SANOFI IN-HOUSE MEDIUM: EXCEEDING EXPECTATIONS IN CELL LINE DEVELOPMENT AS AN ALTERNATIVE TO COMMERCIALLY AVAILABLE BASAL MEDIUM

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Our current CHO cell line development process has used commercially supplied media for all steps from post-transfection recovery through scale-up and screening of clones. Media alternatives have been developed in house to improve cell culture performance, decrease media cost, and enable modification by Sanofi. A current version of the basal medium has been utilized for cell culture production processes for some early stage development programs. With the goal of utilizing the same media for cell line development and cell culture production, we evaluated this basal medium in different steps of the cell line generation process, with the current (commercial) medium used as the control. Overall, the results demonstrated that the in-house medium met or exceeded the performance of the commercial medium in the cell line development workflow.

To assess the in-house basal medium for post-transfection methotrexate (MTX) selection, cell growth and viability were measured during MTX selection, and recombinant protein titers of the MTX-selected pools were assessed. Results show that protein production is comparable between pools selected in the in-house medium versus the control. In addition, use of the in-house medium improved cell growth during selection and decreased the selection timeline by a week. A subsequent MTX kill curve study using the in-house medium showed excellent recovery of transfected cells, even at the higher MTX concentrations used, and high protein titers with less time in selection. Next, the medium was evaluated for single cell cloning in a process using flow cytometry cell sorting to deposit one cell per well in 96-well plates. The initial experiments revealed a minor limitation of the in-house medium for single cell cloning and, based on these results, a cloning version of the basal medium was prepared and tested. Several experiments demonstrated that the cloning version of the in-house medium supported robust cell growth and cloning efficiency that is similar to or better than that obtained with the control. Further studies showed that, for both pools and clones in batch cultures, the in-house medium supports more rapid growth rates and higher cell densities.

Experimental results to be presented demonstrate success of the in-house medium in the MTX selection, single cell cloning and outgrowth, and pool and clone screening steps of the cell line development workflow. Furthermore, the advantages of using the in-house medium for pre-master cell banking will be discussed. Proof of concept work from recent cell line generation projects will further demonstrate the utility and advantage of using our in-house medium in the cell line development workflow for new preclinical development programs.