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LATE STAGE PROCESS DEVELOPMENT FOR A COMMERCIAL FERMENTATION BIOPROCESS

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Late stage process development and technology transfer of a vaccine bioprocess to a new commercial facility requires large bioprocess data sets to define a robust manufacturing process for the lifetime of commercial manufacture. The nature of the experiments to generate these data sets presents significant time and resource burden on industrial bioprocess development. This burden is compounded when the vaccine of interest contains antigens from multiple serotypes of disease-causing bacteria, as serotype specific bioprocess parameters must be defined. To address this burden, it is often necessary to scale down process development studies, execute statistical approaches to experiment design, and implement novel process analytical tools. This talk will review late stage process development for a *Streptococcus pneumoniae* fermentation bioprocess at Merck & Co., Inc., Kenilworth, NJ, USA (MSD). In particular, the successful scale down of the microbial fermentation and subsequent process characterization data will be discussed. To complete the scale down, k_{LA} characterization of various bioreactor scales were completed to successfully scale the process to the Sartorius Ambr 250mL single use bioreactor system. In addition, various studies were performed to develop a closed bottle fermentation process for the first stage of the fermentation, reducing the capital cost of future commercial facilities. The success of these scale down models enabled the subsequent generation of process characterization data to identify parameters at risk of impacting key process attributes, such as the fermentation yield (Figure 1). Ultimately, these efforts and others have led to the successful startup of a commercial facility to complete *Streptococcus pneumoniae* fermentation.

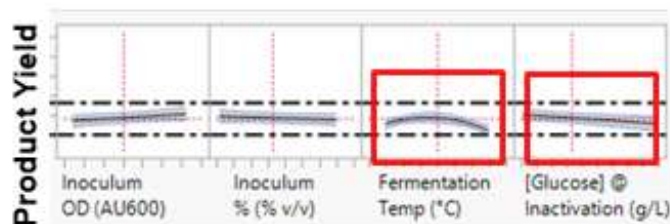


Figure 1 – Design of Experiment (DOE) statistical analysis identified two statically significant process parameter main effects (p value < 0.05, red boxes) for the attribute of fermentation product yield. This figure is representative of serotype specific sensitivities, as the data set includes 18 lab scale batches of one specific serotype. Other serotypes were found to have different statically significant process parameter main effects.