Resin selection to optimize the flexural strength of bioprocess film

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Resin selection to optimize the flexural strength of bioprocess film

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Abstract

Single-use bioprocess technology offers several advantages for manufacturing biopharmaceuticals, such as increased transportability of fluids throughout the bioprocess workflow and a greater diversity of systems to support specific unit operations (e.g., rocking bioreactors). However, due to the flexible nature of the plastic materials used to construct the single-use containers, the flexural properties of the bioprocess film are critical for performance in such applications. This poster focuses on how the resin selection and architecture of a bioprocess film can be optimized to maintain critical performance attributes, such as container integrity and gas barrier properties, under the significant forces during bulk liquid transportation and WAVE Bioreactor™ system applications.

Intoduction

Single-use bioprocess technology is becoming more mainsteam in the biopharmaceutical industry. However, there are a number of challenges that still remain, and system requirements continue to evolve. Over the past several years, materials of construction has been an area of focus due to observations of negative impact of extractable compounds from bioprocess film on the growth of certain sensitive cell lines (1, 2). As a result, the industry is now advancing toward developing single-use films that are better suited to fit the needs of biomanufacturing. Specifically, end users have communicated a need for improved film performance, a breadth of knowledge of material properties, with reliability of the supply. In order to achieve optimal performance of a film for bioprocess applications, it is important to map all of the required material performance attributes in applications across the entire bioprocess workflow. Designing a film with the right balance of attributes is key to achieving the desired performance.

Materials and methods

Material: Fortem™ film post-gamma irradiation (40-55 kGy). Control films are bioprocess films currently on the market.

Bis(2,4-di-tert-butylphenyl) phosphate (bDtBPP) analysis: Extractions in water at temperature = 50°C, surface area to volume ratio: 0.37 cm^2/mL, analysis with liquid chromatography-mass spectroscopy, limit of detection (LOD) and limit of qualification (LOQ): 2 ppb and 5 ppb, respectively.

Cell growth analysis: Test article: 2L containers made from Fortem film containing 200 mL of media (8 cm^2 of film/mL), control: media stored in glass containers. Control stored at 4°C for 7 days. Test containers rocked (6°, 20 rpm) for 3 days at 37°C and 4 days at room temperature (test and control protected from light). Three day cell culture with mAb-producing CHO DG44 cells in shaker flasks (initial viable cell density = 0.3×10^6 cells/mL). The CHO DG44 cell line is sensitive to bDtBPP down to 0.1 mg/L (100 ppb).

$$\text{Growth performance [\%]} = \left(\frac{PD_{bag}}{PD_{ref}}\right) \times 100$$

Materials selections

Fluid contact layer – polyethylene and cyclic olefin copolymer (COC)

- COC is compliant with EP 3.1.3, EP 3.1.5, JP 7.02, USP Class VI
- COC acts as macromolecular slip agent, eliminating need for traditional small molecule additives

Gas barrier – two different types of EVOH (alcohol substitution) incorporated into structure

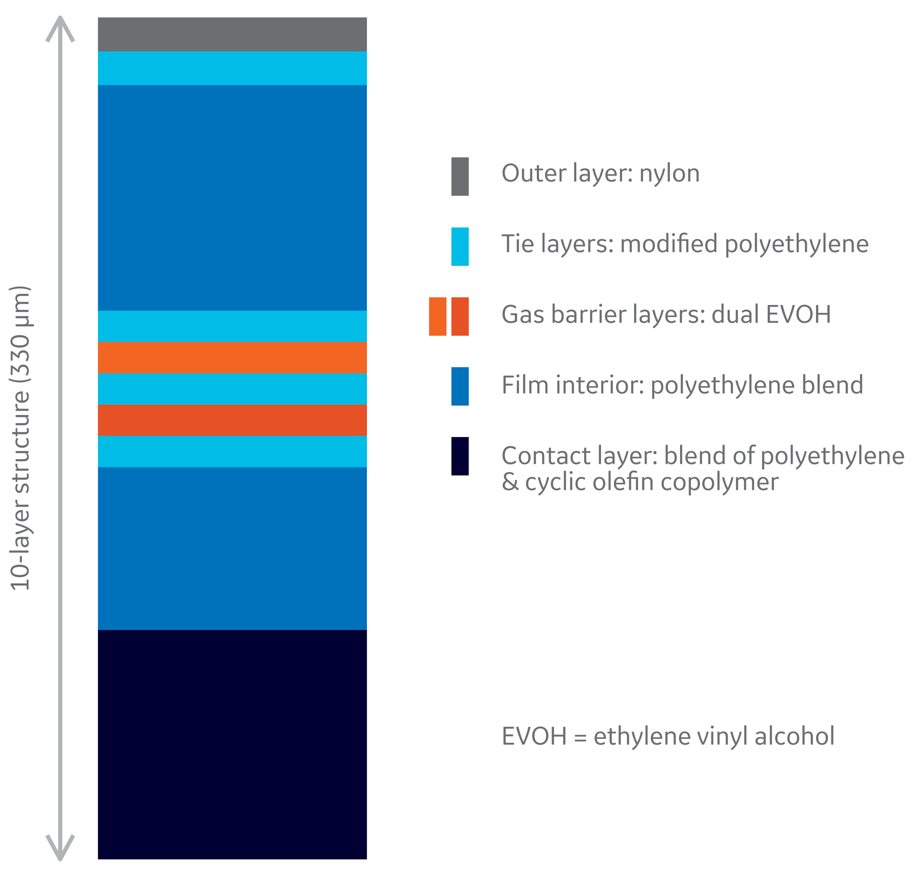
- Provides barrier to gases in both wet and dry conditions

Outer layer nylon and interior polyethylene blend

- Specific nylon chosen for outer layer to provide strength even in humid conditions
- Interior layers composed of polyethylene blend for robustness and flexibility over wide temperature range

Antioxidant package – selection of additives and placement in film optimized for minimal impact on mammalian cell culture performance

Fortem™ film sturcture

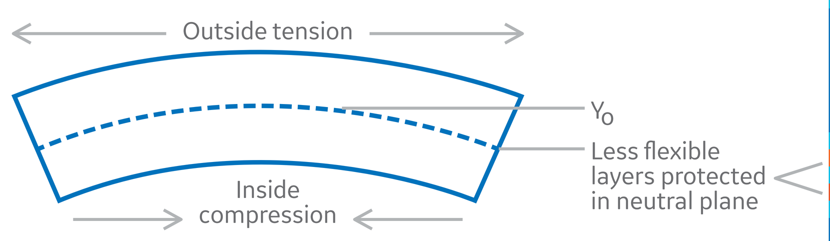


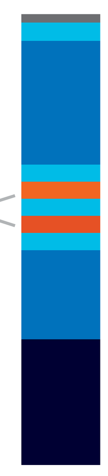
Co-extruded film manufactured in Class 8 cleanroom. Supplied as double ply; contact layer only exposed to Class 5 air (Sealed Air Corp. film design patent).

Connecting materials to architecture

Robustness vs flexibility: a challenge for rocking bioreactors and fluid transportation

Rocking motion and wave impact forces create unique forces on film.





$$y_o = \frac{1}{2} \times \frac{\sum_{i=1}^{n} E_i \times \left(h_i^2 - h_{i-1}^2\right)}{\sum_{i=1}^{n} E_i \times (h_i - h_{i-1})}$$

h – Layer thickness
E – Young's modulus
Y_O – Neutral plant

Translation of film design to performance

Improved extraction profile

Concentration of bDtBPP found in extract (ppb)

Sample	Day 3	Day 7
Control (glass bottle)	below LOD	below LOD
Control film 1	6000-6500	6000-6500
Control film 2	800-1000	800-1000
Control film 3	25-35	25-35
Fortem	**below LOD**	**below LOD**

Cell culture performance – Fortem

Population doubling (%)	Cell viability (%)
98 ± 3	94 ± 1

Summary

To keep pace with the needs of the biomanufacturing industry, the films used in single-use bioprocess technology should be purposefully designed for bioprocess applications. With the new Fortem film, the combination of resin selection and film architecture has been carefully selected and skillfully optimized to deliver innovation.

- Achieves critical to quality attributes across applications– selected data shown here.
- Meets industry needs (e.g., extractables data, supply chain transparency).
- Serves as a cornerstone technology for future advances in biomanufacturing applications.

References

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