Spring 5-12-2016

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INCORPORATION OF QbD ELEMENTS INTO THE DEVELOPMENT AND CHARACTERIZATION OF A SECOND GENERATION PROCESS

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Key Words: QbD, scale down model, scale up, design of experiments, design space

QbD principles are readily incorporated into mammalian cell processes to streamline process development and characterization. A key enabler of the implementation of these principles has been widespread adoption of platform technologies by the industry. This allows easy and efficient navigation of the QbD roadmap laid out in the A-Mab case study over the course of the development lifecycle of a product.

Here we examine the case of a 2nd generation process for a legacy product that was originally developed and approved using the traditional approach to process development and characterization. The goal of the 2nd generation process was to achieve several fold increases to productivity while achieving similar process performance across scales. Furthermore, comparability profiles of quality attributes must be maintained to ensure treatment efficacy and patient safety, and to streamline the regulatory approval process. To meet these constraints, it was necessary to make significant deviations from the platform process.

This presentation outlines some of the challenges encountered during process development, tech transfer, and process characterization and how QbD principles were incorporated at each of the stages. Specifically, advanced metabolomics and proteomics methods were used to understand and eliminate differences in process performance after tech transfer to manufacturing scale and small scale bioreactor operations were optimized to ensure an appropriate scale down model. Risk assessments were used to guide process characterization efforts and custom DOE approaches were used to minimize bioreactor experiments. The experimental data were then fit to models to understand the design space and used to establish quantitative criteria to guide parameter classification. The models were verified through additional experiments and raw material variability was accounted for to improve robustness. The examples provided here demonstrate the advantages of incorporating QbD principles into the development cycle of biologics processes even in situations of compressed timelines and off-platform processes.