Advanced Materials for Single-Use Biomanufacturing Systems

with Michael W. Johnson

Advanced fluoropolymer materials offer distinct advantages in single-use systems regarding chemical compatibility, extractable levels, and cold-temperature performance. In a 5 April 2017 webcast, Michael W. Johnson (business development engineering manager for life sciences at Entegris) examined data from pilot-scale testing of a new single-use bag system for freezing, storage, and shipping of formulated bulk biologics.

Johnson's Presentation

Factors restricting disposables use in biopharmaceutical development include bag breakage, concerns over extractables and leachables, and material incompatibility. Bioprocessors want new and improved plastics. Possible material innovations include homogeneous films that eliminate the lamination and adhesives of multiple layers. Such innovations can improve the cost-effectiveness of single-use technology.

Fluoropolymers were developed for challenging applications in which durability, inertness, purity, and cleanliness are important. These polymers retain their chemical inertness when exposed to strong acids and bases, salt solutions, alcohols, esters, and aldehydes. No other polymers can match their broad operating temperature range: 260 °C down to –240 °C.

Such advanced materials offer an advantage when it comes to extractables and leachables. Sources for detrimental extractables from typical polymers in single-use bags include oligomers; additives such as antioxidants, plastisizers, and lubricants; adhesives; and catalysts. The Aramus brand fluoropolymer uses no additives, adhesives, or catalysts and has a nearly nonexistent extractable profile.

Case Study: We tested the new Aramus single-use bag (made of a single layer of gamma-stable fluoropolymer film) for extractables and durability. To compare this bag with a typical multilayer polyethylene bag for extractables, we used an aggressive 100% ethanol reflux extraction process. The multilayer bag had 144× greater total organic carbon (TOC) than the fluoropolymer film. And an aggressive isopropanol reflux extraction process showed the multilayer bag having 60× greater TOC.

In durability tests, the Aramus bag either equaled or surpassed multilayer polyethylene bags. Both bags were equal in puncture strength and elongation at break. For tensile strength at break, the fluoropolymer film was 2–3× better; in haze testing, it was 2–5× clearer. In cold-crack testing (assessing the brittleness of plastic film and sheeting at low temperatures), the fluoropolymer bag far exceeded the polyethylene multilayer bag. A fluoropolymer film strip did not fracture or break during testing, even below –188 °C. Even after immersion in liquid nitrogen, the fluoropolymer film remained flexible and did not become brittle.

An independent test performed by PDS Labs assessed durability of bags made from different types of material. After several freezing and thawing cycles, bags were dropped from various heights and inspected for pinholes, rips, and tears. Only the Aramus fluoropolymer bag passed all temperature exposures (down to –85 °C), and it was the only one to pass a 1-m drop at –85 °C.

Fluoropolymers have nearly universal chemical inertness, enabling their use in a wide range of upstream and downstream applications. The absence of additives, processing agents, and adhesives greatly reduces extractables risk, especially in critical bulk-drug storage and final filling. The broad temperature range and robustness at cold temperatures provide high security for frozen drug products.

Questions and Answers

How does the Aramus bag tolerate autoclaving? The Aramus bag can withstand a typical autoclave cycle. The ability of the tubing and fittings to withstand autoclave conditions depends on those selected by end users.

Is this fluoropolymer a USP-class thick plastic? And is it gas permeable? The product is going through USP Class VI testing and is required to meet this. The Aramus bag has a higher permeation rate for gases than EVOH-based multilayer bags.

Fluoropolymer also is used as a material for disposable tubing. What advantages does it provide over silicone? End users specify the type of tubing that they would like on an Aramus assembly. Compared with silicone, fluoropolymer will be much cleaner from an extractable standpoint.

How does its gas permeability compare? The single homogeneous fluoropolymer film contains no EVOH layer for moisture/gas permeation. Moisture permeation is similar to that of a multilayer PE bag, but gas permeation is higher. To further quantify what this means to end users, Entegris has performed pH stability studies of frozen products in dry ice to check for CO_2 permeation. We will report those results in another webinar or at a conference in the next couple of months.

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