

## PPROCESS ANALYTICAL TECHNOLOGIES FOR A CONTINUOUS CAPTURE AND CONNECTED DOWNSTREAM PROCESS

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As we move towards the implementation of continuous and connected processes, it becomes apparent that we can no longer avail ourselves of traditional sampling points (pools). Therefore, the implementation of Process Analytical Technologies (PAT) to demonstrate process robustness or to monitor process consistency, becomes necessary. Methodologies to monitor mass and yield are still necessary and the need to have at- or on-line analytics becomes more real. In-between, it may be necessary to bridge between the traditional analysis of unit pools to a more dynamic process monitoring.

Recovered product mass and step yields per unit operation are commonly used to monitor process robustness. This is however more challenging in a connected/continuous mode, where there are no longer pools. The presented approach will demonstrate how UV absorption measurements can be utilized to track yield and to show process consistency. To tackle the issue of signal saturation, variable pathlength measurements as well as UV measurements at 300 nm were used. While univariate UV measurements were used for post-Protein A steps, multivariate measurements in conjunction with Partial Least Squares Regression modelling were evaluated for mass tracking in harvest.

The monitoring of quality attributes within continuous processes also requires an adapted approach. The most straightforward approach in this context is the automation of already existing assays. The poster will present how the turnover time of an offline SEC assay was reduced to 1 min and how the method was applied for automated aggregate analysis. Furthermore, it will be shown how an Online-UPLC assay was used to control the aggregate level in chromatography runs with variable column load densities and aggregate levels in the load.

Until at- or on-line analytics can be developed for all critical quality attributes, a bridging method is required. Here, a testing strategy based on pseudo-product pools will be presented, which allows bridging of quality data from a continuous process stream to a traditional standard batch pool concept. Slip stream pumps were used to generate pseudo pools, whenever product pools were not available. It was demonstrated, that the pseudo pools are representative and that the data is applicable for statistical comparison with historical batch data.