CONTROLLING THE PRODUCT QUALITY ATTRIBUTES OF A COMPLEX RECOMBINANT PROTEIN IN A HIGH CELL DENSITY PERFUSION BIOREACTOR PROCESS
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Perfusion processes for biopharmaceutical manufacturing have gained significant attention over the last few years as a means to significantly improve productivity and product quality over conventional fed batch processes. A few cases have recently been reported that higher cell densities (100-200E6 vc/mL) and higher productivities (2-4 g/L/day) were successfully achieved with perfusion processes. At Shire, perfusion platforms have been established and multiple perfusion processes for the production of complex and heavily glycosylated proteins have been developed and scaled up to clinical and commercial scales successfully. In this presentation, we will discuss our experience and challenges encountered during the development of a high cell density perfusion process for a complex and heavily glycosylated recombinant protein and our approaches to overcome these challenges.

A baseline perfusion bioreactor process at 50-60E6 vc/mL utilizing an ATF retention device was initially established but some of the product quality attributes could not be maintained robustly when the cell density was further increased to 80-90E6 vc/mL. The impact of nutrient availability, inhibitor accumulation & product retention were investigated to understand the product quality differences at different cell densities. The overall strategy and approach to control and improve product quality attributes will be discussed.