Biolife Solutions®

Cell Processing Solutions

CellSeal® CryoCase™

Rethink the standard.
Replace the bag.

An innovative primary container for smarter cell and gene therapy

Addressing Particulate Challenges in Cell and Gene Therapy

In cell and gene therapy (CGT), the presence of particulates in injectable or infusible drug products is a growing industry-wide concern, with potential risks that include embolization, contamination, or triggering adverse immune reactions. The CGT sector, still in its early stages, often draws from practices in blood-based research and large pharmaceuticals, where particulate contamination has been a longstanding challenge. Over the past five years alone, there have been 189 drug recalls, with 20 of those attributed to particulate contamination. Significantly, in at least 35% of cases, the particulates were suspected to come from the container itself.[1]

Determining the exact source of particulates—whether intrinsic or extrinsic to the container—remains complex. Comparative data from final product containers (such as vials, bottles, and bags) shows that bags present a significantly higher particulate rate than vials or bottles.[2] Factors contributing to particulate presence include the materials used, manufacturing processes, tube sets in fill and formulation steps, filtration systems, and the environment in which production takes place.

Advancements in cleanroom technology and drug manufacturing processes have enabled greater control over extrinsic particulates, but managing inherent particulates remains one of the most challenging aspects. At BioLife Solutions, we recognize this challenge and its impact on product integrity, making particulate management a top priority.

To address these issues, BioLife Solutions has undertaken a thorough review of suppliers and implemented rigorous inspection protocols across multiple container types. This approach has identified several key areas where particulate risk can be mitigated:

- **Material selection:** Certain plastics, prone to electrostatic charges, may attract particles during production.
- **Material construct:** Welds on bags can harbor particulates that may remain undetected until the container is filled.
- **Manufacturing standards:** Only bags produced in regulated cleanroom environments are considered for use.

The evaluation of bag types in particulate management remains an area of ongoing investigation at BioLife Solutions, as shown in recent testing data. Table 1 highlights the percentage of particulate rejects across various bag types, emphasizing the need for robust container solutions.

Bag Type	Number of Bags Filled	% Particulate Rejects
EVA Bag 1	38	30%
LDPE Bag 1	40	50%
EVA Bag 2	10	30%
LDPE Bag 2	10	100%
FEP Bag	10	60%
ULDPE	15	53%
Fluoropolymer	>50	<10%

Table 1: Particulate evaluation of bag types.[3]

Paving the way forward

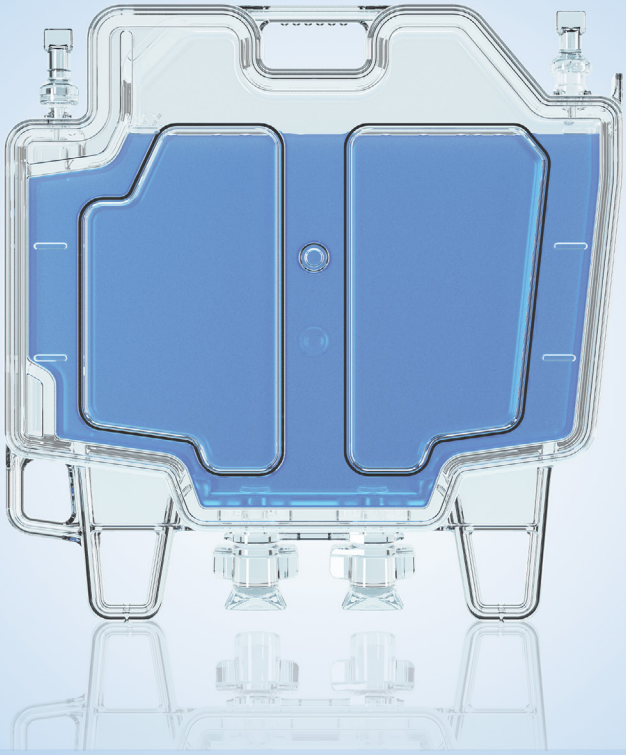
Addressing the particulate issue is crucial to advancing CGT therapies and ensuring patient safety. At BioLife Solutions, we are committed to exploring new container options and the container presented in this brochure has been developed to address particulate contamination from multiple angles. Our focus is on enhancing the industry standard through continued innovation and rigorous quality control, bringing us closer to a more reliable future for CGT product storage and delivery.

1. *PDA JPST May 2020, 74 (3) 359-366*
2. *Internal testing data.*
3. *S. Werner, A. Shields, K. Aoki, M. Eitner, M. Said. Are new options needed for primary packaging? It is time to address particulates and fractures. Poster presented at: ISCT 2024. May 29. Vancouver*

CellSeal
CryoCase

CryoCase and conquer

An innovative solution for smarter CGT



Rethink
the standard.
Replace
the bag.

Confidence

Rigid and fracture resistent structure surpasses bag standards

Control

Streamline processes, simplify handling and eliminate need to remove air

Certainty

Transparent design boosts inspectability

CONFIDENCE.

“Too often we discover that a bag has fractured or sprung a leak and must be rejected post-freeze because the suspension inside has now been exposed to the environment.”

Sean Werner, Chief Technology Officer

Observational study demonstrates a more-rigid primary container structure may be more fracture resistant than standard cryogenic bags.

Product evaluation

During an early product evaluation of the CellSeal CryoCase, Immatics Biotechnology Company tested container design and material selection strength. The CellSeal CryoCase is made of Cyclic Olefin Copolymer (COC) plastic to protect any sample suspended within the storage compartment.

To prepare the containers for drop testing, they were frozen in liquid nitrogen (LN2) for a week. Once removed from the freezer, each container was dropped off the top of an 8 ft. (2.4 m) ladder, 10 times in a frozen state. Once thawed, the containers were evaluated for leaks or noticeable fracture, and no noticeable injuries to the storage compartment were observed.

CryoCase legs are designed as shock absorbers and could break off when the unit is dropped. The container stays intact and will not affect the contents inside.

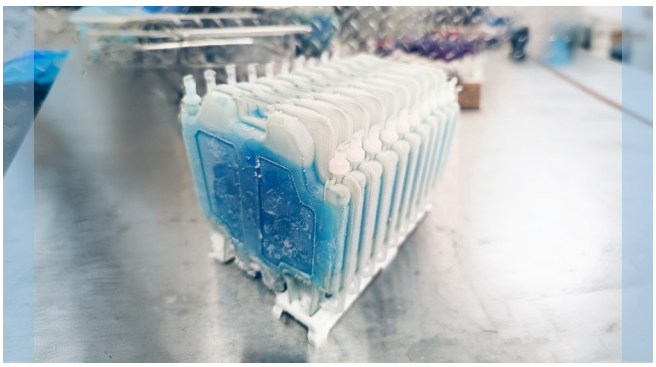


Figure 1: Frozen CellSeal CryoCases.

Early product evaluations from Immatics Biotechnology Company and adthera bio found the CellSeal CryoCase demonstrates equivalent cell performance metrics, when compared with cryobags.

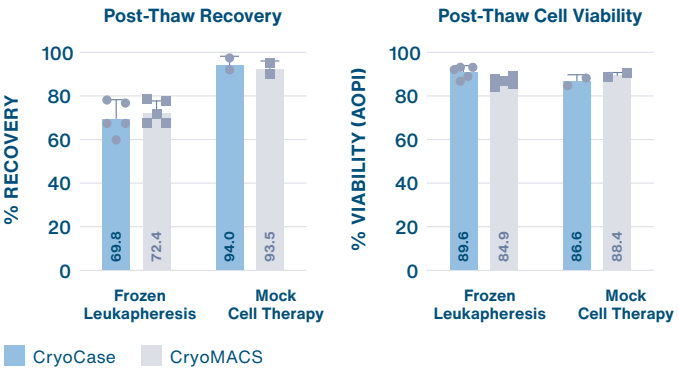


Figure 2 and 3: Immatics froze and tested fresh LP cells and final product in the CellSeal CryoCase and used the CryoMACS® as control. Post-thaw data shows equivalent percent viability and recovery measures for both CryoCase and CryoMACS bags.

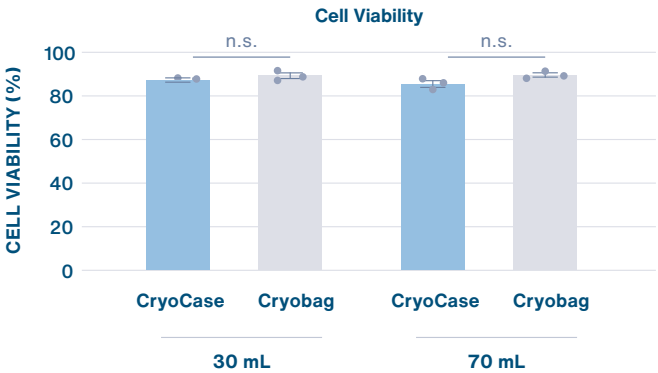


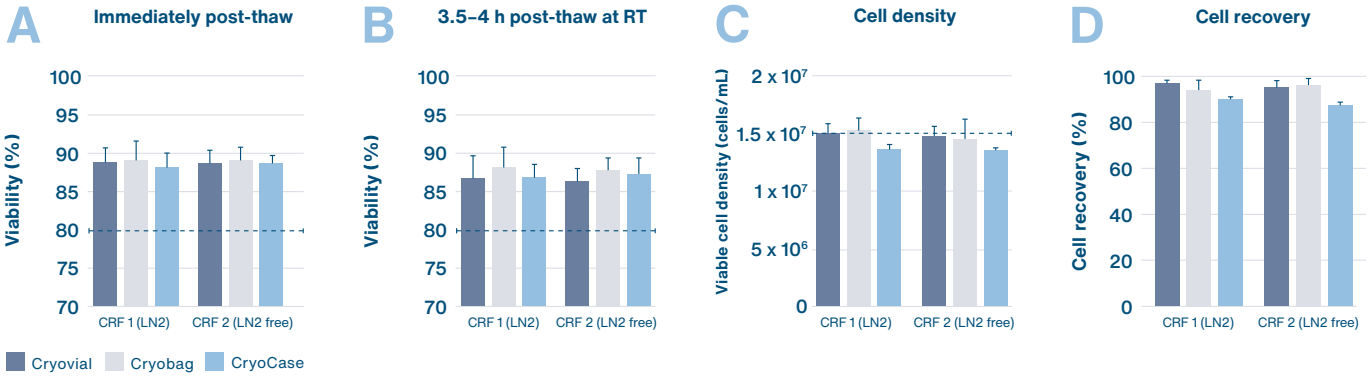
Figure 4: adthera bio’s test results demonstrated equivalent T-cell viability 24 hours post-thaw between the CryoCase and their preferred cryobag.

CONTROL.

In many therapy manufacturing operations, the fill step can be tedious and often require two operators to complete, when filling cryogenic bags. We believe if the primary container is designed specifically for these processes that significant streamlining may be possible.

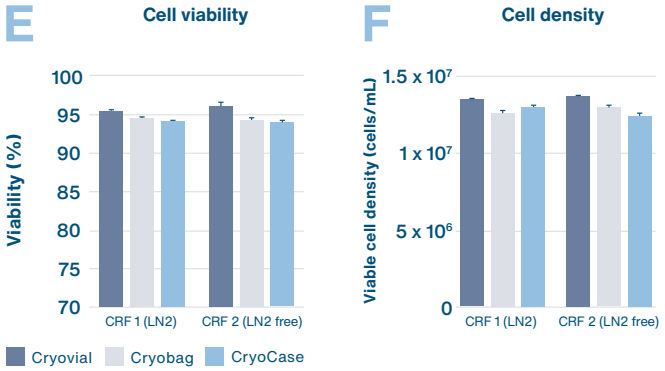
Early user feedback* demonstrates fill process improvements with the CryoCase while maintaining cell viability and recovery.

A recent study by Charles River Laboratory demonstrated that CAR-T cells can be effectively cryopreserved in the CryoCase, **using the same freezing profiles as standard cryobags**. The CryoCase maintained CAR-T cell viability and recovery above 85%, with similar CAR expression and T cell phenotype distributions compared to cryobags and cryovials.[4]



(A) Cell viability immediately after thawing each cryogenic container and (B) after 3.5–4 h post-thaw in each cryogenic container at room temperature. (C) Cell density and (D) cell recovery after cryopreservation and controlled thawing in each type of cryogenic container.

The CryoCase was also deemed compatible with an automated CAR-T manufacturing process, **reducing the number of required operators and the time it takes to complete a fill**; offering a robust solution for product fill and finish. These findings highlight a novel cryopreservation method and container for CAR-T cells, analyzing cell function across different storage conditions.[4]



(E) Cell viability, (F) Cell density and (G) Cell recovery of CAR-T cells using an automated manufacturing process, after cryopreservation in each type of container.

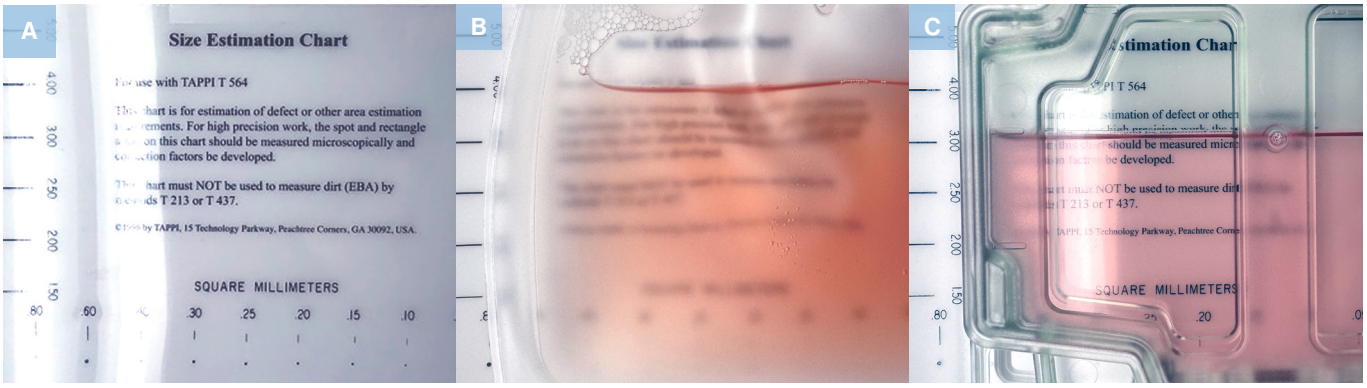
4. Pleitez D, Park M, Safford M et al. Cryopreserving CAR-T cells in a novel rigid container maintains their phenotype and function compared to conventional cryobags and cryovials. Cell & Gene Therapy Insights 2024; 10(7).

*See page 8 for early user feeback.

CERTAINTY.

'Inspectability' can be defined as the quality of being inspectable, or ability to be inspected. In science, inspectability often includes methods for detecting real and anticipated failures. Knowing and anticipating failures when they may not be visible makes certainty harder to obtain – cue in particulate challenges.

The most common feedback received during early client evaluation was that the CellSeal CryoCase was much easier to inspect for particulates or risk of fracture.



TAPPI chart

Images of TAPPI chart A alone, B viewed through a common bioprocessing container, and C viewed through a CryoCase. Containers are partially filled with unfiltered cell culture media containing 5% human platelet lysate.

Bag suppliers have inherent limitations in particulate detection:

- Components are dry when inspected for release
- Adding fluid for Pharmacopeia testing adds risk of new particulates
- Detection is different in filled vs. unfilled containers
- Automated inspectors may detect bubbles as particulates

Evaluation of the CryoCase

Prototype units were evaluated under two inspection conditions. First, 30 units were inspected for 5 seconds in front of a white background and 5 seconds in front of a black background. In the second condition, 10 units were inspected for 60 seconds in front of a black background. Under the conditions of the study, no particulates or fibers were identified.

Particulate Evaluation		
CryoCase	Number of Containers Filled	Number of Particulates Identified
5-second evaluation	30	0
60-second evaluation	10	0

TECHNICAL DATA SHEET

CellSeal® CryoCase™

An innovative primary container for smarter cell and gene therapy

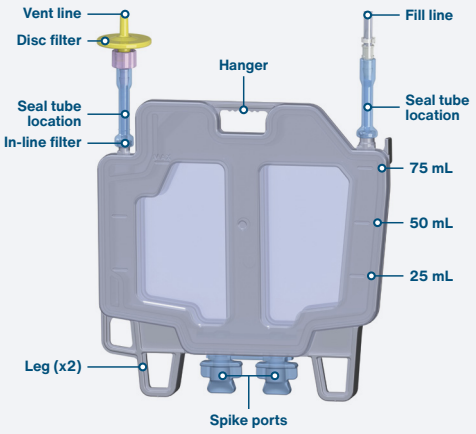


Figure 1: CellSeal CryoCase with labeled features.

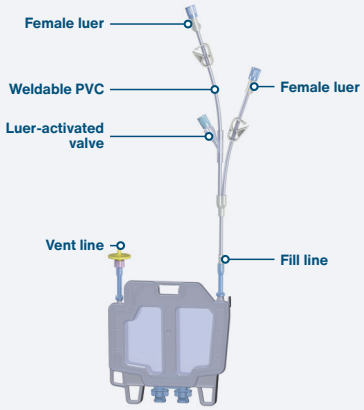


Figure 2: CellSeal CryoCase with fill line connected.

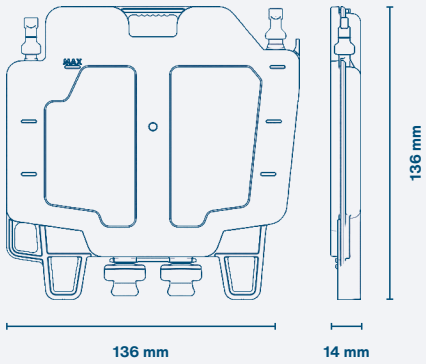


Figure 3: CellSeal CryoCase is shown sealed with dimensions.

Specification

Exterior Dimensions, Sealed, Figure 3 (H x W x D)	136 mm x 136 mm x 14 mm
Fill Line Length	316 mm
Weight (Empty with fill lines connected)	89 g
Weight (Sealed without fill lines)	74 g
Fill Line Weldable Tubing	PVC (DEHP-free), 2.4 mm x 4.0 mm (ID x OD)
Seal Tube & Spike Port Material	EVA (Ethylene Vinyl Acetate), Seal Tube 5.2 mm OD
Cassette Material	COC (Cyclic Olefin Copolymer)
Recommended Fill Volume	15 – 75 mL
Sterile Disc Filter Material	Hydrophobic PTFE, 0.2 µm
Usage	Single use only
Unit of Purchase	10 individually double-pouched CryoCase units per box
Fill Orientation	Upright / Vertical (Stand accessory available)
Shipping Box Dimensions (L x W x H)	568.3 mm x 438.2 mm x 76.2 mm (22.375 in x 17.25 in x 3 in)
Shipping Box Weight:	1.7 kg (3.85 lbs)

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Replace the bag.

Early user feedback:

Please contact your BioLife Solutions sales representative for more information

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