

PROCESS OPTIMIZATION FOR HIGH VOLUMETRIC PRODUCTIVITY WITH PRODUCT QUALITY CONTROL

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High commercial demands of biotherapeutics require high volumetric productivities to accommodate their production with the existing manufacturing infrastructure. While titers are exceeding 5 grams per liter in fed-batch processes, it is imperative that these processes result in consistent and desirable product quality. Here we describe a fed batch process optimization effort resulting in significant increased titer than the initial process. During the optimization, we identified a medium component capable of impacting productivity and two different critical product quality attributes. Through complex screening, the component concentration was shown to be proportional to these product quality modifications in opposing directions, thereby requiring a careful optimization of the delivery range. One of these modifications was recapitulated in a cell free system with media and protein indicating that this was not a result of shift in cellular metabolism unlike the other modification. The mechanism of action and strategies to mitigate this issue were also evaluated. Through this work, a well-controlled process without impacting productivity during large scale manufacturing was designed.