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Validation of the New Single-Use Freeze-Pak™ STS: Storage and Transport Solution Containers

Production of biologics whether for clinical development or large scale manufacturing campaigns intended to be converted to final drug product is often times stored frozen. Frozen storage provides manufacturing process flexibility while enabling long-term product stability. Products are frozen and stored using a variety of technologies including stainless steel vessels, bottles, carboys and disposable bags. While single-use freezing bags are a common choice for storage of biologics, challenges with film durability continue to exist.

Single-use bags intended for freezing and storage are often made with films using EVA and/or LDPE with product routinely blast frozen and stored to -30°C in a cold storage warehouse. During freezing and transport, the bags will typically experience temperatures well below -30°C ranging from -50°C to -80°C. Under these conditions, the bags have to endure a wide variety of stresses (film brittleness, volume expansion, etc.) that could impact integrity. While improvements have been made, mainly by adding a specifically designed secondary protective freezing/storage shell, film fractures and breaks are still common with commercially available bags.

The new single-use Freeze-Pak™ STS (FP-STS) were engineered for frozen storage. They are manufactured using a unique polyolefin monolayer film which remains flexible to temperatures as low as -196°C. Maximum fill volumes for freezing range up to 17 Liters while the “boat” port design offers a wide array of tubing configuration options to support process variation. FP-STS bags deliver the flexibility and durability required for frozen storage and transport.

The purpose of this study was to validate the new Freeze-Pak™ STS bags (Charter Medical, Ltd. Winston-Salem, NC) for freezing and storage. The results herein demonstrate that FP-STS freezing bags can be used for freezing and subsequent storage to -80°C.

Methods

Film Properties: Basic film properties for the FP-STS polyolefin film were completed using standard validated methods. Properties and associated test protocols can be located in Table 1.

Freeze Bag Validation Testing: To validate the FP-STS containers for their intended use, a selection of tests were performed.

Physical integrity: Prior to freezing, bags were evaluated for potential leaks or failures using an unconstrained pressure leak test (1.0 psi). Additional testing was performed by filling 2L and 20L bags to nominal fill volumes and hanging (liquid state) for a minimum of 72 hours.

Table 1: Film Property Physical Test Data

Property	Test Protocol	Value (Ave)
Tensile Strength	ASTM D638	3400/3700 psi
Elongation at break	ASTM D638	670/700%
Elastic Modulus	ASTM D638	540/480psi
Durometer Hardness Shore A	ASTM D2240	74
Tear Resistance	ASTM D1004	225/239
Tg (glass transition)	DSC	-48°C

Freezing integrity: 20L bags (worst case) were filled to at least 85% of nominal capacity and frozen to -80°C. Bags were then hung and thawed for a minimum of 72 hours and the process was then repeated (2 freeze/thaw cycles/bag). Additional robustness testing was achieved by performing a drop test. 1L, 5L and 20L bags were filled to 85% nominal volume before being dropped. Bags were then frozen to -80°C, thawed and dropped a 2nd time. Drop heights were 6ft, 3ft and 2ft for 1L, 5L and 20L bags respectively. For all testing, bags, ports, tubing and connectors were assessed for possible damage or leaks. No damage or leaks were deemed acceptable.

Data Summary

This study introduces the new Freeze-Pak™ STS disposable freezing bags and describes the validation testing performed to support the efficacy and utility where frozen storage of products is required. Prior to building a bag intended for storing products frozen, a robust, flexible film designed for freezing is necessary. The testing and data shown in table 1 represent some of the key physical aspects of the polyolefin film used for the bags. The film combines both durable (resistance to tearing, hardness) and flexibility (elongation, elastic modulus) features along with a low glass transition (Tg = -48°C) temperature.

Table 2: Freeze-Pak™ STS Bag Validation

Property	Test Protocol	Result
Integrity	2L, 20L unconstrained pressure leak test	Pass
Integrity	Nominal fill volumes (2L, 20L); hang 72 hours	Pass
Freeze/Thaw	20L bag freeze, thaw (hanging), repeat	Pass
Robustness	1L, 5L, 20L freeze, thaw, drop	Pass

To ensure bags were suitable for low temperature freezing applications, validation testing was performed (Table 2). All bags were initially tested for leaks and then filled and hung for at least 72 hours to confirm bag seal, port and tubing integrity pre-freeze. Bags were then subjected to freeze/thaw integrity and robustness testing. All bags passed the multiple freeze/thaw cycle and freeze/thaw drop tests (Figure 1; A, B). As a final test, bag ports and handles were folded over and then frozen (See Figure 1; C). No cracks or leaks were found when thawed. These tests represent worst case scenarios and help to demonstrate the overall durability of the FP-STS for frozen storage use.

Figure 1: Freeze-Pak™ STS Validation

A. **B.** **C.**

A New Solution to an Ongoing Challenge

The Freeze-Pak™ STS disposable freezing bags are designed to support frozen storage product needs. The validation studies support the efficacy and durability of the FP-STS containers to storage temperatures as low as -80°C. Supporting studies are currently in progress to validate secondary storage and transport container options to be used with FP-STS bags. The data will be reported in a separate study. In conclusion, the single-use Freeze-Pak™ STS containers from Charter Medical, Ltd. offer a new durable yet flexible freezing, storage and transport solution.

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Freeze-Pak™ STS bio-containers are intended for frozen storage and transport