

MARCHING TOWARD IMPLEMENTATION OF AN ULTRA-HIGH DENSITY DYNAMIC PERFUSION PROCESS

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The tremendous interest and momentum gained in integrated continuous biomanufacturing (ICB) process as the next generation manufacturing platform for our industry needs no further explanation or justification. Many companies have developed their own version of ICB processes, with various implementation strategies based on one's specific drivers and priorities. In the past 6 years, Boehringer Ingelheim has been in collaboration with Pfizer to co-develop an integrated continuous biomanufacturing system, iSKID™.

A highly intensified short-term dynamic perfusion process was developed at BI with similar culture duration as any typical fed-batch process. The intensified process utilized concentrated media at low volume to overcome the large media usage challenge inherited from historical perfusion processes. By utilizing concentrated media, our process requires only 0.5 vvd (volume of media per bioreactor volume per day). Average volumetric productivity up to 4 g/L/d, with a peak reaching up to 5 g/L/d, was accomplished in a 14-day perfusion process. This process was demonstrated at bench-scale, as well as pilot scale, and was successfully reproduced in multiple cell lines to ensure that the platform is widely applicable. In this case study, we will walk through the steps we took to develop and demonstrate a scalable upstream perfusion process that was comparable to our large-scale fed batch processes. This work has opened the door to various paths of implementing ICB processes in biologics production.