Advanced Therapies Week 2026

Mitigating Cryopreservation Risks with a Single-use Solutions Partner

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Thank you for joining us and welcome

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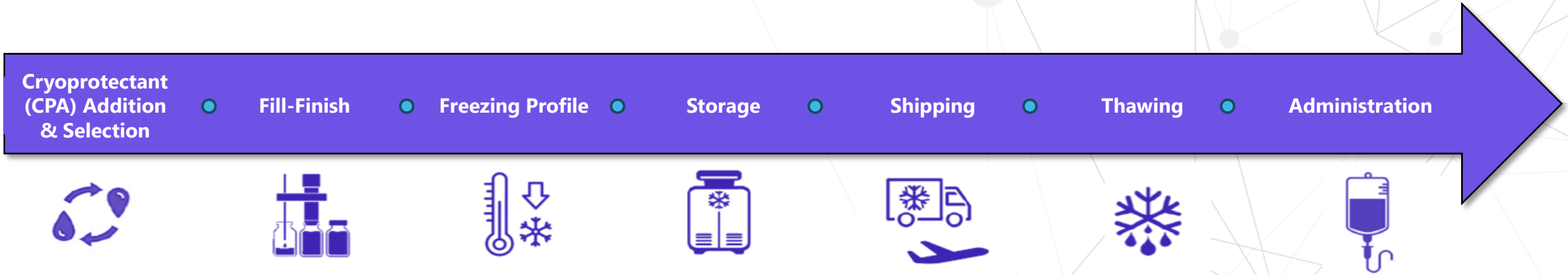
1. Exploring Cryopreservation Risks
   - Unit operations
   - Design in isolation
   - Late changes
   - Regulatory pressure
2. Mitigating Risk with an Early Single-use Partnership
3. About Charter Medical

Cryopreservation Unit Operations: What They Enable



✓ Long-term storage of cells and biologics	✓ Consistent delivery of therapies to patients
✓ Global transport and supply chain flexibility	✓ Scalability, logistics, product quality, and safety

Early cryopreservation workflow design decisions determine downstream risk.

Challenges in Cryopreservation Unit Operations

Multiphysics Challenges

Biology

- Osmotic stress & ice formation
- CPA protection vs. toxicity
- Post-thaw handling

Heat Transfer

- Controlled cooling and warming rates
- Temperature gradients across volume
- Container geometry

Materials & Containment

- Polymers: Seal integrity, brittleness at sub-zero temps
- Mechanical stress through temperature cycling
- Surface interactions

Process & Workflow

- Fill, freeze, storage, transport, and thaw
- Interfaces between unit operations
- Operator handling and intermittent exposure events

Logistics & Scalability

- Scale-up and scale-out
- Equipment and chain of custody, including thermal history
- Thermal and handling variability

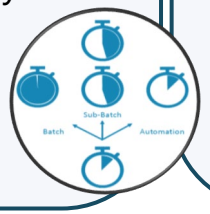
Early cryopreservation workflow design decisions determine downstream risk.

Design in Isolation Fuels Cryopreservation Risk

Risk emerges when biology, materials, process, and logistics are designed separately.

How Risk Is Introduced

- Inconsistent methods
- Process transfer:
  - Scaling batch sizes
  - Sites and operators
  - Multi-site distribution
- Changes are often incremental and individually acceptable, but not cumulatively acceptable

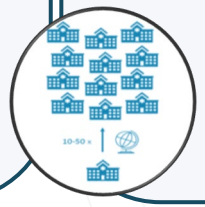


Drift & Accumulation

- Failures occur at interfaces, not steady state
- Containers, materials, and geometry directly impact performance
- Thermal, mechanical, and handling stresses accumulate across transitions
- Drift is introduced through suppliers, equipment, and human factors

Latent Failures

- Many failure modes are latent and only revealed post-thaw
- Damage may not be apparent during storage or transport
- Failures are often detected only via:
  - Recovery & potency assays



When Do Issues Surface?

- Scale-up
- Tech transfer
- Validation

Failures are rarely driven by a single variable event.
They emerge from cumulative drift and are often only revealed at the end of the process.

Avoiding the Expense and Risk of Late Changes

As processes mature, early design decisions lock in and significantly reduce flexibility.

Process & Workflow Constraints

- Container geometry, tubing routing, and port placement are difficult to modify once locked in
- Operator handling and logistics variability amplify at scale
- Process corrections inevitably introduce trade-offs

Design decisions constrain process flexibility long before validation.

Material & Containment Constraints

- Material selection and interfaces become fixed post-validation
- Late material changes require new extractables & leachables assessments and container integrity data

Reversing containment decisions becomes difficult, costly, and time-consuming.

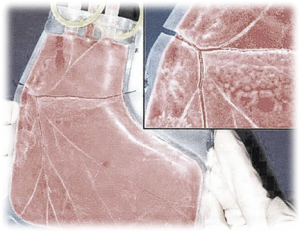
Post-validation Impact

- Comparability risk
- Creates requalification and revalidation burden
- Regulatory exposure

Even technically sound fixes create cascading downstream impact.

Regulatory Pressure Pushes for Early Design Decisions

Regulators do not evaluate cryopreservation as an isolated step.



System Reality

1. Regulatory accountability spans cryopreservation lifecycle
2. Product quality is formally assessed post-thaw
3. Containers & packaging evaluated under real handling, thaw, and stability conditions
4. Late changes introduce comparability risk and carry disproportionate cost

Where Regulation Evaluates the Workflow

1. Storage and transport stability
2. Clinical site usability instructions (thawing protocol, handling, comparability studies, site data, and CQAs)
3. Post-thaw quality and in-use hold
4. Chain of identity and traceability

What this Signals: The Need for an Early Single-use Solutions Partnership

1. Addressing risk before validation
2. Co-designing container, handling protocols, and thawing interfaces
3. Earlier testing of realistic use conditions
4. Planning for scale and variability in advance
5. Creation of sound operational logistics workflows

Why Engage Early with a Single-use Solutions Partner?

The regulatory landscape feeds the need for early engagement.

An Early Partnership Enables:

- ✓ Freeze-thaw workflow simulation under representative conditions
- ✓ Phase-appropriate container material selection and design
- ✓ Alignment between design and downstream handling
- ✓ Early visibility into scale-up and tech transfer constraints
- ✓ Adaptation to dosage form and site-of-care workflows

A Credible Single-use Solutions Partner:

- ✓ Documents design controls
- ✓ Utilizes change notification systems
- ✓ Communicates raw material specs and traceability workflows
- ✓ Establishes scalable phase-appropriate quality systems
- ✓ **Acts as a development partner, not just as a component supplier**

Where a Single-use Partner Can Provide Guidance

Product Performance and Patient-facing Quality

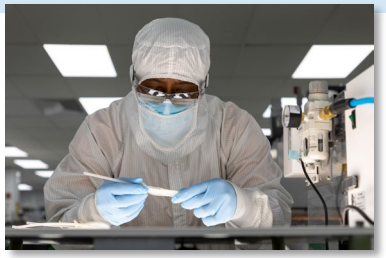
- Shelf life and post-thaw viability considered up front
- Consistent post-thaw quality across handling conditions and workflows

Risk Governance and Change Resilience

- Shared understanding and alignment on risk
- Support during changing regulatory expectations
- Support during material and supplier changes

End-to-end Containment System Integrity

- Fully integrated design (fill → administration)
- Barrier integrity in a closed single-use workflow
- Support for particulate risk reduction:
  - USP <1207> — Container Closure Integrity (CCI)
  - USP <1663>/<1664> — Extractables & Leachables
  - USP <790> Particulate Matter in Injections (considerations)



Operational Workflow Knowledge and Scale Evolution

- Early workflow knowledge enables informed scale-up testing
- Guidance on future experiments as processes mature

The Value of the Single-use Partnership: Confidence & Data

Portfolio Solutions

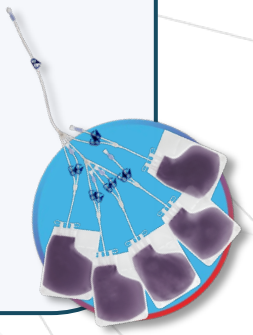
- Work as a starting point
- Effective & validated
- Enable rapid feasibility, early development, and risk reduction
- Reduce time to first data without over-committing on design

Customization Becomes Necessary

- Accommodates process evolution:
  - Scale
  - Automation
  - Site-of-care requirements
- Design diverges from standards

Customization Is Evolution, Not Reinvention

- Transition to purpose-built solutions with a single-use design team
- Modular customization:
  - Manifolds
  - Integrated sensors
  - Filters and pump elements
- Reduce late-stage changes and comparability risks



- ✓ Early partnership reduces risk *before* validation lock-in and comparability constraints
- ✓ Portfolio solutions accelerate early development, but customization adapts to scale and workflow evolution
- ✓ Purpose-built single-use solutions reduce late-stage rework, deviations, and regulatory exposure

Charter Medical: Experience Where it Matters Most

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35+ Years of Experience

Charter Medical designs and manufactures **portfolio and custom single-use solutions** for biological fluid management, cell growth, and cryopreservation.

Supporting Your Process

Our single-use solutions are designed with customer's processes in mind, from **initial process development** to **therapy administration.**

- Activation
- Administration
- Apheresis
- Biological Fluid Transfer
- Cell Banking
- Cell Culturing
- Collection
- Cryopreservation
- Expansion
- Fill/Finish
- Filtration
- Formulation
- Processing
- Separation
- Selection
- Storage
- Transfection
- Transport
- Waste

Key Therapeutic Areas

We have focused efforts in these therapeutic areas with **YOUR processes in mind:**

- **Advanced Therapies**
  - Cell Therapies
  - Gene Therapies
- **Bioprocessing**
  - Monoclonal Antibodies
  - Drug Substances
  - Vaccines
  - Buffers/Media
  - Lentiviral Vectors
- **Blood Management**

Freezing Studies for Data-backed Decisions

Design freezing studies with Charter Medical's engineers to generate actionable data to help you better understand the freeze/thaw steps to produce your clinical or commercialized therapy:

1. Controlled-rate
2. Long-term
3. Therapy containment/protection
4. Transportation

Our Freezing Studies provide you with the data needed to determine the optimal containment options and processes for the success of your therapy.

Key Takeaways: Early Engagement with a Single-use Partner

1. **Risk in cryopreservation is system-level:** It is not isolated to a single component or step
2. **Regulatory scrutiny evaluates real use:** Storage, transport, thaw, and handling – not just design intent
3. **Early partnership reduces risk** – before validation lock-in and comparability constraints
4. **Portfolio solutions accelerate early development** – customization is inevitable as scale and workflows evolve
5. **Purpose-built containment systems reduce** late-stage rework, deviations, and regulatory exposure

The greatest value of early engagement is confidence and data-backed decisions – not just compliance.

Discover how single-use solutions can bring efficiency and flexibility to your biological product development processes.

Visit Charter Medical on *Cell & Gene* to explore portfolio and custom solutions for:

- Biological fluid handling
- Cell growth
- Cryopreservation
- Freezing studies

Scan to explore Charter Medical

Thank you for your time.

Questions?

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