ENABLING END-TO-END CONTINUOUS BIOMANUFACTURING BY EXPLORING INTEGRATION APPROACHES OF CONTINUOUS TFF

Dejan Arzensek, Novartis Technical Operations - BTDM Menges, Lek Pharmaceuticals d.d., Menges 1234, Slovenia
dejan.arzensek@novartis.com

Key Words: continuous, UF/DF, SPTFF, disposable, biopharmaceuticals

The Downstream Processing (DSP) production/process line comprises of several chromatographic process unit operations (techniques for protein isolation and purification), several liquid filtrations process unit operations and final Ultrafiltration/Diafiltration (UF/DF) process unit operation (process for product concentration to the desired final protein concentration and for exchange into final formulation buffering condition). UF/DF step is conventionally performed with the batch tangential flow filtration (TFF). However, several pump passes and a recirculation skid are required to achieve the target concentration in conventional TFF. Thus, it is impractical to implement batch TFF as continuous UF/DF step or in-line concentration step between different DSP chromatographic steps.

In this work the use of single-pass tangential flow filtration (SPTFF) will be examined as continuous TFF step and as the integrational process unit operation allowing both final UF/DF step and in-line protein concentration before chromatographic step. SPTFF integration approach will be explored as continuous TFF delivering a new robust solution with a potential to overcome manufacturing bottlenecks and thus enabling the end-to-end fully continuous biomanufacturing. In this study, the process stability, volumetric concentration factor (VCF) ranges, and process economics of operating SPTFF as continuous in-line UF/DF will be explored in detail. Additionally, the placement of the SPTFF before Protein A capture chromatography unit operation will be explored. This allows coupling of these two steps and as such the potential solution to overcome low and variable protein concentration in the harvest to intensify continuous process. Limitations and requirements for a continuous TFF will be identified. Unique challenges to use technology in a fully continuous UF/DF process step, which is at an earlier phase in development, will also be presented.

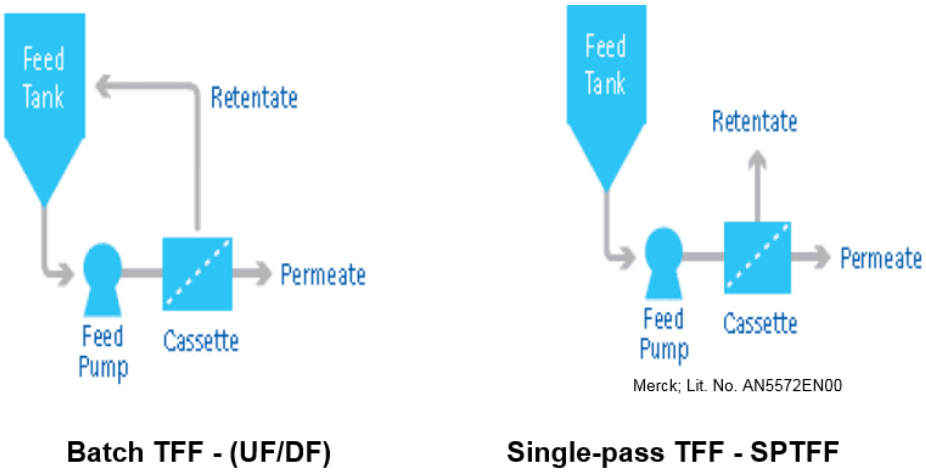

Figure 1: Comparison of batch UF/DF vs. continuous single pass TFF (SPTFF)

Acknowledgements:
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 635557.