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APPLICATION OF ONLINE CO_2 MONITORING TO ENABLE A BETTER UNDERSTANDING OF CELL CULTURE PERFORMANCE VARIATION BETWEEN GMP-SCALE AND SCALED-DOWN BIOREACTORS

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Dissolved carbon dioxide (dCO_2) or partial pressure of carbon dioxide (pCO_2) is an important process parameter that may impact process performance (product titer and viability) and product quality attributes (such as glycosylation) during mammalian cell culture process in a bioreactor. The impact of altered level of pCO_2 on the cell culture process may manifest itself upon process scale-up if the CO_2 removal rate is not consistent between the development scale and the manufacturing scale. The pCO_2 level during cell culture process is normally determined through offline measurement; however, the offset between online and offline pCO_2 may conceal the true effect of pCO_2 on the cell culture process. In this presentation, several studies using online pCO_2 monitoring will be summarized and discussed, including 1) implementation of online pCO_2 probe for measurement of actual pCO_2 levels in a large scale bioreactor, 2) comparison of online and offline pCO_2, 3) correlation between pH and pCO_2, 4) estimation of CO_2 stripping rate in large scale bioreactors, and 5) effect of sample handling on pCO_2 level measurement. The key findings in this presentation are intended to establish biopharmaceutical manufacturing process knowledge, which is valuable for all partners in the cell culture manufacturing network.