# µRAMOS: ONLINE MONITORING OF RESPIRATION ACTIVITIES IN 96-DEEPWELL MICROTITER PLATES

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Online monitoring systems for single-use micro bioreactors are powerful tools for the characterization of microbial cultures in bioprocess development. Among these bioreactor platforms, 96-deepwell microtiter plates are well established for process development and clone screening in high-throughput applications. Yet, a suitable non-invasive online monitoring device for 96-deepwell microtiter plates is still missing. For process characterization and a subsequent transfer to larger scales, one essential online parameter is the respiration activity. It is defined by the oxygen transfer rate (OTR), the carbon dioxide transfer rate (CTR), and the respiration quotient (RQ). The RAMOS technology (Respiration Activity MOnitoring System) is one available system for the measurement of respiration activities, yet it is limited to shake flasks. Hence, this study focuses on a transfer of the RAMOS technology to commercially available single-use 96-deepwell microtiter plates. The novel µRAMOS system provides insights into the respiration activity of microorganisms cultured in 96-deepwell microtiter plates, and thereby, enhances the throughput in early-stage process development.

A new miniaturized optical sensor system was developed to allow an accurate and sensitive measurement of the gas composition within each individual well of the microtiter plate. Cultivations of microbial model organisms were conducted to show the application potential for process characterization using the µRAMOS technology. To evaluate the measurement accuracy, parallel experiments in shake flasks and 96-deepwell microtiter plates were performed. Results from both scales are in very good agreement.

In conclusion, a non-invasive high-throughput online monitoring device for 96-deepwell microtiter plates was developed, allowing accurate and sensitive measurements of respiration activities. Hence, with the µRAMOS technology monitoring of the respiration activity becomes available in the µL-scale and provides important scale transfer criteria. Thus, the new technology has the potential to accelerate process development for industrial applications.