GORE® STA-PURE®
Flexible Freeze Container

Looking Beyond the Spec Sheet

Understanding the cold durability performance of fluoropolymer bags

With an increasing number of biologic therapies being developed, selecting the best containment to store and transport these products is becoming more of a concern. Because the bulk substances used to make biologic therapies are usually stabilized by being deep frozen to temperatures between 40°C to 80°C, they need containers that work well at these low temperatures. The fact that many of these products are high value and produced in small batches means that even a single leak could be problematic.

When comparing containment systems for cold chain use, it is critical to understand all the factors that can affect performance. Although polymer bags are an excellent choice for this application, not all polymer films perform the same way, even if their specifications rate them for use at low temperatures. A full suite of application testing is necessary to determine whether a bag will hold up to all the rigors of handling and shipping at extremely cold temperatures.

Selecting a containment system

Bags are often a good choice for biologics because they use aseptic closures that create a closed system throughout processing, even during the freezing process. When other containers such as bottles are frozen, the different materials used to make the screw top and bottle can expand and contract at different rates, compromising the integrity of the product.

Another benefit of bags compared with other types of containers is that when scaling from smaller volumes manufactured during the development stages to full-scale drug production, the surface-area-to-volume ratio of bags remains mostly consistent. This makes it easier to predict how freezing and interacting with the bag material will impact stability of the bulk drug substance when moving from development to the manufacturing stage.

The type of film used to make the bag is one of the most important considerations. A film's glass transition temperature must fall below – be colder than – the application use temperature to ensure that the material doesn't become brittle. Staying above – warmer than – the glass transition temperature gives the molecules within the polymer chains room to move relative to each other and respond to external forces during freezing and thawing. Because of this, the material remains in its rubbery, ductile phase and does not transition into a hard and brittle phase.

For cold chain storage, bags made of fluoropolymers are a great option because they remain durable and flexible over a wide temperature range. However, it is important to realize that even fluoropolymers with a similar wide temperature range can vary greatly in cold durability performance.

Application-specific evaluation

For cold storage containment systems, the glass transition temperature of the film is the property most often referred to – and sometimes the only property cited. However, it does not provide a complete picture of performance for a specific application. Films with similar glass transition temperatures typically perform very differently.

To demonstrate the importance of looking beyond this single property, we examined the glass transition temperatures of fluoropolymer films commonly used to make bags for transporting and storing drug substances at cold temperatures. We then submitted the same films to cold flex testing, which simulates conditions that might be experienced during frozen handling and transport of the bags.

We analyzed the glass transition temperatures using a machine known as a dynamic mechanical analyzer (DMA) that measures the physical properties of materials as a function of parameters such as time, temperature, and frequency. The samples were held in a tension fixture over a wide temperature range with three measured outputs: storage modulus, loss modulus, and dimensional changes.

Storage and loss moduli measure the elastic and viscous characteristics of a polymer, respectively. The ratio of the loss to the storage modulus provides what is known as the tan delta curve, which is a measure of the polymer's ability to dissipate energy and is otherwise known as the dampening factor. For a given polymer, the tan delta curve contains peaks at important temperatures, such as phase transitions, conformational reordering, and glass transition temperatures. During freezing applications, the glass transition temperature, which indicates a polymer's transition from being ductile to brittle, is the most critical of these peaks. Polymers with higher peaks in the tan delta curve can absorb more energy at that temperature, but it is important to note that the magnitude of the peaks cannot be compared across different polymers. Instead, the temperature at which those peaks occur can be compared because it indicates the estimated coldest application use temperature for that material.

In Figure 1, you can see that all the films tested have peaks, which indicate transition points, at or below -80°C. Even though this indicates these materials are all rated for use at cold temperatures, additional testing is needed to find out if a bag made of either of these materials will hold up to the rigors of handling or being dropped at very cold temperatures. Thus, we took these same materials and submitted them to cold flex testing.

Fluoropolymer Transition Temperature

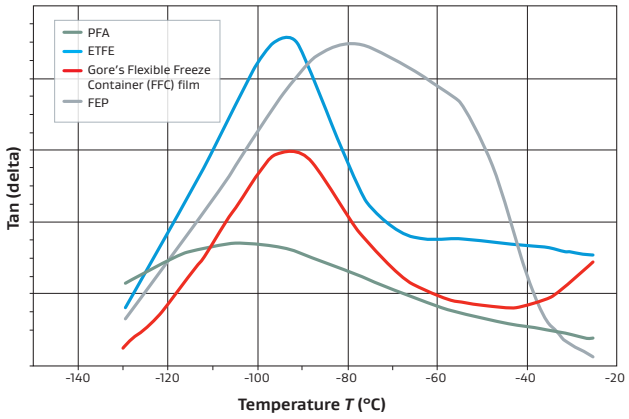

Figure 1. The glass transition temperatures of Gore's Flexible Freeze Container (FFC) film and three other commonly used fluoropolymer films, all fall below -80°C.

Table 1. Cold flex testing results

Film	Cold Flex Testing Pass Rate
GORE Flexible Freeze Container Film	100%
ETFE	60%
FEP	85%
PFA	80%

Cold flex testing was performed by flexing the film in an environmental chamber set at -80°C. This is done by wrapping film samples around two 1.5-inch diameter cylinders with a gauge length of 2.0 inches (Figure 2). The top cylinder actuates through a 1.5-inch stroke 36 times to simulate handling or use once per month over about three years of a bag filled with frozen product. After testing, the samples were brought back to room temperature and each sample was wetted with isopropyl alcohol to reveal any pinholes, cracks, or defects. Table 1 shows the results for each material.

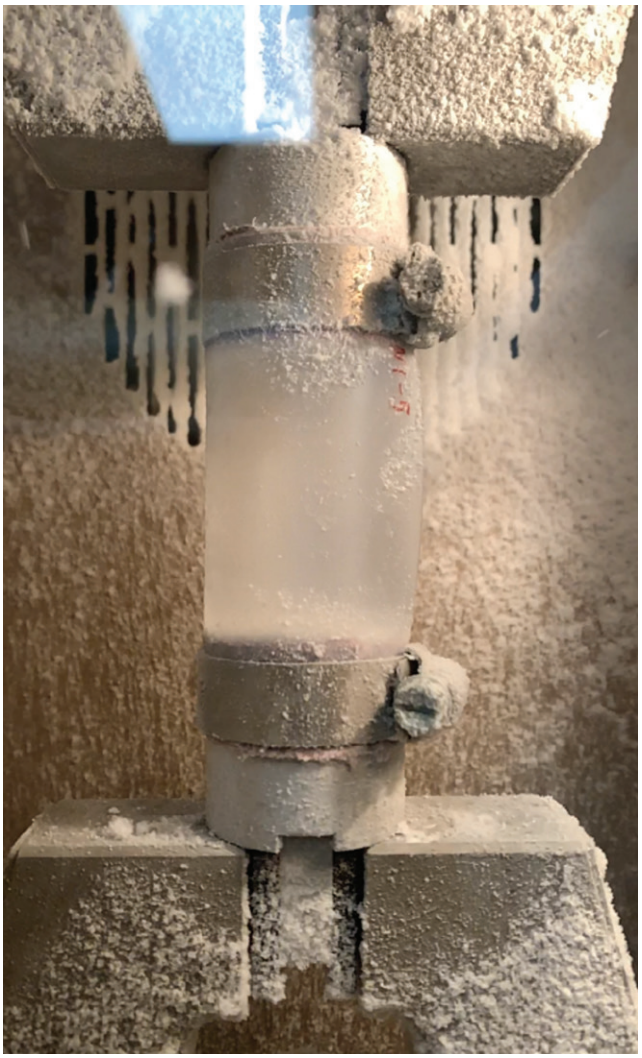

Figure 2. Cold flex testing involves flexing the film in an environmental chamber set at -80°C to simulate handling or use of a bag filled with frozen product.

The polytetrafluoroethylene (PTFE) film used to make the GORE® STA-PURE® Flexible Freeze Container was the only material to exhibit a 100% pass rate for cold flex testing.

Testing for additional real-world stresses

Performing a single additional test reveals the importance of looking at more than the glass transition temperature to determine how a specific polymer will perform in a filled bag at very cold temperatures. However, Gore takes this several steps further by performing a wide range of testing to understand how our fluoropolymer films will react to real-world use.

For example, after freezing in either plate or blast freezers, we make sure our bags can withstand multiple freeze-thaw cycles. This test puts stress on the container's seams and tests the bag construction as the bulk drug product inside expands and contracts during freezing and thawing. Our fluoropolymer bags also show high robustness when undergoing a standardized shipping test performed by an independent lab. This test simulates the worst conditions a container might experience during shipping, including vibrations and drops. It even replicates the horizontal moving that would occur if a whole skid were to come loose within a truck and move or drop.

One of the most unique analyses we perform is frozen impact testing. We conduct this test by filling our STA-PURE® Flexible Freeze Containers with a phosphate-buffered saline solution and freezing them in both blast and plate freezers until completely frozen. The filled and frozen containers showed no failures and maintained product integrity even after dropped from a height of 3 feet onto a concrete floor.

Choosing a packaging partner

When designing our fluoropolymer bags, we look at more than just the glass transition temperature. We use a full suite of testing to assure biopharmaceutical manufacturers that these advanced containment systems will reduce the risk of product loss during cold chain processing, storage, and transportation.

Our containers maintain integrity even in harsh conditions because of our thorough understanding of how single-use materials are affected by handling in the cold chain and our knowledge in how to manipulate the structure of PTFE to maximize durability at cold temperatures. Partnering with Gore for your container needs gives you access to a team of experts with years of materials science and experience in improving the processing and delivery of pharmaceutical products.

To learn more, visit https://www.gore.com/products/gore-sta-pure-flexible-freeze-container.

About Gore

W. L. Gore & Associates is a global materials science company dedicated to transforming industries and improving lives. Since 1958, Gore has solved complex technical challenges in demanding environments — from outer space to the world's highest peaks to the inner workings of the human body. For the pharmaceutical and biopharmaceutical industry, Gore is helping those in drug discovery and manufacturing compete in this increasingly regulated landscape with reliable solutions for purifying, transferring, storing, filtering, processing, and packaging. These solutions include durable, multi-use process components and single-use products that enable researchers and manufacturers to control costs through process improvements.

Gore PharmBIO Products

Our technologies, capabilities, and competencies in fluoropolymer science are focused on satisfying the evolving product, regulatory, and quality needs of pharmaceutical and bioprocessing customers, and medical device manufacturers. GORE STA-PURE Flexible Freeze Container, like all products in the Gore PharmBIO Products portfolio, are tested and manufactured under stringent quality systems. These high-performance products provide creative solutions to our customers' design, manufacturing, and performance-in-use needs.

NOT INTENDED FOR USE in medical device or food contact applications or with radiation sterilization.

All technical information and advice given here is based on our previous experiences and/or test results. We give this information to the best of our knowledge, but assume no legal responsibility. Customers are asked to check the suitability and usability of our products in the specific applications, since the performance of the product can only be judged when all necessary operating data is available. Gore's terms and conditions of sales apply to the purchase and sale of the product.

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PBI1662-R1-ARC-US-MAY22