HIGHLY AUTOMATED BIOBURDEN-FREE CONTINUOUS MANUFACTURING BIOLOGICS GMP OPERATIONS: HOW TO GET THERE?

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Standard batch monoclonal antibody biologics manufacturing processes are costly and time-consuming. A switch to intensified continuous processing enables much higher productivity, notably > 1.5 g/L/day over 25+ days of bioreactor and 17+ days of downstream operation.

Our innovative platform has been tested across multiple scales and locations. It automatically operates end-to-end between staggered startup and shutdown operations. After the upstream process starts and specific thresholds are reached, the downstream process is automatically initiated. When stable mass throughput is achieved, the next unit operation begins.

After gaining experience during 50L end-to-end runs and multiple 500L engineering runs across different sites, two GMP continuous manufacturing runs were successfully completed. These runs were performed within a shared facility with ongoing GMP fed-batch production, which was able to continue with no clinical supply interruptions.

A major achievement was to complete these end-to-end runs intervention in a fully automated manner with little manual intervention and reduced number of quality critical alarms. In addition, aseptic operations in the bioreactor and low bioburden conditions in downstream were achieved thanks to aseptic shopfloor operations. Sterile sampling, assembly-column-filter manifolds, and pre-use sanitization procedures were all found to be critical to maintain a controlled bioburden environment.

Less tangibly, the diligent planning and partnerships behind this milestone showcase the importance of having key organizational tools in place including an assembly/component tracker, a master sampling plan and daily ground plans. These tools alongside the strong collaboration required between process, analytical and automation teams are essential to succeed in establishing future continuous manufacturing teams.
Lessons learnt from these first two GMP continuous manufacturing runs will be directly leveraged and used to project process, automation, and analytical requirements for next generation commercial facilities. Facility design strategies including modularity, flexibility, ‘lights-out operation’, and reduced scale will be key concepts for future highly automated and intensified processes.