MODALITY SOLUTIONS

Building + Validating a Resilient Cell Therapy Supply Chain

What You Need to Know

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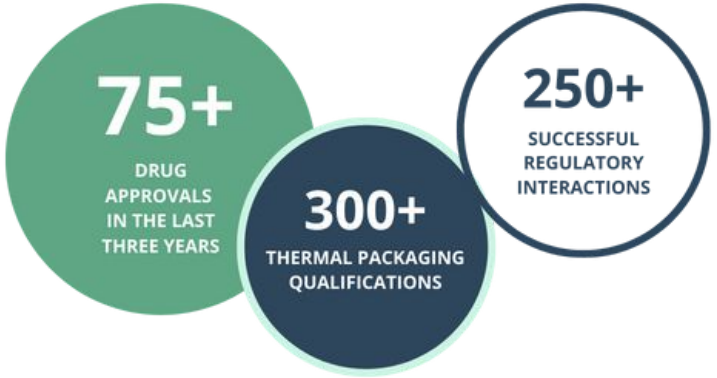
Who is Modality Solutions?

We're **experts in optimizing the biopharmaceutical cold chain** for novel, fragile, and controlled-temperature therapies and meeting the rigorous filing requirements for these advanced drug products.

With an **unmatched track record of regulatory filing success**, the only contract transport simulation lab of its kind, and deep cold chain expertise, Modality Solutions is the trusted Cold Chain Engineering™ partner for leading pharmaceutical and biopharmaceutical companies.



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- Validation: confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled

- Supply Chain Validation: demonstration that the supply chain processes will consistently deliver therapy to patients with all safety and efficacy intact

- Supply Chain Resilience: the ability of a supply chain to prepare for and adapt to unexpected events.

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Importance of Supply Chain Resilience

1. Timely delivery to patients
2. Flexibility to work with the best solution, not just the expedient one
3. Simplifies scale up and expansion
4. Compliant, safe, and effective

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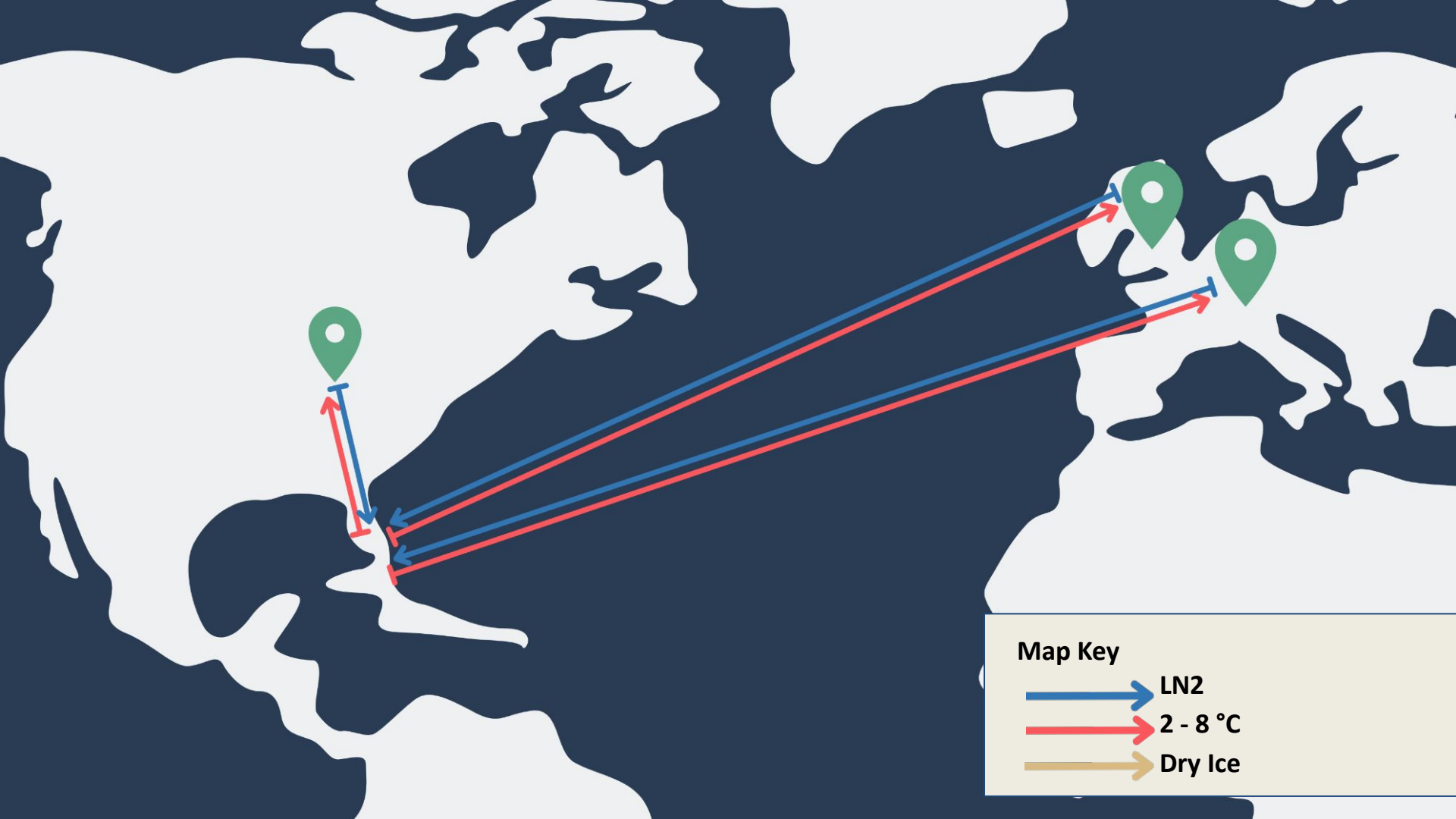
Principles of a Resilient Cell Therapy Supply Chain

1. Multiple shipping solutions should be available for for any given shipping route
2. Multiple couriers can be leveraged to ensure access to on demand shipments
3. Proper shipper qualification and process validation for each segment of the supply chain


Map Key
LN2
2 - 8 °C
Dry Ice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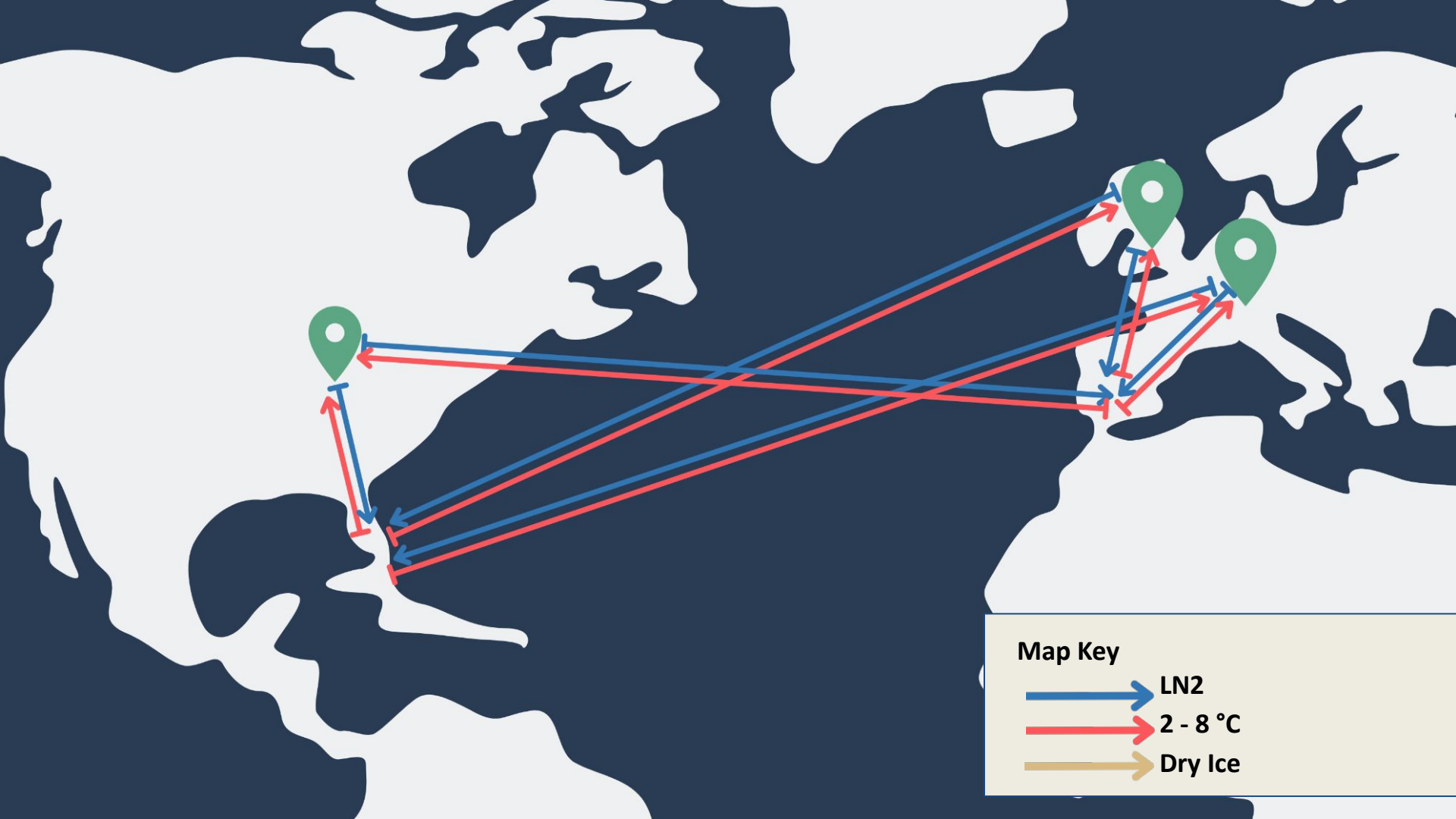
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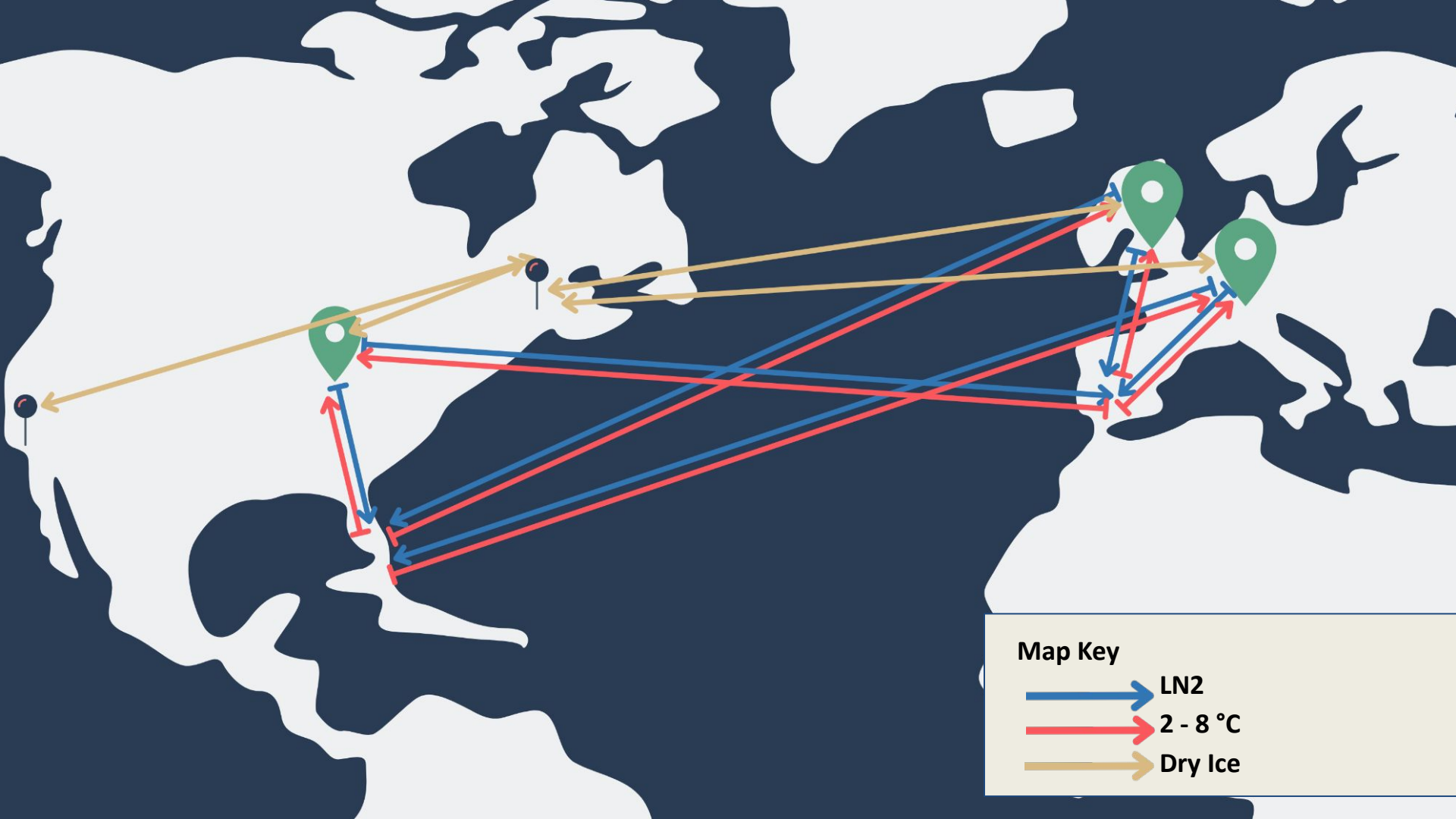
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How We Built in Supply Chain Resilience:

1. Implemented four unique 2 – 8 °C shippers for collected material
2. Two unique dry ice shippers for precursors
3. Three unique LN2 shippers for final DP
4. Multiple eligible couriers for all shipping lanes

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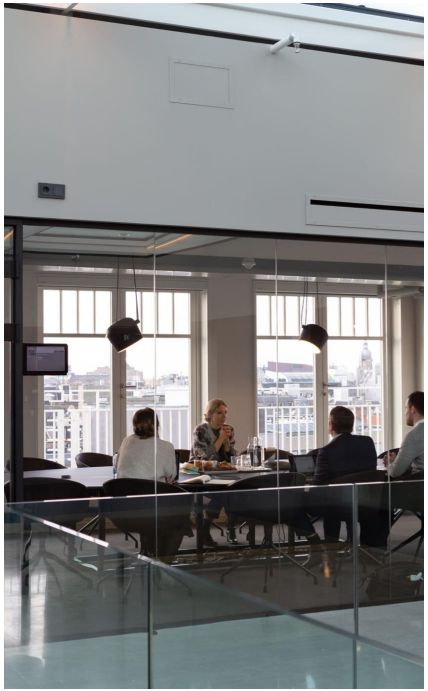
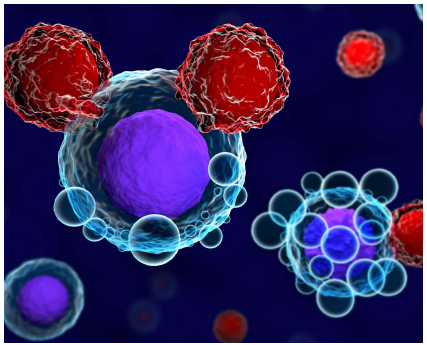
Validation Planning

- A Validation Master Plan should be created to guide the execution of validation activities
- Appropriate flexibility must be allotted to manage the increased complexity of cell therapy supply chains
- The VMP should state the “How To’s” and not be specific to unique solutions
- Acceptance criteria for product quality analytics should be separated from temperature control during shipping





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Two Types of Assurance

Product Quality Assurance

Demonstrate that product quality is not adversely affected by distribution through:

- Exposure to worst-case supply chain hazards (shock, vibration, temperature, humidity, and/or pressure)
- Release and/or stability studies to assess product quality

Thermal Control Assurance

Demonstrate that storage & shipping temperatures will be maintained through:

- Operational Qualification (OQ) of equipment (shippers, freezers, etc.)
- Performance Qualification (PQ) of shipping process (real-world shipments)

Qualification Studies

Operational Qualification

- OQs demonstrate that the equipment will meet baseline specifications under controlled conditions
- OQs should cover all ‘worst-case’ considerations
- Most vendor qualifications are adequate but it is the product owner’s responsibility to confirm that it meets their requirements

Performance Qualification

- PQs generate data on process performance for the qualified equipment interacting with human processes.
- PQs do not need to include ‘worst-case’ conditions
- A bracketing strategy is strongly recommended to account for the complexity of Cell Therapy supply chains

PQ Bracketing

- Traditional methods would not work: Three PQ shipments per lane per unique thermal solution was inefficient
- Bracketing should be applied:
    - Comparable lanes can be studied together: especially applicable for patient/donor collection
    - Shipper types can be bracketed: if the usage process for different LN2 shippers are comparable, results can be leveraged across the different solutions
    - Special scrutiny should be paid to extra circumstances such as customs clearance
- Separating product quality from temperature control in your validation plan enables much greater flexibility in PQ strategy

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Your Resilient Supply Chain

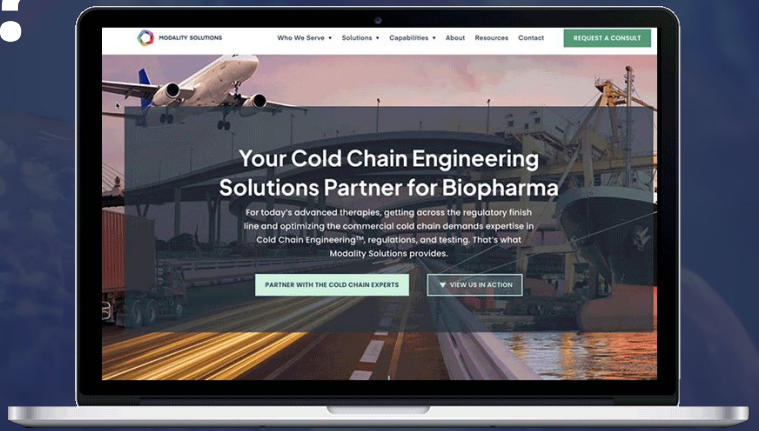
Through a strong design and validation program, **you can ensure that your supply chain has the flexibility to operate in an ever changing global landscape.**

Why does it matter?
Your supply chain operations need to be reliable to ensure that patients across the globe have timely access to safe and efficacious therapies.

Need support?

Through validation engineering, regulatory guidance, advanced testing and cold chain optimization, we have helped hundreds of clients achieve successful and rapid approval of their therapy. **We're ready to help you too.**

Reach out to us directly - or submit an inquiry at modality-solutions.com/contact.



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