eBook

Building Supply Chain Readiness into Advanced Therapy Development

How early decisions around cryopreservation, logistics and documentation can help reduce downstream risk

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Contents

Executive Summary

Early supply chain choices can set the direction for an advanced therapy program. Shipping lanes, cryopreservation, packaging and manufacturing workflows are strategic development choices. They can become the foundation for regulatory readiness, scalability and long-term execution.

This eBook is based on an Xtalks webinar featuring Lorraine Hicks, Dominic Clarke, PhD and Gwendolyn Erskine. The speakers discussed how advanced therapy companies can build supply chain readiness from the earliest stages of development, especially when programs involve time-sensitive biological materials, cryopreservation and complex clinical logistics.

A central message was that regulatory readiness depends on how well teams capture decisions, rationale and changes as the program advances. Decisions need to be documented as they happen. Shipping risk should be considered during site feasibility. Cryopreservation should be evaluated early enough to understand its impact on product handling, comparability and scale.

Early planning means matching evidence to the stage of development. Teams need to know which decisions require support now, which assumptions should be tested by phase and which choices may become harder to change later (Fig. 1). The goal for advanced therapy teams is to create a supply chain strategy that supports the next milestone while preserving the ability to scale.

Fig. 1. *Choices made before clinical entry can shape regulatory readiness, operational flexibility and long-term execution for advanced therapy programs.*

Introduction: Early Decisions Set the Development Path

Advanced therapy development often involves sensitive biological materials, specialized handling requirements and tight movement timelines. The supply chain is part of the development pathway for programs that depend on fresh or cryopreserved materials.

Many early-stage teams are focused on reaching the clinic. They are building protocols, selecting sites, generating data and preparing for first-in-human studies, while supply chain choices are already shaping what the program can support later.

A **shipping lane** selected early may shape future site feasibility.

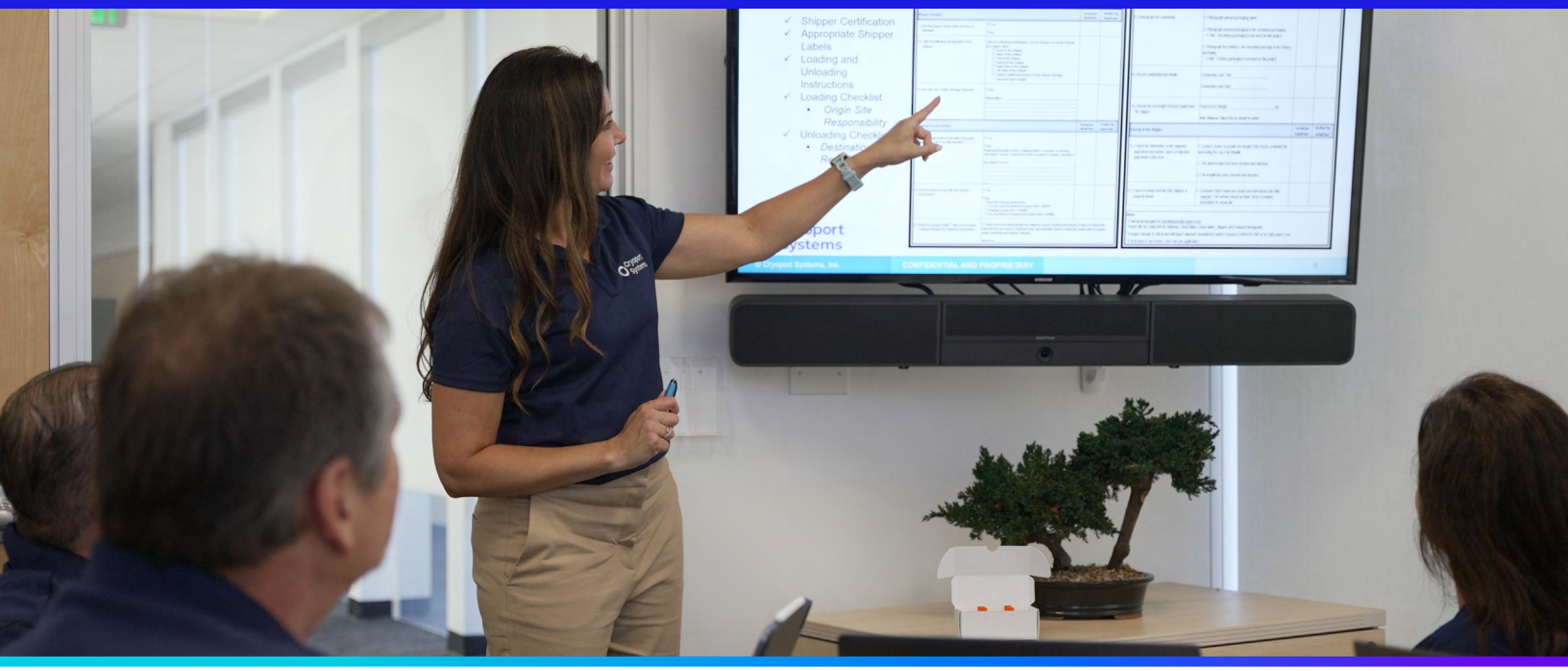
A preliminary **packaging assumption** may later affect stability data.

A decision to begin with **fresh material** may raise comparability questions if the program later needs to introduce cryopreservation.

A **documentation gap** may be harder to explain once the program is preparing for later-stage review.

The webinar focused on the decisions that advanced therapy teams should think through before pivotal milestones. Each speaker brought a different perspective on clinical logistics, regulatory readiness, cryopreservation, technical operations and consulting services.

Chapter 1:
The Regulatory Readiness Mindset



Regulatory readiness begins with the decisions teams document around product handling, logistics and control.

From the logistics and shipping perspective, readiness includes showing that the product is safe and can be delivered safely and reliably. Effective planning requires an understanding of the route, packaging system, shipping risks and real-world conditions that could affect execution, not just the sites involved or the courier moving the material.

In early development, companies are already gathering information to support clinical decisions, including site feasibility. Sponsors may look at a site's performance, experience and ability to support a protocol. Gwen Erskine emphasized that logistics should be part of this feasibility process.

Shipping risk assessments can help teams consider issues such as weather, airport and customs clearance delays earlier in development.

This provides teams with better information for Phase I and Phase II decisions and helps prepare them for later packaging and shipping lane qualifications.

Building a Decision Trail Over Time

A common issue is that early-stage companies treat documentation as something they can catch up on later.

That approach can create problems as the program advances. Development decisions are usually made quickly, and the reasoning behind them can be lost if it is not captured at the time. When teams later need to explain how the program advanced, they may be forced to reconstruct the rationale.

> *"Regulatory readiness is not necessarily just about the paperwork. It's being able to tell your story."*

Lorraine Hicks

Supply Chain & Clinical Logistics Expert / Cell & Gene Therapy Specialist

A clear regulatory narrative should show:

- Why a site or lane was selected
- What shipping risks were identified
- Why a fresh or cryopreserved approach was chosen
- How packaging assumptions changed
- How decisions changed from Phase I to later stages
- What evidence was gathered along the way

A clear decision trail can help teams explain what they did, why they did it and how each decision supported the program's development.

Chapter 2:
Make Cryopreservation Decisions Early

Fresh Material and Timing Risk

Fresh biological material can have a limited window for movement. If a program depends on a 24-hour or 48-hour timeline and a delay occurs, the quality of the material may be affected. In cell therapies, those delays can have serious implications because each step is tied to a specific patient and product.

Teams using fresh starting material need to assess the timing, logistics and handling requirements early, as well as whether the approach can scale as the program grows.

The Role of Cryopreservation

Cryopreservation should be considered on both the front end and the back end. If material is frozen, teams need to understand what that means for biological characteristics such as viability, phenotype and function.

By helping decouple collection from manufacturing, cryopreservation can support scalability as a program moves from a small, single-site Phase I study to a larger, multi-site or multi-country program.

A shift from fresh to frozen material, or even a change in freezing parameters, may raise comparability questions. The impact depends on the product and the level of change, but the need to understand those effects should not be delayed.

Each program needs a handling strategy that fits its product, process and development path. Cryopreservation should be evaluated early enough for the team to understand its implications before options narrow.

> *"If you rely on 24 or 48 hours to get that product where it needs to be, and you have a delay, you're in trouble."*

Dominic Clarke, PhD

Associate Chief Scientific Officer, Cryoport, Inc. / Vice President - Technical Operations, Integricell®, Cryoport Systems

When Decisions Become Hard to Change

Product-handling decisions can become harder to change as programs approach later-stage qualification and filing. By Phase III, teams should have full qualification completed for packaging and shipping systems. If a program is fast-tracked, the timeline can tighten further, and teams may need key packaging and shipping answers much earlier than expected.

The science may continue to change through Phase I and Phase II, and those changes should be documented as the program moves forward. Early planning does not prevent change, but it gives teams a clearer way to manage it.

Chapter 3: Staging Supply Chain Decisions by Phase

Developing the Chapters of a Program

Lorraine Hicks described the process as unfolding like chapters, with each stage built carefully as the program moves forward. In preclinical development, teams should begin by establishing product identity and characterization.

Even if the early work is informal, it should still be captured and documented.

Phase I and Phase II are where programs start to encounter early regulatory friction. Documentation becomes important, but so does flexibility. Teams need to build flexibility into the process because the science and program design may continue to evolve.

A useful question for teams is:

What will we need to show regulators two or three years from now, and are we building that evidence today?

Phase-Appropriate Rigor Without Overbuilding

Balancing early planning with phase-appropriate rigor means avoiding two extremes: over-engineering too early and waiting too long to build evidence. Teams can start with the final goal, then work backward to determine what each phase needs to support the next step.

In Phase I, that may mean shipping risk assessments. In Phase II, it may mean another risk assessment or a shipping lane study to test whether the assumptions in the risk assessment hold up in real-world conditions. By Phase III, documentation and packaging should be finalized, and shipping lane qualifications may require repeated execution.

Each step serves a different purpose:

- A shipping risk assessment is a paper-based exercise
- A shipping lane study tests selected assumptions in the real world
- A shipping lane qualification is more formal and may need repeated execution

Teams do not need every answer in Phase I, but they should know what outcome is needed at each stage to support the final goal.

Gwendolyn Erskine

Senior Director – Consulting Services, Cryoport Systems

Chapter 4:
The Questions Teams Should Ask Early

Packaging and Validation Needs

Teams should think through packaging validation needs.

Full validation may not be needed in Phase I, but planning should start that early (Fig. 2).

Packaging affects stability data, distribution and product quality.

FDA expectations also require teams to show end-to-end control.

Questions to ask include:

- Have we thought through packaging validation needs?
- What will we need for future filings?
- Are stability data and packaging assumptions aligned?
- Are distribution and product quality being considered together?
- Do we have the right decision-makers in the room?

Cryopreservation Options

Teams should assess the option to cryopreserve, especially for starting material. If a team evaluates cryopreservation during process development, it can build a process upfront and generate comparison data to fresh material. Even if the program starts fresh in Phase I, the impact of moving to cryopreserved material later may be reduced if the option is evaluated early.

Dominic Clarke noted that going back to develop cryopreserved starting material after a program is already in the clinic could be "10x to 20x in cost" and come with "a significant loss in time." Teams need sufficient knowledge of how the process performs, even if full validation is completed later.

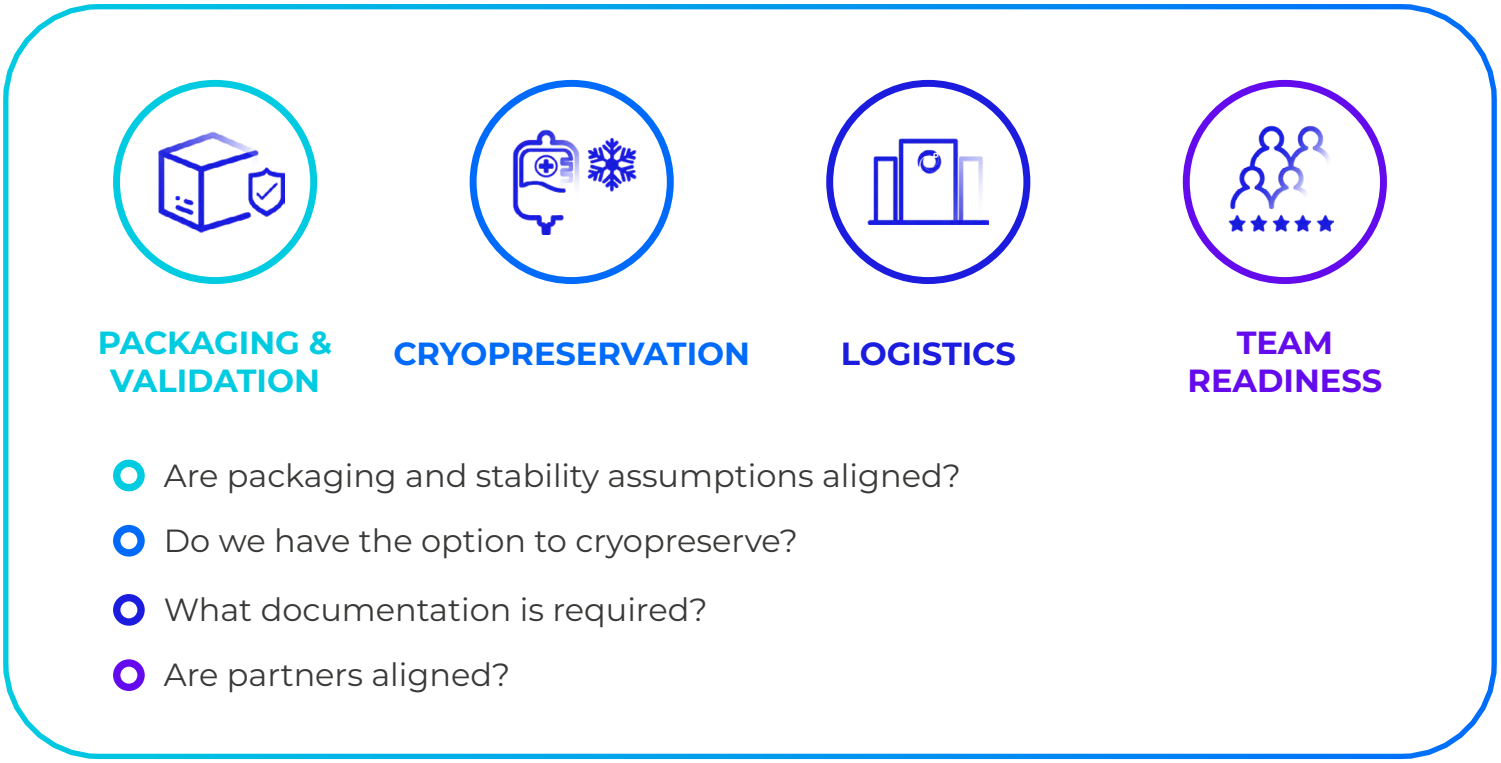


Fig. 2. *Early planning questions can help teams identify packaging, cryopreservation, logistics and regulatory considerations before later-stage pressure builds.*

Domestic and International Planning

It is equally important to think about whether materials will stay domestic or cross borders. Cross-border movement introduces additional documentation and compliance questions. Teams should be clear on what will be required for each regulatory agency and geography involved. This is especially important when shipping sensitive biological materials across jurisdictions.

Chapter 5: Breaking Silos Across Teams and Partners

Cross-functional Alignment is Critical

Teams may begin by asking what they need for the current phase, but the discussion should include broader questions.

If the program is domestic or international, who is thinking through customs needs? Is a packaging design engineer involved? Has quality weighed in on validation needs? Is internal regulatory guidance available, or does the team need outside support?

Cryopreservation sits at the intersection of clinical operations, hospitals, manufacturing and quality. Misalignment across those groups can lead to inconsistent processes, poorly defined specifications and downstream comparability challenges.

Alignment should also include logistics service providers, clinical sites, CDMOs, packaging partners and other external groups. The supply chain depends on all of them (Fig. 3).

Fig. 3. *Advanced therapy supply chain readiness depends on alignment across internal teams and external partners.*

Internal and External Readiness

Supply chain strategy cannot sit with one function. It requires coordination across:

- Clinical operations
- Manufacturing
- Quality
- Regulatory
- Packaging
- Logistics
- Clinical sites
- CDMOs
- Commercial teams
- Customs or import/export support, when relevant

When these groups are involved too late, teams may discover gaps after decisions have already been made. When they are included earlier, the program can make more realistic decisions and prepare for the next phase with fewer surprises.

Chapter 6:
Avoiding Late-Stage Rework

Time Can Be a Friend or an Enemy

There are programs that wait to solidify final packaging or execute qualifications, then run into problems when they are short on time.

Gwen Erskine shared an example in which a company in Phase III needed physical testing, thermal testing and a shipping lane qualification.

The company initially opted for a smaller package of work, but after FDA feedback, more data were requested. The team then had to complete additional qualification and thermal work under time pressure. The back-and-forth contributed to an almost six-month delay.

Qualification planning should match the program stage, timeline and evidence needs. Late-stage corrections can create pressure when timelines are already tight.

It Is Not Just a Box

A common pitfall is underestimating the logistics of the trial. Programs may know that patient samples, starting material or drug product need to move, but the details are not always considered early enough.

Teams may not fully budget for specialized packaging, temperature control, short movement windows or the cost of moving materials across sites or borders.

When it comes to advanced therapies, movement is not a routine shipping task.

Teams need to know what will be collected, where it will go, how it will move, whether it crosses borders and what partners are needed to execute the process.

Thinking With the End in Mind

Teams tend to focus on getting to the clinic. That is understandable, given the urgency, cost and pressure of early development.

But if success is defined only as reaching Phase I, teams may cut corners that later affect chemistry, manufacturing and controls (CMC), logistics or cryopreservation strategy.

Dominic Clarke noted that cryopreservation is sometimes treated as a logistics issue when it is also a biological consideration.

Teams should define what success looks like and understand the risk of skipping steps that may later become important (Fig. 4).

PLAN EARLY	VS.	CORRECT LATE
✓ Build the decision trail		✗ Recreate rationale
✓ Test assumptions by phase		✗ Add studies under time pressure
✓ Prepare packaging and lane strategy		✗ Manage budget strain
✓ Align teams and partners		✗ Risk timeline delays
✓ Reduce work pressure		✗ Resolve gaps when options are narrower

Fig. 4. *Planning early can alleviate the pressure of late-stage corrections when packaging, shipping or documentation gaps surface close to filing.*

Chapter 7:
What Teams Wish They Had Done Earlier

Bring Logistics and the Full Package in Earlier

A common lesson is to think through logistics and the full package earlier, including in Phase I or Phase II (Fig. 5). Logistics partners can help teams think end-to-end, connecting early clinical needs with later-stage execution.

Start Earlier and Build a Stronger Data Package

A recurring theme is the value of building a stronger data package sooner. Introducing cryopreservation earlier can help teams understand the process and avoid trying to develop it after the program is already in the clinic.

Process control is also part of the equation. Some programs may rely on clinical sites to perform cryopreservation. That can work, but it requires oversight. If multiple sites are performing the same critical step, teams need to understand whether the process is consistent and whether they can answer future regulatory questions.

Fig. 5. *Earlier logistics planning, stronger data packages and regulatory input can help teams avoid unnecessary rework.*

Bring Regulatory Expertise in Sooner

Regulatory expertise can also be valuable earlier in the process. Regulatory strategy does not begin with the filing. It takes shape as development, documentation, logistics and product handling decisions are made.

Key Takeaways

Advanced therapy teams do not need every answer at the start, but they do need a clear way to make, document and revisit decisions as the program moves forward.

The main takeaways from the webinar, summarized in Fig. 6, highlight the importance of planning early, building evidence by phase and keeping the right teams aligned.

These steps can help reduce extra work and give teams more flexibility as programs move toward later-stage readiness.

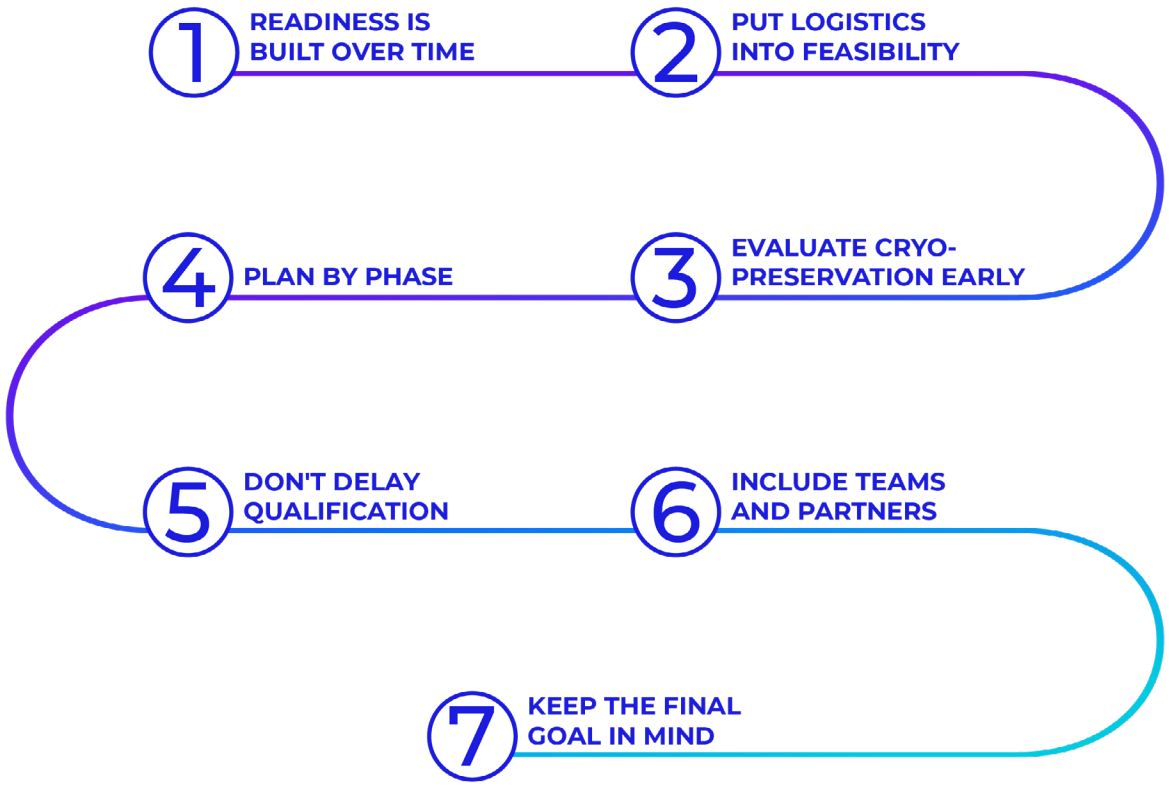


Fig. 6. *Early planning, clear documentation and aligned teams help keep programs on track.*

How Cryoport Systems Can Help

Cryoport Systems is a comprehensive supply chain partner for the life sciences industry focused on meeting the challenges of the global cell and gene therapy market.

We excel in the specialized management of the biopharma supply chain through our comprehensive offerings in logistics, BioServices and biostorage, cryopreservation, and consulting.

With our expansive platform and decades of temperature-controlled supply chain expertise, Cryoport Systems helps Enable the Outcome™ for advanced therapies programs, safely and securely supporting the journey ofcritical therapies to patients in need.

For more information about how Cryoport Systems is Enabling the Outcome™, please scan the QR code.

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