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Bioreactor scale-up harmonization - From process development to manufacturing

Claudia Berdugo-Davis
Cook Pharmica, claudia.berdugo@cookpharmica.com

BIOREACTOR SCALE UP HARMONIZATION – FROM PROCESS DEVELOPMENT TO MANUFACTURING

Claudia Berdugo-Davis, PhD, Cook Pharmica LLC
claudia.berdugo@cookpharmica.com
Kumar Dhanasekharan, PhD, Cook Pharmica LLC
Drew Graves, Cook Pharmica LLC
Steven Perry, Cook Pharmica LLC
Victor Vinci, PhD, Cook Pharmica LLC

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Successful bioprocess scale up requires an understanding of the microenvironment influenced by bioreactor parametric conditions and the effect on cellular metabolism and expression of a recombinant protein. While, significant understanding of best practices exists in scaling up bioprocesses, Contract Development and Manufacturing Organizations (CDMO) have a unique challenge in requiring a working knowledge of our bioreactor capabilities driven by a diverse client network and thus a need for a ready-to-implement scale up platform for a wide range of molecule types. An effective CDMO must be able to scale-up client platform processes (which differ for each client) as well as utilize its knowledge to help smaller client firms with minimal knowledge of scale-up. This challenge is increased for novel innovator molecules, biosimilar candidates, and existing mAb processes transferred from other facilities. Moreover, the addition of novel, disposable bioreactors makes evident the need to harmonize scale up strategies for bioreactors with different geometric characteristics as is typically found in manufacturing settings.

In this work we present an integrated approach to characterizing different scale bioreactors from process development through manufacturing. Approaches include a combination of process mixing empirical correlations for scale-up dependent parameters and computational fluid dynamics (CFD) models as well as experimental data to enable scientific judgment on scale-up. Methodologies used to define scale up model are complementary and represent the starting point for characterizing bioreactors and achieved harmonization across scales. Discussion will be presented on strategies used to achieve comparability between CFD models, correlations and experimental data. Agreement between components of this approach is represented in design charts including mixing time, kLa and power per volume (P/V). (See Figure 1)

The combination of strategies resulted in a structured methodology to define engineering design space for various processes based on models and experimental data. Successful outcomes for multiple products on process performance for cell culture processing such as growth, titer, metabolic performance and product quality attributes are compared between 2L, 20L and 2500L reactors.

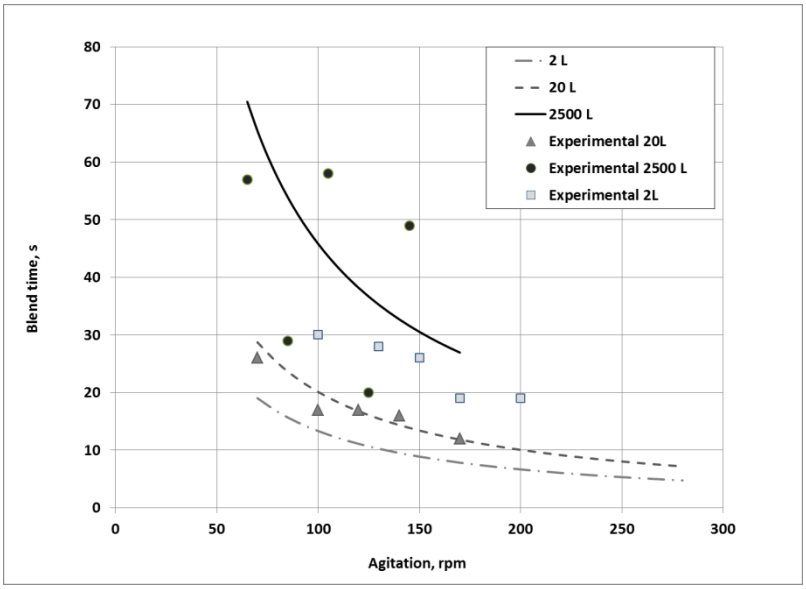

Figure 1 – Blend time design chart and experimental data for different bioreactor scales