Gyrolab applications in industrial monoclonal antibody process development

Elisabeth Wallby, Elin Monié and Tomas Björkman
GE Healthcare Bio-Sciences AB, Björkgatan 30, SE-751 84 Uppsala, Sweden

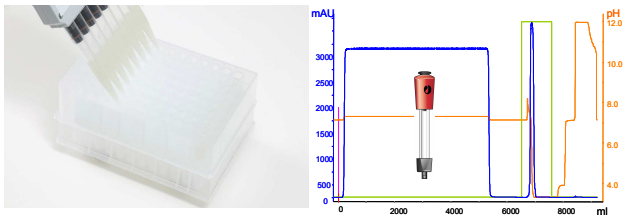
Background

Chromatography is the core technology for protein purification. Monoclonal antibodies (mAbs) are typically purified using Protein A based chromatography resin for capture followed by cation exchange (CIEC) and anion exchange (AIEC) chromatography for intermediate and polishing steps respectively. In these intermediate and polishing steps impurities such as host cell proteins (HCP), DNA, viruses and IgG aggregates are removed. The HCP concentration in samples from different stages of the purification process can be determined with Gyrolab Bioaffy™.

Antibody purification process development

Development of a chromatographic purification method is tedious with a large number of parameters that need to be optimized. It is desirable to systematically explore a number of different variables in a short period of time. 96-well plates containing chromatography resin can be used for high throughput screening (HTS) of different conditions. PreDictor™ plates, 96-well filter plates pre-filled with Capto™ and MabSelect™ chromatography resins are available for this purpose. Optimized conditions can then be verified using column chromatography.

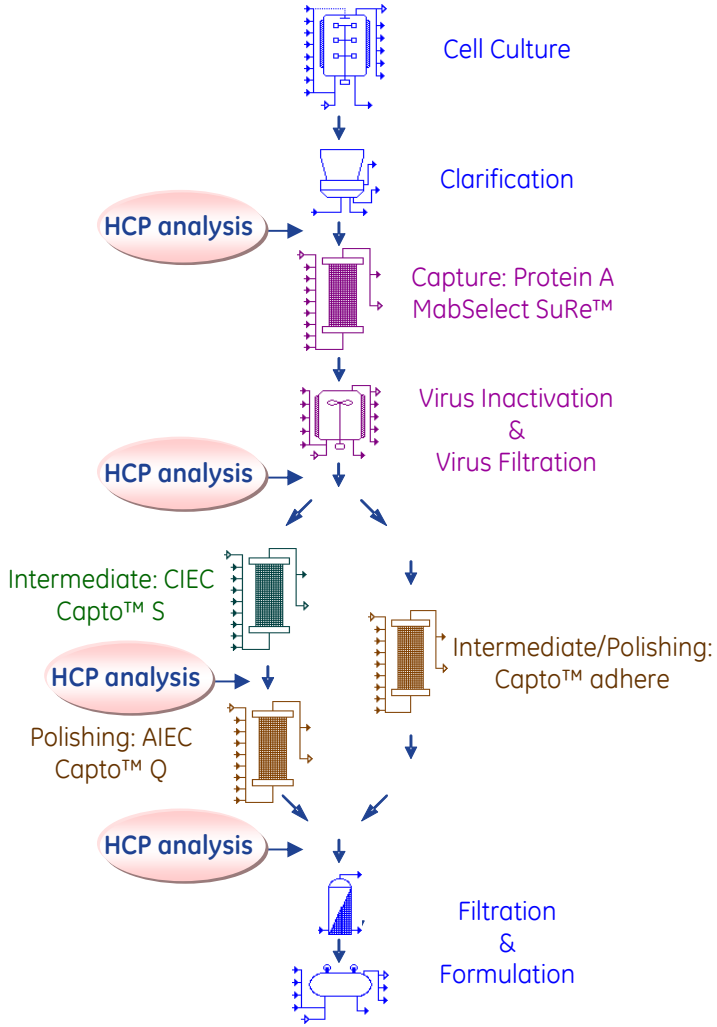
Process development in 96-well and column format



96-well format
≤96 operating conditions/2-3 hours

Chromatography
1 operating condition/2-3 hours

A mAb purification process



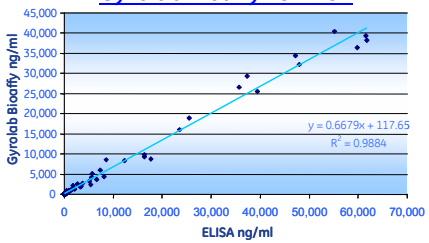
Comparison between Gyrolab Bioaffy and ELISA

ELISA is the golden standard for determination of HCP concentration from different steps in mAb purification processes. The ELISA is a time consuming and laborious method which often becomes a bottle neck in process development. Gyrolab™ Workstation on the other hand is a high throughput instrument that allows 112 data points to be processed in 50 minutes.

Gyrolab Bioaffy	ELISA
• Fast: 112 data points in 50 minutes	• Slow: 96 data points in > 5 hours
• Small sample volumes < 10µl	• Larger sample volumes > 200µl
• Small volumes -> low reagent costs	• Larger volumes -> larger reagent costs
• Reduced need of pre-assay dilution	• Requires accurate dilution of all samples
• Fully automated, less hands on time	• Demand for ELISA trained operator

A comparison between the two methods was done. Samples with HCP concentration measured with Gyrolab Bioaffy were subsequently analyzed in Cygnus HCP ELISA CM015. A good correlation between the two methods was obtained with the reagents used. However, the recovered HCP concentration with Gyrolab Bioaffy was lower compared to the ELISA.

Gyrolab Bioaffy vs ELISA



Conclusions

- The HCP concentration in samples from the different stages of a purification process can be determined with Gyrolab Bioaffy.
- The correlation between ELISA and Gyrolab Bioaffy is very good.
- PreDictor plates combined with Gyrolab Workstation allows high throughput screening of different conditions and rapid sample analysis.

imagination at work