DEVELOPMENT TOWARDS A HIGH-TITER FED-BATCH CHO PLATFORM PROCESS YIELDING PRODUCT TITERS > 10 g/L

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Roche’s current Global Cell Culture Platform (GCCP) using chemically-defined media was implemented in 2012 and has been successfully used in process development and clinical manufacturing for numerous molecules. Several minor version changes have been implemented since its inception mainly to further optimize product quality requirements. However, high lactate levels have been observed in several projects using our CHO-K1-M GS host cell line (Random Integration host), resulting in sub-optimal culture performance when not addressed by process modifications (e.g., off-platform pH changes, etc.). Understanding the “triggers” for undesirable lactate metabolism and identifying levers to control lactate metabolism are keys in improving process robustness and enabling further advances in platform process optimization towards higher titers required for high-demand products.

Using a lactogenic model cell line, we examined numerous potential lactate levers including starting osmolality of production media and other factors that can mitigate the buildup of in-process osmolality (e.g., media components, media powder concentration, feed strategies, and process parameters). The results from these studies were then used to further optimize our existing platform media and process to develop a high titer proof-of-concept fed-batch process yielding > 10 g/L. We also investigated the optimization of media solubility and stability of our proprietary liquid media, thus enabling the development of new highly concentrated liquid media which are required for high titer processes. Case studies that demonstrate the applicability of the newly developed high titer process with numerous mAb producing cell lines including our new Targeted Integration host will be discussed.

The optimized “traditional” fed-batch process may ultimately lead to our next generation platform process, which still fits within our current manufacturing network, but will significantly reduce cost of goods and runs required to support clinical and commercial production of our biopharmaceutical proteins.