CRITICAL QUALITY ATTRIBUTES (CQAS) OF A THERAPEUTIC ANTIBODY PRODUCED FROM INTEGRATED CONTINUOUS BIOPROCESSING

I-Fen Liu, Development Center for Biotechnology
ifen.liu@dcb.org.tw
Ho-Lung Jiang, Development Center for Biotechnology
Ming-Yen Hsu, Development Center for Biotechnology
Ching-Jen Yang, Development Center for Biotechnology
Shih-Lung Hsu, Development Center for Biotechnology
Wei-Kuang Chi, Development Center for Biotechnology

Key Words: Perfusion cultivation, Periodic counter-current (PCC) chromatography, Critical quality attributes (CQAs), Charge heterogeneity

The integrated continuous bioprocess provides an innovative way to produce protein drugs with flexibility and efficiency. However, during the long-term cultivation and complicated production, how to ensure the process stability and product quality is critically important. In this study, the monoclonal antibody (mAb) was produced in a bioreactor operated in a perfusion mode utilizing the ATF cell retention system for up to 32 days. The 2L harvest per day starting at day 10 was continuously purified using the 3-column periodic counter-current (PCC) chromatography system. The first protein A capture purification was performed with the dynamic binding capacity of 50% breakthrough around 60 mg mAb/mL of resin (vs 20 mg/mL resin for batch purification) for 120 cycles or 360 column operations followed by a polishing step of mixed mode chromatography for 20 cycles. The process and quality attributes were monitored daily. The results demonstrate consistency in both the purification process and the mAb qualities (in the aspects of product integrity, aggregates, and glycan profile) between PCC and batch purifications. Culture-related charge heterogeneity was observed accompanied by an increase of bioreactor harvest time using both batch and PCC purification processes. In addition, the impurities such as endotoxin and HCP were also monitored while under this high capacity utilization of chromatography resins. By sharing the insights of process and quality attributes, we hope to provide better understanding on the process-related heterogeneity between batch and continuous production and/or purification.

Figure 1 – Integrated Continuous Bioprocessing