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A Systematic Development Approach to Optimize and Control Biopharmaceutical Product Quality

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The complexity of recombinant protein manufacturing processes, including expression systems (i.e. host cell line, expression vector, cell line engineering process), cell culture process conditions, and choice of media and feeds, present significant challenges to achieve desired product quality of biopharmaceuticals. Significantly more challenging is to develop processes for biosimilar proteins, which must match product quality attributes of the originator molecule, show comparable in-vitro biological activity, and have no clinically meaningful differences as compared to innovator products. To address these challenges, and provide appropriate, flexible, and quick solutions to govern product quality control during manufacturing, Fujifilm Diosynth Biotechnologies (FDB) has developed a unique systematic approach of combining “Media Toolbox” methodology, key chemical components, and cell culture bioprocess “know-how” to optimize and control manufacturing conditions that promote the desired product quality profiles of recombinant proteins.

Case studies will be presented to highlight the efficacy of this approach. Case 1 represents a successful application of the “Media Toolbox” consisting of high-quality media and feeds targeting a variety of CHO parental cell lines that we have established from FDB Innovation program. By using this methodology to optimize a Phase 3 manufacturing process, in less than 3 months, we not only improved the mAb titers ~ 5-fold (> 5 g/L) as compared to original cell culture process, but matched the key product quality attributes including all examined glycan structures and demonstration of scale reproducibility from bench-scale (2L, 10L bioreactors) to manufacturing scale (2000L bioreactor). In addition, on the top of the “Media Toolbox”, the “know-how” of nutrient components (i.e. sugars, trace elements) and cell culture process conditions further expand the ability to optimize and control product quality in a “targeted” manner. This will be outlined with a couple of case studies, to highlight how this concept impacts Glycan structures and functions (i.e. the balance between G0 and G1 glycoforms and relationship with the ADCC).