IMPLEMENTATION OF AN END-TO-END CONTINUOUS BIOPROCESSINGPLATFORM USING NOVEL TECHNOLOGIES

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One significant opportunity for evolutionary change in the biopharmaceutical industry is the widespread adoption of integrated continuous bioprocessing for biologics manufacturing. Key to its success is the availability of novel upstream and downstream technologies that will not only reduce facility footprint, capital expenses and product cost of goods (CoGs), but also will increase process productivity, flexibility and further facilitate the utilization of single-use and/or disposable technologies.

In this context, the suite of cutting-edge technologies we have evaluated to enable cost effective and reliable implementation of continuous bioprocessing of biological drugs, included the Cadence™ Acoustic Separator exploiting acoustic wave separation technology (AWS), Cadence Inline Concentrators within the single-pass TFF (SPTFF) platform, the Cadence BioSMB PD multicolumn continuous chromatography platform using a KANEKA KanCap A™ based platform and novel continuous diafiltration strategies, to address the innovation gap to provide a simplified solution for the continuous final formulation step.

By utilizing a 20L CHO fed-batch cell culture bioreactor with cell density range of $25x10^6$ – $30x10^6$ cells/mL and 65 to 90% cell viability, multiple in-house feasibility runs were conducted through a novel integrated continuous bioprocessing train of unit operations. For instance, while achieving ≥90% continuous clarification yield for the processing of a batch with 1.25 g/L titer, $25x10^6$ cells/mL & ~70% viability this new process platform was able to deliver ≥ 2 g/h mAb for the continuous purification train utilizing a stable 4-fold continuous concentration step for the integration of continuous clarification and continuous capture trains.

We further intensified the process and by running over a 24h period we were able to purify in excess of 100g mAb over this period giving a productivity of this integrated system of ~124g mAb per day. This was carried out in a dedicated Continuous BioProcessing facility within a footprint of just $36m^2$.

With the coupling of the novel continuous clarification, continuous capture, continuous virus inactivation, continuous polishing, continuous viral clearance and continuous final formulation steps, in this platform, using current PD-scale bioreactors, we have demonstrated end-to-end continuous biomanufacture that will generate 1-5 g/h mAb. This presentation will provide a risk-based and data-driven overview of an integrated continuous bioprocessing platform and highlight the requirements, challenges and opportunities for product development, process monitoring, validation, control and automation.