

Spring 5-11-2016

Challenges in the use of scale-down models for understanding and mitigating process variations of a monoclonal antibody production process

Peter Russo

Merck, peter.russo@merck.com

Follow this and additional works at: http://dc.engconfintl.org/cellculture_xv



Part of the [Biomedical Engineering and Bioengineering Commons](#)

Recommended Citation

Peter Russo, "Challenges in the use of scale-down models for understanding and mitigating process variations of a monoclonal antibody production process" 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/129

This Abstract is brought to you for free and open access by the Proceedings at ECI Digital Archives. It has been accepted for inclusion in Cell Culture Engineering XV by an authorized administrator of ECI Digital Archives. For more information, please contact franco@bepress.com.

CHALLENGES IN THE USE OF SCALE-DOWN MODELS FOR UNDERSTANDING AND MITIGATING PROCESS VARIATIONS OF A MONOCLONAL ANTIBODY PRODUCTION PROCESS

A. Peter Russo, Merck & Co., Inc.
peter.russo@merck.com

Key Words: monoclonal antibody, scale-up, scale-down, process robustness

Scale-down models are commonly used to execute process characterization studies, as well as to screen raw materials and to conduct investigations in support of manufacturing operations. During the clinical manufacture of a monoclonal antibody, consistent product quality was maintained; however, large variations in bioreactor harvest titer (> 2X) were observed between lots. Root cause analysis of this variation did not establish a linkage between culture performance and manufacturing execution or deviations. Further, small scale satellite reactor performance displayed lesser variability; thereby eliminating seed train and raw materials as potential root causes. Small scale investigations, using multiple scale-down models, were not able to reproduce the variability in product titer, and other cell culture metrics, observed at large scale. However, these studies were able to establish a correlation between cellular metabolism, feeding strategy and harvest titer. As a result, process modifications have successfully been developed to obtain a more robust production bioreactor process while maintaining product quality.