MANUFACTURING OF THERAPEUTIC ANTIBODIES AND OPPORTUNITIES FOR SINGLE USE TECHNOLOGIES

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An overview of the production of antibodies by CHO cells and its requirements in terms of process development and manufacturing will be presented. Both product quality and process performance are key requirements to enable the manufacturability of therapeutic antibodies. Product quality is often characterized by protein integrity, aggregation, charge and glycosylation, among others. Process performance includes meeting productivity (titer) needs for commercial viability, but is also intrinsically related to the capacity of the purification process to remove unwanted mammalian related impurities (as endogenous CHO proteins, CHO DNA). Product quality is not only monitored and controlled during the production process but also when the product is formulated in its final formulation, and stability determines product shelf life. Production process is developed in scale down models (bioreaction 0.1-20L), with confirmatory scalability at the pilot plant (bioreaction 100-1,000L), and final application in manufacturing (bioreaction 2,000-25,000L). Cell culture environment (cell culture media composition, , pH, temperature, OTR) can have a significant impact upon yield and product quality. Examples showing cell growth and product quality dependency upon cell culture environment will be shown.

The cell culture step of antibody production typically uses stainless steel bioreactors that with decades of use conferred the necessary experience and characterization. Nevertheless, it brings disadvantages as cleaning and product-change over in manufacturing to consider single use technologies. Opportunity to incorporate single use units in cell culture exist, and examples of both challenges and achievements will be discussed.