IMPLICATIONS OF FEEDS AND SUPPLEMENTS ON THE PRODUCTIVITY AND QUALITY OF RECOMBINANT PROTEINS PRODUCED IN CHO CELLS

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Chinese Hamster Ovary (CHO) cells have become the preferred host for recombinant protein production due to their ability to secrete desired proteins with post-translational modifications similar to those observed in humans. Biopharmaceutical companies routinely utilize supplements and feed systems for maximizing the yield of recombinant proteins in processes involving CHO cells. Although high productivity is desirable for monoclonal antibodies (mAbs) production, utilizing supplements and feeds might affect the quality of recombinant proteins. Clinical efficacy and safety of recombinant proteins is dependent on key quality attributes including glycosylation pattern, aggregates, charge variants and low molecular weight species. Our work outlines the comparison of productivity and quality of recombinant proteins produced in fed-batch CHO-cell based processes using commercially available chemically defined (CD) medium for CHO cells, CD feeds and a variety of complex supplements and feed systems. The CD medium, feeds and supplements were tested in three CHO cell lines, each expressing a different IgG molecule. Each cell line was sequentially adapted to all the different CD medium being evaluated. Multiple fed-batch experiments were performed in shake-flasks with combinations of different commercially available supplements and feeds. At regular intervals, samples were assessed for viable cell density, cell viability, nutrient metabolism and IgG titers for the different conditions. The key IgG quality attributes including glycosylation pattern, aggregates, charge variants, low molecular weight species were also evaluated for the samples obtained at the end of the fed-batch process. The medium/feed combinations which demonstrated high protein productivity and high cell viability at the end of the culture process were further tested in bioreactors to evaluate scalability of the medium/feed combinations in the different cell lines. The use of CD medium with either CD feed or complex feed supplements resulted in higher cell viability at the end of the fed-batch process in addition to higher IgG titers. After evaluation of the product quality, the desired glycosylation pattern was obtained in certain combinations of medium, supplements and feeds. Lower amount of IgG aggregation was also observed. Due to the unique nutritional requirements of each cell line, different combinations of medium/supplement/feed were needed for optimal cell growth and productivity without affecting the product quality.