Bioprocess development

The results presented in this section were generated in collaboration with AstraZeneca, Stellrakku, Sweden and with GE Healthcare, Tullinge, Sweden.

Conclusions

- Broader measurement range:
  - Quantification of monoclonal IgG and HCP at concentrations adequate for critical point processes from cell supernatant to purified product
  - Minimum need for pre-dilution
- The open platform makes it possible to adjust assay conditions, such as CD type and reagents, to suit analytical requirements
- Fully automated and avoidance of sample ‘hands-on’ time
- Excellent throughput with 112 data points generated in 60 minutes

Excellent correlation with HPLC and ELISA

Samples were run undiluted or diluted 1:2 or 1:4 in GE Healthcare’s original standard diluent, were spiked with drug molecules in concentrations ranging from <60 ng/mL to 1500 ng/mL. Excellent reproducibility and correlation with HPLC and ELISA were achieved (Figure 10) and are in line with previously published results. Excellent reproducibility and correlation with HPLC and ELISA were achieved (Figure 10) and are in line with previously published results.

Pharmacokinetics of therapeutic antibodies

The results presented in this section were generated in collaboration with a research group performing pharmacokinetics studies of therapeutic antibodies. This group has a deep understanding of pharmacokinetics in clinic and is able to provide insights into the behavior of monomeric antibodies in the body. The data presented here reflects their extensive experience in this field.

Quantification in cynomolgus monkey serum

Samples were collected using a protocol that allowed for the determination of drug concentrations in serum. The samples were run undiluted or diluted 1:2 or 1:4 in GE Healthcare’s original standard diluent, were spiked with drug molecules in concentrations ranging from <60 ng/mL to 1500 ng/mL. Excellent reproducibility and correlation with HPLC and ELISA were achieved (Figure 10) and are in line with previously published results. Excellent reproducibility and correlation with HPLC and ELISA were achieved (Figure 10) and are in line with previously published results.

Automated protein quantification in bioprocess development and pharmacokinetic studies: Improving assay performance

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Introduction

Gyrolab Bioaffy – Single system solution

Gyros offers a unique set of analytical tools to address customer applications within biopharmaceutical development.

The automated solution facilitates protein quantification with a measurement range from micromg to grams per litre. Thus, the need for pre-dilution is minimized.

Examples of customer applications using Gyrolab Bioaffy:

- Quantification of drug product
- Quantification of host cell protein
- Quantification of drug molecule in serum and plasma
- Quantification of anti-drug antibodies (ADA)

Assay methods

The principle for miniaturization and integrating assays on Gyrolab Bioaffy is illustrated in Figure 1. A fully automated instrument is able to process different CD microstructures.

- Gyrolab Bioaffy 20 HC in quantification up to the g/L-range
- Gyrolab Bioaffy 200 in high sensitivity assays

The novel design principles underlying the Gyrolab Bioaffy format facilitate quantification of any target protein for which monoclonal antibodies can be developed and antibody reagents are available up to 20 mg/ml.

Experimental

CD microstructures are used in Gyrolab Bioaffy. Matrix effects and reagents are transferred semi-automatically to provide a high-throughput solution. Liquid phase quantification by automated action and the reagent release are defined within column microstructures, samples and reagents are moved through the microstructure by opening the CD at pre-programmed intervals and speeds to create the desired flow rates. Detection begins as soon as the reactions are completed using a laser-based fluorescence detector integrated at the workstation. Then, an automated vacuum arm moves CDs for analyzing in parallel.

CD microlaboratories can be used in Gyrolab Bioaffy set-up automatically and the reagents results in a measurement range covering three orders of magnitude, allowing for quantification of drug product and contaminants is essential for efficient biotherapeutic development and pharmacokinetics. Current technologies, such as ELISA and IAC, are able to deliver good quality results. However, in several cases of high concentrations of proteins, such as HCP in the biopharmaceutical industry, using the Gyrolab Bioaffy CD microstructures provides an extended measurement range. See Figure 4 for an illustration of how analytical support in the different stages of biotherapeutic development.

Bioprocess development

The approach presented in this section were generated in collaboration with AstraZeneca, Stellrakku, Sweden and with GE Healthcare, Tullinge, Sweden.

Gyrolab Bioaffy 200 (crosses) and Gyrolab Bioaffy 20 HC (boxes) were used for first quantification up to the g/L-range.

The open platform makes it possible to adjust assay conditions, such as CD type and reagents, to suit analytical requirements.

Fully automated and avoidance of sample ‘hands-on’ time.

Excellent throughput with 112 data points generated in 60 minutes.

Excellent correlation with HPLC and ELISA

Samples were run undiluted or diluted 1:2 or 1:4 in GE Healthcare’s original standard diluent, were spiked with drug molecules in concentrations ranging from <60 ng/mL to 1500 ng/mL. Excellent reproducibility and correlation with HPLC and ELISA were achieved (Figure 10) and are in line with previously published results.

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