DESIGN & CONSTRUCTION OF A TRULY CONTINUOUS AND FULLY AUTOMATED PROCESS SKID FOR THE PRODUCTION AND PURIFICATION OF A MONOCLONAL ANTIBODY

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The objective of this project is to design and construct a process skid which allows 20+ days of continuous production and purification of an industrial relevant monoclonal antibody.

The underlying concept of this end-to-end processing skid divides the process train into three major units, the cell culture, the capture and the polishing unit. The first one represents a perfusion system with a tangential flow filtration for cell retention. The capture unit consist of a continuous precipitation and redissolution step including a low-pH virus inactivation. The last one consists of several flow through methods. All units are directly connected with each other allowing a real continuous mass flow with the narrowest possible residence time distribution. The mentioned showcase utilizes a CHO cell line recombinantly producing anti-HER2.

For the first two units we developed the process layout, control algorithms, monitoring concepts and the showcase for the process itself. A major focus was laid on designing a functional closed system, allowing In-Process Maintenance to keep the system running without any sterility issues. In a first step, a lab-scale prototype, a 2 L cell culture unit in combination with a semi-automated capture unit, was built up. This setup were kept running continuously for 6 days in steady state and high yields of ~90% were achieved. Currently we are focusing on the construction of a fully automated pilot scale version (10 L/d) for the first two units. This shall allow us to achieve the desired target of 20+ days of continuous processing without mass flow interruptions.

This study shall highlight the potential but also the issues and challenges in designing and constructing such an integrated continuous process skid.