

# Bioprocess optimisation in shake flasks

**RAMOS**<sup>®</sup>- Respiration Activity MOnitoring System



#### Universal measuring system

RAMOS<sup>®</sup> (Respiration Activity MOnitoring System) has established itself worldwide as the standard for the online determination of the breathing activity of prokaryotic and eukaryotic cultures in shake flasks.

In a number of processes tested so far, RAMOS<sup>®</sup> has contributed to the revelation of key insights and in some cases has given decisive impetus to development work which has taken place over many years.

RAMOS<sup>®</sup> supplies the truly significant metabolic parameters for O<sub>2</sub> (OTR) and CO<sub>2</sub> transfer rates (CTR) and the parameters of the respiration quotient (RQ) and the maximum specific growth rate ( $\mu_{max}$ ) derived from this.

#### Areas of use

- Media optimisation
- » Process development
- » Bioprocess development
- Process optimisation
- Strain optimisation
- » Fermentation validation
- » Reproducible inoculum production
- » Production strain screening
- Scale-up
- » Stability tests



#### You can benefit from the following opportunities

- Continuous monitoring of the growth of prokaryotic and eukaryotic cultures including that of mammalian cells
- Eightfold parallel online measurement of the breathing activity under sterile conditions
- » Easy determination of typical characteristics (OTR, CTR, RQ,  $\mu_{max}$ )
- Bioprocess optimisation through early recognition of oxygen and substrate limitation or product inhibition
- » Bioassays (toxicity test, proliferation assay)
- Determination of appropriate operating parameters for primary and secondary screening (media, test duration, operating conditions)
- Reduction of the development times for media and process optimisation
- » Process balancing and quantification
- » Quality control (e.g. stability of mammalian cell lines)

Tests for the determination of the breathing activity in stirred tank reactors with separate exhaust gas analysis are carried out as standard. Statistically accurate results, however, demand many parallel tests which considerably increase the amount of experimental effort which is required. With RAMOS<sup>®</sup> eight tests may be carried out at the same time in parallel and recorded online, thus making the amount of time and costs only a fraction of that of conventional methods.



With the aid of the measurement curves, basic biological phenomena can be easily detected, examples being:

- Substrate and oxygen limitation
- Product inhibition
- › Diauxia
- Fermentation
- > Overflow metabolism



The RAMOS® measuring flask was designed in such a way that it matches, in terms of gas and hydrodynamics, an Erlenmeyer flask in accordance with DIN 12380/ISO 1773 in its lower section which is filled with liquid.

The patented measuring method enables, purely from the change to the oxygen partial pressure in the gas section of the measuring flask (no invasive electrodes), the determination of the oxygen transfer rate and the carbon dioxide transfer rate, the RQ and the growth rate (for obligate aerobes).

In order to ensure equivalent culture conditions the gas composition above the culture liquid in the measuring system flasks is set identically to that of a normal flask using cotton stoppers.

### The benefits

- More information on your microbiological processes in shaking flasks
- » Differentiation of process-based and biological effects
- » Replaces expensive tests in a stirred tank reactor
- >> Culture conditions equivalent to a standard shake flask
- Simple handling
- » Parallel technique (time saving, comparability, ...)
- Improved reproducibility
- Virtual non-stop operation thanks to extremely short set-up times
- Shortens the "time to market"

## **Expansion options**

- » Gmix<sup>™</sup> precision gas mixture station
- » RAMOS<sup>®</sup> fed batch
- As an option to the glass flasks, disposable Erlenmeyer flasks can also be supplied

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