ASSESSING ALTERNATE SPARGER CONFIGURATIONS TO MITIGATE SUPPLY CHAIN RISKS IN SINGLE-USE BIOREACTORS

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Consumable shortages throughout the pandemic introduced unanticipated challenges for continued manufacture of commercial biologics. With single-use systems, the bioreactors themselves are consumables that were impacted by these supply chain shortages. To ensure patient supply of necessary biologics, risk mitigation planning and determining suitable alternatives was required. In this presentation, we detail work performed to allow for continued manufacturing, while facing stock-out risks for single-use bioreactor bags used at both the seed and production stages. Specifically, this work focused on alternate sparger configurations, as the standard configuration used in the production bioreactor stage was unavailable. Additional options for added flexibility at the seed bioreactor stages were evaluated to address stock-out risks, and are discussed.

Prior experience indicated that differences in sparger configurations negatively impact production bioreactor performance for one legacy bioprocess. At-scale manufacturing and follow-up laboratory studies indicated that the use of a micro-sparger, as compared with the standard drilled-hole sparger, resulted in higher rates of cell death (Figure 1), and ultimately impacted product quality attributes. With advances in media technologies for newer bioprocesses, it was imperative to understand if the sensitivity to micro-sparging would be observed in two active campaigns in our single-use manufacturing facility, and which alternate sparger configurations would ultimately be acceptable.

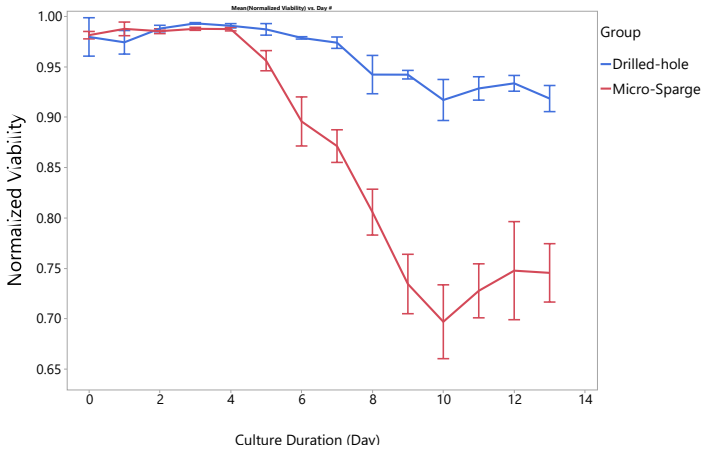

Figure 1 - Micro-sparge impacts viability in a legacy bioprocess

Using 5-L lab-scale bioreactors, with an innovative dual-sparger configuration, we were able to examine the impact of micro-sparging and potential impact to cell growth, process performance, and quality attributes and determine which programs to prioritize our standard sparging configuration and which could use an acceptable alternative. While the initial legacy program demonstrated cell sensitivity to micro-sparging, the same sensitivity was not observed with the two additional programs studied.

Future looking work to mitigate supply chain challenges necessitates strategically incorporating flexibility into bioprocesses. Building flexibility into the bioprocess will allow for quick adaptation and response to supply chain issues. A discussion of the studies required to support these alternatives, the benefits of building in this flexibility during process development, as well as potential challenges arising for retrospectively adding flexibility to commercial processes is presented as well.