

# Raman single-use measurement precision

Real-time composition analysis for biopharmaceutical development and manufacturing with the Raman Rxn portfolio



## Raman sampling portfolio for reusable or single-use bioprocessing

Get to market faster, boost productivity, and manage risk

Single-use technology has transformed the world of biopharmaceutical production from process development to commercial drug manufacturing. Single use refers to any process contact equipment designed to be used once, whether for one batch or an entire manufacturing cycle, before being replaced.

Built upon a long history in cGMP manufacturing with many proven successes, Endress+Hauser has developed an innovative portfolio of Raman single-use bioprocess analysis tools that meet all the stringent requirements of biomanufacturing in the Life Sciences industry.



**Raman optic system for single use**  
Bioprocess probe with sterile, disposable fittings for single-use bioreactors (SUBs). Gain better process insight, speed up process development, improve process efficiency, and improve outcomes.



**Raman bio multi optic and bio sleeve**  
Flexible Raman sampling portfolio for reusable or single-use bioprocessing composition analysis. Maintain sterility and spectral quality while reducing maintenance and cleaning burdens.



**Raman Rxn-46 probe**  
Raman interface adapted and optimized to fit the BioPAT® Spectro platform by Sartorius to enable high-throughput development through single-use commercial manufacturing.

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## Raman optic system for single use

Ensure sterility and reliability for single-use biopharmaceutical development and manufacturing

The Raman optic system for single use is comprised of two key components - a reusable optic and a disposable fitting for SUBs. In conjunction with the Rxn-10 probe, this system offers the same quality data as reusable Raman probes. It allows customers to develop products and processes without limitations of the final production reactor type.

- Developed to industry standards for single-use sensors
- Spectral quality to match standard Raman bioprocess probes
- Gamma sterilizable
- E & L testing conducted by an independent agency
- Patented self-focusing lens for automatic alignment
- Tested and supplied by multiple SUB vendors
- Full data compatibility across our bioprocess probe portfolio
- Qualification complete with leading SUB vendors
- Quick and easy calibration and verification



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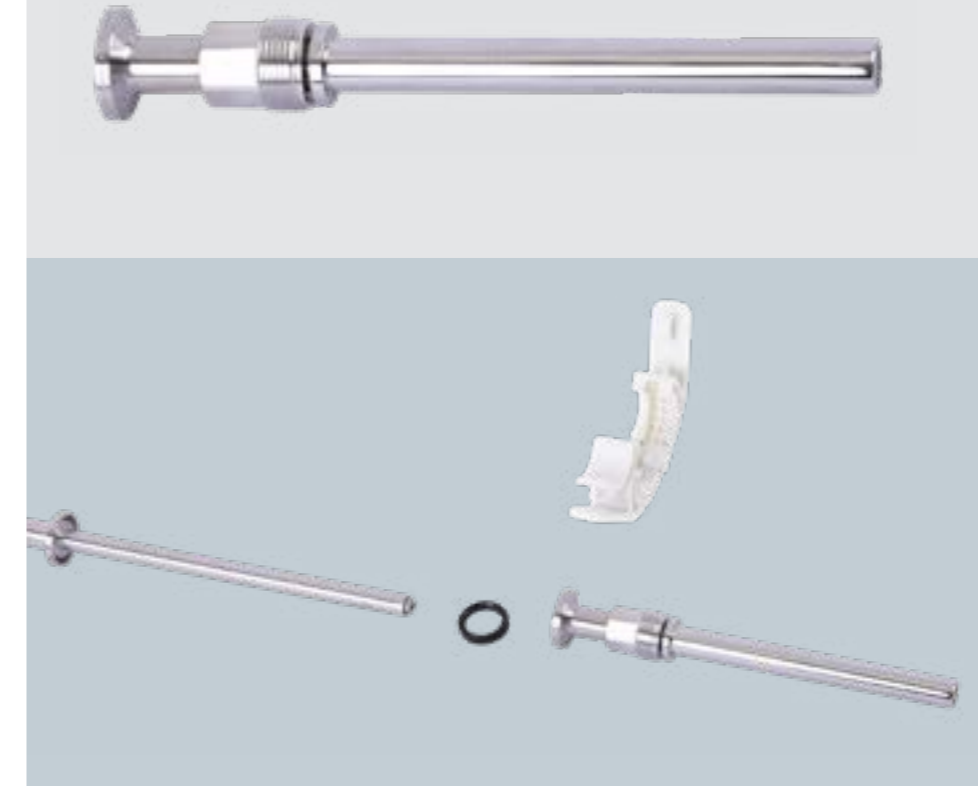
## Raman bio multi optic and bio sleeve

Versatile immersion optic system with disposable sleeve offers the utmost flexibility for reusable or single-use benchtop bioreactor setups

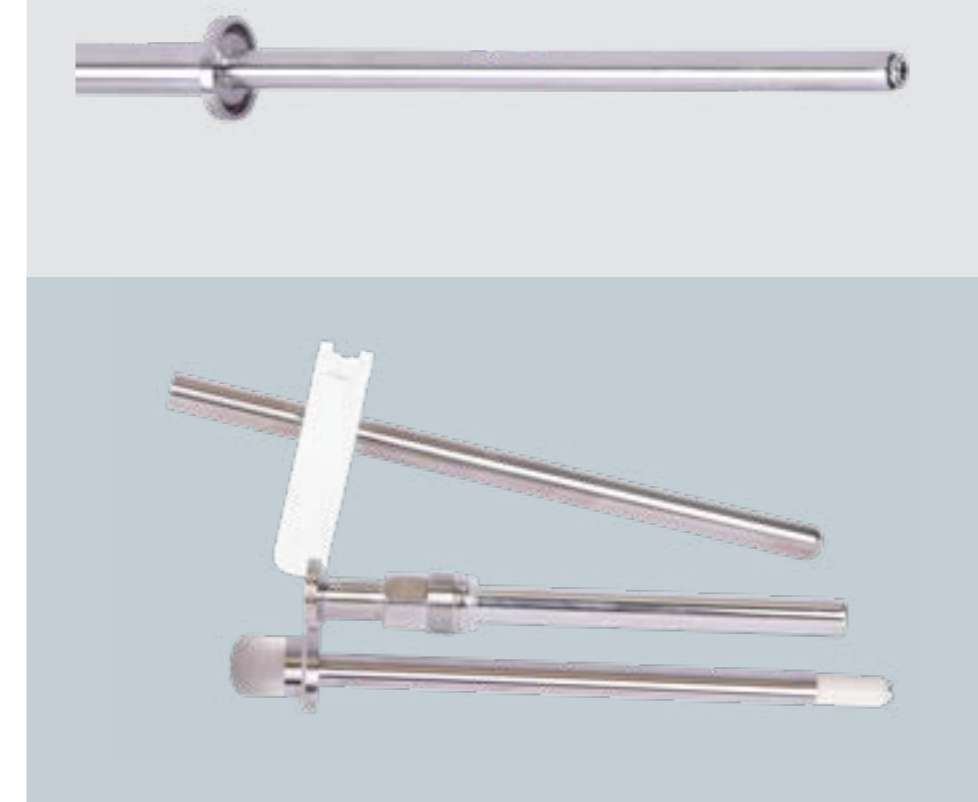
The Raman bio multi optic and bio sleeve offering takes disposable sampling innovation to the next level. Pairing the Rxn-10 probe with a specially designed multi-use optic that fits into a disposable sleeve delivers reliable composition measurement with greater ease of use, less maintenance, and lower cross-contamination risk. The use of disposable parts improves the user experience for bioprocessing applications and offers flexibility for use in either reusable or single-use benchtop bioreactor setups.

- Patented self-focusing lens with automatic alignment for optimal spectral quality and transferability
- Improved ease of use and calibration
- Reduced probe service and maintenance
- Simplified workflow for greater process efficiency
- PG13.5 threaded connector for headplate entry
- Autoclavable, gamma sterilizable, and compatible with standard cleaning protocols
- Expanded compatibility with additional SU bioprocessing containers
- Cross-contamination risk eliminated for single-use set ups
- Compatible with Endress+Hauser flow assembly [CYA680](#)

### Raman bio sleeve



### Raman bio multi optic





## Raman Rxn-46 probe

Bioprocess probe compatible with BioPAT® Spectro by Sartorius for Ambr® 15, Ambr® 250, and Biostat STR®

The Raman Rxn-46 probe is optimized specifically to fit the BioPAT Spectro platform by Sartorius. This collaboration represents the first instance of Raman being brought down to the Ambr-scale and Biostat STR single-use product lines. It offers the market an ideal interface to high throughput development through single-use commercial manufacturing. By providing fast, reliable, and accurate measurement of key process variables from lab-to-process, the Rxn-46 probe empowers bioprocessing companies to more easily scale up and scale out from development to cGMP while complying with strict quality standards.

- Enables faster, easier, and more robust model building via integration with Ambr 15 and Ambr 250
- Allows high throughput process development which supports QbD
- Provides efficient transfer to Biostat STR for single-use manufacturing
- Offers a scale-independent interface from 15 ml in the laboratory to 2000 L in the production suite
- Requires no probe cleaning, sterilization, or frequent maintenance due to non-contact sampling



# Benefits at a glance

Better process insights, faster process development, and improved outcomes

Endress+Hauser's single-use Raman systems are designed to be used for one or several batches before being replaced. This eliminates the need for additional cleaning, sterilization and component validation. It also provides opportunities for reduced material use, costs, cross-contamination risks, and manufacturing times.

Endress+Hauser's latest single-use Raman innovations are also user-friendly and efficient. With these offerings, biopharmaceutical manufacturers can progressively convert their disposable production facilities into interconnected, fully enclosed unit operations with continuous processing.

**Simplified workflow for greater process efficiency**  
Enjoy flexibility to interchange probes in process without downtime and for calibration and verification scheduling

**24/7 process monitoring and control**  
Continuously monitor multiple process attributes with a single *in situ* Raman probe



**Accurate and reliable bioprocess measurement**  
Assure consistent data accuracy and precision, with high-quality probe windows optimized for bioprocessing



**Total process transparency**  
Gain valuable process insights for better decision making, adaptability, and optimization

**Less risk**  
Eliminate cross-contamination risk for single-use set ups



**Lower cleaning burden**  
Use instrumentation that is autoclavable, gamma sterilizable, and compatible with cleaning protocols



**Seamless scalability**  
Experience smooth method, model, and technology transfer from lab to GMP manufacturing



**Improved product quality and easier cGMP compliance**  
Rely on devices designed to meet industry standards for single-use sensors and pre-qualified from leading SUB vendors



**Tight data protection**  
Maintain data compliance and protect against cybersecurity threats

**Maximize profitability**  
Realize fast ROI from process automation, reduced product loss, and higher yields



# Challenges in Life Sciences

To satisfy the latest new requirements of biopharmaceutical manufacturing, more effective single-use sensing technologies are in demand.

Most single-use instrumentation available on the market so far have not sufficiently met the needs for accuracy and repeatability. While material quality standards need to be maintained to ensure product quality, improvements in accuracy, resilience, and robustness are required to allow for tighter process control and minimize the chances of batch loss.

## Single-use bioprocess measurement requirements:

- Real-time bioprocess monitoring for tight quality control
- Equivalent reliability and measurement accuracy as reusable counterparts
- Compatible with industry-standard sterilization protocols
- Enabling quick and easy calibration and verification
- Full compliance to regulations and cGMP standards
- Same technology in the lab and manufacturing scales for safe and fast tech transfer
- Non-invasive application to safeguard sterility



## Solution

Endress+Hauser has risen to the challenge to develop versatile single-use sampling technology for the future of biopharmaceutical manufacturing. We offer scalable single-use and reusable Raman sampling systems that provide full bioprocess transparency from development to cGMP, regardless of your bioreactor setup mix. For critical bioprocess monitoring and control, you can rely on our suite of single-use instrumentation and global service experts to fully support your single and multi-use biopharmaceutical manufacturing operations.

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# Raman spectroscopy measurement

Illuminating molecular secrets

## Technology overview

Utilizing visible or near-infrared light, Raman spectroscopy reveals intricate details about molecular vibrations. As light interacts with these vibrations, it undergoes inelastic scattering, resulting in a unique “molecular fingerprint.” This powerful tool enables identification, quantification, and monitoring of specific chemistries.

## Role in biopharmaceuticals

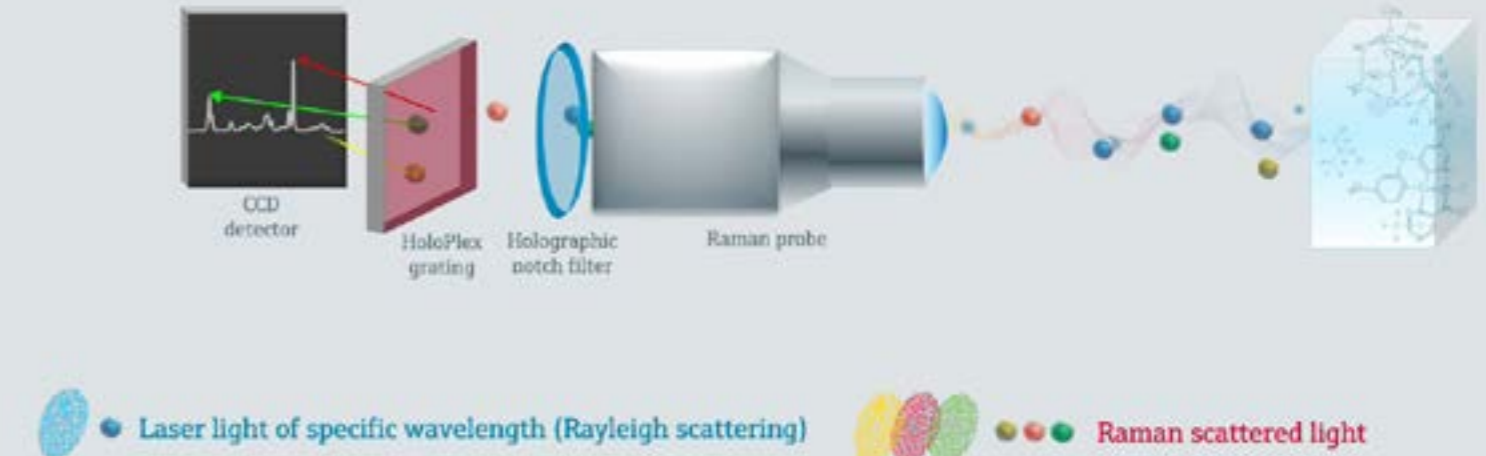
Raman spectroscopy, traditionally used in laboratory settings, has now become a crucial process analytical technology (PAT) solution in biopharmaceutical process development and commercial manufacturing.

## Why Raman is well suited for bioprocessing

- **Real-time measurement** – Raman provides real-time, *in situ* measurements during various bioprocessing operations.
- **Insensitivity to water** – unlike other techniques, Raman measurements remain accurate even in aqueous environments, making it ideal for bioprocess applications.
- **Specificity** – Raman can distinguish between different molecules, even those with similar structures, enabling precise analysis of complex mixtures in biopharmaceutical processes.
- **Inline sampling** – directly inserted into bioreactors or flow paths, a single probe can simultaneously measure multiple parameters and quality indicators without disrupting the process.

## Raman technology illustrated

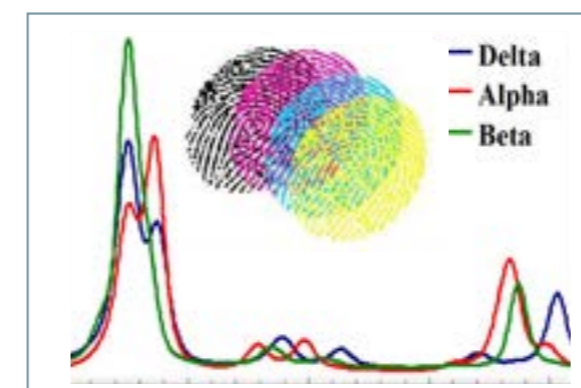
- Laser light of specific wavelength interacts with molecules which causes scattering
- 1 out of  $10^8$  photons is frequency-shifted due to specific energy transfer (Raman shift)
- Result: specific photons allow identification and quantification of materials (solvent, products, substrate)



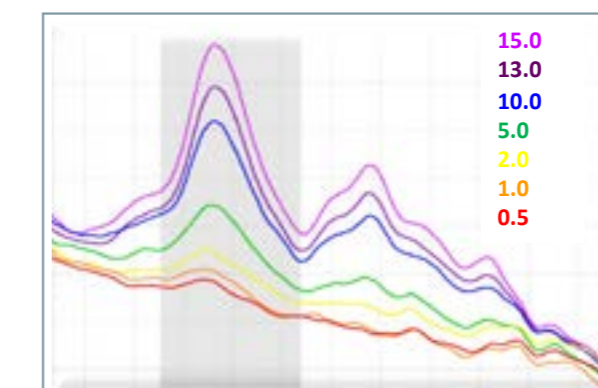
The collected light is interpreted as a spectrum by the camera, creating a “molecular fingerprint” of the material being sampled.

## Raman spectra from a lab sample or process can tell us...

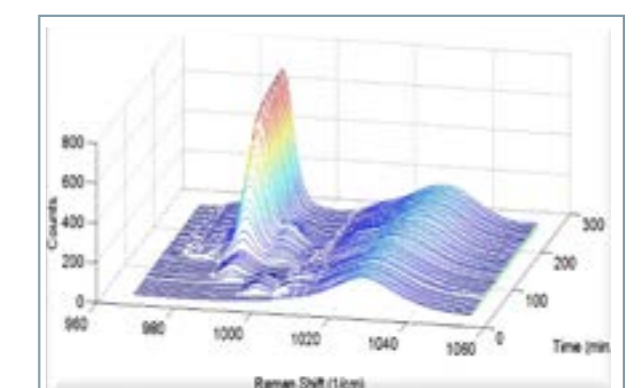
What is it?



How much?



Has it changed?





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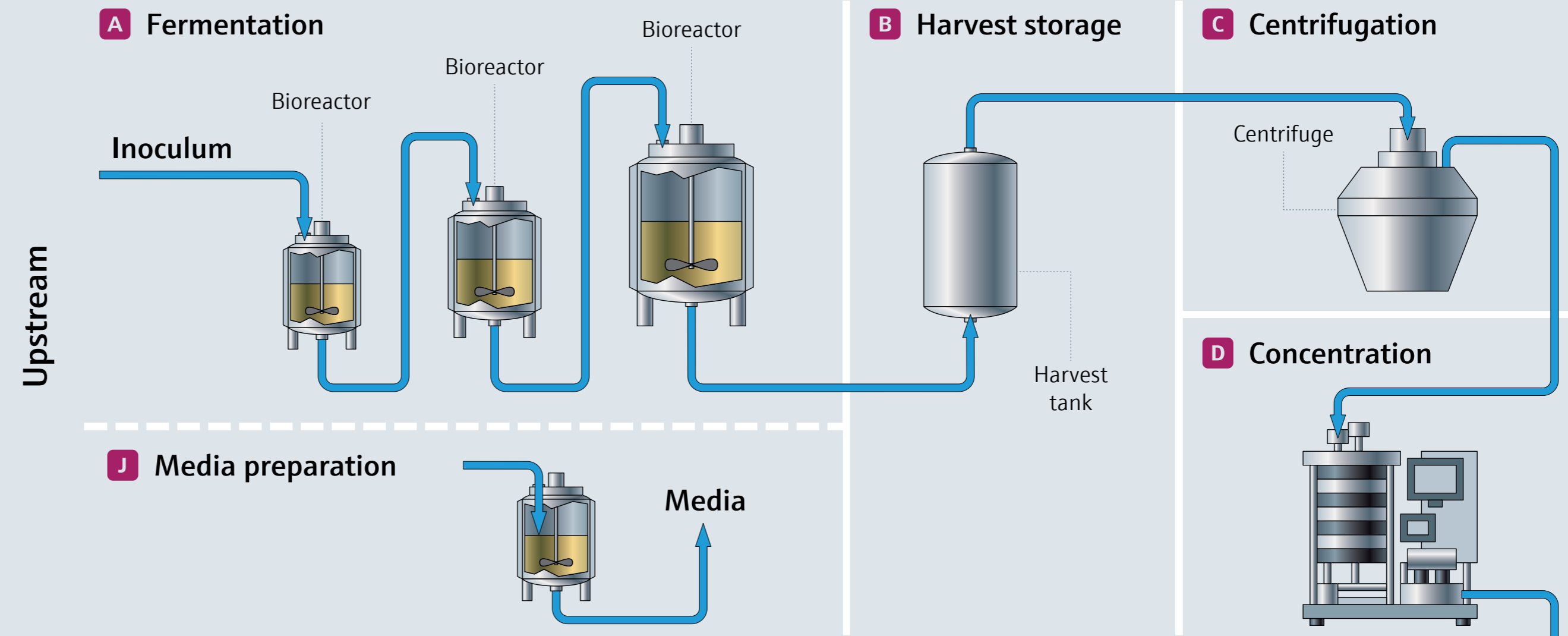
# Applications in Life Sciences

Harness the power of Raman for robust chemical composition analysis in upstream bioprocesses

Real-time, inline analysis is an indispensable tool for upstream process optimization. Recent advances have made it possible for Raman analysis to be introduced into the smallest bioreactor setups, as well as large-scale single-use bioreactors (SUBs).

With 24/7 process monitoring and control, Endress+Hauser's latest single-use devices help biopharmaceutical manufacturers optimize bioreactor conditions and feed control, ensuring optimal growth for microorganisms and cell cultures.

## Bioprocess overview



Overview of fermentation process steps in bioprocessing with opportunities for composition analysis measurement.

### Upstream bioprocessing

In the upstream realm, Endress+Hauser Raman systems shine, revealing molecular composition process insights that could not be "seen" before. Endress+Hauser has collaborated with leading technology providers to extend our Raman portfolio with single-use offerings for critical upstream, inline bioprocess measurements.

### Upstream applications well suited to Raman measurement include:

- Metabolite monitoring
- Feed control
- Cell growth
- Monitor capsid integrity and filling
- Yield predictability
- Many other PAT/QbD applications

# Technical data

Understanding our Raman single-use portfolio technical details

Everything you want to know about our Raman single-use portfolio for bioprocessing.

## Analyzer compatibility

- Raman Rxn2 or Raman Rxn4 embedded analyzer\*

## Sampling compatibility

- Rxn-10 probe (for single-use and multi-use optic)
- Rxn-46 probe is compatible with BioPAT Spectro for Ambr and Biostat STR by Sartorius

## Probe configuration

- Single or four channel (for single-use and multi-use optic)
- Single channel for Ambr (with the Rxn-46 probe)
- Single or four channel for Biostat STR (with the Rxn-46 probe)

## Laser wavelength

- 785 nm, 1000 nm (single-use optic)
- 785 nm (multi-use optic and Rxn-46 probe)

## Spectral coverage

- Limited by the coverage of the analyzer being used

## Maximum laser power into probe head

- < 499 mW

\*For the Rxn-46 probe, analyzers with Raman RunTime v6.2.2+ software are required





> Single use

# Raman optic system for single use

Let's focus on the technical details

The Raman optic system for single use offers a disposable pathway to a ready-to-use gamma-sterilized window, allowing operators to get Raman data from a SUB without compromising sterility or optical performance. Its disposable SUB couplings not only facilitate precise Raman sampling, but the reusable part of the probe features a patented self-focusing lens for automatic alignment. This optical design assures the ultimate spectral quality and reproducibility.

Endress+Hauser Raman disposable fittings come in multiple configurations, such as Barb-shaped or PG13.5 port compatible. The Raman optic system for single use has been tested and qualified by multiple SUB vendors and implemented at multiple biopharmaceutical companies from process development to cGMP.

## Raman optic system for single use



### Sample interface

- **Temperature:** 0 to 100 °C (32 to 212 °F)

### Wetted materials

- **Wetted materials (SUB fitting):** 316L stainless steel
- **Window:** proprietary material, optimized for bioprocesses
- **Process connection:** varies according to single-use bioreactor vendor port and fitting type
- **Surface finish:** Ra 0.38 µm (Ra 15 µin) with electropolish
- **Adhesive:** USP Class VI and ISO 10993 compatible

### Immersible length

- Dimensions vary according to single-use bioreactor vendor port and fitting type

### Immersible diameter

- Dimensions vary according to single-use bioreactor vendor port and fitting type

### Sterilization method

- Gamma sterilized

### Calibration method

- **785 nm:** multi optic calibration accessory\* (recommended) or HCA-785 with single-use calibration adapter
- **1000 nm:** HCA-1000 with single-use calibration adapter

### Verification method

- **785 nm:** multi optic verification accessory with 70% IPA (recommended) or bIO Sample Chamber with 70% IPA and single-use calibration adapter
- **1000 nm:** bIO Sample Chamber with 70% IPA and single-use calibration adapter

\*Requires analyzers with Raman RunTime v6.2.2+ software



# Raman bio multi optic and bio sleeve

## Get a more in-depth look

The dual-part bio multi optic and bio sleeve, paired with an Rxn-10 probe, provide accurate, real-time, *in situ* measurements of crucial parameters in your bioprocess.

Like our single-use optic, the bio multi optic features a patented self-aligning lens for the utmost spectral quality and reproducibility. Since it does not contact the process, the multi optic allows calibration and verification steps to be conducted at any time, even mid-batch if necessary. This convenience significantly boosts the overall efficiency of the entire bioprocessing operation.

## Raman bio multi optic

Reusable component



<b>Sample interface</b>	<ul style="list-style-type: none"> <li>n/a (non-contact)</li> </ul>
<b>Wetted materials</b>	<ul style="list-style-type: none"> <li>n/a (non-contact)</li> </ul>
<b>Immersible length</b>	<ul style="list-style-type: none"> <li>n/a (non-contact)</li> </ul>
<b>Immersible diameter</b>	<ul style="list-style-type: none"> <li>n/a (non-contact)</li> </ul>
<b>Sterilization method</b>	<ul style="list-style-type: none"> <li>n/a (non-contact)</li> </ul>
<b>Calibration method</b>	<ul style="list-style-type: none"> <li>Multi optic calibration accessory* (recommended) or HCA-785 with bio sleeve attached to bio multi optic</li> </ul>
<b>Verification method</b>	<ul style="list-style-type: none"> <li>Multi optic verification accessory with 70% IPA (recommended) or bIO Sample Chamber with 70% IPA and bio sleeve attached to bio multi optic</li> </ul>

\*Requires analyzers with Raman RunTime v6.2.2+ software

## Raman bio sleeve

Disposable component



<b>Sample interface</b>	<ul style="list-style-type: none"> <li><b>Temperature:</b> -30 to 150 °C (-22 to 302 °F)</li> <li><b>Maximum pressure:</b> 13.8 barg (200 psig)</li> </ul>
<b>Wetted materials</b>	<ul style="list-style-type: none"> <li><b>Wetted material - Body:</b> 316L stainless steel</li> <li><b>Window:</b> proprietary material, optimized for bioprocesses</li> <li><b>Process connection:</b> PG13.5</li> <li><b>Surface finish:</b> Ra 0.38 µm (Ra 15 µin) with electropolish</li> <li><b>Adhesive:</b> USP Class VI and ISO 10993 compatible</li> </ul>
<b>Immersible length</b>	<ul style="list-style-type: none"> <li>120 and 220 mm (4.73 and 8.67 in)</li> </ul>
<b>Immersible diameter</b>	<ul style="list-style-type: none"> <li>12 mm (0.48 in)</li> </ul>
<b>Sterilization method</b>	<ul style="list-style-type: none"> <li>Autoclave, with the use of the sleeve desiccator rated for 10* autoclave cycles (30 minutes each) at 131 °C (268 °F)</li> <li>Compatible with gamma sterilization</li> </ul>
<b>Calibration method</b>	<ul style="list-style-type: none"> <li>n/a unless attached to bio multi optic with HCA-785</li> </ul>
<b>Verification method</b>	<ul style="list-style-type: none"> <li>n/a unless attached to bio multi optic and bIO Sample Chamber with 70% IPA</li> </ul>

\*Potential to last many more cycles based on your site-specific autoclave protocols and process conditions



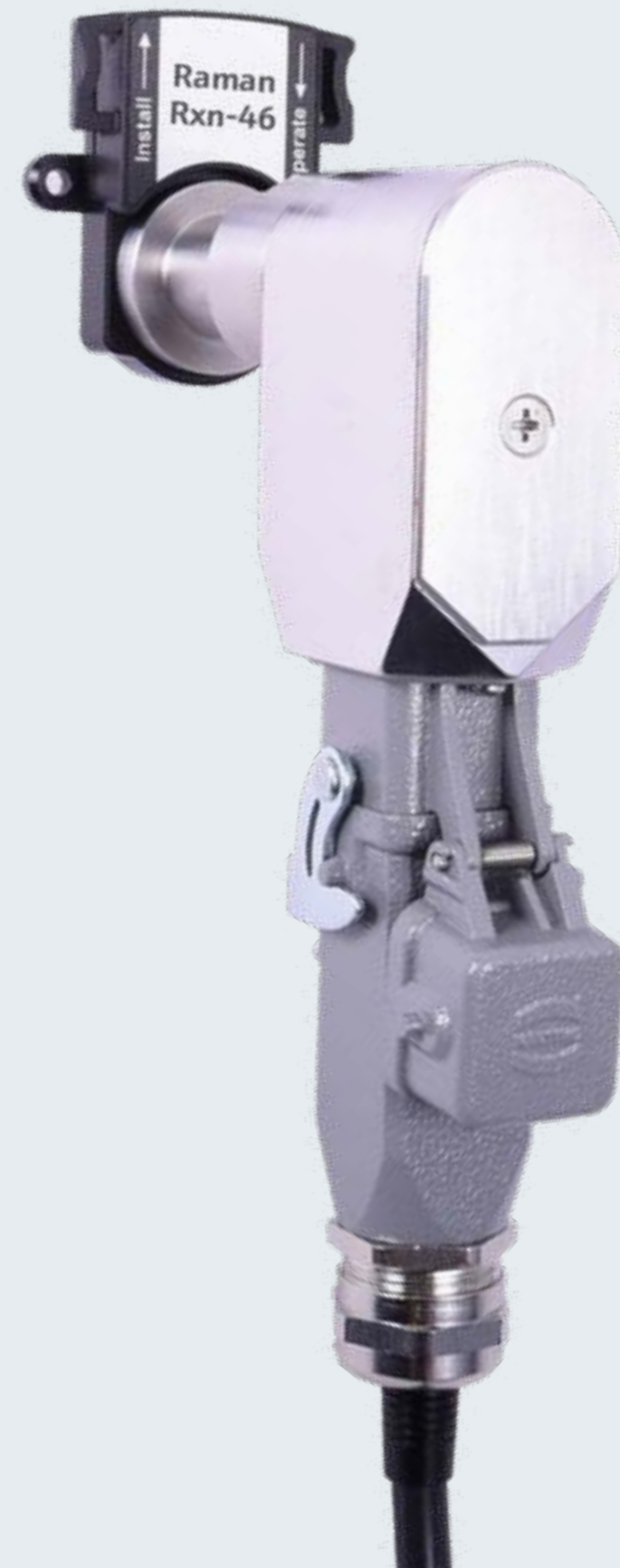
# Raman Rxn-46 probe

How the Rxn-46 probe works with BioPAT Spectro by Sartorius

Integrating Endress+Hauser Raman spectroscopy into Ambr enables Quality by Design (QbD) methods that are scalable to all sizes of Biostat STR single-use bioreactors. When paired with a Raman Rxn analyzer, the Rxn-46 probe works together with the Sartorius system as follows:

- Raman probes attach to the BioPAT Spectro single-use port.
- Ports come ready to use and fully qualified.
- Probe connection to the port is fast and simple.
- Raman collection is isolated from bubbles and light (no additional light blocking is required).

## Raman Rxn-46 probe



### Sample interface

- **Temperature:** probe is non-contact; operating temp: 10 to 50 °C (50 to 122 °F)

### Wetted materials

- **Process connection:** Sartorius BioPAT Spectro

### Immersible length

- n/a

### Immersible diameter

- n/a

### Sterilization method

- n/a

### Calibration method

- Rxn-46 probe calibration cell\*

### Verification method

- Rxn-46 probe verification cell

\*For analyzers with Raman RunTime v6.2.2+ software

## Quick and easy calibration and verification

A specially designed Rxn-46 calibration and verification kit is available that includes all the necessary hardware for calibration of the Rxn-46 probe when paired with a Raman Rxn analyzer (note: kits are also available for the single-use optic and multi optic).





## Why partner with Endress+Hauser?

30+ years of Life Sciences innovation, expertise, and customer success

Endress+Hauser is the global leader in Raman instrumentation for laboratory, process, and manufacturing environments in the Life Sciences industry. In particular, biopharmaceutical manufacturers rely on our Raman analyzers and probes to help drive lab-to-process optimization.

Our Raman bioprocessing technology stands apart from other alternatives in the market because we offer:

- 30+ years of lab-to-process Raman leadership, expertise, innovation, and reliability
- 20+ years of cGMP expertise (10+ years leading the bioprocess PAT journey), with proven compliance, method transfer, and up time
- Proven successes documented in countless biopharmaceutical customer publications and other industry publications
- ISO 9001:2015 certification and experience hosting many successful audits by leading pharma/biopharma companies and suppliers
- The security of partnering with the Endress+Hauser Group and its network of global and local support process automation experts
- The most trusted, robust, scalable, and reliable Raman analyzer systems on the market
- Superior bioprocessing probes known for having the highest quality of contact materials and the most flexible sampling capabilities
- A demonstrated ability to simplify process equipment complexity and ease method transferability from lab-to-manufacturing
- Experience, training, support, data modeling, and advanced analytics services to allow companies to achieve rapid ROI
- Pharma Manufacturing's 2020 Pharma Innovation Award for the Rxn-46 bioprocessing probe





> Other single-use offerings

## Additional Endress+Hauser single-use devices

Did you know that Endress+Hauser also offers these other single-use products for biomanufacturers?

### Liquicap FTZ61 single-use foam detector

Foam detection in single-use bioreactors.

### Proline Promass U 500 single-use Coriolis flowmeter

The first single-use flowmeter with premium performance and cGMP compliance for the biopharmaceutical industry.



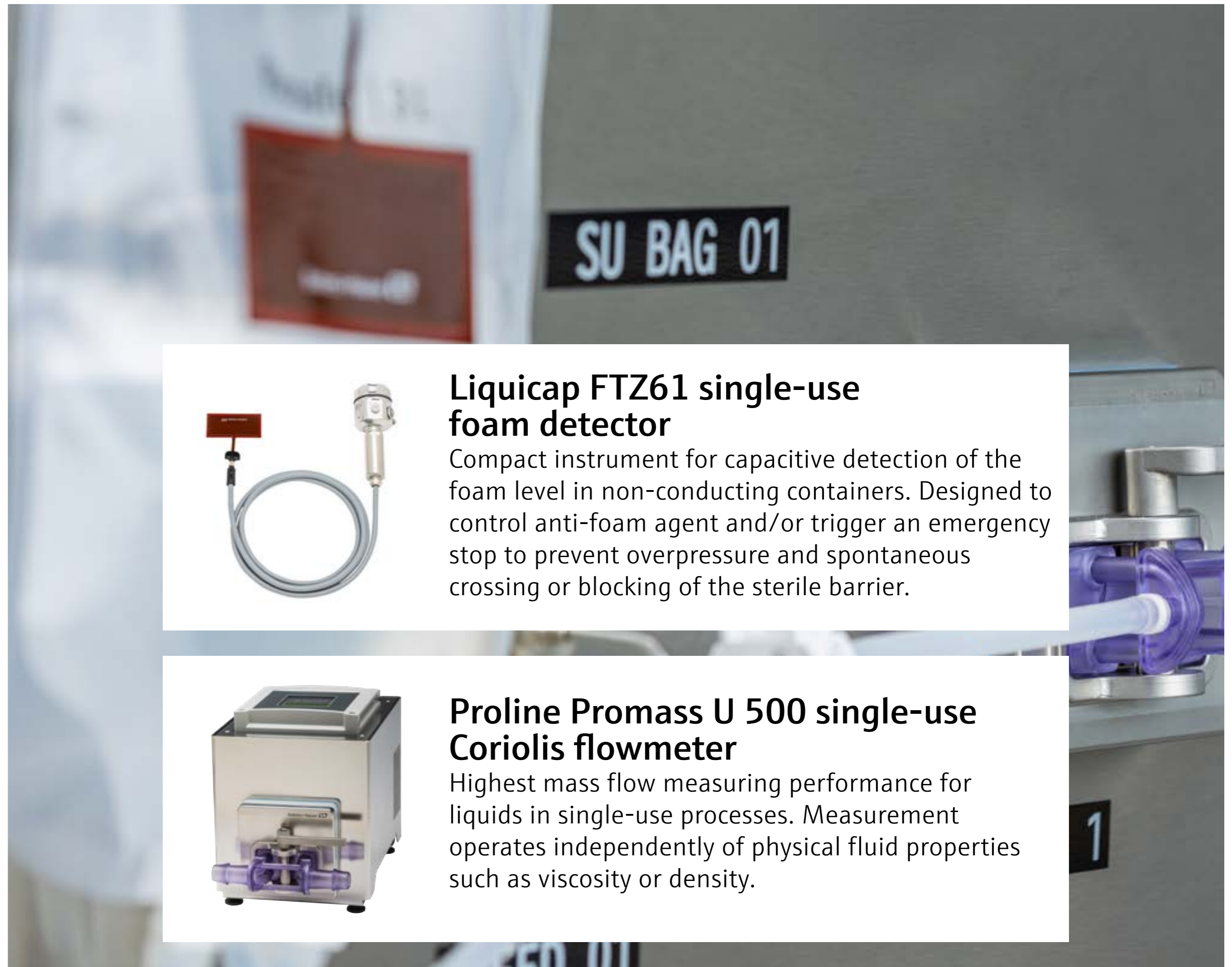
### Liquicap FTZ61 single-use foam detector

Compact instrument for capacitive detection of the foam level in non-conducting containers. Designed to control anti-foam agent and/or trigger an emergency stop to prevent overpressure and spontaneous crossing or blocking of the sterile barrier.



### Proline Promass U 500 single-use Coriolis flowmeter

Highest mass flow measuring performance for liquids in single-use processes. Measurement operates independently of physical fluid properties such as viscosity or density.



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