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Process Robustness and Cell Line Variation in N-1 High Density Perfusion System

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In newly developed Biogen manufacturing processes, we are using perfusion technology to shift the cell growth phase into the seed train from the production reactor. This change improves facility throughput 30% by reducing time within the production bioreactor. In order to implement this approach, a hollow fiber based tangential flow filtration (TFF) system has been utilized in both lab and manufacturing settings. In defining the laboratory scale model, a case study showed that inadequate pumps and tubing can result in significant cell damage which was only observed at high cell densities. After integrating the non-spallation tubing with peristaltic pump, a TFF perfusion bioreactor can work as well as ATF system (Alternate Tangential flow filtration). To ensure successful scale-up, we also assessed the impact of volumetric throughput, hydrodynamic shear, and perfusion medium feeding strategy within laboratory experiments. Process robustness were also evaluated including cell damage from high sparging, the impact of low mass transfer capability and the extended residence time during recirculation. Given the associated capital costs and long term production needs, assessing the robustness of the approach for inclusion in current and future programs becomes critical. Work on several CHO cell lines has begun in order to compare the cellular response to the addition of this step. Within this work, we will present a perfusion TFF model for scale up of cells in the N-1 bioreactor and report on methods assessing its suitability as a platform approach.