

INTENSIFICATION OF A MULTI-PRODUCT PERFUSION PLATFORM THROUGH MEDIUM AND PROCESS DEVELOPMENT

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Integrated Continuous Biomanufacturing (ICB) provides many important strategic advantages for therapeutic protein production through process intensification, simplification and integration. The success of this technology will be significantly enhanced by the platform's ability to push towards high productivity in conjunction with minimizing the associated perfusion rate, resulting in dramatic reductions in cost of good manufactured. We have previously demonstrated that an in-house chemically defined medium can support cell densities exceeding 100 million viable cells/mL in 10L perfusion bioreactors with an average productivity of 2 g/L/day. Further optimization utilizing high throughput technology specifically tailored to improve cell specific productivity (SPR) resulted in an intensified medium that is capable of achieving greater than 2X increase in SPR while maintaining low cell specific perfusion rate (CSPR). When combined with process knowledge and efforts to improve shear protection in a high oxygen demand environment, we were able to achieve 4 g/L/day volumetric productivity of an IgG for over 30 days in a state of control. In this talk, recent case studies on the application of this intensified perfusion platform to cell lines producing different classes of biologics will be described, effects on product quality will be illustrated, and engineering and economic considerations for commercial scale will be discussed.