DESIGN OF A GMP-READY SINGLE-PASS TANGENTIAL FLOW FILTRATION (SPTFF) AND INLINE DIAFILTRATION (ILDF) SYSTEM FOR CONTINUOUS MANUFACTURING OPERATIONS

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Intensified continuous manufacturing (CM) processing enables significantly higher volumetric productivity than a traditional batch/fed-batch approach with 2 to 5-fold higher cell density, extended cultivation duration and greater mass throughput. Its adoption in the biopharmaceutical industry is being driven, among other factors, by cost reductions per gram of protein and the potential for fully automated single-use end-to-end operations. One key difference of CM compared to traditional processes lie in the final ultrafiltration/diafiltration step. This unit in CM, often overlooked yet ‘under-developed’, is a highly complex and manual operation. Typically, two separate filtration modules are required: a single-pass tangential flow filtration (SPTFF) module for volume reduction/concentration and an inline diafiltration (ILDF) module for buffer exchange.

This work covers the multiple iterations of SPTFF/ILDF technologies at Merck, from initial prototypes in development lab operations to the transition to GMP operations at 500L scale. Multiple internal groups across several sites were engaged along with a third-party vendor to build upon the knowledge gained in these runs and work towards a commercial SPTFF/ILDF skid design.

This work was done in an accelerated timeframe (<10 months) from proof of concept to site acceptance test (SAT) execution. Informed fast decisions on single-use consumable design, P&ID drawings, automated sanitization and process flow schemes, and choice of skid component will be covered here.

This work covers the culmination of years of work across sites and scales by many team members, with the end goal of designing and commissioning a highly flexible scale-agnostic future-proof continuous UF skid.