

Monoclonal Antibodies in GALAXY Containers

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Abstract

Purpose: To develop a series of feasibility tests that can be performed with monoclonal antibodies to determine their suitability for packaging in flexible containers (GALAXY®).

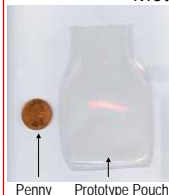
Methods: Prototype plastic flexible containers were fabricated from film samples, filled with antibody solution, sealed, and incubated at either 5, 25, or 40 °C. Antibody aggregation and total soluble protein were monitored over time using size exclusion chromatography with multi-angle light scattering (SEC-MALS). SEC separation was carried out using a Waters BioSuite 250 HR SEC 5 µm column (7.8 × 300 mm) at a flow rate of 1.0 mL/min with an analysis time of 16 minutes. The mobile phase was phosphate buffered saline, pH 6.8 – 7.2. Triple detection was accomplished using a Wyatt Technologies DAWN Helios multi-angle light scattering detector coupled with a Wyatt Technologies Optilab rEX differential refractive index detector and an Agilent 1100 Series variable wavelength UV detector. The pH of the antibody solution was tracked, and its potency was also measured using either a binding competition assay via flow cytometry with fluorescein-labeled antibody or ELISA. In addition to these analyses, some of the samples were analyzed using asymmetric flow field flow fractionation with multi angle light scattering (aFFF-MALS) using a Wyatt Technologies Eclipse 2 aFFF separations module.

Results: Antibody testing with SEC-MALS showed that the monomer content of the antibody remained at or above 98% in all of the film types tested, which was in agreement (to within 1%) with the aFFF-MALS data. Two of the four film types showed water vapor transfer losses, as indicated by an apparent increase in total soluble protein to as high as 140% of control values. The pH and binding activity of the antibody both remained nearly constant over the course of the study.

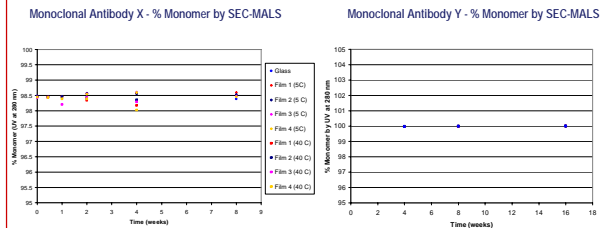
Conclusions: Monoclonal antibody therapeutics administered via IV infusion could potentially be provided in ready-to-use plastic flexible containers (GALAXY®) with appropriate container closures. Film compatibility was assessed with two commercially available monoclonal antibodies. The entire study was conducted using only 100 mL of each antibody solution. These results show that GALAXY® containers are suitable for monoclonal antibody therapy packaging.

Methodology

- Prototype pouches fabricated from plastic films allow for small sample volumes.
- Compatibility testing included:
 - SEC-MALS (aggregation, total soluble protein)
 - aFFF-MALS (comparison to SEC-MALS)
 - pH
 - Bioactivity assays (ELISA or binding competition assay)



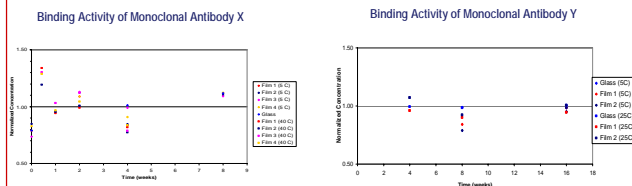
No Aggregation Over Time



Percent MAb X monomer remaining in solution after being held at 5 or 40 °C over time in four different films as well as a glass control as determined using SEC-MALS analysis.

Percent MAb Y monomer remaining in solution after being held at 5 or 25 °C over time in two different films as well as a glass control as determined using SEC-MALS analysis.

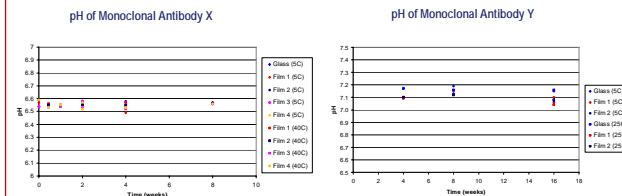
No Loss of Binding Activity



Binding activity (assayed using a competition binding assay) of MAb X after being held at 5 or 40 °C for 8 weeks in four different films as well as a glass control. The concentrations have been normalized to a time zero glass control and corrected for WVTR effects.

Binding activity (assayed using ELISA) of MAb Y after being held at 5 or 25 °C for 16 weeks in two different films as well as a glass control. The concentrations have been normalized to a time zero glass control and corrected for WVTR effects.

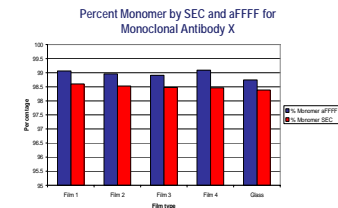
No pH Drift



pH of MAb X solution after being held at 5 or 40 °C over time in four different films as well as a glass control.

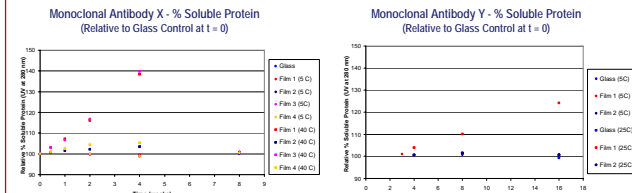
pH of MAb Y solution after being held at 5 or 25 °C over time in two different films as well as a glass control.

Agreement between SEC and aFFF



Percent monomer remaining in solution for MAb X after being held at 5 °C for 8 weeks in four different films as well as a glass control. The percentages were determined by analysis with SEC-MALS as well as with aFFF-MALS.

Tracking Water Loss by Protein Concentration



Apparent percent MAb X remaining in solution after being held at 5 or 40 °C over time in four different films as well as a glass control as determined using SEC-MALS analysis.

Apparent percent MAb Y remaining in solution after being held at 5 or 25 °C over time in two different films as well as a glass control as determined using SEC-MALS analysis.

Summary

The data collected in this study shows that monoclonal antibodies are compatible with GALAXY® containers as well as with other film types. When commercially available monoclonal antibody solutions are incubated in prototype containers, monomer content was at or above 98%. This data was collected with both size exclusion chromatography (SEC) and asymmetric flow field flow fractionation (aFFF). The two techniques were in agreement to within 1%. Also, the pH did not drift over time, the monoclonal antibodies did not lose biological activity, and two of the four films tested showed no water vapor transfer losses.