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A closed system container for shipping non-frozen cellular therapy products for direct clinical use

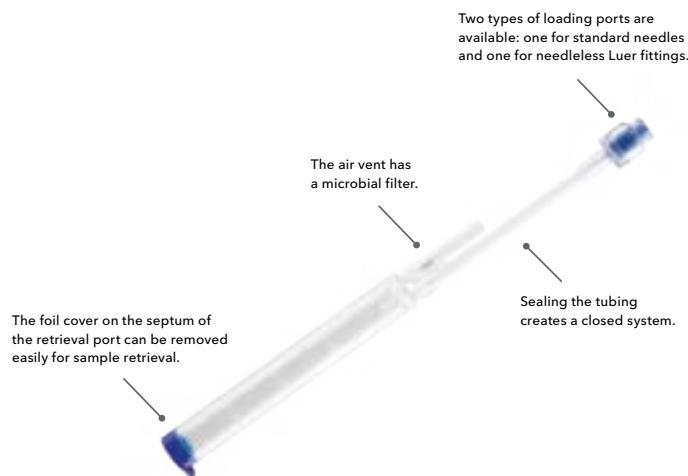
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Introduction

The current study evaluates the CellSeal® Closed-System Cryogenic Vial as a container for shipping cellular therapy products that have never been cryopreserved. The objective of the study was to ascertain the effect on cellular therapy product viability, integrity, and functionality during shipping overnight from a manufacturing facility to the bedside of the patient. The fresh cells were shipped overnight in a shipper validated to maintain a temperature of 4-8°C. The autologous mesenchymal multipotent stem cells (MSCs) were derived from equine skin punch biopsies. The purpose of the cellular therapy was to treat various naturally occurring tendon/ligament injuries of the distal extremities. The study included 25 horses with 23 completing the study to be followed one year postinjection.

A dose of 10-20 million cells were suspended in autologous peripheral plasma lysate at a concentration of 10 million cells/mL. The recovery, viability, and functionality of the cells were within the acceptable range set forth for this study. Upon arrival, the veterinarian used a standard syringe and a 20 g needle to withdraw the cells from the closed CellSeal® system and injected them via ultrasound guidance into the core lesion of the tendon or ligament injury. No adverse effects were noted in the horses postinjection, efficacy standards of the cellular therapy were promising, and no complications were reported by the attending veterinarians regarding use of the CellSeal® closed system.

CellSeal® Closed-System Cryogenic Vial



- The CellSeal® vial is a completely closed system equipped with an inlet septum and microbial barrier vent for easy fluid transfer. It is specifically designed to meet the demands of the cell therapy industry.
- The inlet tubing can be sealed using any standard blood tubing sealer to create a closed system. A separate test segment can also be sealed off.

Equine skin derived MSC (E-SMSC)

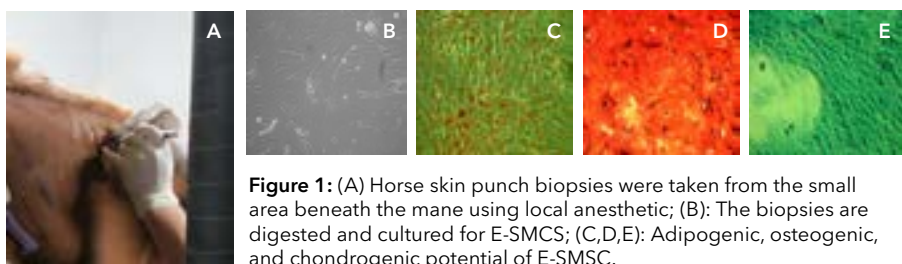


Figure 1: (A) Horse skin punch biopsies were taken from the small area beneath the mane using local anesthetic; (B) The biopsies are digested and cultured for E-SMSCs; (C,D,E) Adipogenic, osteogenic, and chondrogenic potential of E-SMSC.

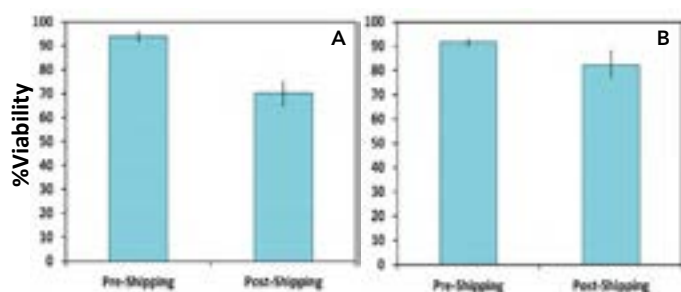


Figure 2: (A) Effect of overnight shipping on the viability of non-frozen E-SMSC. (B) The viability of cells after 48 hour culture. Both attached and floater cells were harvested and counted for viability.

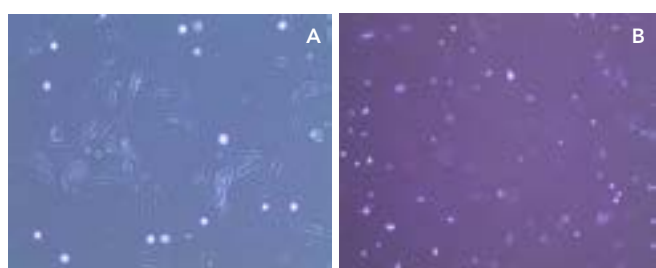
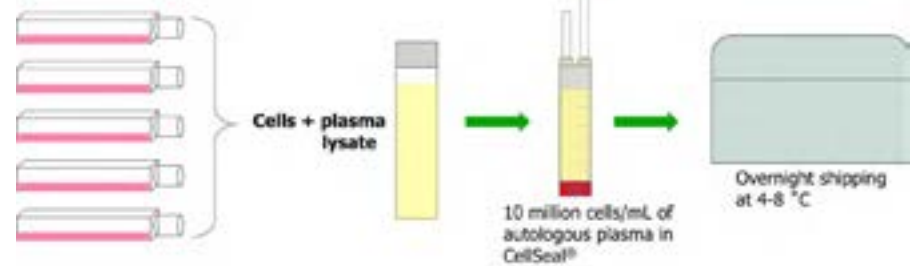


Figure 3: (A) Morphology of pre-shipped E-SMSC at 48 hour culture time. (B) Morphology of post-shipped E-SMSC at 48 hour culture time.

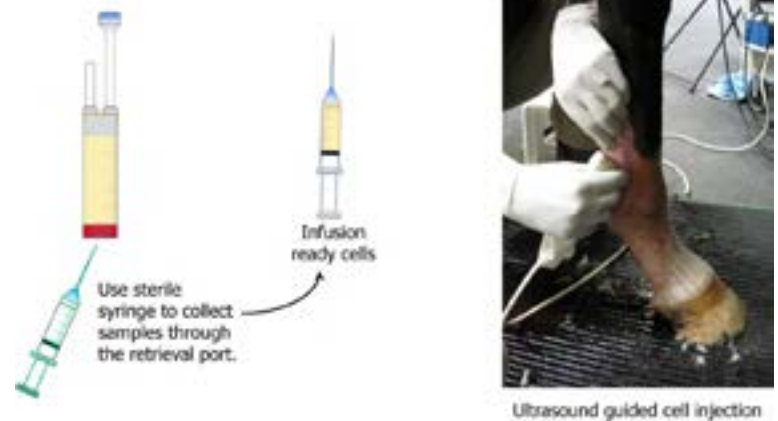
Cell manufacturing facility

Cell manufacturing, packaging and shipping



E-SMSC were cultured to a known, viable dose, then suspended in autologous peripheral plasma lysate at a concentration of 10 million cells/mL and packaged in CellSeal® vials. The fresh cells were shipped overnight to the participating veterinary clinics in a shipper validated to maintain a temperature of 4-8°C.

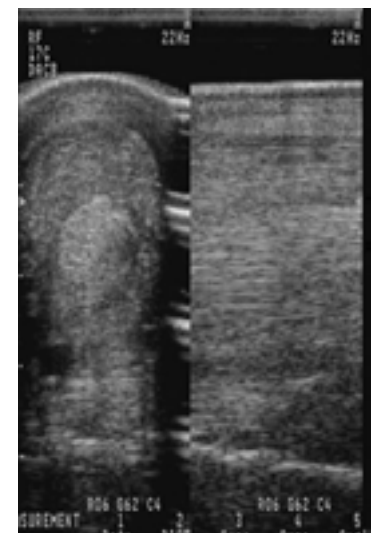
Treatment Facility



The veterinarian used a standard 3 ml syringe and a 20 g needle to withdraw the cells from the closed CellSeal® system and inject them via ultrasound guidance into the core lesion of the tendon or ligament.



Figure 4: A: Before Cell Therapy
Right front superficial and deep digital flexor tendons showing tendonitis. Tendon borders outlined in color: Red=superficial digital flexor tendon (SDFT), Blue=deep digital flexor tendon (DDFT). Lesion of each tendon outlined in white.



B: 1 Month Post-Cell Therapy
Post stem cell injection showing tendon filling and fiber alignment.

Conclusions

- Cellular therapy products can be shipped non-frozen using the CellSeal® Closed-System Cryogenic Vial. The recovery, viability, and functionality of the E-SMSC were tested to be within the acceptable range set forth.
- No adverse effects were noted in the horses postinjection. Efficacy standards of the cellular therapy were based on clinical improvement and ultrasound images pre-injection and at various time points postinjection.
- No complications were reported by the attending veterinarians regarding use of the CellSeal® vials. Efficacy and safety evaluation were followed for one year postinjection with no adverse reports at 12 months.