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Critical process parameter identification using the ambr15(tm) for process characterization

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Process characterization is a critical phase in the development of a commercial process for biotherapeutic production. Knowing the critical quality attributes of your molecule prior to beginning process development and/or characterization is imperative when using a quality by design (QbD) approach. Here we use a (QbD) approach for the characterization of a fed-batch process using an NSO cell line to express an IgG. For this molecule, the glycosylation profile, and in particular, the total fucosylation was identified as a critical quality attribute. After performing a primary hazard analysis, several process inputs were determined to potentially have an impact on this critical quality attribute. These parameters were then studied in a screening DoE using the ambr15™ to model the first and second order effects for each parameter on both the critical quality attributes and process performance. Of the 9 parameters studied, 5 were determined to have a statistically significant effect on the fucosylation of the molecule. In addition, 6 parameters were identified to have a significant impact on process performance. Through process modeling using JMP, a design space was determined for further studies to determine the proven acceptable range (PAR) for each parameter using the 10L, qualified scale down model. An example of the predicted PAR for pH and the timing of the temp shift can be seen in figure 1. Following the 10L studies, a PAR was determined for each parameter and compared with the predicted PAR from ambr. Here we demonstrate the feasibility to use the ambr15™ as a tool for key and even critical process parameter identification to reduce timelines for process characterization.

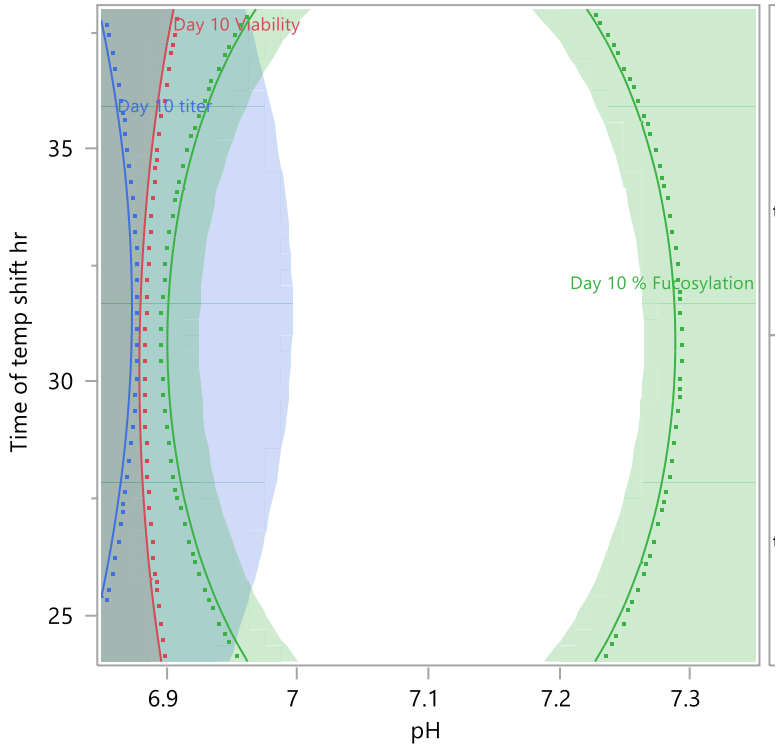

Figure 1 – Design space for critical process parameters satisfying the critical quality attributes of an IgG