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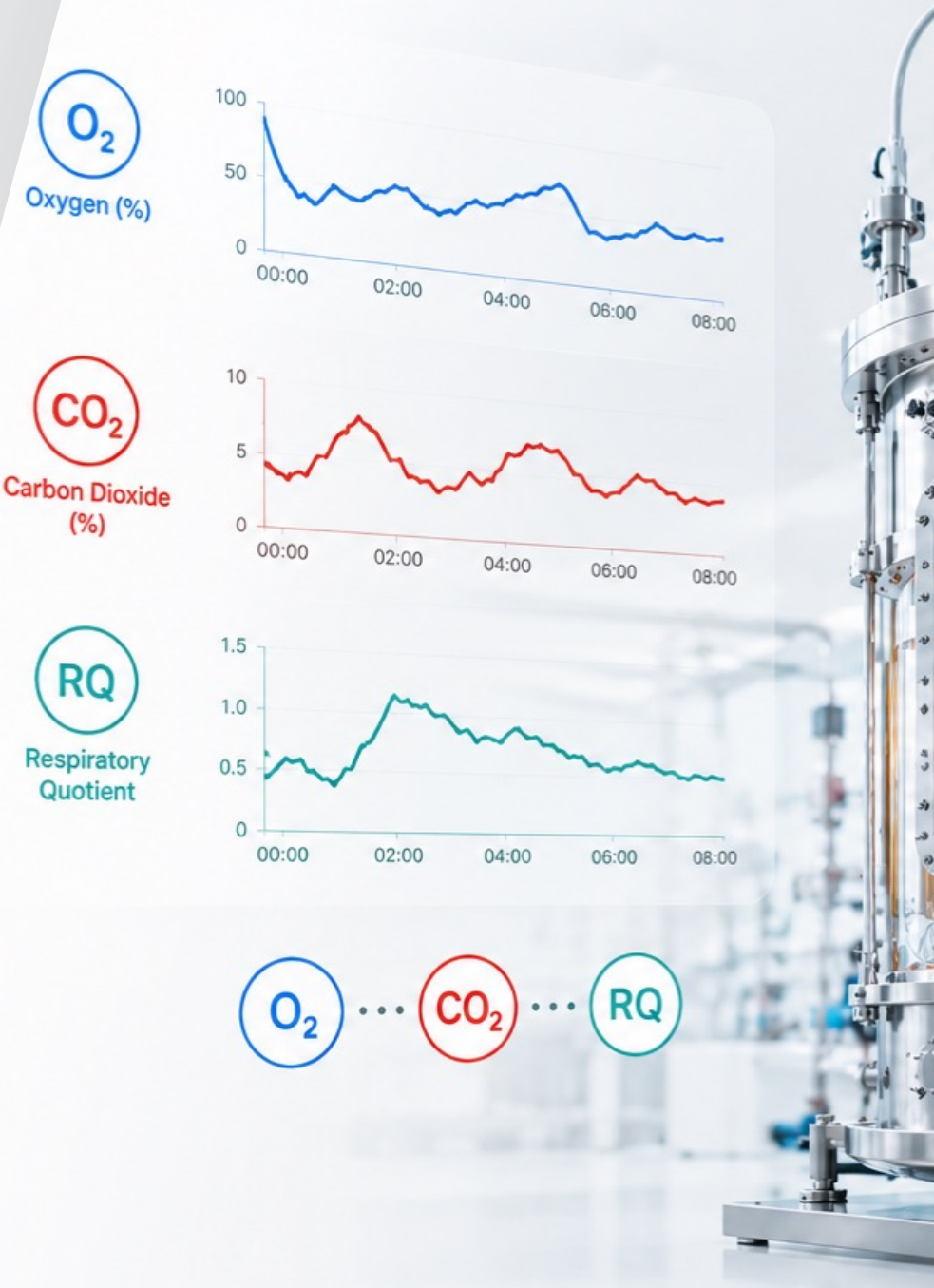
Improving fermentation and cell culture performance through real-time respiratory gas analysis

A practical guide to understanding cell metabolism, optimizing process performance, and supporting Process Analytical Technology (PAT) initiatives through continuous off gas monitoring.



Author: Dan Merriman

What you will learn

Why real-time bioprocess monitoring matters

Understanding the limitations of traditional sampling methods and the need for continuous process insight.

What respiratory gases reveal about cell metabolism

Using oxygen and carbon dioxide measurements to better understand biological activity and process performance.

Monitoring fermentation and cell culture performance

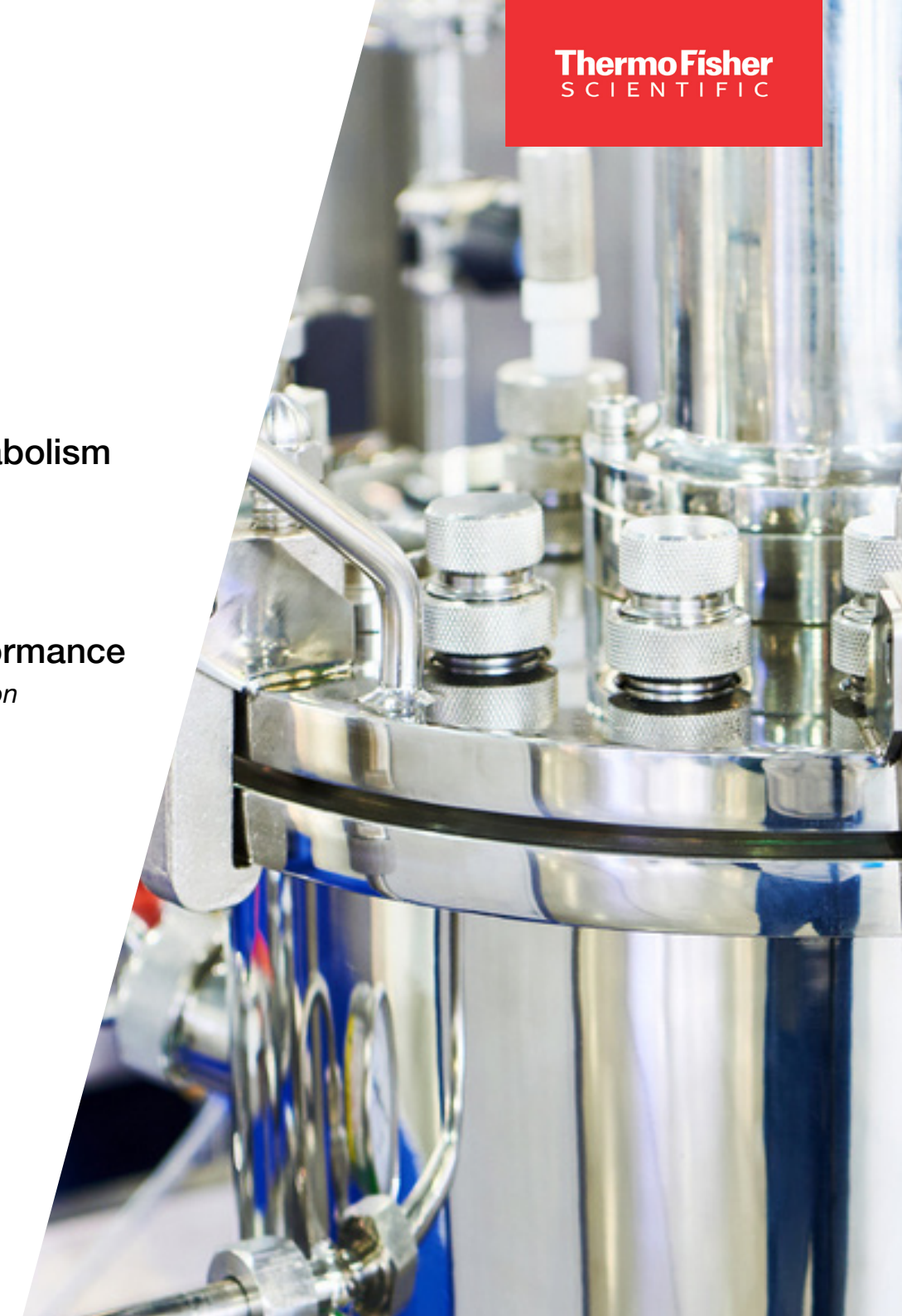
Tracking growth, viability, substrate utilization, and contamination through off-gas analysis.

Using OUR, CER, and RQ to optimize performance

Applying key respiratory measurements to support process understanding and control.

Implementing respiratory gas analysis from lab to production

Considerations for deploying gas analysis technologies across R&D, pilot, and manufacturing environments.



Bioprocesses are dynamic and constantly changing

Challenge

Fermentation and cell culture performance can be influenced by nutrient availability, oxygen transfer, metabolic activity, contamination, and environmental conditions.

Limitation

Traditional offline measurements often provide delayed insight, making it difficult to identify process deviations before they affect productivity or product quality.

Opportunity

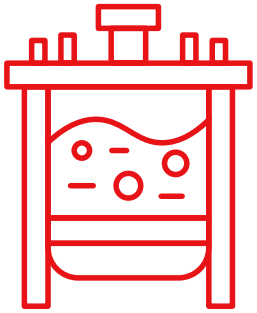
Continuous respiratory gas monitoring provides real-time visibility into cellular activity, supporting better process understanding and decision-making.

Respiratory gas analysis workflow

From raw gas measurements to optimized bioprocess performance

1.

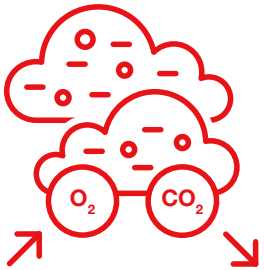
Bioreactor



- Fermentation
- Cell culture

2.

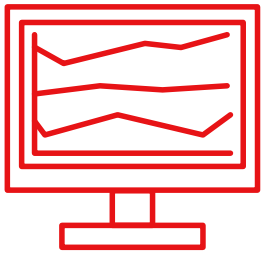
Respiratory gas measurements



- Oxygen Uptake Rate (OUR)
- Carbon Dioxide Evolution Rate (CER)
- Respiratory Quotient (RQ)

3.

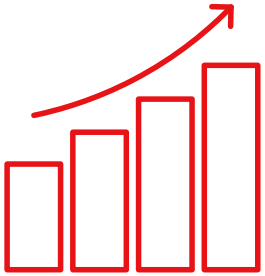
Process understanding



- Metabolic activity
- Nutrient utilization
- Process health

4.

Process optimization



- Feed optimization
- Process consistency
- Data-driven decision making

Continuous respiratory gas analysis provides the real-time understanding needed to optimize bioprocess performance and drive consistent, high-quality production.

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What respiratory gases reveal about cell metabolism

Cells continuously consume oxygen and produce carbon dioxide as part of their metabolism. Measuring these respiratory gases provides valuable insight into cellular activity and process performance.

By monitoring respiratory gases entering and leaving a bioreactor, teams can gain real-time insight into culture health, growth, substrate utilization, and overall process performance.

Changes in oxygen consumption and carbon dioxide production can provide early indication of:

- Cell growth and productivity
- Nutrient depletion
- Metabolic shifts
- Process deviations
- Contamination events

Respiratory gas analysis provides a continuous, non-invasive window into cellular activity throughout fermentation and cell culture processes.

Author: Dan Merriman

Monitoring fermentation and cell culture performance

Respiratory gas analysis provides valuable process insight throughout the fermentation and cell culture lifecycle, helping teams monitor biological activity and make more informed process decisions.

Monitor:

- Initial oxygen demand.
- Culture establishment.

Track:

- Cell growth
- Oxygen uptake
- Nutrient utilization

Identity:

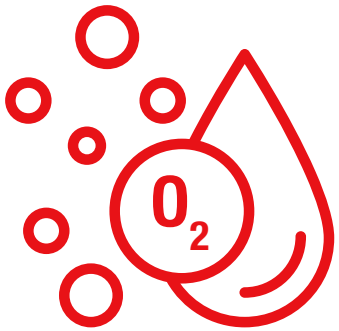
- Metabolic shifts
- Nutrient limitations
- Feed optimization

Determine:

- Optimal endpoint
- Batch consistency
- Product quality

Understanding OUR, CER, and Respiratory Quotient (RQ)

Respiratory gas analysis enables the calculation of several key measurements that provide insight into biological activity and process performance.



Oxygen Uptake Rate (OUR)

- Measures: Oxygen consumption
- Indicates: Cellular activity and viability

Carbon Dioxide Evolution Rate (CER)

- Measures: Carbon dioxide production
- Indicates: Cellular respiration and metabolic activity and viability

Respiratory Quotient (RQ)

- Calculated as: CER ÷ OUR
- Substrate utilization
- Provides insight into metabolic state and substrate utilization.

Together, OUR, CER, and RQ provide a more complete understanding of culture performance than gas concentrations alone.

Author: Dan Merriman

Using RQ to understand metabolic shifts

RQ compares carbon dioxide production to oxygen consumption, providing insight into metabolic activity and changes in substrate utilization throughout a process.

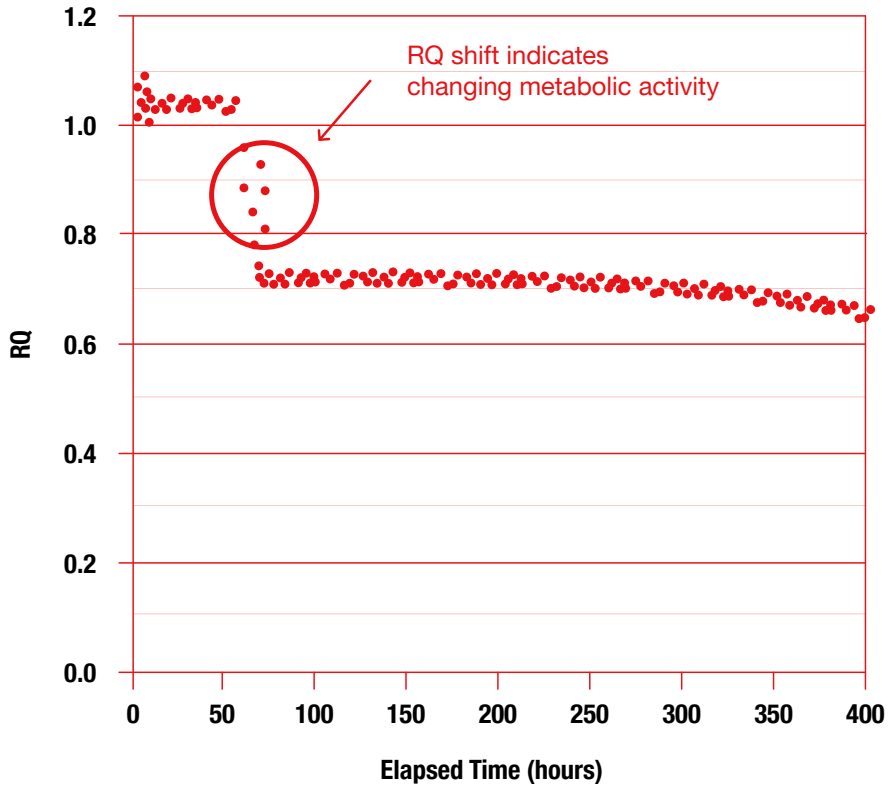
Changes in RQ can indicate shifts in metabolic activity, helping teams identify nutrient depletion, changes in carbon source utilization, and opportunities for process optimization.

RQ can help identify:

- Changes in cellular metabolism
- Nutrient depletion events
- Carbon source transitions
- Process deviations
- Opportunities for feed optimization

When viewed alongside OUR and CER, RQ provides a more complete picture of culture performance and metabolic behavior.

Real-time monitoring of RQ value



Changes in RQ can help identify shifts in metabolism, nutrient availability, and carbon source utilization during fermentation.

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Supporting process optimization and control

Respiratory gas measurements can support process optimization by helping teams monitor performance, interpret process conditions, and take informed action.

Process optimization

Track respiratory gas measurements in real time

Identify metabolic shifts and changing process conditions

Adjust process parameters and nutrient feeds as needed

Process understanding

Collect continuous process data

Build deeper process understanding

Support batch consistency and continuous improvement

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Detecting process deviations earlier

Respiratory gas measurements can provide early indication of changing process conditions, helping teams identify deviations before they significantly impact process performance, productivity, or product quality.

Nutrient limitations

Changes in respiratory activity may indicate depletion of critical nutrients and shifts in metabolic behavior.

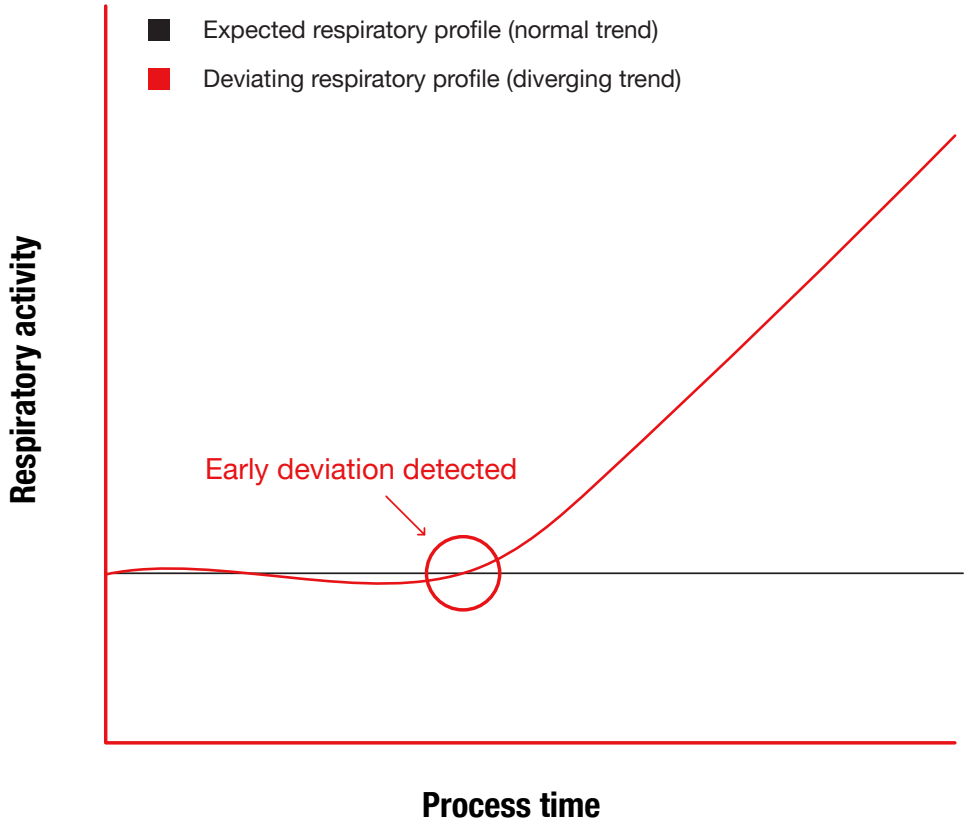
Contamination events

Unexpected changes in oxygen consumption or carbon dioxide production can signal the presence of unwanted biological activity.

Process deviations

Variations from expected respiratory gas profiles can help identify abnormal process conditions and support investigation.

Early detection of process deviations



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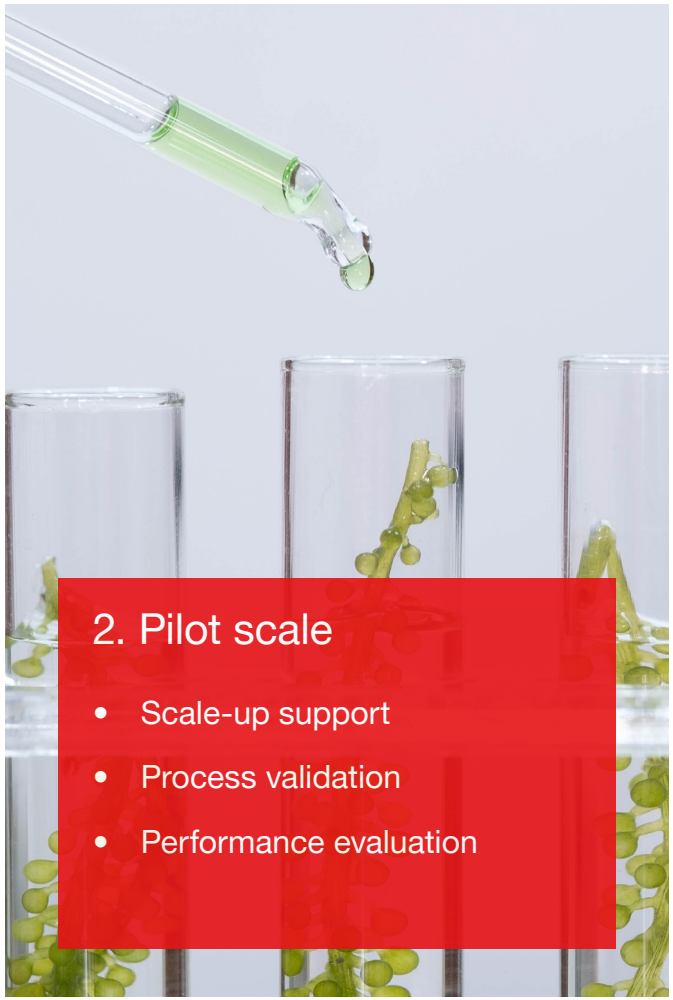
From laboratory development to manufacturing

Respiratory gas analysis can support process monitoring throughout the entire development and production lifecycle, from early-stage process development through pilot-scale studies and commercial manufacturing.

1. Research & development

- Process characterization
- Method development
- Experimental optimization



2. Pilot scale

- Scale-up support
- Process validation
- Performance evaluation

3. Manufacturing

- Continuous monitoring
- Process consistency
- Operational efficiency

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Selecting the right respiratory gas monitoring solution

From early-stage process development to commercial manufacturing, process mass spectrometry can support respiratory gas analysis throughout the biotechnology workflow.

	Thermo Scientific™ Prima BT	Thermo Scientific™ Prima PRO 710
Typical environment	Laboratory / R&D	Pilot & manufacturing
Application focus	Process development	Process monitoring & control
Scale	Bench-top and lab-scale systems; supports multi-point sampling depending on configuration	Pilot and manufacturing environments; supports high-capacity multi-stream monitoring depending on configuration.
Key benefit	Process characterization and optimization	Continuous monitoring and process control

Both systems provide rapid, multi-component respiratory gas analysis to support process understanding, optimization, and scale-up activities.

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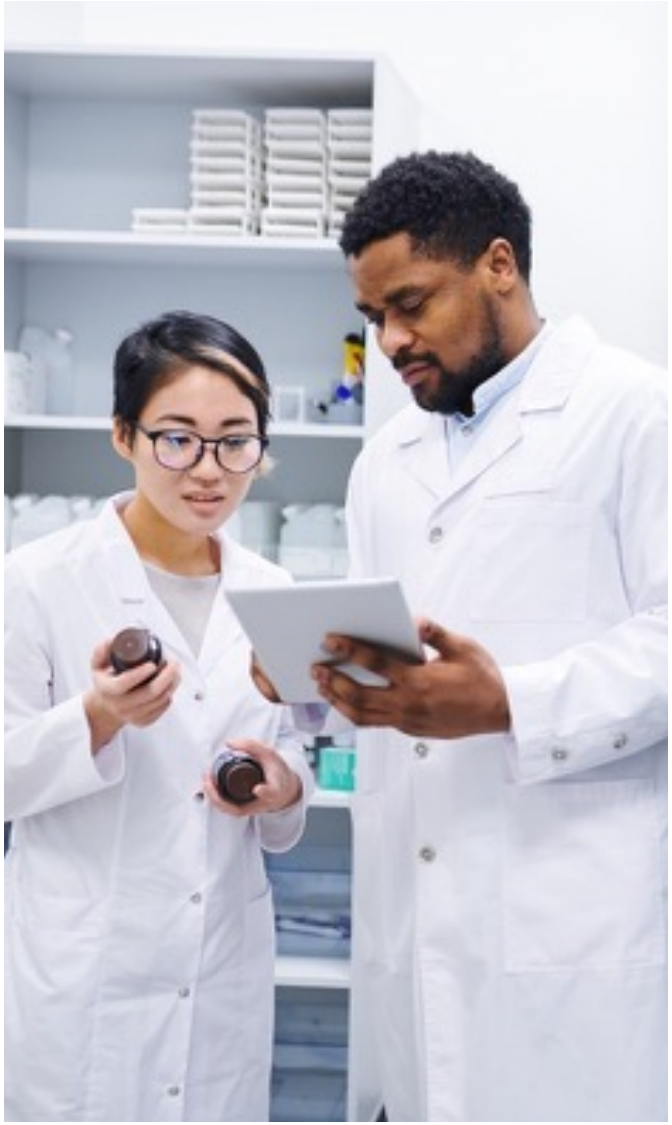
Resources

Continue exploring respiratory gas analysis



- PharmTech eBook: The role of advanced analytics
- Webinar: Fermentation elevated
- eBook - A Guide to Improving Biotech Processes with Process Mass Spectrometry Gas Analysis
- Webinar: Unlock the future of food innovation
- Learn more: Thermo Scientific™ Prima PRO 710 Process Mass Spectrometer
- Learn more: Thermo Scientific™ Prima BT Bench Top Mass Spectrometer

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