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**APPLICATION OF ONLINE CO₂ 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 (dCO₂) or partial pressure of carbon dioxide (pCO₂) 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 pCO₂ on the cell culture process may manifest itself upon process scale-up if the CO₂ removal rate is not consistent between the development scale and the manufacturing scale. The pCO₂ level during cell culture process is normally determined through offline measurement; however, the offset between online and offline pCO₂ may conceal the true effect of pCO₂ on the cell culture process. In this presentation, several studies using online pCO₂ monitoring will be summarized and discussed, including 1) implementation of online pCO₂ probe for measurement of actual pCO₂ levels in a large scale bioreactor, 2) comparison of online and offline pCO₂, 3) correlation between pH and pCO₂, 4) estimation of CO₂ stripping rate in large scale bioreactors, and 5) effect of sample handling on pCO₂ 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.