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Adapting an in-licensed/acquired cell culture process to platform conditions

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Title: Adapting an in-licensed/acquired cell culture process to platform conditions.

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The use of platform materials and processes for new products help streamline process development, enhance predictability and efficiency during manufacturing, and simplify the raw materials supply chain. Although common, adaptation of cell expression systems can require a significant amount of process development work to achieve desired product yield, quality, and comparability. Here, we present a progressive development approach for evaluating platform media and feeds for an acquired cell culture process.

A CHO-DG 44 cell line expressing a novel antibody product was procured through acquisition. The original non-platform media and fed-batch process yielded titers of approximately 3 g/L. A study was performed to evaluate the cell line performance in the platform media and feeds that are designed mainly for CHO-K1 based cell lines with the aim of determining whether the platform media and feed system would be suitable as-is, or with only minor alterations. The cell growth and titers with the platform media and feeds were found to be approximately 1g/L. While the per-cell specific productivity (pg/cell-day) was found to be comparable to the non-platform process, cell growth was substantially less with the platform media. As a next step, minor modifications were made to the platform basal media including modifications to the starting osmolality, and the use of amino acid supplements. The modifications resulted in an increase in the cell growth comparable to the non- platform conditions only during the early phase of production. This was possibly due to high ammonia levels observed in most platform conditions after the first few days of production culture. While improved, the culture performance with small modifications to the platform system was not considered adequate. Therefore, based on cell biology considerations, existing process knowledge, and literature review, two redesigned platform media were evaluated and further improvements were realized – i.e. an overall 40-50% increase in titer and cell growth compared to control platform conditions under shake flask conditions. Further work is ongoing to confirm this observation in bioreactors. This study clearly demonstrates the cell culture challenges that come with adapting new and different cell lines to platform media and feed systems, the benefits and limitations of small adjustments, and the occasional need for larger media redesign efforts.