EVALUATION OF CELL CULTURE WITH A SIMULATED CONTINUOUS MANUFACTURING (sCM) PROCESS IN 50mL TUBESPINS FOR CLONE SCREENING

Natalia Gomez, Drug Substance Technology, Amgen, Thousand Oaks
nagomez@amgen.com
Jonathan Lull, Drug Substance Technology, Amgen, Thousand Oaks
Mike Pritchard, Drug Substance Technology, Amgen, Thousand Oaks
Kristi Daris, Drug Substance Technology, Amgen, Thousand Oaks

Key Words: simulated perfusion, clone screening

Continuous Manufacturing (CM) is a process where perfusion cell culture for >30 days is performed with a pre-defined constant biomass set point achieved by bleeding extra cells from the bioreactor (BR). Requirements for cell lines cultured in CM include: (1) good growth to achieve biomass set-point and maintain viability >90%; (2) constant cell-specific productivity as function of culture time (and consequently, volumetric productivity); and (3) constant product quality as function of culture time. In comparison to traditional batch or fed-batch cultures, early screening of numerous clones for a CM process may need to include further evaluation of these three additional attributes to better choose the top performing clones in a CM-like culture. With this purpose, we evaluated a small-scale simulated CM process (sCM) in 50mL Tubespins to screen up to 20 different clones simultaneously. This sCM small-scale model mimics a BR CM process with a simulated perfusion via daily medium exchange. Additionally, sCM can match the cell-specific perfusion rate (CSPR) in the CM BR and includes a discrete daily manual bleed to maintain a target cell density.

We performed two sets of experiments to determine sCM performance including (1) evaluation of 16 cell lines expressing a model molecule and cultured in both sCM and small-scale fed-batch process, and (2) evaluation of 5 clones in both sCM and 2L CM BR. Our results indicate clone ranking accordingly to product quality is comparable between small-scale fed-batch and sCM, but ranking accordingly to viability and growth could differ between the two formats. Comparing to BR CM results, sCM predicts well daily volumetric productivity and overall growth performance, but final viability is lower in sCM for some clones. Overall product quality trends as function of culture time were similar between BR CM and sCM. In summary, we established a small-scale Tubespin model for CM that could be used as an additional tool during clone screening.