Evaluating In-Line Volume Reduction using Single-Pass TFF during mAb Production

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In-line concentration using single Pass TFF solves problems found in mAb production, including insufficient storage capacity and process tank volumes, extended process times, and large hold-up loop volumes for UF concentration. This optimizes the ion-exchange step following capture, reduces costs and process times for virus filtration and polishing, and significantly improves the UF/DF yield, all without large hardware investments. Biopharmaceutical manufacturers are under pressure to reduce costs and increase the robustness and flexibility of their manufacturing operations. Optimization of downstream purification steps is required to achieve these goals. In-line concentration of dilute solutions prior to various downstream unit operations, can result in both cost and time efficiencies. This study investigated the performance and scale-up possibilities for in-line concentration on a mAb production platform using a patented SPTFF technology approach designed by Pall Life Sciences for a simplified control scheme with a fixed retentate resistor known has Inline concentrator (ILC).

For the tested mAb, the in-line concentration process performed in the present study reduced the capture step pool volume by a factor of 3X or 4X. The ion exchanger pool was reduced by a factor of 3X. Notably, the in-line concentration performance was affected by the conductivity (salt concentration) of the chromatographic pools. At the same feed flux, adding salt to increase the capture step pool conductivity to 20 mS/cm increased retentate concentration to nearly twice that without salt. Conversely, removing the salt from the ion exchanger pool via DF significantly reduced concentration. For final concentration after the UF/DF step, this study's in-line process increased a 50 g/L mAb solution to a final concentration of > 100 g/L in a single pass. It was also shown that controlling in-line concentration by the feed flux provides a robust dampening effect for small variations in the feed product concentration. If the processing objective is to obtain a similar retentate concentration, the feed flux should be the controlling parameter. If the aim is to obtain

a similar VCF, the feed concentration and the mass throughput should serve as the controls.

The study was made in collaboration with Novo Nordisk.