CLONE SELECTION AND PROCESS LEVER OPTIMIZATION USING AN AMBR® 15 SYSTEM FOR CONVERSION OF A ROLLER BOTTLE PROCESS TO A SUSPENSION, PERFUSION BIOREACTOR PLATFORM

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Due to the high capital costs for a new roller bottle facility, a new suspension bioreactor perfusion platform was pursued as a potential option to improve the supply network for an existing commercial roller bottle cell culture process. The first step in developing the bioreactor process was the adaptation of the current commercial working cell bank to serum-free, suspension conditions. Subcloning of this serum-free, suspension adapted pool was performed to reduce the pool to the top 50 clones based on titer and activity. In deep well plates and shake flask cultures, the top 50 clones were further screened to yield the top 10 clones based on yield, activity, and important product quality attributes including sialylation and Mannose-6-Phosphate (M6P) content, which were determined by high throughput analytical methods specifically designed for this molecule. In parallel with these activities, an ambr® 15 perfusion scale down model was developed to evaluate multiple process levers (e.g. medium osmolarity, target viable cell concentration, cell specific perfusion rate, etc.) for the serum-free, suspension adapted pool using definitive screening designs. After ambr® 15 scale down model development, the Top 10 clones identified in subcloning were evaluated in the top conditions identified from the process lever optimization study. Several of the best combinations of clones / bioreactor conditions were then repeated in 10L bench scale bioreactors to ensure reproducible cell culture performance. Furthermore, the 10L cultures were harvested and purified to mock drug substance to confirm significant product quality attributes were consistent between the ambr® 15 scale down model and bench scale bioreactors and within desired commercial specification ranges. These results suggest that the ambr® 15 perfusion scale down model can be deployed for clone selection, process optimization, and process characterization activities for the current suspension, perfusion bioreactor process, as well as development of future perfusion processes, to ensure successful launch at large scale.