STRATEGIES TO MODULATE CHARGE VARIANTS OF A BIOSIMILAR MONOCLONAL ANTIBODY THROUGH CELL CULTURE CONDITIONS

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Monoclonal antibodies (mAb) are the most successful and rapidly growing class of biopharmaceuticals used in treating several diseases. Biosimilar mAb, an approved version of an original biological medicinal product (reference product) with demonstrated similarity to the reference in terms of critical quality attributes, safety and efficacy, is an increasingly accepted solution to provide greater access at affordable cost to the patients across the world. But, given the complex nature of mAbs, developing a biosimilar using a new cell line and a process is challenging, especially with regards to matching the glycosylation and charge profiles to the appropriate level.

It is reported that culture environment during the production of monoclonal antibody affects its various quality attributes including charge variant profiles[1]. The charge variants are usually formed due to chemical modification of amino acids by deamidation, oxidation, glycation and methylglyoxal adducts[2], and may lead to increase in acidic charge variants. These unintended changes in the protein are mainly due to it being exposed during the long duration of the cell culture to an environment, like elevated temperature, nutrients from media and feed, metabolites from live and lysed cells, culture pH, which favours certain chemical modifications.

Understanding and controlling cell culture process parameters are vital in developing a protein biologic to ensure process consistency and product quality. In the present study, we discuss a case study of development of a cell culture process to produce a proposed biosimilar mAb using a CHO cell line, and ways to modulate its charge variants in the cell culture. The initial screening experiments were performed in an ambr® 15 cell culture micro bioreactor system, from which an optimal 12-day process was chosen and subsequently tested in 3L and 10L bioreactors. Significant time-dependent increase in acidic charge variants was observed from day 10 to 12 at both bioreactor scales, while all other quality parameters remained largely unchanged during the last days of the culture.

Further various strategies such as use of different basal media, feed, and additives (amino acids/metal ions and insulin), and changes in culture temperature and pH, were applied during the cell culture process to control the charge variants, in particular the acidic charge variants. The impact of various additives, cell culture pH, temperature on the charge profiles, as well as on productivity and glycosylation, during the development of this biosimilar mAb using a CHO cell line is discussed in detail.

References:

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