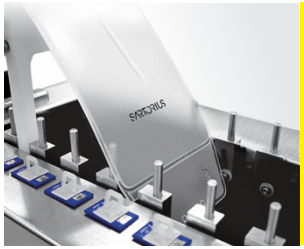
Unprecedented Performance and Assurance of Supply

Celsius® Freeze & thaw solutions for frozen storage and shipping applications
Building on more than 15 years experience in designing single-use freeze & thaw solutions, we have established lab-scale and production-scale Celsius® Pre-designed Solutions (PDS) for every process step when frozen storage and frozen shipment are required. Celsius® PDS are configured with the features needed to decouple downstream process steps and securely transport Drug Substances to Drug Product sites.

The performance and assurance of supply (AoS) of Celsius® PDS are based on the complete control of our manufacturing process for resins, film, bags, filters and the assemblies.

Other fluid-contact components are secured by strategic partnerships, long term contracts and quality agreements and are available off-the-shelf to provide best delivery reliability.





Lab-scale Freeze & Thaw

Pre-designed solutions for laboratory-scale validation studies, process development and sampling

When you select a Celsius® PDS, you get the assurance of consistent quality and robust change control. At least 24-month notification in case of a change on a critical fluid-contact component.

Cell Harvest & Downstream Intermediates

Pre-designed solutions for frozen storage of cell harvest and downstream intermediates to decouple DSP process steps

Drug Substance | Drug Product

Pre-designed solutions for frozen storage, transfer and shipment of drug substances to drug product sites

Celsius® pre-designed solutions

Material Science and Film Extrusion Expertise

The S71 EVA film is the foundation for the excellent performance of Celsius® PDS and is the result of combining material science and film extrusion expertise in collaboration with our resin suppliers and film partner. Such partnerships ensure a full understanding of the resins formulation and the film manufaturing process.

Following the principles of QbD, we have selected the raw materials to achieve superior assurance of supply and best performances.

We have established the resin specification, extrusion design space and process controls that provide consistent quality and reproducible characteristics of the S71 film.

The resins and additive package formulation is optimized to reduce the generation of extractables during film extrusion and gamma irradiation processes.

Welding and sealing parameters have been optimized and are routinely controlled to ensure bag making process consistency.

Characterized for use at low temperatures, the properties of the S71 film demonstrate its suitability for freezing applications when used in conjunction with the Celsius® products. Extensive testing of the Celsius® assemblies has shown that they can be safely used at frozen temperatures.

Heat-laminated EVA | EVOH | EVA structure

- 360 µm thickness for all Celsius® bags
- Outstanding robustness by combining strength and flexibility
- Large sealing window of welds for bag robustness
- Gas and water barrier structure

S71 film features & benefits

- Superior strength and flexibility: The film strength offers safety during handling and thawing while flexibility ensures integrity during frozen storage and shipment
- High gas and water barrier properties: Suitable for long term frozen storage of downstream intermediates and drug substances
- Low extractable profile: Ideal for drug substance and drug product process steps
- Excellent biocompatibility: Ideal for every process steps from cell harvest and downstream intermediates to drug substances and drug products

Resins + additives

Specifications & controls
- Optimized resin & additives
- Minimized antioxidant level
- Use of EP listed antioxidant for the contact layer

Film extrusion and welding

Design space, operating ranges & controls
- No slipping agents
- Mechanical anti-blocking (SiO_2)

Bag making

Performance testing in process qualification

Benefits
- Best film performance and quality attributes
- Proven robustness
- Superior Assurance of supply
- Consistent extractable profile

The lot to lot consistent performance of Celsius® bags is ensured by specification and controls of raw materials, the definition of the design space for the film extrusion and the control of the welding and overall bag making process.

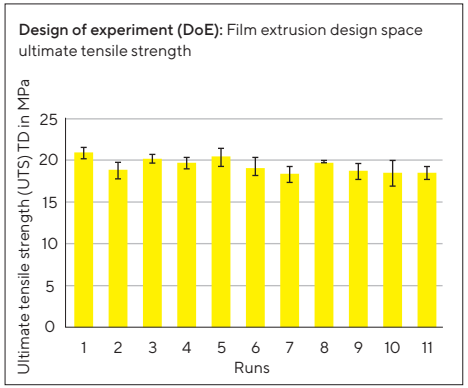
Backbone:
- Superior strength and flexibility
- High gas barrier properties

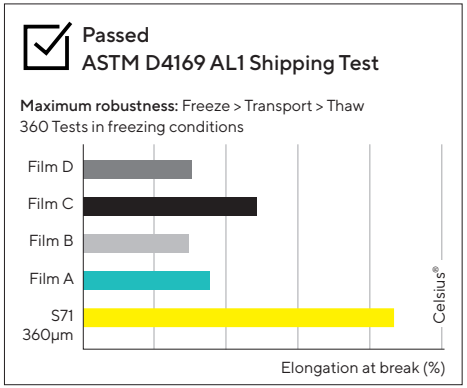
Contact layer:
- Superior strength and flexibility
- Weld strength
- Low extractable level
- Excellent biocompatibility

Celsius® pre-designed solutions

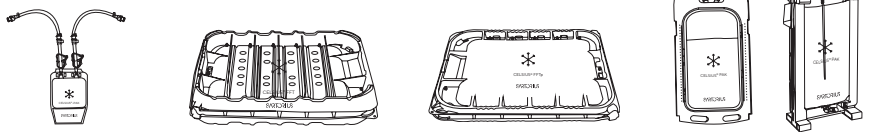
Control of the Entire Manufacturing Process

The complete control of our manufacturing process and our quality management for critical fluid-contact components ensure reliable and consistent performance of our Celsius® PDS.
The establishment of long term supply contracts and quality agreements for resins, film and fluid-contact components ensure unprecedented assurance of supply.





Same performances for all Celsius® PDS



30 mL –100 mL Celsius®-Pak | 2 L –12 L Celsius® FFT | 6 L –12 L Celsius® FFTp | 1 L –16.6 L Celsius®-Pak

Resin – S71
Resin specification & process control
- Resin & additives traceability
- Lot to lot raw material consistency

Long term contract
- 2-year last time buy option
- 2-year stocks of resin & film

Film – S71
Extrusion design space & control
- Reproducible robustness
- Lot to lot consistent extractable

10-year supply & quality contract
- 2-year last time buy option
- 2-year stocks of resin & film

- 4-year guaranty of unchanged film
- 2-year of unchanged critical fluid-contact components for our Pre-Designed-Solutions

Components
Long term supply contracts
- 2-year change notification

Quality agreements & controls
- Bioburden, particle & endotoxin
- Extractable characterization

Final SU assembly
Business continuity plan
- Back up equipment & safety stocks

Multiple manufacturing sites
- 7000m² of clean room in EU, US & Asia
- Resin-to-bag process control

Film performance and quality
The formulation of the resins and additives is completeley known to reduce material variability and the extrusion process parameters are controlled within the established design spaces to ensure lot to lot performance consistency.
Robustness is routinely controlled in production by mechanical testing providing the best quality, identical for all Celsius® bags.

Proven robustness
The strength and flexibility of Celsius® bags make them perfectly suitable for freezing and thawing operations. Supported by protective frame or integral shell, Celsius® PDS have been qualified in typical handling processing conditions and validated with the most stringent ASTM D4169 shipping test Assurance Level 1 (AL1) to offer maximum security for frozen storage and frozen transportation of drug substances.

Assurance of supply
Long-term supply contracts and quality agreements with suppliers and partners guarantee the traceability and control of the raw material and the film formulation. The control of the entire manufacturing process provides consistent quality, change control and business continuity.

Consistent extractable profile
Specification and control of the resins and the film eliminate lot to lot variability ensuring well characterized and consistent extractables. Extractable data is readily available for risk assessment, thus saving end-users the time and money required for generating validation data. The validation studies and toxicological assessments remain valid and reproducible from lot to lot.

Celsius® pre-designed solutions

Assurance of Supply for Fluid-Contact Components

Component quality and change control

Critical fluid-contact components used for Celsius® PDS are secured by long term contracts and quality agreements to offer the best assurance of supply.

Our supply contracts and quality agreements ensure at least a 24-month change notification on critical fluid-contact components thus providing robust change control and business continuity.

Critical fluid-contact components are also available off-the-shelf to offer the best delivery reliability.

Material qualification

Celsius® PDS components are evaluated for conformity against the EP and USP standards after reviewing technical documentation and certificates of quality available from our suppliers. Additional internal qualification tests are performed to establish extractable profiles, post gamma sterilization shelf life and consistent functional properties.

Criteria for component selection	Reference
Biological safety (USP Class VI)	USP<87> & USP<88>
TSE-BSE questionnaire	Compliance with EMA/410/01 and E.P 5.2.8
Endotoxin	USP<85> or EP 2.6.14
Bioburden	ISO 11737
Sub-visible particulates	USP<788> or EP 2.9.19
Visible particulates	Internal reference
Others	Bisphenol A free, REACH compliance

Our core expertise in plastics and polymers enables the selection of the cleanest and most inert materials to minimize chemical interactions with biopharmaceutical fluids and leacheable substances.

Design qualification

Component designs are selected to maximize tubing engagement tensile strength and tightness. All engagements with tubings on Celsius® PDS are qualified for a 3-year shelf-life (after exposure to freezing and thawing conditions). Test samples are visually inspected for absence of defect and tested for leak, burst pressure, traction and compression.

Using a Celsius® Pre-designed solution in your drug manufacturing processes provide you with best performance and assurance of supply.

Celsius® PDS

Components	Biocompatibility USP <87> or USP<88> Class VI	Endotoxin sub-visible particulates	TSE-BSE EMA/410/01 & REACH	Notification period time
Celsius® bags	Yes	Yes	Yes	48 months
Tubings	Yes	Yes	Yes	24 months
Opta® sterile connectors	Yes	Yes	Yes	24 months
Midisart® BV filters	Yes	Yes	Yes	24 months
Fittings	Yes	Yes	Yes	24 months
Connectors	Yes	Yes	Yes	24 months

Celsius® pre-designed solutions

Validation and Quality Assurance

Celsius® PDS are qualified against extensive biological, chemical, physical, extractable and functional testing to provide reliable validation data applicable to a wide range of process conditions. Sartorius Stedim Biotech Quality Systems for single-use products follow applicable ISO 9001 and ISO 13485 for Medical Devices. Design, manufacture, quality control and sterilization of Celsius® PDS are conducted under conditions that mirror biopharmaceutical operations and meet cGMP like requirements to ensure they are supplied clean, pure, non-pyrogenic fluid path and sterile.

Celsius® PDS are validated for a 3-year shelf-life post gamma-sterilization and routinely controlled to provide consistent performance.

Robustness
- ASTM D882 and ISO527, ASTM D1004, F392 and ISO7765 for tensile properties, tear resistance and flex durability
- Qualification of the bag manufacturing process capabilities following recommendations from standards (ASTM F-2097, ISO15747) and other publications (PDA, FDA-CBER)
- Internal standardized methods for connection tests and functional qualification in real process conditions
- ASTM D4169 (AL1): Standard Practice for Performance Testing of Shipping Containers and Systems
- 100% bag chamber leak test by pressure decay (ASTM D2095)

Gas transmission (S71 film)
- ASTM D3985, ISO 15106-3, ASTM F2476: Oxygen, Water Vapor and Carbon Dioxide Transmission Rate

Thermal Properties (S71 film)
- ISO 8570: Cold Crack temperature
- ASTM D3418 and ISO11357-2, ISO 6721-1 and ISO 11359-2: Tg

Biocompatibility & chemical compatibility (fluid-contact components)
- USP<87> and ISO 10993-5: Biological reactivity tests, in Vitro
- USP<88>: Biological reactivity tests, in Vivo
- USP<661> and EP 3.1.7: Containers, physico-chemical tests – Plastics
- ASTM D543-06: resistance of plastic to chemical reagents

Purity, extractable & leachable
- Extractable data based on knowledge and control of resins and film manufacturing process

Cleanliness, particulates & sterilization
- TSE/BSE: EMA/410/01 and EP 5.2.8
- USP<788> and EP 2.9.19: Particulate Matter in Injections
- USP<71> and E.P 2.6.1 : Sterility test
- Visible particles: Representative product has been analyzed for particles with sizes > 100 µm according to internally developed and validated method. Results are monitored.
- USP<85> and E.P. 2.6.14: Bacterial endotoxins sterility
- Other tests listed in section "Sterile Water for Injection" of USP and EP
- ISO 11737: Sterilization of medical devices – Microbiological methods: Bioburden
- ISO 11137: Sterilization by irradiation of Medical Devices: Sterilization of Medical Devices
- ISO 14644: Cleanroom environmental controls
- Gamma radiation dose mapping

Celsius® PDS are released on the basis of a weekly quality control for bioburden, sub-visible particulates and endotoxin performed on representative finished products.

In addition, categorized as Drug Product, Celsius®-Paks (excluding 30 mL and 100 mL sizes) and Celsius® FFTp are released via Lot Release Testing.

Media, buffer, harvest & downstream intermediates | Drug substance	Drug product
Weekly testing of bioburden, sub-visible particulates and endotoxin on representative finished product	Lot release testing of bioburden, sub-visible particulates and endotoxin on representative finished product

For the most critical drug product process step bioburden, sub-visible particulates and endotoxin testing is performed on representative finished products for every production batch.

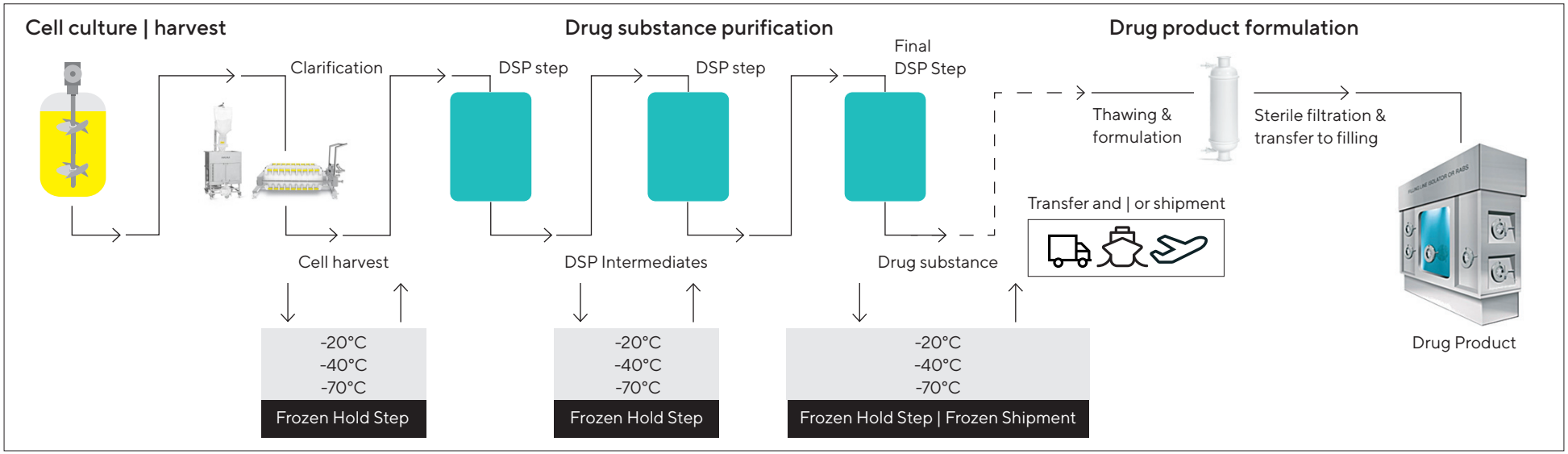
Certificate of release

Statement	Monitoring[1]	100% Batch testing		Particles prevention program
USP Class VI USP<87> and ISO 10993-5: Biological reactivity tests, in Vitro USP<88>: Biological reactivity tests, in Vivo **Physico-chemical testing** USP<661> and EP 3.1.7 **TSE-BSE Status** EMA/410/01 and E.P 5.2.8	**Bioburden** ISO 11737 **Endotoxin** USP<85> and E.P. 2.6.14 **Sub-visible Particulates** USP<788> and EP 2.9.19 **Sterility** ISO 11137	**Bioburden**[2] ISO 11737 **Endotoxin**[2] USP<85> and E.P. 2.6.14 **Sub-visible Particulates**[2] USP<788> and EP 2.9.19	**Gamma radiation** Dose irradiation **Visual inspection** Film, bag, seal and packaging **Technical drawing conformity** Batch record review **100% Leak testing** Bag chamber & immediate connections	**Visible particles monitoring**

[1] performed weekly on representative finished products (all Celsius® PDS)
[2] performed on each batch on representative finished products (Celsius®-Paks excluding 30 mL and 100 mL sizes, and Celsius® FFTp only)

Celsius® pre-designed solutions

Freezing Operations in Biomanufacturing



Why establish freezing operations?

- To maintain product quality and improve its stability over long period of time
- To reduce microbial growth risk
- To minimize protein interactions with the container closure system and eliminate stresses during shipment
- To provide longer shelf-life
- To maximize productivity and flexibility by allowing process step decoupling, stockpiling or by enabling batch processing (real-time commercial campaign or clinical demands)

Frozen storage and shipment in biomanufacturing

Freezing and thawing operations are commonly used along the entire downstream purification process steps of biomolecules up to the transition towards the drug product manufacturing for which shipping in frozen state may be required.

Celsius® PDS have been designed to be used in all biomanufacturing process steps. Indeed, the versatile range and the functionalities offered by the different Celsius® PDS configuration allow the transfer of all biopharmaceutical fluids from and to most common single-use or stainless steel containers.

Drug substance transfer to drug product sites worldwide

Due to increasingly complex networks in the industry, the drug substance is generally manufactured at a different location from the drug product site. High value Bulk Drug Substance has to be stored and shipped worldwide to remote location.

To maintain the product quality and stability, this critical operation requires frozen storage in robust containers and a complete logistic solution for an easy, reliable and safe transfer. This represents the majority of the application served today by the Celsius® products.

Celsius® PDS are designed for safe and easy storage and shipment of high value biopharmaceutical products across campus, production sites or world-wide manufacturing networks.

Celsius® pre-designed solutions

Robust, Complete and Scalable Solutions

Robustness qualified down to –70°C

- A single-use freeze & thaw platform dedicated to maximize product security throughout its life cycle
- Proven S71 single-use bag protected by structural containers and complete logistics for proven freeze & thaw performances through extensive low-temperature functional qualification
- Maximum Robustness for worldwide frozen shipment of high value drug substances validated according to ASTM D4169 Assurance Level 1 (AL1)

360 tests in real process conditions

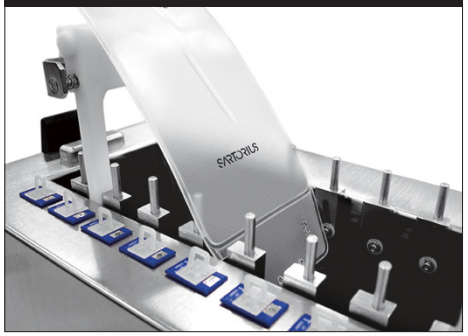
Connection tests
Liquid robustness
Extreme F&T conditions
Pass

Functional tests
Freeze & thaw cycles
Shipping: simulated + real
Frozen robustness
Rotate | lift | drop
Pass

Meet your frozen Storage and transfer needs

From process development to clinical and commercial production, Celsius® PDS offers a common S71 film and a complete range of single-use containers for process matching and scalability. Process Development tools offer easy feasibility studies.

Lab-scale Celsius®-Pak



For Celsius® S³ Benchtop System (30 mL – 100 mL)

Celsius® FFT

For Conventional Freezer (2 L – 12 L)

Celsius® FFTp

For Horizontal Plate Freezer (6 L – 12 L)

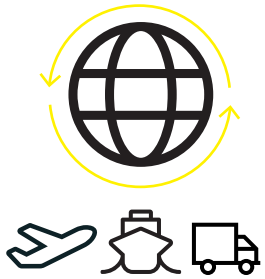
Celsius®-Pak

For Celsius® FT33 | 66 | 100 (1 L – 100 L)

Complete solution for safe and robust frozen transfer in increasingly complex networks

Complete frozen storage and logistics solutions from one supplier to transfer world-wide Drug Substances to Drug Product Sites.

- Passed ASTM D4169 AL1 Shipping Test
- Passed ISTA7D Shipping Test
- Freeze & Thaw



Full control of process logistics –
Optimized accessories from fill to drain

Safe and robust handling –
Qualified shippers and shipping methods

Celsius® PDS features & benefits

- Full control of manufacturing processes ensure best assurance of supply
- Long term contract and stocks of raw materials, films and components ensure best assurance of supply and delivery reliability
- Process controls ensure performances and quality for superior robustness and consistent extractable profile
- Versatile range of configurations to implement freezing in all process steps
- Maximum robustness for safe frozen storage of high value biopharmaceutical products with complete solutions
- Scalable platforms to meet any frozen storage and transfer needs
- Ready to use extractable data save time and money by avoiding specific leachable studies for drug substance

Celsius® pre-designed solutions

Select Your Celsius® Platform for Your Process Requirements

Lab-scale Celsius®-Pak

30 mL – 100 mL
Lab-scale
Celsius®-Paks

Celsius® S³
Benchtop system

Lab-scale Celsius®-Paks are sterile, singleuse containers intended for use in the Celsius® S³ Benchtop System, a scalability tool for process development studies.

These bags are commonly used for stability, compatibility and other developmental tests, or for small aliquots (e.g., ID samples). Two sizes of lab-scale Celsius®-Pak are available, 30 mL and 100 mL nominal volume.

Celsius® FFT

2 L – 12 L
Celsius® FFT

Frozen Celsius® FFT
in lab freezer

Celsius® FFT are sterile, single-use containers for freezing and thawing biopharmaceutical solutions in commercially available equipment such as laboratory (walk-in) freezer, cold room, temperature controlled cabinet or water bath.

Celsius® FFT combines a unique design of a flexible bag with an integral protective shell. The robustness of this single-use assembly ensures protection, support and ease of handling.

Pre-qualified shippers for world-wide shipment of Celsius® FFT is also offered as part of the complete logistics solution. Four sizes of Celsius® FFT are available, 2 L, 4 L, 6 L, and 12 L nominal volume.

Celsius® FFTp

6 L – 12 L
Celsius® FFTp

Frozen Celsius® FFTp
in horizontal plate
freezer

Celsius® FFTp are sterile, single-use containers for use in horizontal plate freezers (not provided by Sartorius Stedim Biotech).

It also combines a flexible single-use bag with an integral protective shell design but more compact and more flat compared to Celsius® FFT for uniform, fast and reproducible freeze & thaw processes in horizontal plate freezers. Two sizes of Celsius® FFTp are available, 6 L and 12 L nominal volume.

Celsius®-Pak

1L – 16.6 L
Celsius®-Paks

Celsius®
FT33 | 66 | 100

Production-scale Celsius®-Paks are sterile, single-use containers specifically designed to be used in the Celsius® FT33 | 66 | 100 equipment offered by Sartorius Stedim Biotech for uniform, fast and reproducible freeze & thaw processes.
The combination of a structural protective frame with a sterile container provide protection to the contents during all processes, making the assembly robust and reliable during handling.

A complete logistics solution from filling to transfer, storage and shipping is offered through a series of accessories to easily manage large volume batches of frozen biopharmaceutical solutions. Four sizes of Celsius®-Pak are available, 1 L, 2 L, 8.3 L and 16.6 L nominal volume.

Celsius® pre-designed solutions for

Lab-scale Freeze & Thaw

Lab-scale freeze & thaw

- Sanitary or aseptic connection for filling
  - Luer connection with Thermowell
  - Quick coupler connection without Thermowell

Freeze & thaw kinetics studies
Stability studies
Sampling

- Sanitary or aseptic connection for draining
  - Luer connection with Thermowell
  - Quick coupler connection without Thermowell

Lab-scale Celsius®-Pak are 30 mL and 100 mL single-use bags designed to support the implementation of freezing and thawing operations at production-scale with the Celsius® technology.

These bags are made with the same product contact layer as the production-scale Celsius® bags (360 µm S71 film) and will support all validation activities linked to freezing and thawing:

- Process development activities
- Freeze & thaw kinetic studies to establish the best process conditions at production-scale
- Formulation studies and optimization
- Sampling for QC test analysis
- Stability Studies
- Explore future use of the Celsius® FT33 | 66 | 100 with the Celsius® S³ Benchtop system and its pre-defined freeze & thaw recipes matching performances at 100 L production-scale

Lab-scale Celsius®-Pak PDS are configured with all the needed features to conduct properly your studies:

- with thermowell for non-invasive temperature measurement during freeze & thaw kinetics studies or for stability studies to mimic 8.3 L and 16.6 L Celsius®-Pak
- without thermowell for stability studies to mimic production-scale Celsius® bags not equipped with thermowell (Celsius® FFT | FFTp, 1 L and 2 L Celsius®-Pak)
- MPC quick couplers are used for either sanitary connection or aseptic connection under ISO5 laminar air flow to single-use systems
- Luer connectors are used for either sanitary connection or aseptic connection under ISO5 laminar air flow to single-use systems

Inlet and outlet lines are made with EVA, Clear C-Flex® or Dow Corning® Pharma-50 silicone tubes to reproduce the different production-scale Celsius® bags transfer lines. EVA tube is directly sealed to the bag chamber at both inlet or outlet and allows for sterile seal disconnection with radio frequence sealer device after filling and draining. Sterile seal disconnection with BioSealer® after filling and draining is also allowed for lab-scale Celsius®-Pak PDS equipped with Clear C-Flex®.

Option with or without Thermowell
- Sealed-end EVA tube (3/16" ID) for non-invasive temperature measurement during freezing and thawing operations
- Luer connector female

Filling and draining lines
- EVA tube
- Clear C-Flex® tube
- Dow Corning® Pharma-50 Silicone tube

Inlet Sanitary or aseptic connections
- MPC quick coupler male
- Luer connector female

Outlet sanitary or aseptic connections
- MPC quick coupler male
- Luer connector female

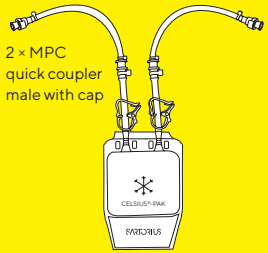
Celsius® pre-designed solutions for

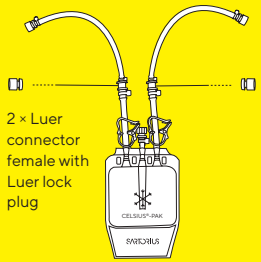
Lab-scale Freeze & Thaw to Match Large-scale Conditions

Lab-scale freeze & thaw

Sanitary or aseptic connection for filling

- Luer connection with Thermowell
- Quick coupler connection without Thermowell





Thermowell for non-invasive temperature measurement

Sanitary or aseptic connection for draining

- Luer connection with Thermowell
- Quick coupler connection without Thermowell

Select your pre-designed solutions for the required lab-scale freeze and thaw activities

Lab-scale activities	Recommended lab-scale Celsius®-Pak PDS			Related production-scale Celsius® PDS
	Inlet & outlet connector	Thermowell	Inlet & outlet tubing	
Freeze & Thaw Kinetics Studies	Luer connector	Yes	EVA	All Celsius®-Pak
Stability Studies and Sampling	Luer connector	Yes	EVA	8.3 L & 16.6 L Celsius®-Pak
	Luer connector	Yes	EVA + Dow Corning® Pharma-50 Silicone	8.3 L & 16.6 L Celsius®-Pak equipped with Dow Corning® Pharma-50 Silicon
	Luer connector	Yes	EVA + Clear C-Flex®	8.3 L & 16.6 L Celsius®-Pak equipped with Clear C-Flex®
	Quick coupler connector	No	EVA + Dow Corning® Pharma-50 Silicone	– 1 L & 2 L Celsius®-Pak equipped with Dow Corning® Pharma-50 Silicon – Celsius® FFTp
	Quick coupler connector	No	EVA + Clear C-Flex®	– 1 L & 2 L Celsius®-Pak equipped with Clear C-Flex® – Celsius® FFT – Celsius® FFTp

Overpouch for lab-scale Celsius®-Pak

The overpouch for lab-scale Celsius®-Paks provides a highly restrictive gas barrier that eliminates oxygen and water vapor transmission. This accessory is primarily used for stability tests with a lab-scale Celsius®-Pak to overcome effects of high surface area to volume ratio.

Part number	Description	Units per box
FDP102653	Overpouch for 30 mL Celsius®-Pak	250
FDP102667	Overpouch for 100 mL Celsius®-Pak	100

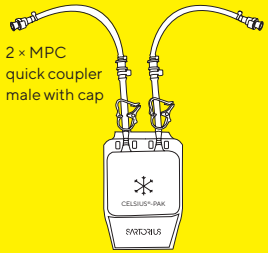
Celsius® pre-designed solutions for

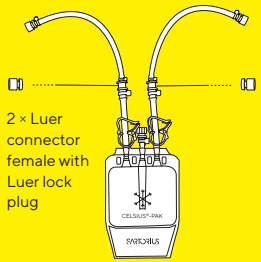
Lab-scale Freeze & Thaw in 30 mL and 100 mL Celsius®-Paks

Lab-scale freeze & thaw

Sanitary or aseptic connection for filling

- Luer connection with Thermowell
- Quick coupler connection without Thermowell





Thermowell for non-invasive temperature measurement

Sanitary or aseptic connection for draining

- Luer connection with Thermowell
- Quick coupler connection without Thermowell

Lab-scale Celsius®-Paks with luer connector and Thermowell

			Inlet	Outlet	Tubing
Bag volume	Part number	Units per box	Distal connector	Distal connector	Inlet & outlet
30 mL	FZB114804	10	¼" Luer Female + luer lock plug	¼" Luer Female + luer lock plug	EVA[1]
	FZB129264	10	¼" Luer Female + luer lock plug	¼" Luer Female + luer lock plug	EVA + Dow Corning® Pharma-50 Silicone[2]
	FZB114866	10	⅛" Luer Female + luer lock plug	⅛" Luer Female + luer lock plug	EVA + Clear C-Flex®[3]
100 mL	FZB114839	10	¼" Luer Female + luer lock plug	¼" Luer Female + luer lock plug	EVA[1]
	FZB129261	10	¼" Luer Female + luer lock plug	¼" Luer Female + luer lock plug	EVA + Dow Corning® Pharma-50 Silicone[2]
	FZB114908	10	⅛" Luer Female + luer lock plug	⅛" Luer Female + luer lock plug	EVA + Clear C-Flex®[3]

Lab-scale Celsius®-Paks with quick coupler and without Thermowell

			Inlet	Outlet	Tubing
Bag volume	Part number	Units per box	Distal connector	Distal connector	Inlet & outlet
30 mL	FZB129265	10	MPC Male + sealing cap	MPC Male + sealing cap	EVA + Dow Corning® Pharma-50 Silicone[2]
	FZB129266	10	MPC Male + sealing cap	MPC Male + sealing cap	EVA + Clear C-Flex®[4]
100 mL	FZB129262	10	MPC Male + sealing cap	MPC Male + sealing cap	EVA + Dow Corning® Pharma-50 Silicone[2]
	FZB129263	10	MPC Male + sealing cap	MPC Male + sealing cap	EVA + Clear C-Flex®[4]

[1] Tubing from bag to end line: ¼"ID 5/16" OD EVA 0.1 m (4")
[2] Tubing from bag to end line: ¼"ID 5/16" OD EVA 0.1 m (4")+ ¼"ID 3/8"OD Dow Corning® Pharma-50 Silicone 0.15 m (6")
[3] Tubing from bag to end line: ¼"ID 5/16" OD EVA 0.1 m (4")+ ⅛"ID ¼"OD Clear C-Flex® 0.15 m (6")
[4] Tubing from bag to end line: ¼"ID 5/16" OD EVA 0.1 m (4")+ ¼"ID 3/8"OD Clear C-Flex® 0.15 m (6")

Celsius® pre-designed solutions for

Frozen Storage & Shipment in Celsius® FFT and Celsius® FFTp

Celsius® FFT

Celsius® FFT advanced solutions for flexible freezing and thawing feature a variety of connections which allows the transfer of biopharmaceutical fluids across the entire drug manufacturing process:

- Opta® SFT enables sterile connections to single-use systems
- MPC quick couplers are used for either sanitary connection or aseptic connection under ISO5 laminar air flow to single-use systems
- Clear C-Flex® tubing enables sterile weld with BioWelder® TC and sterile seal with Biosealer®

Celsius® FFT are equipped with three transfer lines, for inlet, outlet and sampling, all made with Clear C-Flex® for welding and sealing. The sampling line feature a luer connector for either sanitary connection or aseptic connection under ISO5 laminar air flow. EVA tube is directly sealed to the Celsius® FFT bag chamber for both transfer lines.

Inlet sterile connections
- Opta® SFT male
- Clear C-Flex® tube for sterile weld with BioWelder® TC

Inlet sanitary or aseptic connections
- MPC quick coupler male

Sampling
- Luer connector female
- Clear C-Flex® tube for sterile weld with BioWelder® TC

Filling and draining lines
- Clear C-Flex® tube

Celsius® FFT

Outlet sanitary or aseptic connections
- MPC quick coupler male

Outlet sterile connections
- Opta® SFT male
- Clear C-Flex® tube for sterile weld with BioWelder® TC

Celsius® FFTp

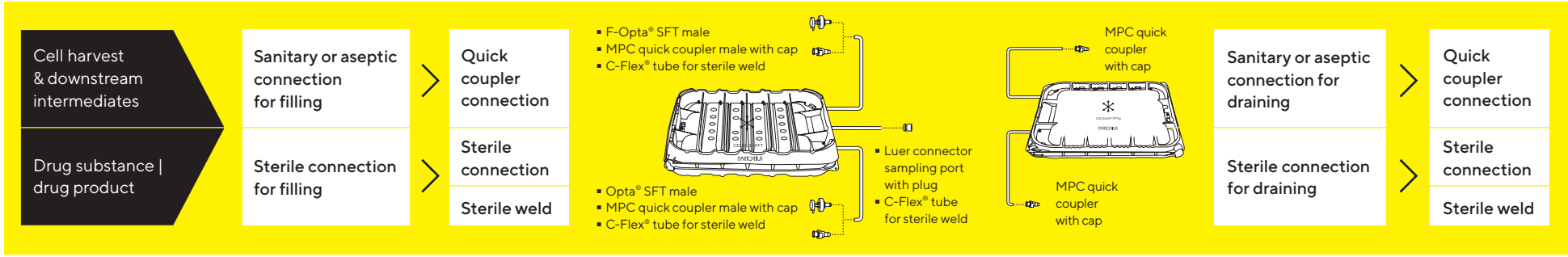
Celsius® FFTp are equipped with two transfer lines for inlet and outlet (no sampling line). Both inlet and outlet connectors are MPC quick coupler for sanitary connection or aseptic connection under ISO5 laminar air flow.

Inlet and outlet lines are made entirely with EVA tube which allows for sterile seal disconnection with radio frequence sealer device after filling and draining.

Celsius® FFTp

Celsius® pre-designed solutions for

Frozen Storage & Shipment in Celsius® FFT and Celsius® FFTp



Celsius® FFT pre-designed solutions

			Inlet[1]	Outlet[1]	Sampling[2]
Bag volume	Part number	Units per box	Distal connector	Distal connector	Distal connector
2 L	FZB114906 FZB129267	6 6	MPC Male + sealing cap ⅜" Opta® SFT Male	MPC Male + sealing cap ⅜" Opta® SFT Male	⅛" Luer Female + luer lock plug ⅛" Luer Female + luer lock plug
4 L	FZB212401	6	MPC Male + sealing cap	MPC Male + sealing cap	⅛" Luer Female + luer lock plug
6 L	FZB212241	6	MPC Male + sealing cap	MPC Male + sealing cap	⅛" Luer Female + luer lock plug
12 L	FZB212435 FZB129268	3 3	MPC Male + sealing cap ⅜" Opta® SFT Male	MPC Male + sealing cap ⅜" Opta® SFT Male	⅛" Luer Female + luer lock plug ⅛" Luer Female + luer lock plug

Celsius® FFTp pre-designed solutions

			Inlet[3]	Outlet[3]	Sampling
Bag volume	Part number	Units per box	Distal connector	Distal connector	Distal connector
6 L	FZB114079	6	MPC Male + sealing cap	MPC Male + sealing cap	NA
12 L	FZB115784	2	MPC Male + sealing cap	MPC Female + sealing cap	NA

[1] Tubing from bag to end line:
⅜"ID ⅝"OD Clear C-Flex®
– 0.38 m (15") for 2L Celsius® FFT
– 0.5 m (20") for 4L Celsius® FFT
– 0.75 m (30") for 6L and 12L Celsius® FFT

[2] Sampling line tubing:
⅛"ID ¼"OD Clear C-Flex®
– 0.5 m (20") for 2L, 4L and 12L Celsius® FFT
– 0.75 m (30") for 6L Celsius® FFT

[3] Tubing from bag to end line:
⅜"ID 15⁄32"OD EVA tubing
– 0.15 m (6") for 6L Celsius® FFTp
– 0.3 m (12") for 12L Celsius® FFTp

Celsius® pre-designed solutions for

Frozen Storage & Shipment in Celsius®-Paks

Celsius®-Pak advanced solutions for controlled-rate freezing and thawing feature a variety of connections which allows the transfer of biopharmaceutical fluids across the entire drug manufacturing process:

- Opta® SFT enables sterile connections to single-use systems
- MPC quick couplers are used for either sanitary connection or aseptic connection under ISO5 laminar air flow to single-use systems
- Clear C-Flex® tubing enables sterile weld with BioWelder® TC and sterile seal with Biosealer®

After filling, the venting line, on top of the bag, is used to pressurize the Celsius®-Pak with air or nitrogen to guarantee performances of the controlled-rate freeze & thaw process:

- Midisart® BV Air Filter for sterile venting
- CPC quick couplers for non-aseptic venting with sanitary connection

Inlet and outlet lines are made with C-Flex® or Dow Corning® Pharma-50 silicone for welding, sealing and pumping. EVA tube is directly sealed to the Celsius®-Pak bag chamber at both inlet or outlet and allows for sterile seal disconnection with radio frequence sealer device after filling only.

1 L and 2 L Celsius®-Paks

1 L & 2 L Celsius®-Pak PDS are also equipped with three transfer lines for inlet, venting and outlet. They differ from the 8.3L and 16.6L Celsius®-Pak configuration as they are not equipped with Thermowell.

Sanitary or sterile venting
- MPC quick coupler male
- Midisart® BV Air Filter

Thermowell
- Sealed-end EVA tube (3⁄16" ID) for non-invasive temperature measurement during freezing and thawing operations
- Luer connector female

Inlet sterile connections
- Opta® SFT female
- C-Flex® tube for sterileweld with BioWelder® TCIe

Filling and draining lines
- Clear C-Flex® tube
- Dow Corning® Pharma-50
- Silicone tube

Inlet sanitary or aseptic connections
- MPC quick coupler male

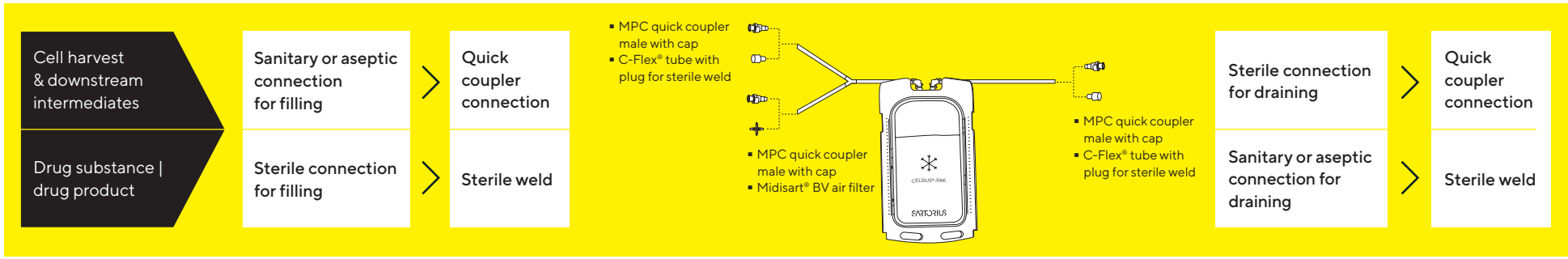
8.3 L and 16.6 L Celsius®-Pak

Outlet sterile connections
- Opta® SFT male
- C-Flex® tube for sterile weld with BioWelder® TC

Outlet sanitary or aseptic connections
- MPC quick coupler male

Celsius® pre-designed solutions for

Frozen Storage & Shipment in 1 L and 2 L Celsius®-Paks



1 L & 2 L Celsius®-Pak pre-designed solutions

			Inlet[1]	Outlet[2]	Venting line[3]
Bag volume	Part number	Units per box	Distal connector	Distal connector	Distal connector
1 L	FZB129260	8	MPC Male + sealing cap	MPC Male + sealing cap	MPC Male + sealing cap
	FZB115319	8	MPC Male + sealing cap	MPC Male + sealing cap	Midisart® BV
	FZB115358	8	¼" Press in plug	¼" Press in plug	Midisart® BV
2 L	FZB129259	4	MPC Male + sealing cap	MPC Male + sealing cap	MPC Male + sealing cap
	FZB115322	4	MPC Male + sealing cap	MPC Male + sealing cap	Midisart® BV
	FZB115366	4	¼" Press in plug	¼" Press in plug	Midisart® BV

[1] Tubing from bag to end line:
- ¼"ID ⅜"OD Dow Corning® Pharma-50 Silicone 0.3 m (12") for PDS equipped with MPC quick coupler
- ¼"ID ⅜"OD Clear C-Flex® 0.5 m (20") for PDS equipped with Press in plug

[2] Tubing from bag to end line:
- ¼"ID ⅜"OD Dow Corning® Pharma-50 Silicone 0.3 m (12") for 1 L Celsius®-Pak and 0.45 m (18") for 2 L Celsius®-Pak equipped with MPC quick coupler
- ¼"ID ⅜"OD Clear C-Flex® 0.36 m (14") for 1 L Celsius®-Pak and 0.5 m (20") for 2 L Celsius®-Pak equipped with Press in plug

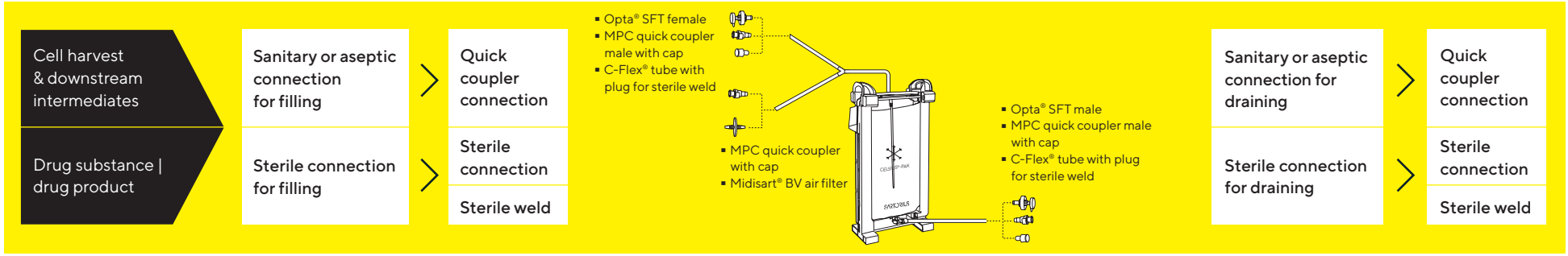
[3] Venting line tubing:
¼"ID ⅜"OD Dow Corning® Pharma-50 Silicone
- 0.1 m (4") for PDS equipped with MPC quick coupler
- 0.15 m (6") for PDS equipped with Press in plug

Addressing drug substance and drug product sites different practices for connections

Should the drug substance and drug product sites may have different practices and technologies to connect and disconnect Celsius®-Pak (eg. Opta® SFT male at the DS site and BioWelder® TC at the DP site) or different process requirements, 8.3 L and 16.6 L Celsius®-Pak PDS offer the possibility to combine all the different connection | disconnection types at both inlet and outlet in the same design (please see details on the next page).

Celsius® pre-designed solutions for

Frozen Storage & Shipment in 8.3 L and 16.6 L Celsius®-Paks



8.3 L Celsius®-Pak pre-designed solutions

			Inlet[1]	Outlet[2]	Venting line[3]
Bag volume	Part number	Units per box	Distal connector	Distal connector	Distal connector
8.3 L	FZB103152	12	MPC Male + sealing cap	MPC Male + sealing cap	MPC Male + sealing cap
	FZB115334	12	MPC Male + sealing cap	MPC Male + sealing cap	Midisart® BV
	FZB129252	12		⅜" Opta® SFT Male	
	FZB129253	12		⅜" Press in plug	
	FZB129254	12	⅜" Opta® SFT Female	MPC Male + sealing cap	Midisart® BV
	FZB115370	12		⅜" Opta® SFT Male	
	FZB129255	12		⅜" Press in plug	
	FZB129256	12	⅜" Press in plug	MPC Male + sealing cap	Midisart® BV
	FZB129257	12		⅜" Opta® SFT Male	
	FZB129258	12		⅜" Press in plug	

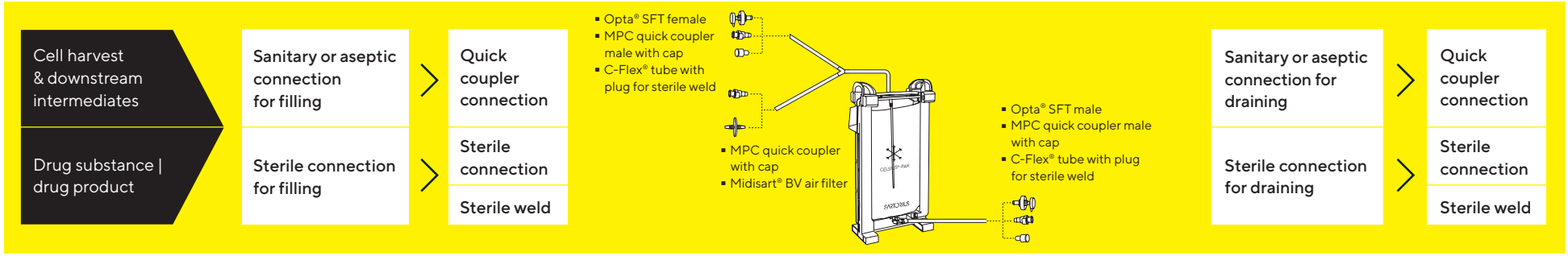
[1] Tubing from bag to end line:
⅜"ID ⅝"OD Dow Corning® Pharma-50 Silicone
– 0.9 m (36") for PDS equipped with Opta®
– 1 m (40") for PDS equipped with MPC quick coupler, 1.05 m (42") for those with Midisart® BV on the venting line
⅜"ID ⅝"OD Clear C-Flex® 1.25 m (50") for PDS equipped with Press in plug

[2] Tubing from bag to end line:
⅜"ID ⅝"OD Dow Corning® Pharma-50 Silicone
– 1.82 m (72") for 8.3L Celsius®-Pak and 2.05 m (80") for 16.6L Celsius®-Pak equipped with Opta®
– 1.5 m (60") for 8.3L Celsius®-Pak and 2 m (79") for 16.6L Celsius®-Pak equipped with MPC quick coupler
⅜"ID ⅝"OD Clear C-Flex® 1.5 m (60") for 8.3L Celsius®-Pak and 2 m (79") for 16.6L Celsius®- Pak equipped with Press in plug

[3] Venting line tubing:
⅜"ID ⅝"OD Dow Corning® Pharma-50 Silicone
– 0.1 m (4") for PDS equipped with MPC quick coupler on the venting line
– 0.15 m (6") for PDS equipped with Midisart® BV on the venting line

Celsius® pre-designed solutions for

Frozen Storage & Shipment in 8.3 L and 16.6 L Celsius®-Paks



16.6 L Celsius®-Pak pre-designed solutions

			Inlet[1]	Outlet[2]	Venting line[3]
Bag volume	Part number	Units per box	Distal connector	Distal connector	Distal connector
16.6 L	FZB114861	6	MPC Male + sealing cap	MPC Male + sealing cap	MPC Male + sealing cap
	FZB115377	6	MPC Male + sealing cap	MPC Male + sealing cap	Midisart® BV
	FZB129245	6		⅜" Opta® SFT Male	
	FZB129246	6		⅜" Press in plug	
	FZB129247	6	⅜" Opta® SFT Female	MPC Male + sealing cap	Midisart® BV
	FZB115289	6		⅜" Opta® SFT Male	
	FZB129248	6		⅜" Press in plug	
	FZB129249	6	⅜" Press in plug	MPC Male + sealing cap	Midisart® BV
	FZB129250	6		⅜" Opta® SFT Male	
	FZB129251	6		⅜" Press in plug	

[1] Tubing from bag to end line:
⅜"ID ⅝"OD Dow Corning® Pharma-50 Silicone
– 0.9 m (36") for PDS equipped with Opta®
– 1 m (40") for PDS equipped with MPC quick coupler, 1.05 m (42") for those with Midisart® BV on the venting line
⅜"ID ⅝"OD Clear C-Flex® 1.25 m (50") for PDS equipped with Press in plug

[2] Tubing from bag to end line:
⅜"ID ⅝"OD Dow Corning® Pharma-50 Silicone
– 1.82 m (72") for 8.3L Celsius®-Pak and 2.05 m (80") for 16.6L Celsius®-Pak equipped with Opta®
– 1.5 m (60") for 8.3L Celsius®-Pak and 2 m (79") for 16.6L Celsius®-Pak equipped with MPC quick coupler
⅜"ID ⅝"OD Clear C-Flex® 1.5 m (60") for 8.3L Celsius®-Pak and 2 m (79") for 16.6L Celsius®- Pak equipped with Press in plug

[3] Venting line tubing:
⅜"ID ⅝"OD Dow Corning® Pharma-50 Silicone
– 0.1 m (4") for PDS equipped with MPC quick coupler on the venting line
– 0.15 m (6") for PDS equipped with Midisart® BV on the venting line

Equipment and accessories

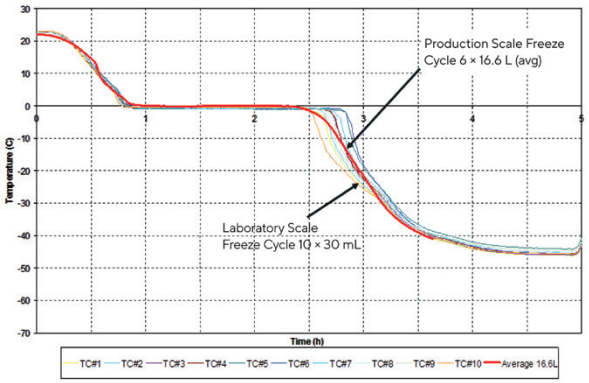
Develop Your Freeze & Thaw Process with Celsius® S³ Benchtop System

Celsius® S³ benchtop system

The Celsius® S³ is the only lab-scale freeze & thaw system in single-use containers that is scalable to production-scale. This system is a tool to execute freeze & thaw process development and stability studies using a minimal amount of product:

- Scalability
  The Celsius® S³ System models a 16.6 L pilot-scale and 100 L production system with a minimal amount of product. Using the same freeze & thaw path length and identical materials of construction in all Celsius®-Pak containers, the Celsius® S³ System ensures unmatched scalability between all scale systems.
- Ease of Use
  The CryoPilot Control Unit provides automated operation and data collection. The Celsius® S³ System freezes and thaws from 1 to 10 product samples per run. Celsius®-Pak is available in 30 mL and 100 mL with different filling port and thermowell configurations.
- Improved process validation
  Celsius® S³ System offers excellent batch to batch reproducibility and consistent product stability after freezing, thawing and storing. The Celsius® S³ System provides documented and reproducible freeze & thaw processes, thus facilitating validation of your freeze & thaw operations.

Part number	Drug substance
FTH-CS00000-0001	Celsius® S³ System with US voltage
FTH-CS00000-0002	Celsius® S³ System with EU voltage



Celsius® S³ Applications

Process development	Storage & transportation studies	Formulation development	Stability studies
Studies to understand decoupling (hold) steps during i.e., frozen storage of process intermediates, frozen storage of Drug Substances. **Investigate the Celsius® CFT technology for future scale up (Celsius® FT33 | 66 | 100)**	Scale-down studies (using minimal volumes as low as 20 mL) for understanding extended Bulk Drug Substance storage (time and temperature) & transportation	Formulation development of freeze & thaw compatible formulations for Bulk Drug Substance	Stability Studies in accordance to industry guidelines, conducted in a container closure system that is the same as or simulates the packaging proposed for storage and distribution at production-scale

Equipment and accessories

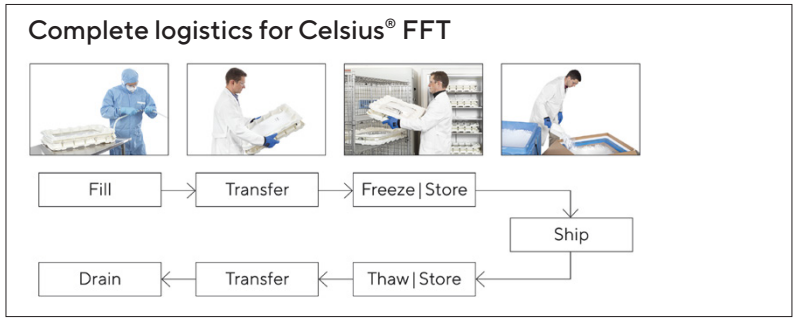
Complete Logistics Solutions for Celsius® FFT

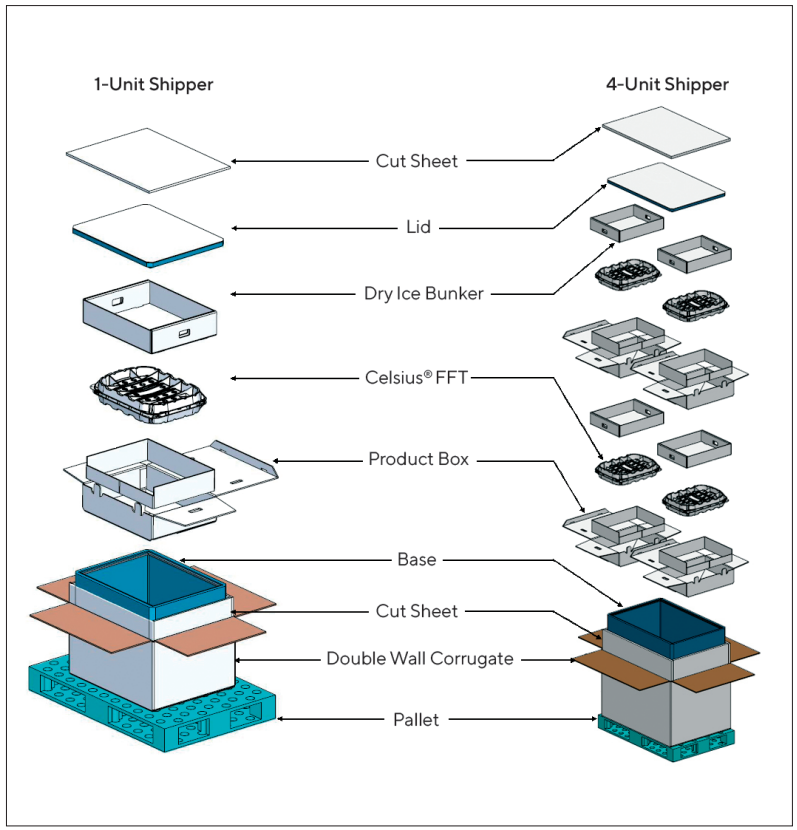
Celsius® FFT Box Shippers
The Celsius® FFT Box Shipper is a robust, qualified solution allowing safe shipment of frozen Celsius® FFT to remote locations.

The Celsius® FFT Box Shipper has been qualified according to the most restrictive regulations for shipping containers. Validations include ASTM-D4169 Assurance Level 1 for mechanical integrity and ISTA 7D extreme summer profile for thermal performance to ensure proper safety and integrity of your high-value drug product during frozen shipment. The shipper provides adequate insulation and refrigeration to maintain the Celsius® FFT below –40°C for at least 96 hours.

Celsius® FFT Box Shipper is offered for the shipment of the 4 sizes of the Celsius® FFT: 2 L, 4 L, 6 L and 12 L.

Each Celsius® FFT size has dedicated Shippers: a one-unit and a four-unit Shippers are available for the 2 L, 4 L and 6 L FFT while the 12L FFT has a one-unit version.





Part number	Description
FTH-SM00103-0006 Shipper	Celsius® FFT 2 L 1-unit Shipper
FTH-SM00103-0007 Shipper	Celsius® FFT 2 L 4-unit Shipper
FTH-SM00103-0003 Shipper	Celsius® FFT 4 L 1-unit Shipper
FTH-SM00103-0004 Shipper	Celsius® FFT 4 L 4-unit Shipper
FTH-SM00103-0001 Shipper	Celsius® FFT 6 L 1-unit Shipper
FTH-SM00103-0002 Shipper	Celsius® FFT 6 L 4-unit Shipper
FTH-SM00103-0005 Shipper	Celsius® FFT 12 L 1-unit Shipper

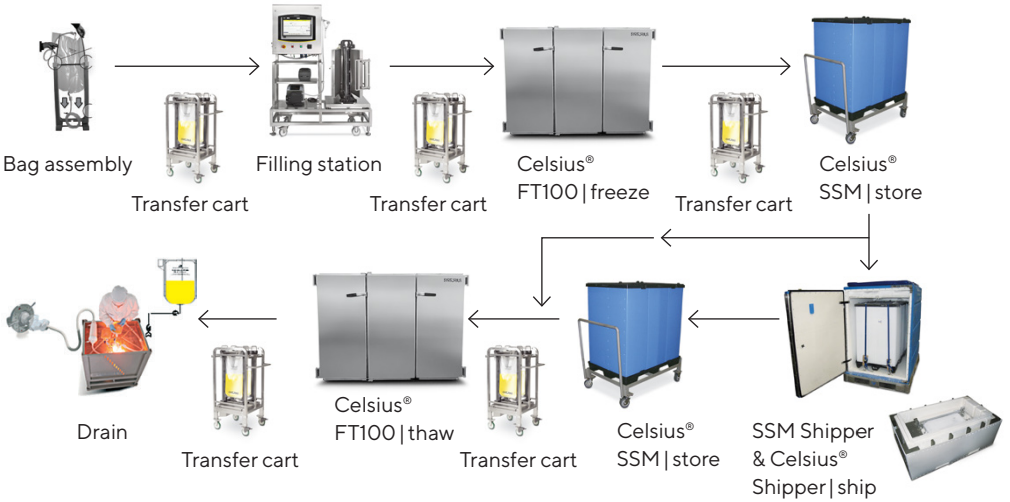
Equipment and accessories

Complete Logistics Solutions for Celsius®-Paks

Celsius® FT33 | 66 | 100
Celsius® FT33 | 66 | 100 is a controlled-rate freeze & thaw system designed to minimize the adverse effects of the cryoconcentration in your biopharmaceutical products. This modular equipment uses a patented heat transfer technology which provides unprecedented freeze & thaw performances and gives flexibility by processing up to 100 L of solution with single-use Celsius®-Paks.

Celsius® FT33 | 66 | 100 can be customized according to process specifications. Please consult your SSB Sales representative for any additional information.

Complete logistics for Celsius®-Paks



Transfer carts
Transfer carts are designed to minimize the operator efforts when transferring Celsius®-Paks to and from the Celsius® FT33 | 66 | 100. The Transfer Carts are available in two sizes: TC33 with a maximum carrying capacity of 33 L and TC100 with a maximum carrying capacity of 100 L.

Filling station
The FS16 Filling station optimizes the logistics of filling and pressurizing the Celsius®-Pak. Connected to the platform balance, the controller with HMI (Human Machine Interface) allows accurate and automatic filling process with minimal operator intervention.

Filling station insert
The Filling Station Insert allows using the FS16 to fill and pressurize 1L and 2L Celsius®-Paks.

Equipment and accessories

Complete Logistics Solutions for Celsius®-Paks

Celsius®-Pak 1L and 2L Carrier
The Celsius®-Pak Carrier allows processing the 1L or 2L Celsius®-Paks in the Celsius® Freeze-Thaw Modules.

SM100 – Storage Module
The SM100 – Storage Module allows storage of up to 100 L of product in frozen Celsius®-Paks. This is a stainless steel cart with a reduced footprint compared to the Transfer Cart to optimize space in the storage area.

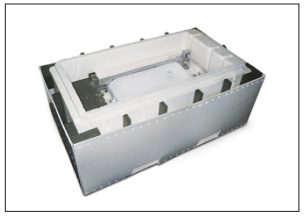
Celsius® SSM
The Celsius® Shippable Storage Module (SSM) allows storage of up to 100 L of product in frozen Celsius®-Paks.

SSM Trolley
The Celsius® SSM is mounted on a Celsius® SSM trolley that permits the easy rolling of the module into freezers while allowing removing the SSM for storage.

Insulated Cover for Celsius® SSM
This is an optional insulated cover composed of polyethylene bubble film with a metalized exterior which will protect the Celsius® SSM during transfer operation over warming-up.

SSM Shipper
The Celsius® SSM can be shipped to remote locations by using the Celsius® SSM Shipper. The shipper provides adequate insulation and refrigeration to maintain all Celsius®-Pak in a maximally or minimally loaded SSM.

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



Celsius® Shipper
The Celsius® Shipper 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.

Accessories	Part number	Description
Celsius®-Pak frames and accessory	FTH-CF00016-0009	16.6 L Celsius®-Pak Frame 2G
	FTH-CF00008-0015	8.3 L Celsius®-Pak Frame 2G
	FTH-CF00000-0029	Celsius®-Pak Frame 2G RTD Holder
	FTH-CF00004-0020	Celsius®-Pak 1 L and 2 L Carrier
Filling Station and accessory	Upon Request	Filling Station FS16-S2
	FTH-CF00004-0050	Filling Station Insert for 1 L and 2 L Celsius®-Pak
Storage Solutions and accessory	FTH-TC00033-0001	TC33 – Transfer Cart 33 L
	FTH-TC00100-0001	TC100 – Transfer Cart 100 L
	FTH-SR00080-0003	Adaptor, Freezer Storage, 80 L, 20" deep
	FTH-SM00100-0070	SM100 – Storage Module
	FTH-SM00101-0010	Trolley for SM100
	FTH-SM00101-0024	Celsius® SSM (Shippable Storage Module)
	FTH-SM00101-0020	SSM Trolley
	FTH-SM00101-0027	SSM Insulated Cover
Shipping Solutions and accessory	FTH-SM00101-0028	SSM Shipper
	FTH-SM00102-0002	Celsius® Shipper

Celsius® pre-designed solutions

Design, Applications Development and Validation Services

Design configuration options
All Celsius® pre-designed solutions are available in our Sartorius corporate configurator for easy selection of the right solution for your process and application requirements.

Should our pre-designed solutions need to be adjusted to more specific requirements, they can serve as a base for designing your specific best design.

Our Engineered to Order (ETO) solutions then allows the selection of a larger variety of solutions with added features, lines, manifolds, filters, connectors and sampling systems.

Please contact our sales representatives and application specialist to support you with the selection and design of your best solution for your specific process and application.

Application support
Our expert FMT Application Specialists provide global support for:
- Single-use process URS definitions and application development
- Process design with standard and custom solutions
- Technical support during lab-scale l aboratory or process development freeze & thaw studies
- SOP development, process validation and operator training
- Technology transfer and process optimization

Validation service
Our global validation services network offers:
- Installation start up, FAT, IQ and OQ, calibration and maintenance
- Consultancy service and process specific validation studies including
- Extractables | leachables
- Chemical compatibility
- Integrity testing
- Bacterial challenge test
- Particle shedding
- Shipping test

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