Fall 11-2-2015

Innovations in bioreactor operational modes – Hybrid semi-continuous processes to push beyond the limits of conventional fed-batch cultures

Gregory Hiller
Pfizer, gregory.hiller@pfizer.com

Matthew Gagnon
Pfizer

Ana Maria Ovalle
Pfizer

Wenge Wang
Pfizer

Elizabeth Eydelman
Pfizer

INNOVATIONS IN BIOREACTOR OPERATIONAL MODES – HYBRID SEMI-CONTINUOUS PROCESSES TO PUSH BEYOND THE LIMITS OF CONVENTIONAL CULTURES AND DOVETAIL WITH CONTINUOUS DOWNSTREAM OPERATIONS

Gregory Hiller, Pfizer, Inc.
gregory.hiller@pfizer.com
Matthew P. Gagnon, Pfizer, Inc.
Ana Maria Ovalle, Pfizer, Inc.
Wenge Wang, Pfizer, Inc.
Elizabeth Eydelman, Pfizer, Inc.

Key Words: Hybrid continuous processes

Due to the limits of feed volume addition and the problem of amino acid counter ion, miscellaneous osmolyte, and cell growth inhibitor accumulation, the fed-batch mode of bioreactor operation for CHO cell production of protein therapeutics is inherently limited with respect to the cell densities and productivities that are achievable. Continuous or perfusion culture with cell retention can overcome some of these limitations, but suffers from the disadvantages of large volume media consumption, long times to reach peak cell densities, and complications with cell retention devices. We will describe hybrid versions of continuous culture that overcome many of these limitations and utilize a unique and simple technology which allows cells to control their own rate of perfusion with continuous feedback. Volumetric productivities of greater than 1 gram/L/day (more than double the optimized fed-batch culture) for several moderate specific productivity cell lines have been achieved with very modest medium volumes, comparatively simple bioreactor operations, and a batch length that fits in a standard fed-batch window. Methods of operation and experimental results obtained at the pilot scale when coordinating these hybrid continuous cultures with a continuous downstream process will also be discussed.

Figure 1 – Arial 10 pt Italics