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INVESTIGATING THE IMPACT OF PROCESS OPTIMIZATION ON PRODUCTIVITY, PRODUCT QUALITY, CELL METABOLISM, AND INTRACELLULAR ENVIRONMENT

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One of the key goals in process development for monoclonal antibodies is to improve productivity and product quality as needed. The early stage cell culture process developed for an antibody had titers averaging 4 g/L and variable aggregate levels within cell culture. Through process optimization work, involving changes in media formulations, feeding strategy, and process parameters, the final optimized process achieved industry leading titers (greater than 10 g/L) with consistently lower aggregate levels. To understand the impact of process optimization on the CHO cell metabolism and intracellular environment we evaluated 4 conditions: Early stage cell culture process, 2 intermediate processes, and the final optimized process. In this study we monitored multiple process performance attributes, cellular metabolites and indicators of intracellular health. The higher productivity processes had increased nutrient consumption, moderate oxidative stress and a more active unfolded protein response when compared with the early stage process. Additionally, aggregate levels were impacted by many process parameters. These findings shed important understanding into how cell culture process changes affect productivity and internal cell metabolism and are applicable to process optimization efforts to enhance productivity and product quality.