Spring 5-11-2016

Performance consistency of fed-batch cultures across multiple systems used in upstream process development

Matthieu Stettler
Merck Serono, matthieu.stettler@merckgroup.com

Jean Marc Bielser
Merck Serono

Yolande Rouiller
Merck Serono

Martin Jordan
Merck Serono

Herve Broly
Merck Serono

PERFORMANCE CONSISTENCY OF FED-BATCH CULTURES ACROSS MULTIPLE SYSTEMS USED IN UPSTREAM PROCESS DEVELOPMENT

Matthieu Stettler, Merck Serono SA, Switzerland
matthieu.stettler@merckgroup.com
Jean-Marc Bielser, Merck Serono SA, Switzerland
Yolande Rouiller, Merck Serono SA, Switzerland
Martin Jordan, Merck Serono SA, Switzerland
Hervé Broly, Merck Serono SA, Switzerland

Key Words: Screening and selection, clonal cell lines, high-throughput,

Each stage of cell culture process development requires fit for purpose tools. The selection of a fed-batch cultivation system is often based on throughput and cost. However, the process knowledge derived from different systems and scales is not necessarily identical. Hence, a careful evaluation of systems which are already established or newly implemented is essential. We recently introduced a novel high throughput fed-batch screening system (1) and the objective of this study was to provide data on how it compares with other systems used in early and late stage cell culture process development. We describe the performance of 12 different recombinant CHO cell lines expressing the same antibody in fed-batch culture systems ranging from a few hundred microliters to lab scale. The 12 cell lines were selected based on distinct phenotypes covering a range which can be expected in typical industrial process development projects. The cell lines were cultivated using the same expansion and fed-batch protocol (proprietary fed-batch system). The following cultivation systems were evaluated: shaking 96-deepwell plates, 50 mL vented shake tubes, micro-scale bioreactors (ambr15^{TM} system) and lab-scale bioreactors (3L). The results of this study show both the limitations and the potential of each cultivation system and their suitability for process development, process characterization and scale-up. The shaking systems offer unprecedented parallel throughput but are limited with respect to culture control (e. g. lack of pH and pO_2 control). Despite their limitations, they are expected to be used in the future as important tools for early process development and for the improvement of fed-batch platform processes. On the other hand, the data obtained from this study show that micro- and lab-scale bioreactors represent ideal tools for the confirmation of process consistency. Both micro- and lab-scale systems will be extensively used in the future to support tech transfers and perform process characterization studies.

(1) Rouiller Y. et al. Modulation of mAb quality attributes using microliter scale fed-batch cultures. Biotechol Prog 2014, 30(3):571-83.