Spring 5-10-2016

Improved scale-down model development case study for raw materials screening

Angela Au
Bristol-Myers Squibb, angela.au@bms.com

Davanna Marks
Bristol-Myers Squibb

Hugh Graham
Bristol-Myers Squibb

IMPROVED SCALE-DOWN MODEL DEVELOPEMENT CASE STUDY FOR RAW MATERIALS SCREENING

Angela Au, Bristol-Myers Squibb, Syracuse-Drug Substance Manufacturing Sciences and Technology
Angela.Au@bms.com
First name Family name of next author, Affiliation
Davanna Marks, Bristol-Myers Squibb, Syracuse-Drug Substance Manufacturing Sciences and Technology
Hugh Graham, Bristol-Myers Squibb, Syracuse-Drug Substance Manufacturing Sciences and Technology

Key Words: Scale-down Model, Manufacturing-scale, Raw Materials, Screening

The lack of an adequate scale-down model for the cell culture stages of legacy processes is an ongoing issue across the industry. This presentation will describe an existing scale-down model, the modifications made to it, and an example of the utility of the new model. The scale-down model for Process X was originally developed based on power per unit volume, with minimal modification to accommodate other input parameters. This scale-down model performed significantly differently from the manufacturing-scale process with respect to cell growth, metabolites, and productivity. For example, the productivity in the scale-down model was 3 to 4 times higher than at the manufacturing scale, and the peak viable cell density (PVCD) for the scale-down model was two times the PVCD of the manufacturing scale, while cell viability was also consistently higher in the scale-down model. There was a clear need to develop a scale-down model that takes into account additional scaling parameters and better mimics manufacturing scale to increase understanding of the manufacturing-scale process. Analysis of mixing and sparging parameters indicates that the manufacturing scale results differed significantly from the model. The scale-down model was therefore modified to reduce air flow rates, increase the total volume, and to over-sparge air early in the process to better mimic the manufacturing-scale behavior and trends. These changes resulted in a scale-down model which closely matches the large-scale growth, viability, and metabolite profiles. This scale-down model has been used to successfully screen raw materials which are known to impact the manufacturing-scale process. This improved scale-down model will enable process improvement studies, effective satellite runs, improve understanding of manufacturing-scale results, address deviations, and will help ensure robust production.