Portfolio
Life Sciences

Endress+Hauser
People for Process Automation

Get to market faster – manage risk

Dear reader,

Three decades ago, when the first biopharmaceutical manufacturers announced their intention to develop, produce and sell inhalable insulin, Endress+Hauser became the main supplier for all process measurements. Since then, we have been proudly committed to developing products, services and solutions to address the challenges of an industry bound by tight regulatory compliance, quality assurance and product safety requirements.

Today, we see how a wave of innovations is driving the transformation of the life sciences industry. Over the past few years, smart device usage has increased, advanced analytics have been popularized and digital connectivity has been adopted across the board. Single-use systems became a successful alternative to stainless steel equipment, in particular in biopharmaceutical operations. Also, highly automated processes have become increasingly widespread, in combination with real-time monitoring of quality parameters and careful risk management. This is where Endress+Hauser can help you.

This brochure presents a visual selection of the ASME BPE-compliant product portfolio, especially designed for the life sciences industry. In here, you will find a technology, product or service that fits your requirements for every measurement need. Endress+Hauser offers you full solutions, from standardized automation, reliable monitoring and predictive maintenance to expert consulting in process scale-up and calibration services. We remain committed to supporting you to achieve your goals – whether it be to accelerate time to market, sustain operational excellence or manage risk.

Learn more about our life sciences offering:
www.endress.com/life-sciences

8 All from one source

Benefit from our extensive portfolio of industry-conforming products, solutions and services throughout your plant's entire life cycle

22 Service by your side

Our service portfolio was developed to increase production uptime, enable compliance with industry standards and improve overall equipment effectiveness

32 Optical analysis

Industry-proven Raman spectroscopy analyzer and probe portfolio

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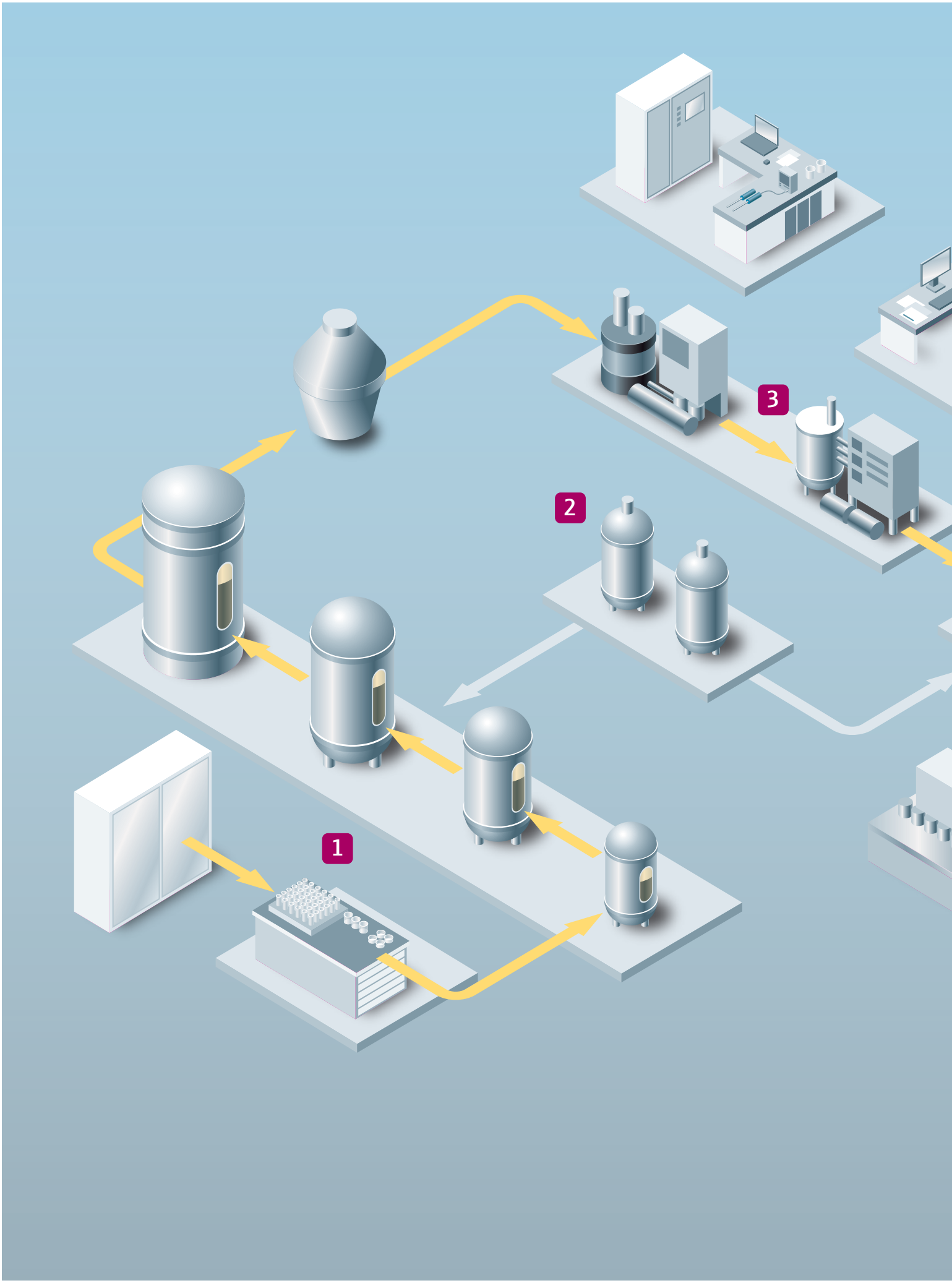
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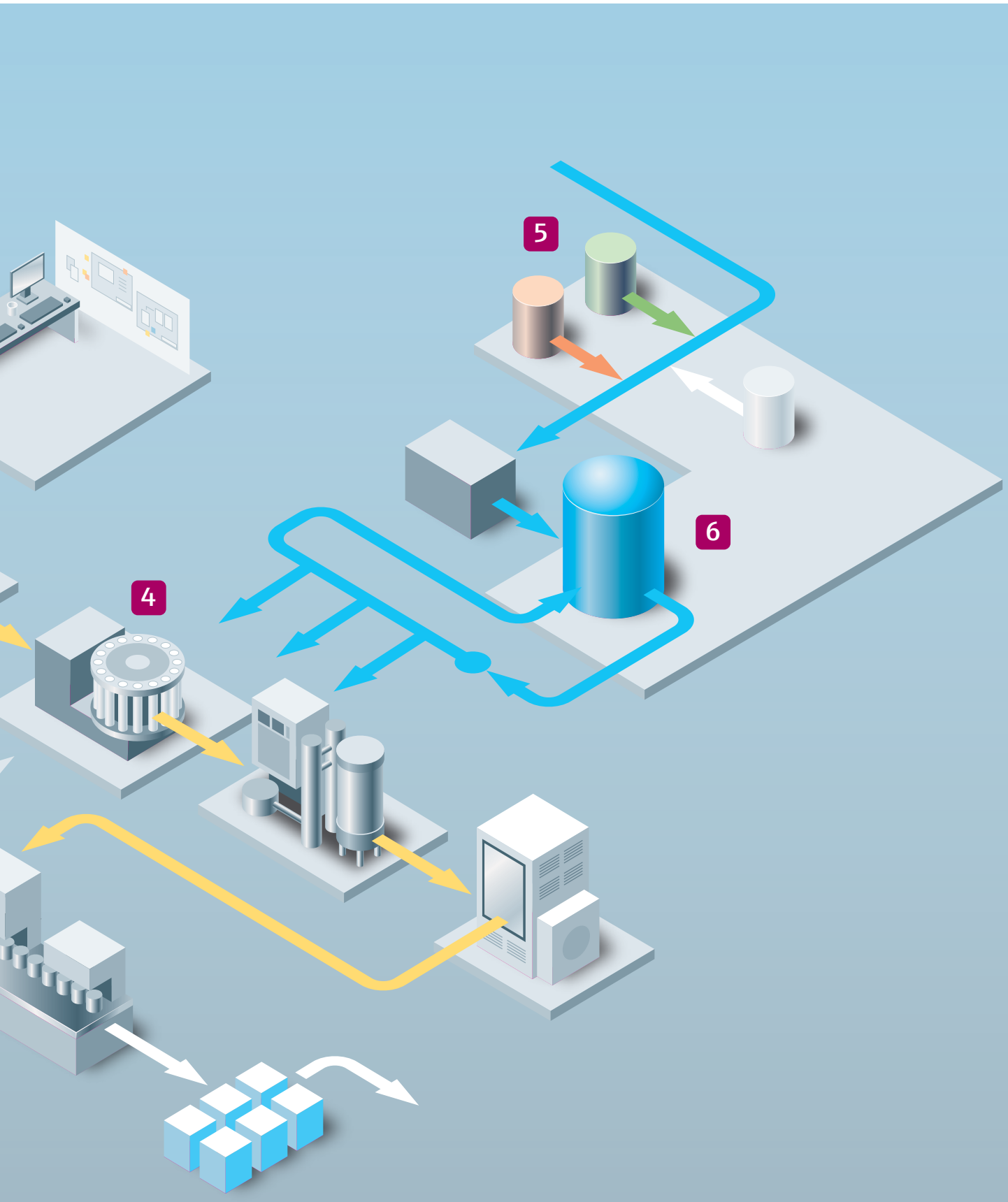


Life sciences process

1. Fermentation (upstream process)
2. Media and buffer preparation
3. Concentration / virus filtration
4. Chromatography
5. Water purification (purified water)
6. Water purification (distribution)

Compliance

Validation Master Plan

Goals The compliance Validation Master Plan (VMP) translates requirements from the current Good Manufacturing Practices (cGMP) for regulated industries into current guidelines, procedures and working instructions. The VMP describes the mandatory requirements for products, processes and services as the foundation, as well as organizational requirements to ensure proper behavior in a globally harmonized way.
The Life Sciences Strategic Industry Group standardizes and manages the implementation with support from its network of members. Aspects of computerized systems validation are dealt with as part of digitalization initiatives. The standard serves as a base for local audits and assessments.

Benefit for Endress+Hauser customers Defining and executing validation plans shows customers in the regulated industries that Endress+Hauser understands their business. Endress+Hauser designs, produces, tests, and delivers measurement devices, solutions, and services that meet pharmaceutical and biopharmaceutical industry regulations. Our support team is specifically trained in the requirements of the life science industry and has in-depth expertise in cGMP.

Benefit of standardization The benefit of standardization is that it provides a common language, terminology and comprehensive flow of procedures and tasks that are essential for the implementation of projects and subsequent maintenance in a heavily regulated industry like the Life Sciences. The FDA's regulations will become more and more stringent in the future and will impact other industries as well. The VMP defines those rules that have to be met by Endress+Hauser.

Scope of the standard This VMP will be applied to each operating unit that handles, produces and services products for the regulated industries (GxP relevant systems).

Who is working with the standard? Roles that will be involved in ensuring that standards are followed include: Technical heads and validation teams of corporate units, system owners for each IT application and process, data owners for GxP relevant systems, human resource managers, and quality managers.

Who is affected by this standard? All associates involved in and working for GxP relevant processes would be affected, including but not limited to: management, R&D, IT personnel, engineering, service and maintenance.

What is standardized?
- Validation fundamentals and responsibilities
- Planning and documentation
- GxP areas and relevant systems at corporate level
- GxP review processes, training
- Related external and internal standards and guidelines

Global standards

Validation and qualification are important steps in the life cycle of any piece of processing equipment. Regulatory authorities such as the FDA provide only general guidelines and few specific details related to the cGMP design and manufacture of equipment for the pharmaceutical industry. Therefore, manufacturers of such equipment must rely on other standards and guidelines, such as the American Society of Mechanical Engineers Bioprocessing Equipment (ASME BPE) standard and the International Society for Pharmaceutical Engineering (ISPE) Good Automated Manufacturing Practice (GAMP®) guidelines.

ASME BPE

ASME BPE is the leading standard on how to design and build equipment and systems used in the production of biopharmaceuticals, which includes bioprocessing, pharmaceutical and personal care products. The standard covers system design, materials, fabrication, inspections, cleaning and sanitization, testing and certification for both multi-use and single-use equipment.

Designing a cGMP-compliant biotech plant requires an intense coordination effort between multiple component vendors and equipment manufacturers. Writing design specifications is a time-consuming task. The ASME BPE standard serves as a way to simplify and improve communication between the user, supplier and manufacturer as every party must adhere to the same requirements. An ASME BPE-compliant system can profit from harmonized mechanical specs as well as from a unified set of documentation.

Audit safety

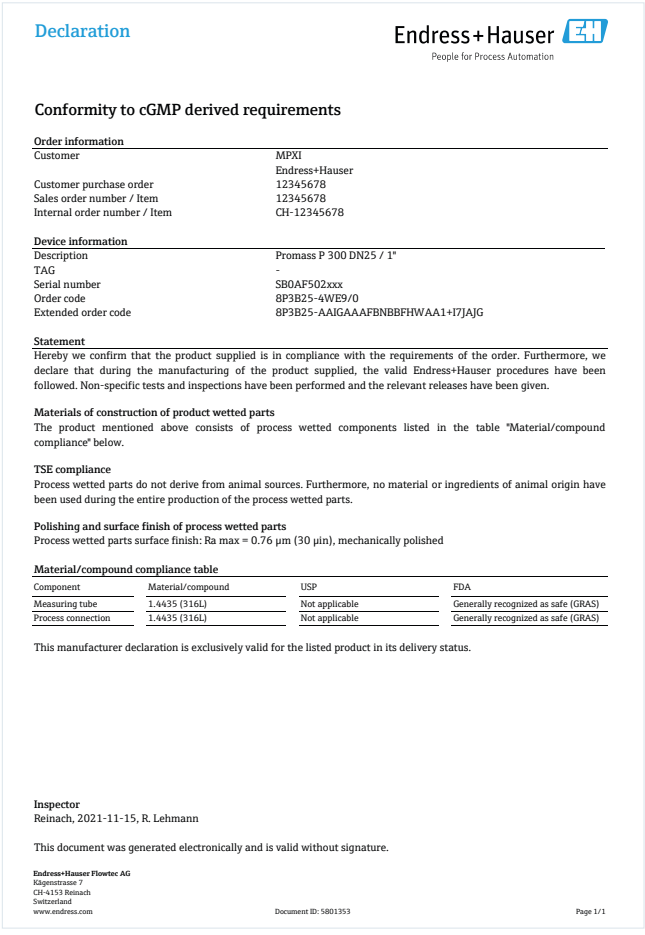
Having the right documentation available is critical during the validation and qualification phase. Every ASME BPE-compliant instrument is delivered with a comprehensive set of documents including a CoC (Certificate of Compliance) according to ASME BPE. This declaration is unique and traceable to the respective instrument by serial number, ensuring that the product meets or exceeds the requirements as specified in the latest revision of the ASME BPE standard.

ASME BPE has become established as one of the most accepted and comprehensive guidelines to define processing equipment for the life sciences industry. Instruments carrying the CoC are recognized by the authorities as components with the greatest compliance and suitability for life sciences applications.

Compliance

For a system or component to be ASME BPE-compliant, adherence to all applicable parts of the standard is required. The stringent requirements of BPE often mean that only devices specifically designed according to the standard can achieve full compliance. Endress+Hauser offers a complete portfolio of instruments that are designed and manufactured according to ASME BPE.

ASME BPE-compliant Promass P 100 Coriolis mass flowmeter



Declaration

Endress+Hauser
People for Process Automation

Conformity to cGMP derived requirements

Order information

Customer	MPXI Endress+Hauser
Customer purchase order	12345678
Sales order number / Item	12345678
Internal order number / Item	CH-12345678

Device information

Description	Promass P 300 DN25 / 1"
TAG	-
Serial number	SB0AF502xxx
Order code	8P3B25-4WE9/0
Extended order code	8P3B25-AAIGAAAFBNBBFHWAA1+I7JAJG

Statement

Hereby we confirm that the product supplied is in compliance with the requirements of the order. Furthermore, we declare that during the manufacturing of the product supplied, the valid Endress+Hauser procedures have been followed. Non-specific tests and inspections have been performed and the relevant releases have been given.

Materials of construction of product wetted parts

The product mentioned above consists of process wetted components listed in the table "Material/compound compliance" below.

TSE compliance

Process wetted parts do not derive from animal sources. Furthermore, no material or ingredients of animal origin have been used during the entire production of the process wetted parts.

Polishing and surface finish of process wetted parts

Process wetted parts surface finish: Ra max = 0.76 µm (30 µin), mechanically polished

Material/compound compliance table

Component	Material/compound	USP	FDA
Measuring tube	1.4435 (316L)	Not applicable	Generally recognized as safe (GRAS)
Process connection	1.4435 (316L)	Not applicable	Generally recognized as safe (GRAS)

This manufacturer declaration is exclusively valid for the listed product in its delivery status.

Inspector

Reinach, 2021-11-15, R. Lehmann

This document was generated electronically and is valid without signature.

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Switzerland
www.endress.com

Document ID: 5801353

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Certificate of Compliance (CoC) ASME BPE

All from one source

Benefit from our extensive portfolio of industry-conforming products, solutions and services throughout your plant's entire life cycle

Now more than ever, the life sciences industry must deal with the ever-increasing pace of the marketplace. To meet your goals, you need a partner that enables you to cover the most critical measurement parameters – from bench to pilot plant, and from there to a fully automated commercial-scale operation. Endress+Hauser has a portfolio carefully designed to meet your needs for high productivity while meticulously aligning with GMP standards and the strictest regulatory requirements.

How can we help you? To start with, you will have only one point of contact right from the inception of your project. We offer products based on different technologies to optimize a wide range of measurement parameters from lab to process. Take level measurement in bioreactors, for example. For smaller bioreactors, radar or guided wave radar are the ideal technologies. For the larger ones, using differential pressure is more advantageous.

When thinking about commissioning or qualification, having instruments from the same provider results in a more standardized, straightforward process. In case you prefer working with a selection of different suppliers, our experienced service technicians can even install, commission and validate their instruments.

Once your plant or application is up and running, you can still benefit from relying on a primary instrumentation vendor like Endress+Hauser. Thanks to our modular instrumentation platform, you can reduce the number of spare parts you need to keep in stock. In addition, services like maintenance, verification and calibration become easier to manage when the instruments are sourced from the same provider.

Standardization of instrumentation early in the project phase can reduce project complexity and risk.

80%

Fewer temperature measurement types through standardization

3%

of initial investment saved on annual operating costs through standardization

100%

Matching instruments to user requirements – perfectly engineered, right the first time

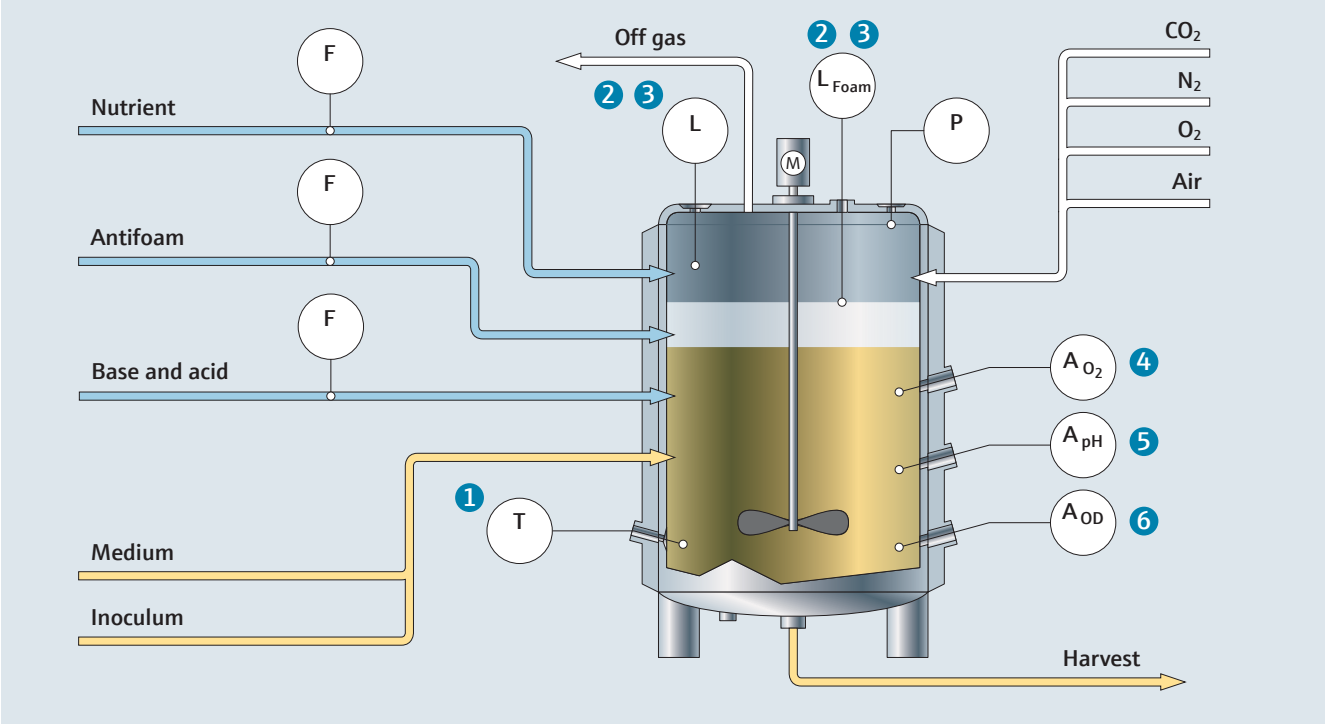
Standardization from the beginning

Manufacturing plants in the life sciences industry are typically assembled from OEM skids from different suppliers, using their individual instrumentation standards. Depending on the size and complexity of the production facility, the number of different measurement devices can rapidly multiply. Their integration, commissioning, calibration, documentation and the spare parts handling becomes unnecessarily cumbersome and expensive, bringing with it a higher risk of human error.

By standardizing the instrumentation at an early project phase and coordinating with the skid suppliers, the installed base can be dramatically simplified. Our knowledgeable instrumentation engineers can support you in defining the right technology for your applications.

Fermentation

Maximum cell growth and titer is achieved at optimal temperature, pH and nutrition supply



1 – iTHERM TrustSens TM371

World's first self-calibrating thermometer

- Risk and cost reduction thanks to self-calibration and Heartbeat technology
- Fully automated, traceable, inline self calibration
- Automatized documentation, memory for 350 calibration points
- Printable calibration certificate – audit proof

F L E X

www.endress.com/TM371

2 – Levelflex FMP53

Guided wave radar level measurement for hygienically sensitive applications with full cleanability

- Reliable level measurement even for changing product (density), process conditions and in the presence of foam
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA

F L E X

www.endress.com/FMP53

3 – Deltabar FMD72

Electronic differential pressure system with metal sensors for level, pressure, volume or mass measurement

- Low temperature effect, high reproducibility and long-term stability
- Low total cost of ownership due to reduced installation time, maintenance and spares requirements
- Small flush-mounted process connections for hygienic applications

F L **E** X

www.endress.com/FMD72

4 – Memosens COS81E

Dissolved oxygen sensor for optimal oxygen supply for the growing organisms

- Precise and stable dissolved oxygen measurement after autoclaving, SIP and CIP cycles
- Easy handling and reliability thanks to Memosens technology and self-monitoring via reference LED
- High long-term stability and enhanced maintenance intervals thanks to optical technology
- Designed for life sciences applications with 12 mm design for standard assemblies and direct insertion into benchtop fermenters

F L **E** X

www.endress.com/COS81E

5 – Memosens CPS61E

Proven pH sensor for process control in enzyme production and control of culture growth

- Stable and reliable measuring values thanks to specific pH-sensitive glass for cell growth process and pressurized gel with fixed pressure indicator
- Highest product safety thanks to full compliance with all relevant regulations like FDA and USP
- Optimized calibration management and advanced sensor diagnosis with Memobase software
- Memosens technology offers safe and reliable communication

F L **E** X

www.endress.com/CPS61E

6 – Optical sensor OUSBT66

Cell growth sensor for biomass measurements during fermentation processes

- Process safety by continuous monitoring of cell density and avoidance of contamination by sampling
- High flexibility since the sensor is available in several lengths to accommodate any fermenter and bioreactor size
- LED lamp provides long lifetime and extended measuring range
- Hygienic and CIP/SIP-resistant design

F L **E** X

www.endress.com/OUSBT66

Fast and easy scale-up with Memosens technology

Simplify your process and boost your efficiency

Pre-calibrated sensors for easy maintenance and minimized process downtime

Memosens CPS61E for process control in fermentation processes and control of culture growth

The development of new vaccines, therapeutic proteins and other biopharmaceutical substances is based on fermentation processes and cell cultivation of gene-manipulated microorganisms or higher cells, e.g., human, mice or hamster cells. This process is very time- and cost-intensive. The drugs are manufactured in a cascade of bioreactors of different sizes. Usually, the production process starts in small bioreactors (1–20 liter) and the volume of the next bioreactor increases with each cycle until the final production scale (up to 20,000 l) is reached.

In upscaling processes it is essential to run the process during each cultivation step in similar environmental conditions and parameters to maximize the product yield and quality. The most critical analytical process parameters are pH and dissolved oxygen, and both parameters need to be controlled permanently. Consistent measurement values can be achieved by using the same sensors in all process steps and scales. Endress+Hauser Memosens technology promotes this consistency.

Ideal environment: pH value in cell cultivation
The product yield from cell cultivation is strongly dependent on the pH value of the nutrient medium. As an example, mammalian cells require a pH value slightly above 7, and for optimal growth and replication the pH needs to be maintained within the range of 0.1 to 0.2 pH units. Since the fermentation tends to decrease the pH value in the medium, continuous inline control is required.

Elixir of life: Oxygen for cell growth
Microorganisms and cells need oxygen to survive, and the propagation as well as the formation of the wanted biomolecule depends on the level of dissolved oxygen in the medium. Since the oxygen is consumed by the microorganism, it is essential to monitor the concentration permanently and precisely. Furthermore, inline monitoring of dissolved oxygen allows an optimal dosing of sterile gas to maintain an optimal oxygen concentration in the medium.

Ensure product quality and yield with Memosens technology

Digital Memosens sensors can help to optimize all steps from lab to process

Memosens technology supports your scale-up process with consistent digital measured values and helps to transfer the values inductively to the transmitter via a non-contact connection. As a result, moisture and corrosion, which could corrupt the measured value or cause the measuring point to fail, do not stand a chance. This is particularly important for glass bioreactors, which are usually autoclaved together with the sensors before use. The bottom line is maximum data transmission safety, which significantly increases the availability of the measuring point and process safety.

In addition, digital sensors with Memosens technology save calibration, sensor and process data, which means they can be calibrated and regenerated in the lab under ideal conditions with Memobase software. This not only increases the operating life of the sensors but also makes commissioning and maintenance considerably easier and cuts process downtime to a minimum. Thanks to a bayonet lock and automatic sensor detection, pre-calibrated sensors can be replaced in the field in next to no time and the data saved can be used for predictive maintenance and process automation. In addition to sensor calibration, Memobase software enables smart sensor and quality management, thereby helping to drive down operating costs.

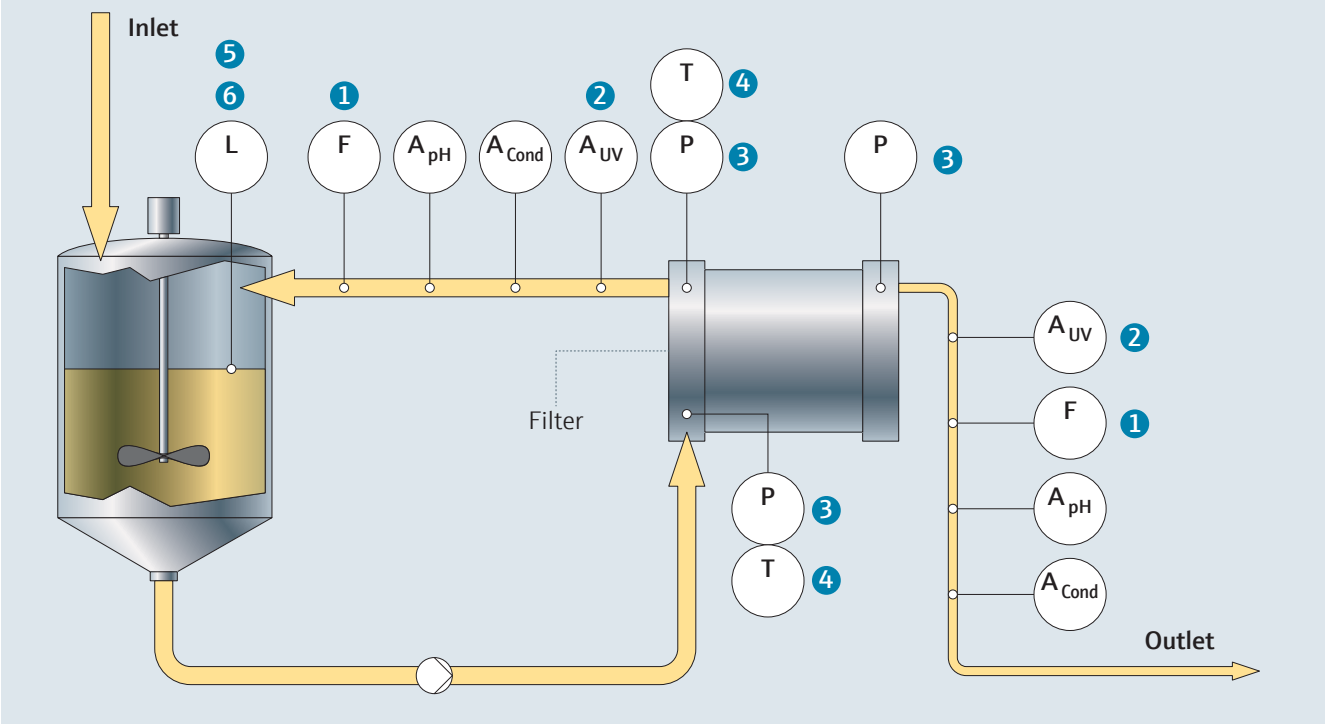
With Memosens technology, it is possible to combine each sensor with a member of the Liquiline transmitter family: from single-parameter to multiparameter devices, from stainless steel field housings to cabinet installations, and from simple handheld devices to devices connected directly to a PC with Memobase software. Memosens and Liquiline offer the utmost in flexibility when it comes to installing and integrating devices in higher-level process control systems. In addition, their standardized, user-friendly operation and menu navigation increase operating reliability, and storage costs are reduced as identical hardware modules are used for the entire platform. Benefit from seamless liquid analysis from one supplier.

All benefits at a glance:

- Decrease time to market while upscaling with Memosens technology
- Reduce your qualification effort
- Maximize your product quality and yield
- Simplify your process control
- Same sensors for all process steps

Concentration and virus filtration

Reliable pressure control leads to the desired concentration



1 – Proline Promass P 100

Coriolis mass flowmeter with a large turndown ratio providing highest accuracy in demanding applications

- Designed according to ASME BPE with all welded stainless steel 1.4435 (316L) wetted parts and electropolished surface finish
- Comprehensive documentation package including ASME BPE CoC ensures maximum audit safety
- Multivariable measuring (flow, density, temperature) for advanced process control
- Digital system integration for full access to extended device and process data

F L E X

www.endress.com/8P1B

2 – Optical Sensor OUSAF44

Inline sensor for UV absorption in concentration measurement

- Maximized product yield thanks to fast and reliable monitoring of measured values for exact concentration and to avoid product loss
- Patented Easycal™ system option for easy, liquid-free online calibration traceable to NIST
- Low-maintenance sensor with long service life and stable operation
- Early detection of breakdowns in filtration thanks to monitoring of the permeate

F L E X

www.endress.com/OUSAF44

3 – Cerabar M PMP51

Pressure transmitter with a compact metal piezoresistive measuring cell

- High accuracy even in changing process temperatures
- Small flush-mounted process connections
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA

F L E X

www.endress.com/PMP51

4 – iTHERM TM411

Easy-to-use metric version with outstanding sensor technology

- User-friendly and reliable from product selection to maintenance
- iTHERM QuickSens: fastest response times (t90s: 1.5 s) for optimum process control
- iTHERM StrongSens: unsurpassed vibration resistance (> 60 g) for ultimate plant safety
- iTHERM QuickNeck – cost and time savings thanks to simple, tool-free recalibration
- Over 50 hygienic process connections

F L E X

www.endress.com/TM411

5 – Micropilot FMR63B

Non-contact radar level measurement for hygienic sensitive applications

- Intuitive and easy guided operation
- Heartbeat Verification enables to check the measuring performance of the device in a traceable and documented manner, without process interruption
- Heartbeat Monitoring secures the process in case of foam or build-up
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA

F L E X

www.endress.com/FMR63B

6 – Liquiphant FTL50H/51H

Vibronic point level switch for hygienic applications in all liquids

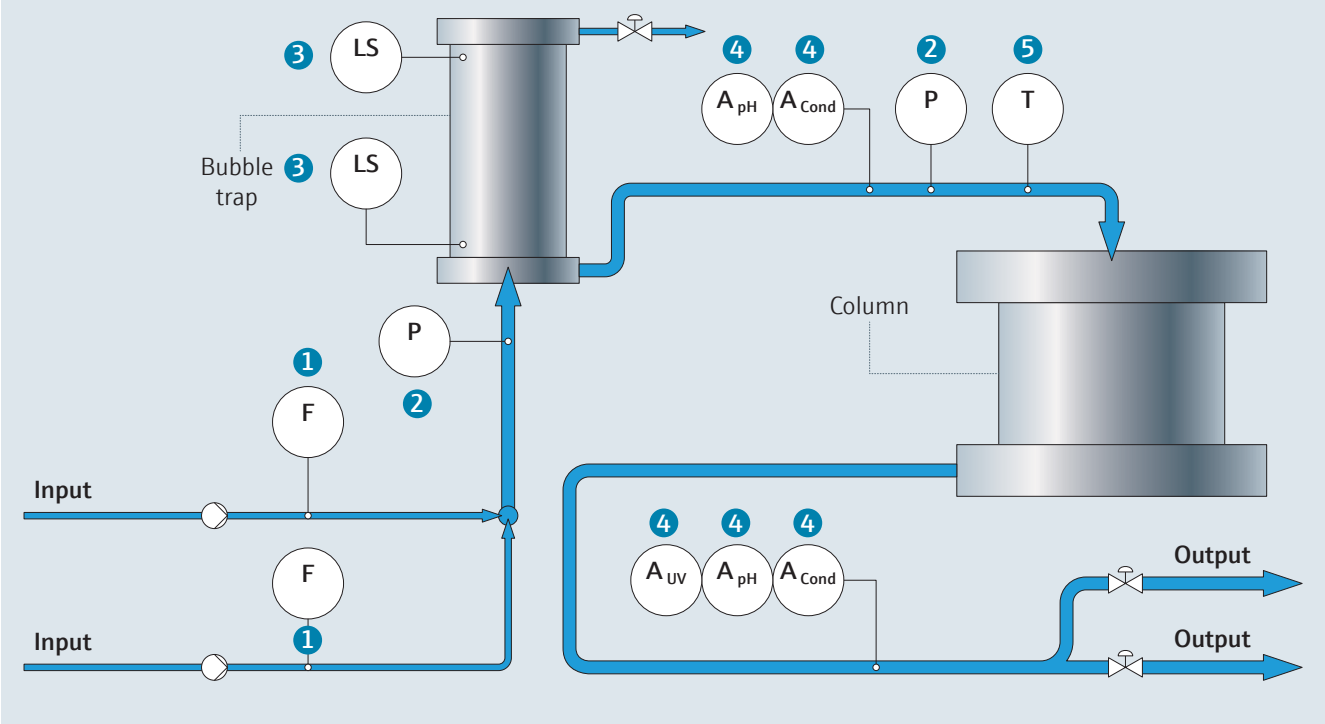
- Real plug & play sensor offered without any need for adjustment even in changing media
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA
- Guaranteed function and mechanical safety due to permanent monitoring of fork

F L E X

www.endress.com/FTL50H

Chromatography

Precise buffer concentration and reliable measurement of the target protein load maximize the yield



1 – Proline Promass A 500

Coriolis mass flowmeter for accurate measurement of smallest quantities

- Delivering highest accuracy for smallest flow rates independent of fluid properties
- Less calibration effort and maximum reliability thanks to Heartbeat Technology
- Easy to clean (CIP/SIP) with a fully-welded stainless steel design in 1.4435 (316L)
- Space-saving installation with a compact single-tube design

F L **E** X

www.endress.com/8A5C

2 – Cerabar M PMC51

Pressure transmitter with oil-free ceramic measuring cell

- Oil-free measuring cell for enhanced product safety
- High mechanical and vacuum resistance
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA

F **L** E X

www.endress.com/PMC51

3 – Liquiphant M FTL50H

Vibronic point level switch for hygienic applications in all liquids

- Real plug & play sensor offered without any need for adjustment even in changing media
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA
- Guaranteed function and mechanical safety due to permanent monitoring of fork

F L **E** X

www.endress.com/FTL50H

4 – Memosens CPS61E / Memosens CLS82E / Optical Sensor OUSAF44

Analytical chromatography package including pH, conductivity and UV sensor

- All analytical instruments for chromatography processes from one supplier, including pH and conductivity measurement, UV photometers and the respective assemblies
- Reliable performance of all components during the process
- Fast response time for process safety
- Accurate pH measurement with the Memosens CPS61E to get the ideal pH value for binding
- Bacteria- and steam-tight conductivity sensor Memosens CLS82E with wide measuring range during all separation steps
- UV sensor OUSAF44 with patented Easycal™ system option for easy, liquid-free online calibration traceable to NIST
- Only one Liquiline CM44P is needed to connect all sensors and photometers and capture values reliably
- State-of-the-art Memosens technology for easy operation and handling

F L **E** X

www.endress.com/CPS61E
www.endress.com/CLS82E
www.endress.com/OUSAF44

5 – iTHERM TM411

Easy-to-use metric version with outstanding sensor technology

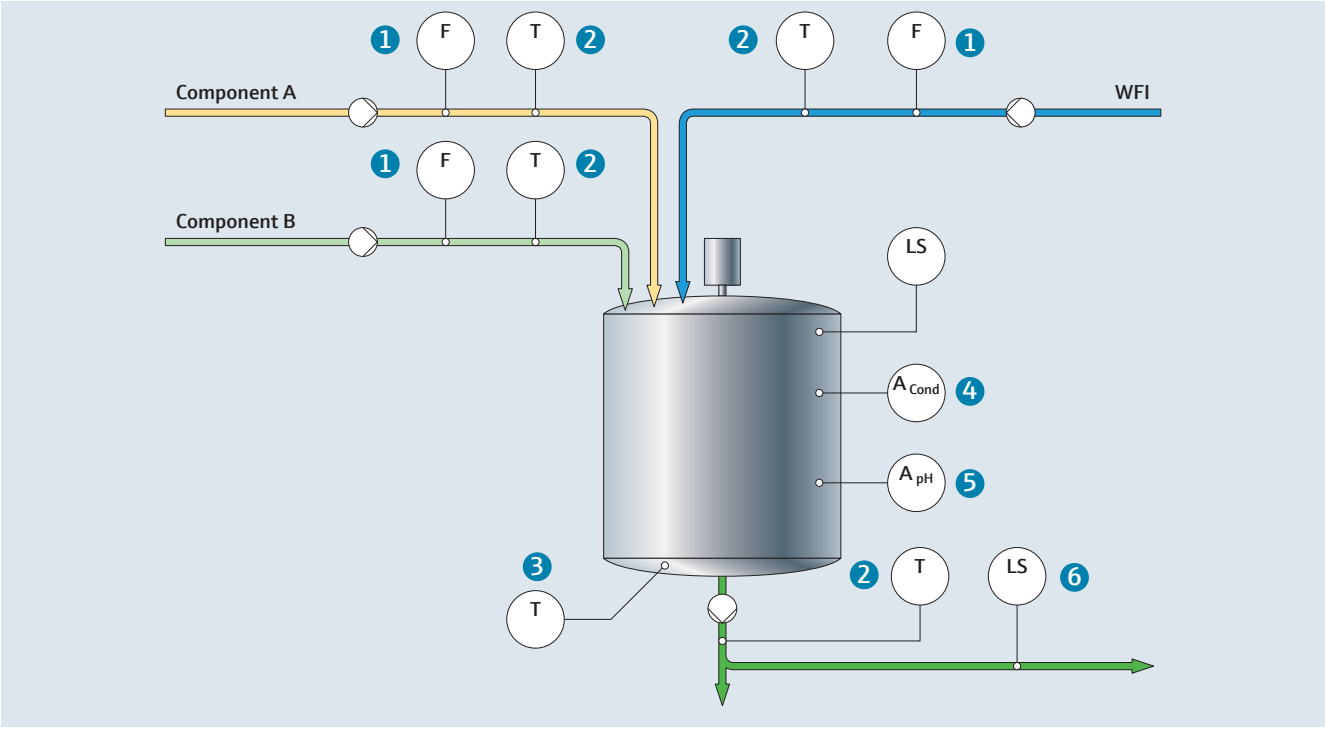
- User-friendly and reliable from product selection to maintenance
- iTHERM QuickSens: fastest response times (t90s: 1.5 s) for optimum process control
- iTHERM StrongSens: unsurpassed vibration resistance (> 60 g) for ultimate plant safety
- iTHERM QuickNeck – cost and time savings thanks to simple, tool-free recalibration
- Over 50 hygienic process connections

F L **E** X

www.endress.com/TM411

Media and buffer preparation

Batch or inline: the perfect composition of buffer and media is key



1 – Proline Promass P 100

Coriolis mass flowmeter with a large turndown ratio providing highest accuracy for dosing and batching

- Designed according to ASME BPE with all welded stainless steel 1.4435 (316L) wetted parts and electropolished surface finish
- Large turndown for accurate dosing and process control
- Small footprint with fully self-drainable design, even in horizontal installations where space is limited
- Digital system integration for full access to extended device and process data

F L E **X**

www.endress.com/8P1B

2 – iTHERM TM411

Easy-to-use metric version with outstanding sensor technology

- User-friendly and reliable from product selection to maintenance
- iTHERM QuickSens: fastest response times (t90s: 1.5 s) for optimum process control
- iTHERM StrongSens: unsurpassed vibration resistance (> 60 g) for ultimate plant safety
- iTHERM QuickNeck – cost and time savings thanks to simple, tool-free recalibration
- Over 50 hygienic process connections

F L **E** X

www.endress.com/TM411

3 – iTHERM TrustSens TM371

World's first self-calibrating thermometer

- Risk and cost reduction thanks to self-calibration and Heartbeat technology
- Fully automated, traceable, inline self-calibration
- Automatized documentation, memory for 350 calibration points
- Printable calibration certificate – audit proof

F L E **X**

www.endress.com/TM371

4 – Indumax CLS54D

Memosens toroidal conductivity sensor for accurate concentration measurement in media and buffer preparation

- High accuracy of the composition of media and buffer solutions
- No contamination of the media thanks to compliant material and hygienic design
- Suitable for clean-in-place (CIP) and sterilization-in-place (SIP)

F L **E** X

www.endress.com/CLS54D

5 – Memosens CPS77E

Reliable non-glass sensor for pH measurement during media and buffer preparation

- Unbreakable and robust PEEK sensor body for highest product safety
- Maximum process safety thanks to non-contact inductive signal transmission which eliminates all problems due to moisture or corrosion
- Suitable for hot steam sterilization offering long-term stable measurements
- Low maintenance: ISFET technology is insensitive to temperature variations and allows long calibration intervals

F L **E** X

www.endress.com/CPS77E

6 – Micropilot FMR63B

Non-contact radar level measurement for hygienic sensitive applications

- Intuitive and easy guided operation
- Heartbeat Verification enables to check the measuring performance of the device in a traceable and documented manner, without process interruption
- Heartbeat Monitoring secures the process in case of foam or build-up
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA

F L **E** X

www.endress.com/FMR63B

The next generation of single-use instruments

The same robustness, accuracy and cGMP compliance

Single-use systems refer to manufacturing equipment designed to be used for one batch or an entire manufacturing cycle before being replaced. Single-use equipment has long been applied in the Life Sciences industry because it 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. Recent developments in single-use systems have rendered them more user-friendly and efficient, enabling fully continuous operation and plug and play modules. With these enhancements, manufacturers can now progressively convert their disposable production facilities into interconnected, fully enclosed unit operations with continuous processing.

No compromise

Nevertheless, the risks of using disposable components remain, primarily the possibility of migration of undesired materials from the plastic materials used in their construction. While material quality standards need to be maintained to ensure product quality, improvements in accuracy, resilience and robustness are required to allow more accurate process control and minimize the chances of batch loss.

"With regard to the process analysis technology (PAT) initiative of the US Food and Drug Administration (FDA), it is necessary to monitor several process parameters to ensure the quality of biotechnological products. In this context, sensors for online monitoring in disposable bioreactor systems are urgently needed." [1]

To satisfy these new requirements, more effective single-use sensing technologies are in demand. Single-use instrumentation must offer equivalent reliability and measurement accuracy as their reusable counterparts, while still providing key attributes such as minimized hold-up volume, an ergonomic design, no required calibration, and the ability to optimize costs.

Next-generation single-use sensors for the future of biopharmaceutical manufacturing

Endress+Hauser has risen to the challenge, collaborating with leading technology providers to extend our portfolio with an equivalent single-use offering for both USP and DSP applications.

Raman Rxn-46 probe connected to a Biostat STR® with BioPAT® Spectro single-use port by Sartorius

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). Whether for single-use or traditional bioreactors, fed-batch or perfusion, lab or cGMP, our Raman systems enable the production of higher volumes, minimize product loss and reduce time to market.

[1] Eibl, Regine. Single-Use Technology in Biopharmaceutical Manufacture. Available from: VitalSource Bookshelf, (2nd Edition). Wiley Global Research (STMS), 2019.

Raman interface to high throughput development through single-use commercial manufacturing

By integrating Raman into high-throughput platforms with our Rxn-46 probe and single-channel Raman Rxn2 analyzer, users can generate enough data to build robust models in a single cycle, enabling streamlined model building. Paired with a Raman Rxn2 or Rxn4 analyzer, the Rxn-46 probe also seamlessly integrates with single-use bioreactors to deliver fast, reliable and accurate measurement of key process variables.

Raman Rxn-46 probe connected to BioPAT® Spectro for Ambr® 15 and Ambr® 250 by Sartorius

Reusable Raman non-contact optic and sensor with disposable SUB fittings

Endress+Hauser also offers one of the only multi-attribute sensors commercially available for single-use bioprocess containers, comprising an integrated disposable fitting for SUBs, plus a reusable non-contact optic. Integrated single-use Raman probe connections eliminate the contamination risks associated with end-user probe sterilization and aseptic insertion. Our Raman optic system for single use is compatible with several leading SUB vendors. The end user receives a sterilized, ready-to-use and fully proficient optic system offering greater ease-of-use, fewer cleaning and maintenance requirements and minimized contamination risk, all without sacrificing performance.

Raman optic system for single use

Foam detection

Another area of development related to bioreactor applications for non-intrusive online monitoring is foam detection. Current systems require direct access to the interior of the bioreactor while maintaining sterility, which can increase production costs. Developed in cooperation with Endress+Hauser's sister company Innovative Sensor Technology (IST AG), Sartorius has launched BioPAT® Foam as part of its Biostat STR® Generation 3 system. The novel BioPAT® Foam uses an auto-adhesive patch that can be attached on the outer wall of the single-use bioreactor, eliminating the need to change the bioreactor design. The BioPAT® Foam System consists of a transmitter and a single-use sensor patch. The transmitter is the first complete system brought to market by Endress+Hauser IST AG.

A leader in measurement instrumentation, services and solutions for process engineering, Endress+Hauser is enabling the life sciences industry to maximize the opportunities of single-use systems.

Service by your side

Our service portfolio was developed to increase production uptime, enable compliance with industry standards and improve overall equipment effectiveness

By your side, with total commitment, today and into the future, Endress+Hauser will help you to meet and surpass your specific industry challenges. By achieving incremental OPEX reductions and plant availability gains, we can make a difference by helping you to compete more effectively in the global 24/7 economy.

New regulations and guidelines put in place to increase patient safety and protect the environment forced the industry to rethink its processes. We help you comply with the ever-increasing regulatory pressures while remaining competitive. Moreover, we are here to ensure that relentless technological progress does not become a threat but an opportunity to improve your processes. With Endress+Hauser Services, you give yourself every chance of success.

Calibration services
From on-site to fully accredited laboratory calibration, Endress+Hauser provides timely, traceable and cost-effective calibration services to ensure both high performance and compliance of your quality critical instruments.

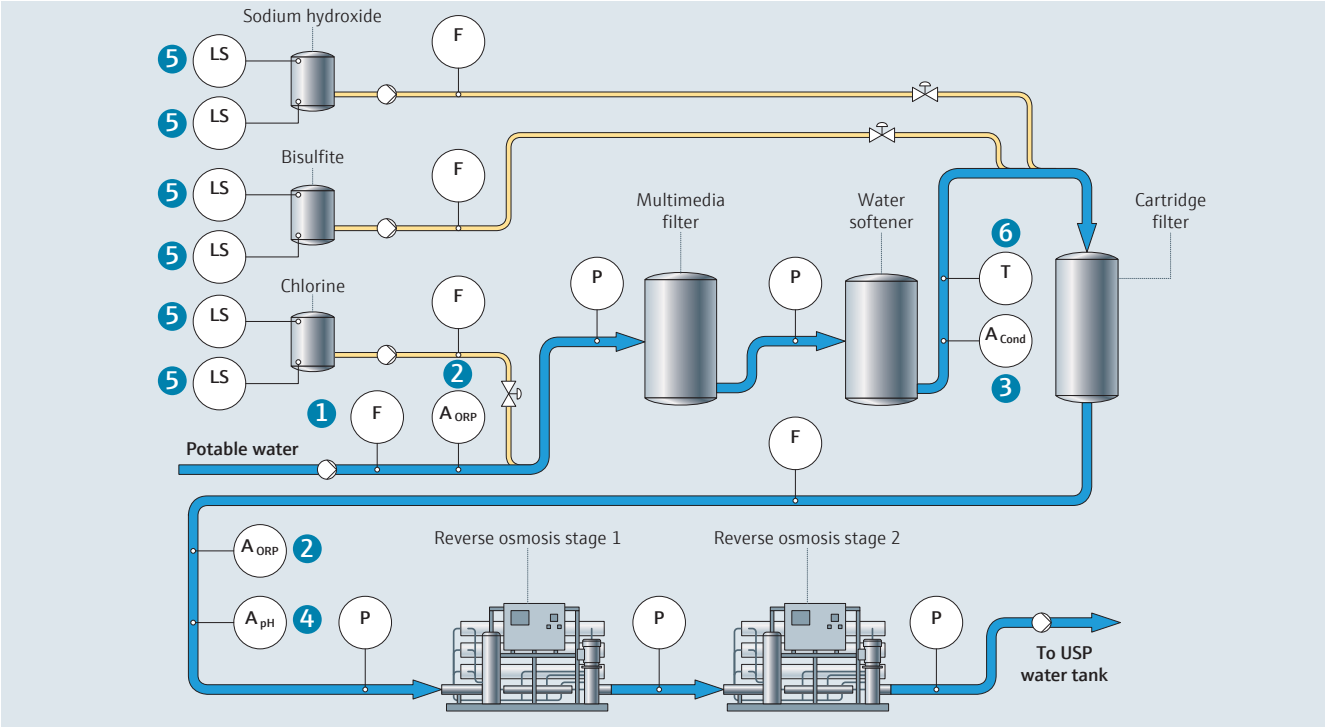
- Rely on Endress+Hauser calibration competence, available anywhere in the world
- Benefit from ISO 17025 accreditation available for many parameters in many regions
- Continuously improve your calibration process and activities with expert insights

Maintenance and calibration optimization How can you find the right balance between costs and maintenance activities without compromising quality? A review and redesign of the maintenance processes in a plant can help its managers decide how to reach their asset management goals. On the one hand, Endress+Hauser consultants analyze calibration data with in-depth metrological expertise to help customers find their optimal calibration intervals. On the other hand, the adoption of digitalization in the life sciences industry makes it possible to obtain detailed insights on the health of your installed base. This further enables optimization of current maintenance processes and reduction of operational costs.

Thorough management of your maintenance processes
With Managed Services, Endress+Hauser takes over the day-to-day management of the field instrumentation responsibilities as a strategic method for improving operations and accelerating the return on instrument investments. We define effective processes to schedule, track and record the maintenance of your critical instruments, and commit to achieving the agreed performance goals. Key performance indicators help measure progress and regular reports help to demonstrate the realized efficiency gains. When you choose Endress+Hauser as your single point of contact on the plant, we also ensure work orders are completed for third-party partners to make sure that all the required service activities are completed on time. We bring peace of mind and enable optimized productivity of your business processes with increased plant availability, transparent cost control, high quality standards and efficient asset management.

Water purification, purified water (PW)

Filters and reverse osmosis skids require complex monitoring and control



1 – Proline Promag W 400

Proven and versatile flow specialist for water applications

- Less unplanned downtime due to integrated build-up detection of magnetite or calcium carbonate
- No pressure loss thanks to full-bore design, even after pipe bends
- Flexible engineering without inlet/outlet run requirements (“0 x DN full bore” option)
- No process interruption for device verification thanks to integrated Heartbeat Technology

F L E X

www.endress.com/5W4C

2 – Memosens CPS12E

Memosens 2.0 ORP electrode for analysis of potable water before and after the purification process

- Extremely reliable measurement with non-contact, inductive signal transmission results in increased process safety
- Large, dirt-repellent PTFE junction protects from soiling by the medium
- Long diffusion path prevents poisoning of the electrode reference
- Lab calibration and fast sensor replacement on site minimize process downtimes and reduce operating costs

F L E X

www.endress.com/CPS12E

3 – Memosens CLS82E

Four-electrode conductivity sensor for conductivity measurement of softened water

- Compact design suitable for small pipe diameters and narrow, space-limited installations
- Hygienic design and materials certified and approved by EHEDG, 3-A and FDA ensure compliance with GMP requirements
- Non-contact, inductive signal transmission ensures high process and data integrity
- Absolute loop safety thanks to Memosens technology and unique detection of build-up on electrodes

F L **E** X

www.endress.com/CLS82E

4 – Memosens CPS11E

Proven pH sensor for wide application range

- Lab calibration and fast sensor exchange in the process result in minimized process downtime and longer sensor lifetime
- Robust, low-maintenance electrode: Long diffusion path and optimized ion trap prevent poisoning of the electrode reference
- Large, dirt-repellent PTFE junction protects from soiling by the medium
- Maximum process integrity through non-contact, inductive signal transmission

F L **E** X

www.endress.com/CPS11E

5 – Liquiphant FTL51B

Vibronic point level switch for applications in all liquids

- Real plug & play sensor offered without any need for adjustment even in changing media
- Developed according to IEC 61508 for highest safety – SIL2/3 applications (3rd party approved)
- Heartbeat Technology allows safe, continuous diagnostics and simple verification without process interruption

F L **E** X

www.endress.com/FTL51B

6 – iTHERM ModuLine TM131

Trend-setting, highly modular and intrinsically safe RTD or TC thermometer

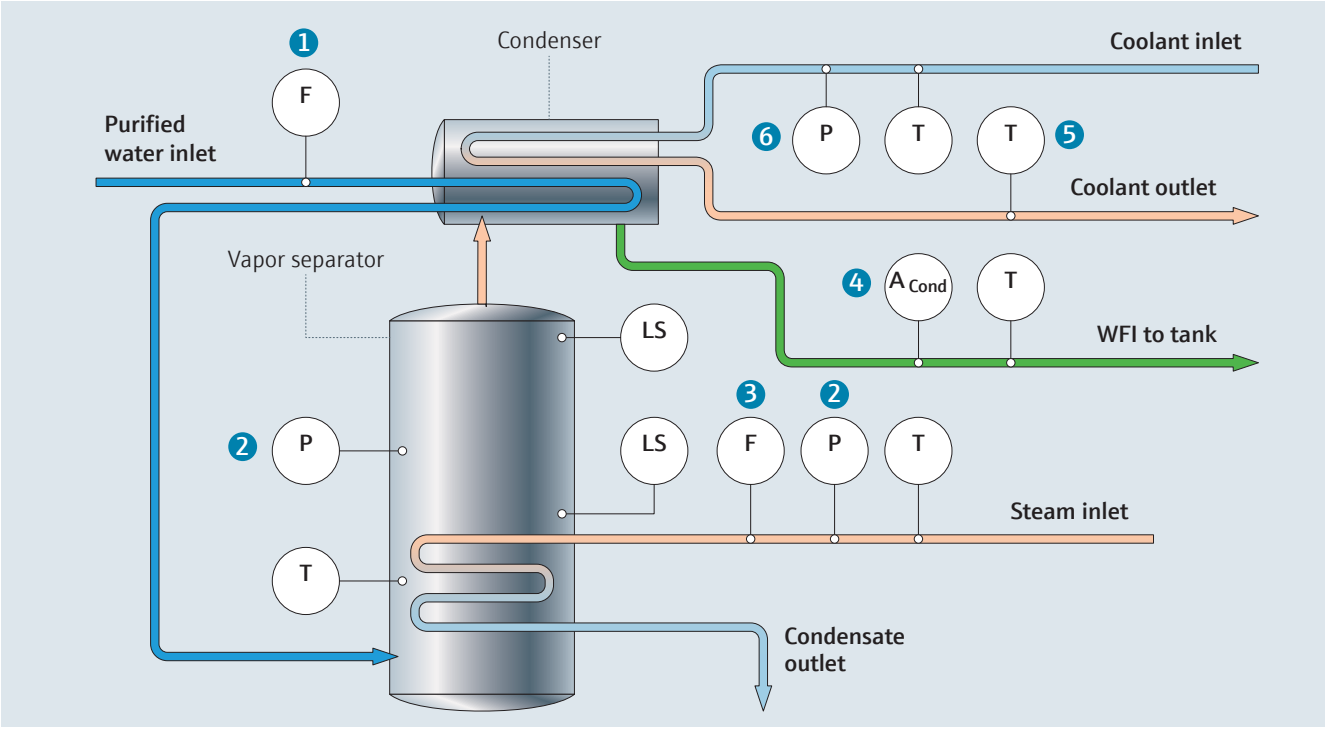
- iTHERM QuickSens: fastest response times 1.5 s for optimum process control
- iTHERM StrongSens: unsurpassed vibration resistance (> 60 g) for ultimate plant safety
- iTHERM QuickNeck: cost and time savings thanks to simple, tool-free recalibration
- Bluetooth® connectivity (optional)

F L **E** X

www.endress.com/TM131

Evaporation (WFI)

Temperature control for energy efficiency and regulatory compliance



1 – Proline Promass K 10

Cost-efficient Coriolis flowmeter for non-conductive liquids featuring simple connectivity and operation

- Coriolis mass flowmeter as an alternative to conventional volumetric and variable-area devices
- cGMP-compliant design and materials including comprehensive documentation
- Easy installation with a light and compact dual-tube sensor design
- Convenient operation and diagnostics in the field – device access via Bluetooth with SmartBlue app

F L E X

www.endress.com/8KBB

2 – Cerabar M PMP55

Pressure transmitter with fully welded compact diaphragm seal for demanding applications and media

- New and patented TempC membrane minimizes temperature influences on the measurement
- Diaphragm seal designed according to ASME BPE
- Enhanced lifetime with high resistance against temperature

F L E X

www.endress.com/PMP55

3 – Proline Prowirl F 200

Vortex flowmeter with wet steam detection, available as compact or remote version

- Integrated temperature measurement for mass/energy flow calculation of saturated steam
- Highest process safety with dualsens version for redundant measurement
- High availability thanks to proven robustness as well as high resistance to vibrations, temperature shocks and water hammer
- No maintenance required, lifetime calibration

F L **E** X

www.endress.com/7F2C

4 – Memosens CLS16E

Memosens conductivity sensor for measurements in pure and ultrapure water applications

- Highest measuring accuracy even at high temperatures and under pressure
- Sterilizable and autoclavable sensor, resists clean-in-place (CIP) and sterilization-in-place (SIP)
- Stainless steel ensures robust, corrosion-free operation and the replaceable seal enables a long operating life
- Extended storage of calibration and process data, providing a future-proof basis for predictive maintenance

F L **E** X

www.endress.com/CLS16E

5 – iTHERM CompactLine TM311

Hygienic compact thermometer with innovative sensor technology and IO-Link communication

- Extremely short response times while highly accurate even with short immersion lengths
- 4-wire, Pt100 or integrated transmitter with 4 to 20 mA output and IO-Link communication
- Breakdown information in event of sensor break or sensor short-circuit, adjustable as per NAMUR NE43
- Hygienic design with 3-A marking and EHEDG certification

F L E X

www.endress.com/TM311

6 – Cerabar PMP21

Compact pressure transmitter with a metal piezoresistive measuring cell

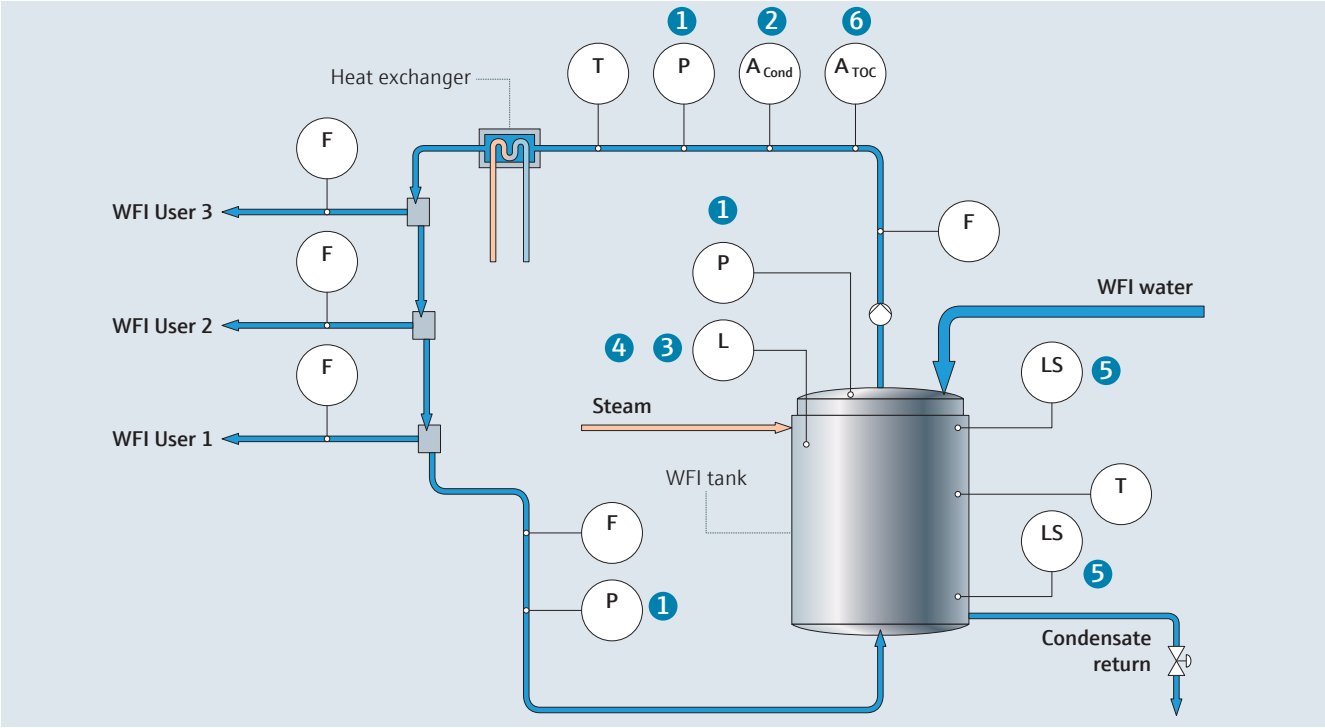
- Easy and time saving installation with customizable measuring ranges
- High quality with cost savings

F L E X

www.endress.com/PMP21

Water distribution

Avoiding microbial load by keeping water in motion and monitoring quality parameters



1 – Cerabar M PMP51

Pressure transmitter with a compact metal piezoresistive measuring cell

- High accuracy even of changing process temperatures
- Small flush-mounted process connections
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA

F L E X

www.endress.com/PMP51

2 – Memosens CLS16E

Memosens conductivity sensor for measurements in pure and ultrapure water applications

- Highest measuring accuracy even at high temperatures and under pressure
- Sterilizable and autoclavable sensor, resists clean-in-place (CIP) and sterilization-in-place (SIP)
- Stainless steel ensures robust, corrosion-free operation and the replaceable seal enables a long operating life
- Extended storage of calibration and process data, providing a future-proof basis for predictive maintenance

F L E X

www.endress.com/CLS16E

3 – Micropilot FMR63B

Non-contact radar level measurement for hygienic sensitive applications

- Intuitive and easy guided operation
- Heartbeat Verification enables to check the measuring performance of the device in a traceable and documented manner, without process interruption
- Heartbeat Monitoring secures the process in case of foam or build-up
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA

F L E X

www.endress.com/FMR63B

4 – Deltabar S FMD78

Differential pressure transmitter with metal sensors for level, volume or mass measurement

- New and patented TempC membrane, available with surface finish Ra<0.38µm electropolished for higher performance, reduced temperature effects and short recovery times

F L E X

www.endress.com/FMD78

5 – Liquiphant M FTL50H

Vibronic point level device for hygienic applications in all liquids

- Real plug & play sensor offered without any need for adjustment even in changing media
- Full compliance: ASME BPE, USP Class VI, 3-A, FDA
- Guaranteed function and mechanical safety due to permanent monitoring of fork

F L E X

www.endress.com/FTL50H

6 – TOC analyzer CA79

Precise online TOC monitoring during water distribution

- Proven UV oxidation and differential conductivity measurement
- Real-time overview of water quality with fast response time
- Clear documentation of relevant events, regular quality reports and system suitability tests (SSTs) to meet compliance requirements
- Maintenance-friendly design in combination with worldwide service network

F L E X

www.endress.com/CA79

The power of Raman spectroscopy

Real-time, lab-to-process composition measurement for process insight, faster development and improved outcomes

The use of Raman spectroscopy to monitor, adapt and control processes in the life sciences industry has grown dramatically in the last decade. The resulting process characterization can provide a roadmap for increased yields, reduced waste and an improved final product. With access to 24/7 data at multiple instances and unit operations, and a proven ability to scale from micro processes to large-scale manufacturing, Endress+Hauser Raman technology can greatly improve the efficiency of your process development by enabling rapid acquisition of process knowledge and creation of analytical models for multiple critical process parameters. This functionality makes it an ideal process analytical technology (PAT) in support of quality-by-design (QbD) initiatives by offering real-time quality assurance and better risk management throughout the process life cycle.

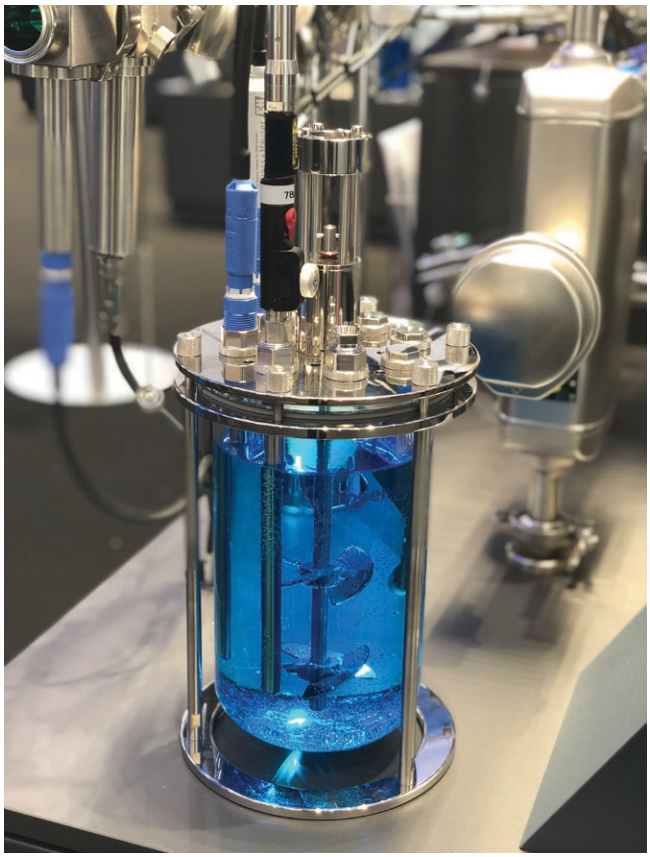
A trusted Raman partner

Endress+Hauser has been a trusted partner for Raman measurement in the life sciences industry for over 30 years. With an established installation base of more than 1,500 units throughout the world, our continued growth speaks to how much we have earned trust from global industry leaders. Our robust and reliable Raman analyzer systems deliver real-time, around-the-clock, *in situ* measurements from the laboratory to the manufacturing floor. Raman provides in-depth process characterization, allowing for enhanced product quality, reduced cycle times, increased yields, compliance with regulatory standards and facilitation of cross-scale method transfer from lab to cGMP.

Raman Rxn4 analyzer with enclosure

Wide application range

Raman spectroscopy is uniquely suited for many unit operations in cell and gene therapy, small molecule and biopharmaceutical development cycles and manufacturing processes. Raman monitoring and control applications for pharmaceuticals include API reactions, crystallization, polymorph, blending, granulations and drying. With biopharmaceuticals, applications include metabolite monitoring, feed control, column loading/elutions and many other PAT/QbD applications. Cell and gene therapy benefits from cell culture innovations, as well as the ability to monitor capsid integrity and filling. From primary reactions to continuous processes, Endress+Hauser Raman technology provides manufacturers with the capability to successfully design a transferable and efficient process for ultimately better patient outcomes.



Tailored to industry standards

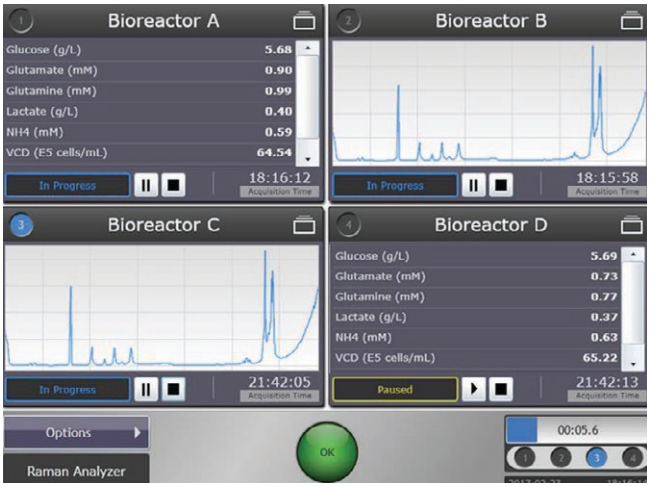
Our bioprocess probes have been designed with industry-specific requirements in mind, including strict material standards, various sterilization methodologies, port compatibility and convenience. The stainless steel surfaces offer compatibility with many industry-standard cleaning and sterilization protocols, and our window material is optimized for bioprocess measurements due to its high purity, low background and lack of interfering peaks. In fact, the Raman probe materials are identical across all our bioprocess probe lines, providing consistent performance with traditional and single-use bioreactors, in batch or continuous mode, from lab to cGMP. As a result, Endress+Hauser Raman technology can drive process optimization while easily integrating into your existing and future systems.

Lab to process scalability

A unique benefit of Endress+Hauser Raman technology is lab-to-process scalability. Our Raman analyzers are designed with a unified internal construction and feature self-monitoring, diagnostics and self-calibration routines for unparalleled method transfer capabilities. The Endress+Hauser design paradigm simplifies equipment complexity, allowing scale-up and scale-out from development to cGMP without significant model overhaul. This scalability accelerates lab-to-process cycles while also improving quality control.

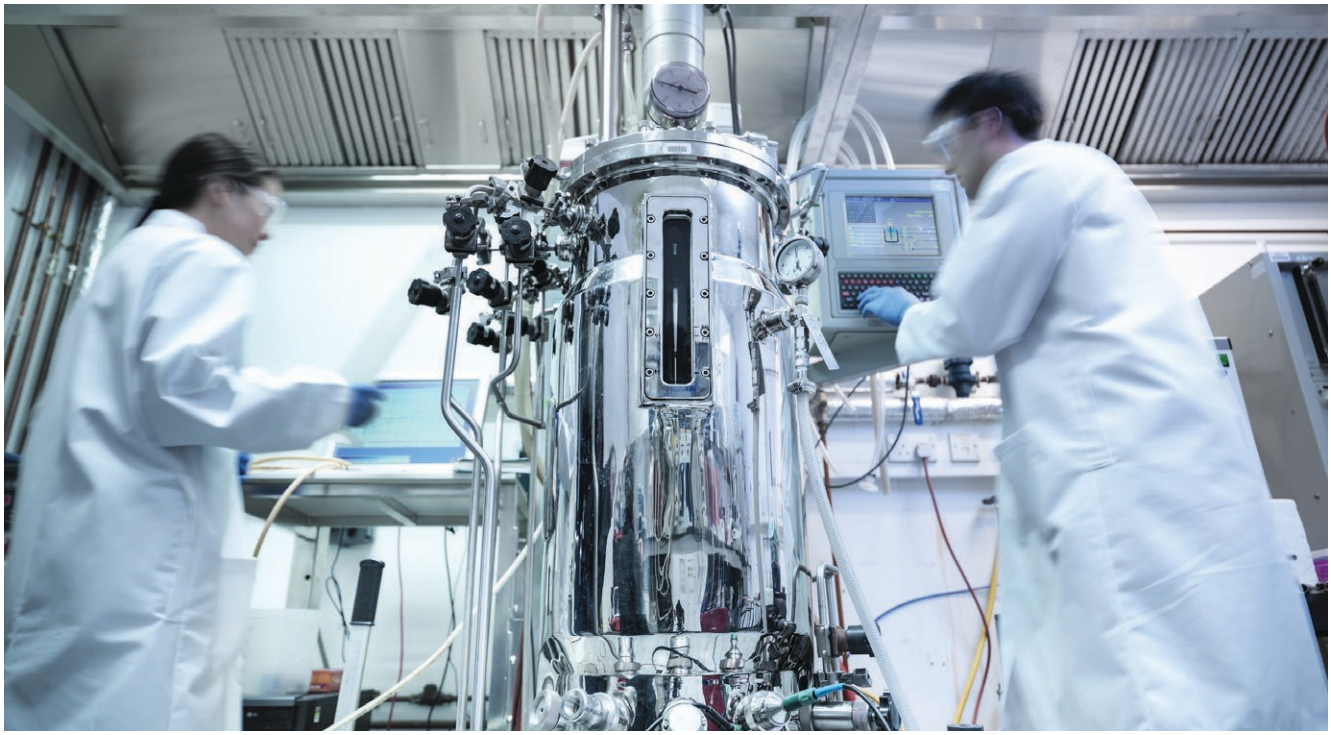
Integrated analyzer and control software with 24/7 automation

Endress+Hauser Raman technology also embodies the IIoT/Industry 4.0 strategy of increased data security, system integration and automated communication. We offer integrated Raman analyzer and control software in a fixed-purpose device with built-in intelligence. With our fully embedded Raman RunTime analyzer control software at the helm, you have constant real-time access to all your process data via a user-friendly touchscreen or remote interface. Raman RunTime can transmit raw data, processed data and diagnostics over standard communication protocols – including OPC UA or DA, Modbus and or HTTPS – to assure data integrity and compatibility with third-party devices. By connecting to leading PAT platforms, our Raman analyzer software also supports 21 CFR Part 11 / cGMP compliance. With 24/7 automation, Endress+Hauser Raman systems allow you to keep an eye on the quality and efficiency of your operations.



Optical analysis

Industry-proven Raman spectroscopy analyzer and probe portfolio



Raman Rxn2 analyzer

Designed for use in analytical laboratories with model transfer capabilities

- Reliable, real-time, *in situ* measurements
- Unified internal construction for easy model transfer
- Intuitive, fully embedded Raman RunTime control software with built-in multivariate predictors
- Configurable with up to four probes with installation via benchtop or mobile wheeled cart

F L **E** X

www.endress.com/KRXN2B

Raman Rxn4 analyzer

Designed for analysis in process and manufacturing settings

- Continuous in-line, on-line, or at-line process measurement
- Intuitive, fully embedded Raman RunTime control software with built-in multivariate predictors
- Scale-up, scale-out, and cGMP/pilot plant compatible
- Designed for rack installation (NEMA 4X enclosure available) and certified for output into hazardous area/classified environments

F L **E** X

www.endress.com/KRXN4B

Raman Rxn-10 probe with bIO-Optic

Bioprocess probe for benchtop reactors with detachable immersion optic

- Autoclavable and compatible with standard cleaning protocols
- Features PG13.5 threaded connector for headplate entry
- Compatible with Flow Assembly CYA680

F L **E** X

www.endress.com/KLBIO1

Raman Rxn-10 probe with Raman optic system for single use

Bioprocess probe with sterile, disposable fittings for single-use bioreactors

- Developed to industry standards for single-use sensors
- Gamma sterilizable
- Tested and supplied by multiple SUB vendors

F L E **X**

www.endress.com/KRSU1

Raman Rxn-45 probe

Liquid immersion probe for bioprocess composition analysis

- Polished to meet the surface finish requirements in cGMP manufacturing
- Compatible with industry standard stainless steel bioreactor ports
- Compatible with CIP/SIP standards

F L **E** X

www.endress.com/KR45

Raman Rxn-46 probe

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

- Provides a more efficient transfer for single-use commercial manufacturing
- Offers a scale-independent interface up to 2000 L in the production suite
- Requires no probe cleaning, sterilization, or frequent maintenance

F L **E** X

www.endress.com/KR46

Get all the insights with Netilion Library

Life science meets data science: drive business with IIoT

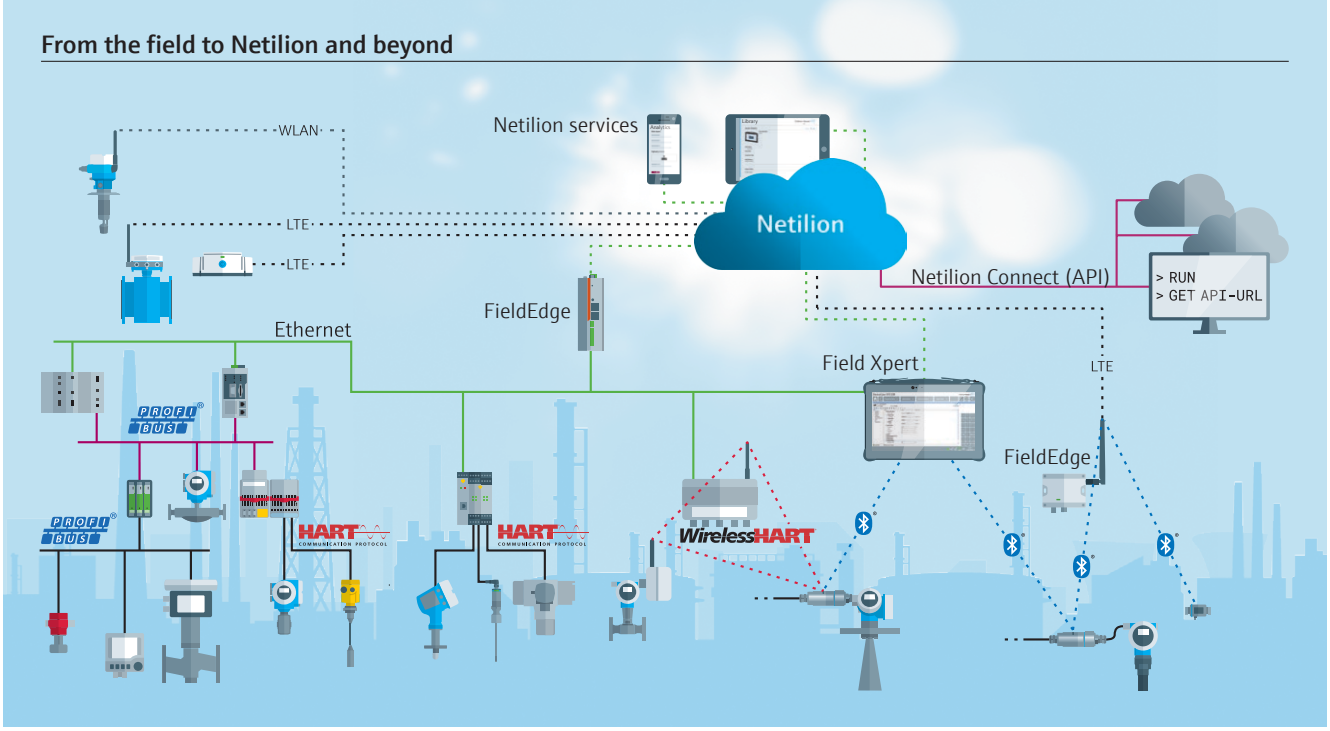
Data gathered in smart field devices delivers valuable insights into the production processes of the life sciences industry. Improving asset management of the installed base leads to better product quality and, subsequently, patient safety.

Digital transformation is already taking place in the life sciences industry. For the production and processing of its product portfolio, this is of particular relevance. The life sciences industry faces the high pressure of running processes at maximum efficiency without compromising quality and patient safety. In the past, there appeared to be few options in addressing this challenge. Now that the Industrial Internet of Things is unlocking data that was barely accessible before, new optimization potential is arising.

One important dimension of process optimization is intact equipment. Regardless of the type of equipment – instrumentation, pumps, valves, etc. – failures of critical components can cause complete production downtimes in the worst case. Key equipment data can become a crucial lever for increasing reliability. At this point, it is revealing to know that 90 percent of Endress+Hauser's field devices are already digital. Their inherent intelligence can deliver relevant information once it is unlocked.

This is where Endress+Hauser's field connectivity and the Netilion IIoT ecosystem come into play. Our technology can access crucial equipment data such as self-diagnostics as well as obsolescence status and instrument documentation. Making the information and files digitally available in a secure way increases control over the processes. Quick responses to emergencies, as well as strategic operational activities, can be based on precise data and perfectly managed documents. This is how an IIoT ecosystem creates opportunities to increase plant availability.

In addition, a data-driven approach to calibration can become an asset that yields many benefits. Primarily, digitalization can optimize calibration intervals, reducing cost and mitigating risk. However, it also gives confidence that processes are operating within tolerance. By eliminating inaccurate measurements, it assures product compliance, reduces energy inefficiency or costly raw material loss, and improves other production KPIs. Additionally, accurate and consistent results from quality-critical devices ensure product quality. As a leading manufacturer of measurement instrumentation, with our approach to facilitate data-driven calibration interval optimization, manufacturers can achieve smarter decision-making, increase outputs, reduce energy costs, improve processes, enhance skills and expand knowledge. A representative case of this is the combination of iTHERM TrustSens TM37x and the modular data manager Memograph M RSG45. The data from the self-calibration of iTHERM TrustSens TM37x is made available for further digital processing, for example in the Netilion IIoT ecosystem.[1]



Typical industrial network topology with Netilion connectivity

Endress+Hauser is a trustworthy partner in implementing digital services. The development process of the products has been certified group-wide according to IEC 62443-4-1. Our IIoT ecosystem Netilion fulfills the requirements of ISO 27017. Further, Endress+Hauser Digital Solutions complies with ISO 27001. Netilion is also easy to implement. The standard offering comprises various digital services. The Netilion Connect API module can be utilized for data integration projects or development of individual applications. There are several ways to ensure field connectivity to unlock the data from your instruments. With a partner like Endress+Hauser, whose expertise covers the hardware automation level and IIoT, you are in a position to take a major step toward the future of manufacturing.

More details on Netilion?
www.netilion.endress.com

[1]Stoll S. Hajek J 2019 iTHERM TrustSens Calibration Monitoring Whitepaper. More details on iTHERM: iTHERM TrustSens Calibration Monitoring Whitepaper

Netilion Services

Netilion Analytics is a digital service that lets you manage all the devices in your plant. Use their data to eliminate obsolescence by optimizing and standardizing your equipment. This is the first step to keeping productivity smooth and continuous.

Netilion Health reduces unplanned shutdowns with appropriate monitoring. Put your maintenance team a step ahead of problems. Netilion Health provides diagnostics from your field devices anywhere at any time, so you can have solutions ready when you need them.

Netilion Library is a file management service designed to organize documents related to your plant's instrumentation. The digital availability of these files will increase your team's performance, thanks to automated administration and simple information sharing.

Netilion Value is a digital monitoring service that connects you to your measurements wherever you are, letting you see what's happening in your facility at any time. With digital access to this information, you can manage operational quality accurately and precisely – even from a distance – and you can document your compliance.

Netilion Inventory is a digital service for inventory management that allows you to control your supplies. No matter where you are, you can monitor your containers and tanks. Having exact data about how much you have is the best way to optimize storage and logistics.

www.addresses.endress.com

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Endress+Hauser

People for Process Automation