

Spring 5-12-2016

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Recommended Citation

Yang Wang, Shawn Barrett, Borka Naumovich, Jessica Nichols, and Steve Gorfien, "Perfusion media development and evaluation with spin tube and ambr15 highthroughput small-scale models" in "Cell Culture Engineering XV", Robert Kiss, Genentech Sarah Harcum, Clemson University Jeff Chalmers, Ohio State University Eds, ECI Symposium Series, (2016). http://dc.engconfintl.org/cellculture_xv/154

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PERFUSION MEDIA DEVELOPMENT AND EVALUATION WITH SPIN TUBE AND AMBR15 HIGH-THROUGHPUT SMALL-SCALE MODELS

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Key Words: perfusion media, CHO-S cells, batch-refeed, ambr15

For over 75 years, continuous manufacturing has been investigated in both academia and industry as an alternative to batch manufacturing. Perfusion is a well-recognized method for continuous production of biomolecules expressed in CHO cell culture and it is known to have certain advantages over batch and fed-batch processes. The major advantage of perfusion processes is that a constant environment is provided to cells through continuous by-product removal and nutrient addition. However, it has proven to be challenging to apply high-throughput approaches routinely used in fed-batch process development while maintaining true continuous culture, and so semi-continuous methods have instead been pursued for perfusion process development. In an effort to confirm how effective each method could be for early process development or as a quick perfusion applicability test for a particular clone, a media panel consisting of ten candidates was developed. In this study, several established high-throughput small-scale models, comprising batch-refeed cultures in spin tubes (Corning® 50mL Mini Bioreactors) and two semi-continuous methods in ambr15™ microbioreactors, were applied to evaluate the performance of the perfusion media panel candidates for up to 18 days with a recombinant CHO cell line expressing IgG. Different observations resulted from the three different approaches, but in each case a simulated steady-state was achieved for several key indicators such as cell density and product titer. Best results were seen in the spin tube batch-refeed process, where a medium exchange strategy of 63% per day was used to mimic metabolic by-product removal of 1 reactor volume per day (RVD). For the spin tube method, viable cell densities up to 30 million vc/mL were observed and the highest daily IgG titer of 525 mg/L ($q_p \sim 14$ pg/cell/day) was achieved with perfusion medium 6 (PM6). Additional verification studies to confirm these findings in small-scale perfusion bioreactors will also be discussed.