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Use of an automated, integrated laboratory environment to enable predictive modeling approaches for identifying critical process parameters and controlling key quality attributes

Brandon Downey
Bend Research, brandon.downey@bendresearch.com

John Schmitt
Bend Research

Jeffrey Breit
Bend Research

Brian Russell
Bend Research

Justin Beller
Bend Research

See next page for additional authors

Authors
Brandon Downey, John Schmitt, Jeffrey Breit, Brian Russell, Justin Beller, Liz Herman, Anthony Quach, and David Lyon

USE OF AN AUTOMATED, INTEGRATED LABORATORY ENVIRONMENT TO ENABLE PREDICTIVE MODELING APPROACHES FOR IDENTIFYING CRITICAL PROCESS PARAMETERS AND CONTROLLING KEY QUALITY ATTRIBUTES

Brandon Downey, Bend Research, Inc.
brandon.downey@bendresearch.com
John Schmitt, Bend Research, Inc.
Jeffrey Breit, Bend Research, Inc.
Brian Russell, Bend Research, Inc.
Justin Beller, Bend Research, Inc.
Liz Herman, Bend Research, Inc.
Anthony Quach, Bend Research, Inc.
David Lyon, Bend Research, Inc.

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An essential part of ensuring a high quality medicine is being able to reliably control Critical Quality Attributes (CQA's). In the cell culture process, bioreactor conditions, feeds, cell state are some of the many variables that affect CQA's. Out of this very large set of possible variables, the small subset of these (i.e., critical process parameters, or CPP's) that have a large effect on the CQA's must be identified and understood such that those CPP's can be controlled to ensure quality product. Here, we demonstrate the use of predictive modeling techniques to supplement experimental bioreactor studies when defining critical process parameters (CPP's) and generating process control strategies. Using predictive models to relate culture process conditions to CQA's has the benefit of enabling both: 1) using model predictions to supplement experimental data when determining critical process parameters (CPP's) and the resulting control strategy, and 2) active control of CQA's based on model forecasts to achieve finer control of CQA's. In order to support this predictive forecasting approach for bioreactor process definition and control, Bend Research has developed a new bioreactor laboratory environment that allows us to run the right experiments, take the right data, and determine which measurements are actually important in determining CQA's, and to generate model predictions based on those data sets. Here we demonstrate the application of this new laboratory paradigm in practice, using galactosylation, an important product quality attribute, as the "CQA" of interest. We show how through using automated, perfusion-type systems identification experiments, combined with automated data-generation and reduction tools, we can generate a prediction of the effect of galactose feeding on product quality.