

# Plug and measure

Proline Promass U 500: The first single-use flowmeter with premium performance and cGMP compliance for the biopharmaceutical industry

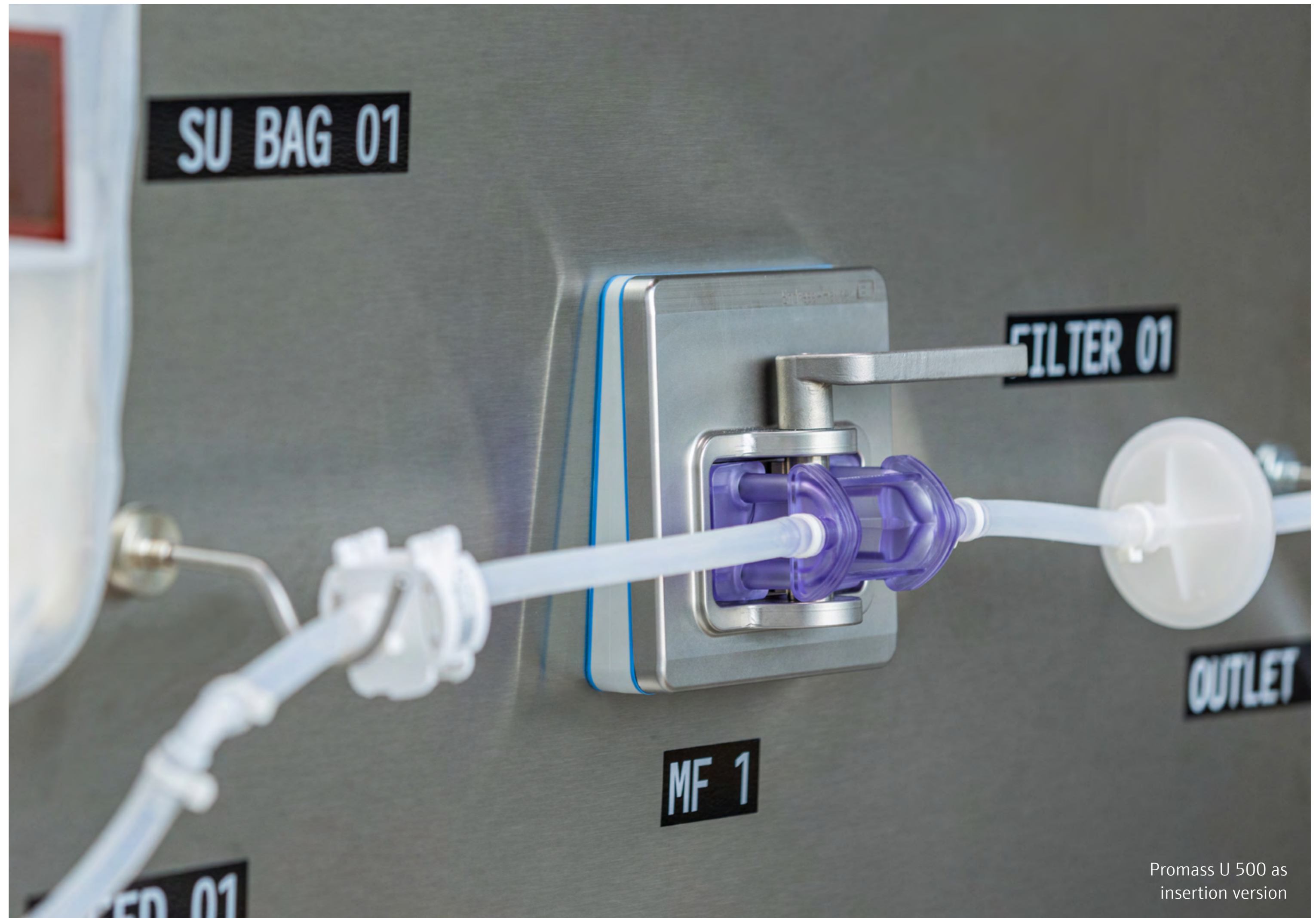


# Proline Promass U 500

Do you need high-precision, reliable flow measurement for biopharmaceutical single-use applications?

The Proline Promass U 500 Coriolis flowmeter is the solution. In addition to unbeatable measuring performance for single-use applications, it also offers multivariable measurement functions (mass flow, density, temperature). It is available as an insertion version for front panel mounting for skids as well as a tabletop version in its own housing for use in laboratories. The disposable component with the gamma-sterilizable measuring tube made of stainless steel is available in four nominal diameters: DN 04 (1/8"), DN 06 (1/4"), DN 15 (1/2") and DN 25 (1"). Both versions are inserted into the permanently installed base unit.

Promass U 500 offers cGMP compliance and automated verification of the factory calibration with Heartbeat Technology (see product features chapter). It makes it possible to achieve the best measuring performance and reliability – and makes on-site calibration unnecessary.



Promass U 500 as  
insertion version

# Benefits at a glance

Customer needs are at the center of our device development. We put great value on tackling their unique challenges in order to maximize the benefits for their processes.

This is also true for Proline Promass U 500.

The advantages at a glance:

## First-class measured values

Coriolis technology with multivariable measurement functions (mass flow, density and temperature) and the highest accuracy ( $\pm 0.5\%$ ) and repeatability ( $\pm 0.25\%$ )

## Time-saving commissioning

Seamless traceability thanks to fully automated verification of the factory calibration with Heartbeat Technology during the installation makes on-site calibration unnecessary

## Simple operation

Commissioning with one hand, even with protective equipment in a cleanroom environment, thanks to an intuitive clamping mechanism

## Flexible use

For all scales of single-use production, from cell and gene therapies to monoclonal antibodies, with flow rates from 0.12 to 75 l/min and with one base unit for all four nominal diameters

## Easy integration

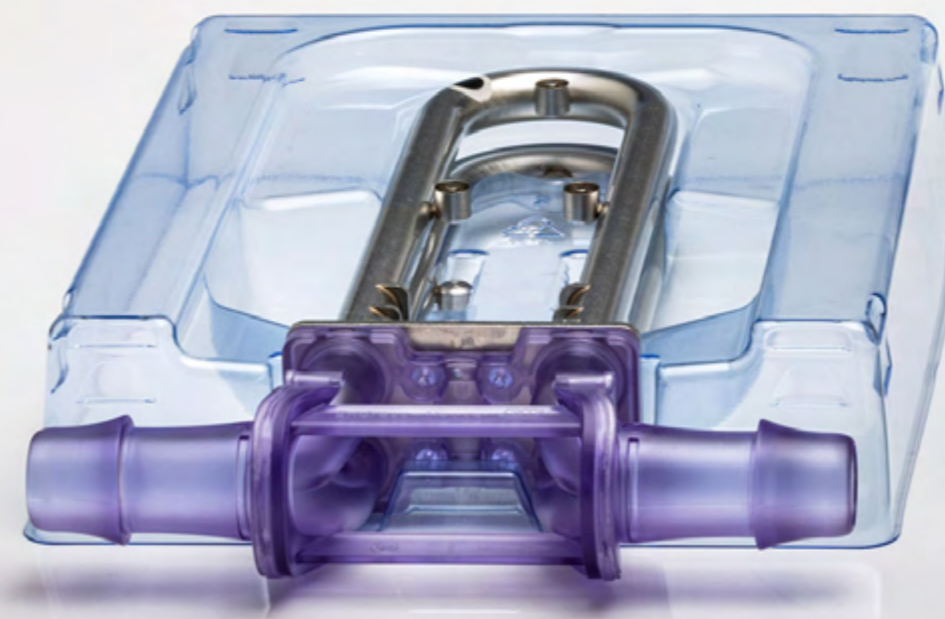
State-of-the-art communication protocols (PROFINET, Ethernet-APL/SPE, 2-wire) based on Single Pair Ethernet

## Extensive data

Full access to process and diagnostic information thanks to several freely configurable I/Os and Ethernet

## Complete industry compliance

Meets all relevant requirements for the life sciences industry (ASME BPE, BPOG, FDA, cGMP)



Promass U 500 as tabletop version with second disposable component

## Product features

Highest measuring performance and a wide range of applications for monitoring flow in biopharmaceutical single-use applications are two of the advantages of Promass U 500. Furthermore, the Coriolis measuring device has several special features in store to help customers tackle their challenges.





## cGMP compliance

Manufacturers of pharmaceuticals have to guarantee the safety of their products, which means processes and manufacturing must meet strict quality and regulatory standards. One of the most widely used standards is the “Current Good Manufacturing Practice” (cGMP) implemented by the US Food and Drug Administration (FDA).

Promass U 500 supports manufacturers with this continuous process improvement:

- Unmatched fulfillment of industry requirements (ASME BPE, BPOG, FDA, cGMP, USP Class VI, TSE/BSE, 3.1), highest measuring accuracy based on multivariable Coriolis measuring technology and plug-and-play-capabilities

- Installation of disposable components in a cleanroom and delivery in double-layer plastic pouches
- Disposable components are gamma-sterilizable, can be traced by serial number and meet all requirements in biopharmaceutical production
- Hygienic, self-cleaning design to meet the highest industry standards

These features enable cGMP-compliant production, shorten cycle times in the process and thus accelerate the time to market.





# Automated verification trail

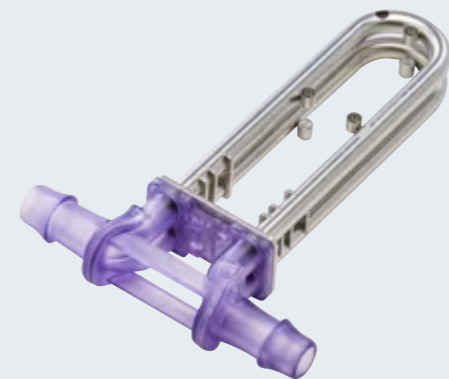
Human errors with a negative impact on function and accuracy occur frequently when commissioning measuring devices.

With Promass U 500, this source of error is minimized thanks to Heartbeat Technology. The functions for diagnostics, verification and monitoring which are integrated into the measuring technology deliver reliable and extensive sensor and process data.

Automated verification trail

## Factory calibration

The data from Heartbeat Technology and the calibration factor are recorded and stored on the measuring tube in the form of a QR code.



## Installation and cleaning

Assembly is performed with hoses and other components, followed by cleaning, packaging and gamma sterilization.



## Installation on site

To commission the single-use device, the data from the factory calibration and Heartbeat Technology are automatically loaded to the transmitter using the QR code and a camera integrated in the base unit.



## Commissioning

### 1. Verification

Heartbeat Verification is performed automatically after the installation of the disposable component in order to check the validity of the factory calibration data.



On-site verification



Factory calibration

### 2. Zero-point adjustment

After that, a zero-point adjustment is performed automatically to ensure the best measuring performance under process conditions.

## Production

The flowmeter is now verified and ready for cGMP-compliant operation.



Uninterrupted, fully automated data trail – Heartbeat Technology checks the validation of the original factory calibration



## Simple clamping mechanism

In cleanrooms and laboratories, wearing bulky protective equipment is obligatory. As such, replacing disposable parts as well as commissioning and operating measuring technology must be kept simple. The intuitive clamping mechanism of Promass U 500 makes it easy to exchange disposable components and can be operated even with protective equipment.



1. The clamping mechanism can be easily opened with one hand



2. The disposable measuring tube can then be removed



3. The QR code on the disposable part contains the factory calibration data



4. The calibration data is read out by the camera in the base unit



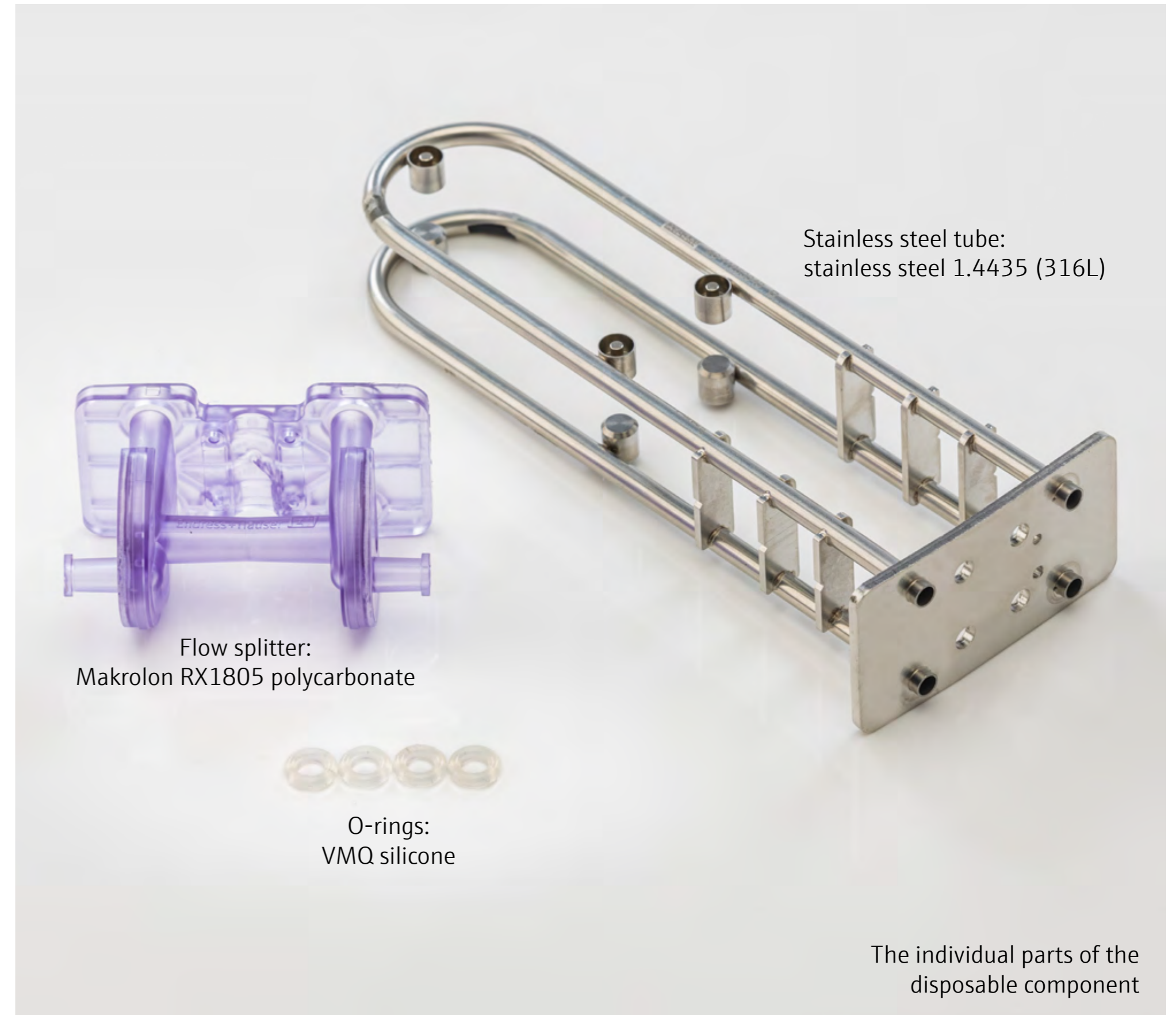
# Sustainability and recycling

From the perspective of sustainability, terms like “single-use” or “disposable” may sound questionable. But even though disposable components in biopharmaceutical applications are thrown away or recycled after a production process, they have advantages in comparison to equivalent multi-use instrumentation:

- Location-based cleaning (CIP) and sterilization (SIP) is not necessary.
- This reduces the water and energy consumption by up to 40 percent.
- CO<sub>2</sub> emissions are lowered due to the lack of CIP and SIP, which offsets the energy consumption for the production of the disposable components.

One advantage of Promass U 500 in the recycling process is the separability of the individual assemblies of the disposable component: The flow splitter can be disconnected from the stainless steel tube, and then the O-rings can also be removed. The stainless steel measuring tube can be completely recycled as scrap metal after autoclaving.

Due to the combination of different plastics in the flow splitter, specialized recycling processes are required for separation and further processing. The two packaging films and the secondary containment for the disposable measuring tube do not touch any fluids and can therefore be recycled as household plastics.





## Challenges in Life Sciences

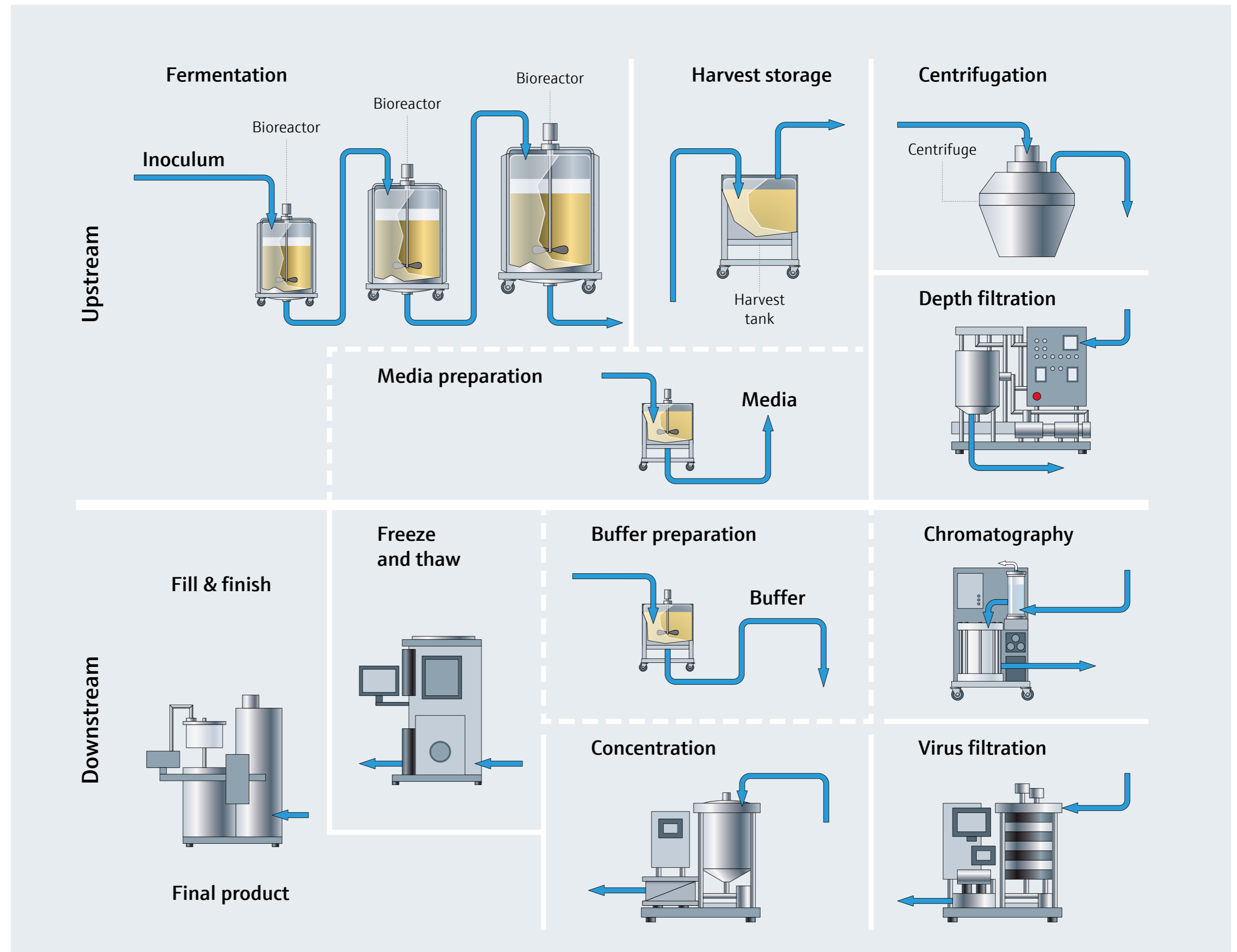
The need for single-use measuring technology has been increasing sharply for several years due to the rising demand for biopharmaceuticals. This is especially true for processes with mammalian cell cultures, where the focus is on the rapid development and efficient manufacturing of therapeutic antibodies, hormones, enzymes or vaccines – also in smaller quantities. Significant savings in both costs and time compared to multi-use instrumentation are a clear advantage of single-use technology. In addition, the risk of cross-contamination is drastically reduced and the flexibility during process setup is increased.

At the same time, a change is taking place from a traditional batch process to continuous production, leading to a higher need for high-grade flow measuring technology. Most single-use flowmeters available on the market so far have not sufficiently met the needs for accuracy and repeatability. Promass U 500 takes single-use instrumentation to a new level.



# Applications in Life Sciences

Promass U 500 can be used in many different places in upstream and downstream processes for high-accuracy flow measurements. The overview shows four marked measuring points (+) for application examples.



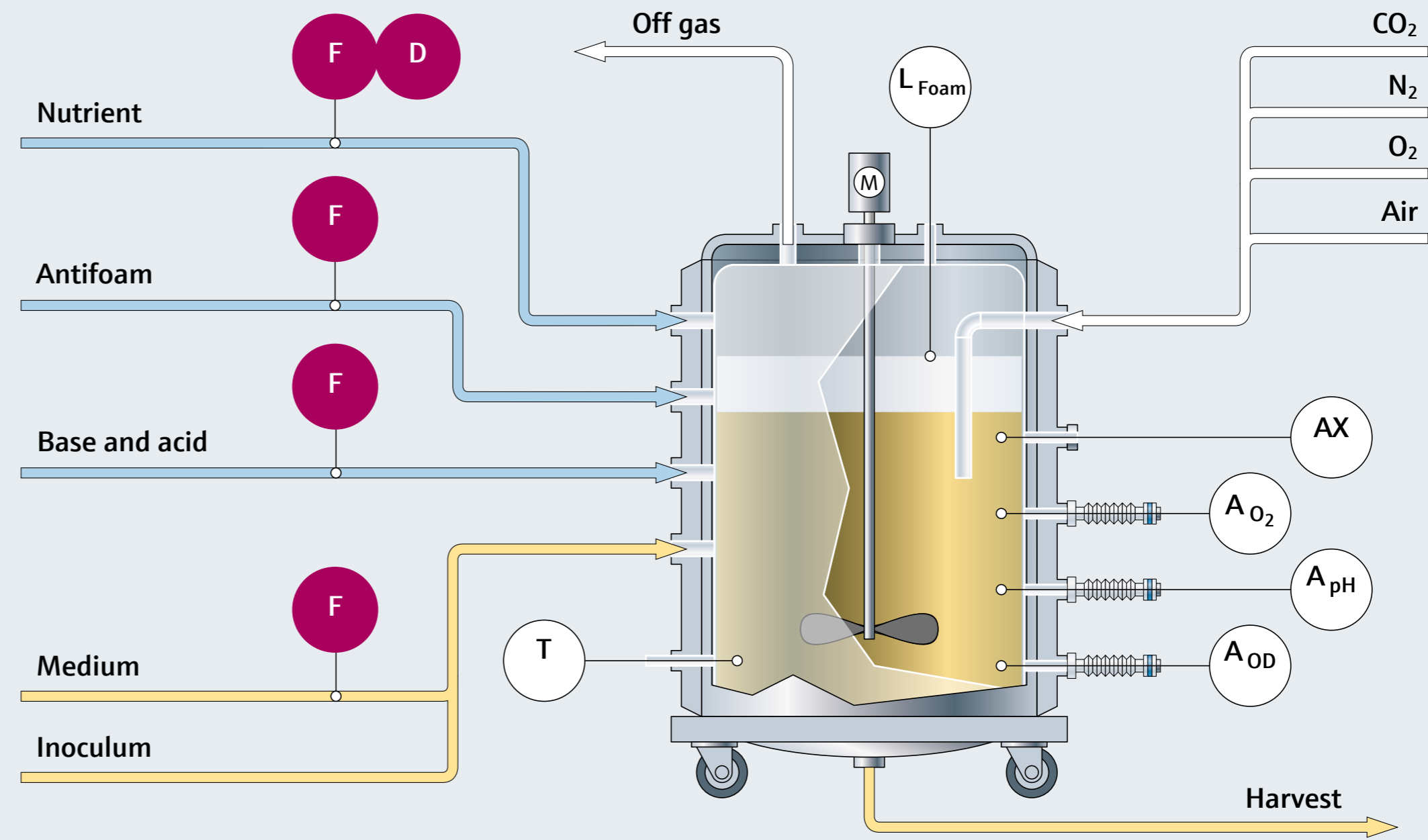


# Single-use fermentation

The prerequisites for fast growth of the biomass and maximization of the yield are met in fermentation. The most important parameters are pH value, dissolved oxygen, temperature and turbidity. By installing the appropriate measuring and control technology, growth can be regulated, monitored, recorded and documented. This ensures an optimal yield and compliance with legal requirements.

Precise flow measurements for the medium and culture medium supply, antifoam dosing as well as base and acid dosing are required here.

The measuring device must be able to measure water for injection (WFI) and other, changing liquids without readjustment.



### Your challenge

**Medium:** Various, sometimes highly viscous fluids

**Process temperature:** 5 to 50 °C (41 to 120 °F)

**Density:** 0.8 to 1.25 g/cm<sup>3</sup>

### Our answer

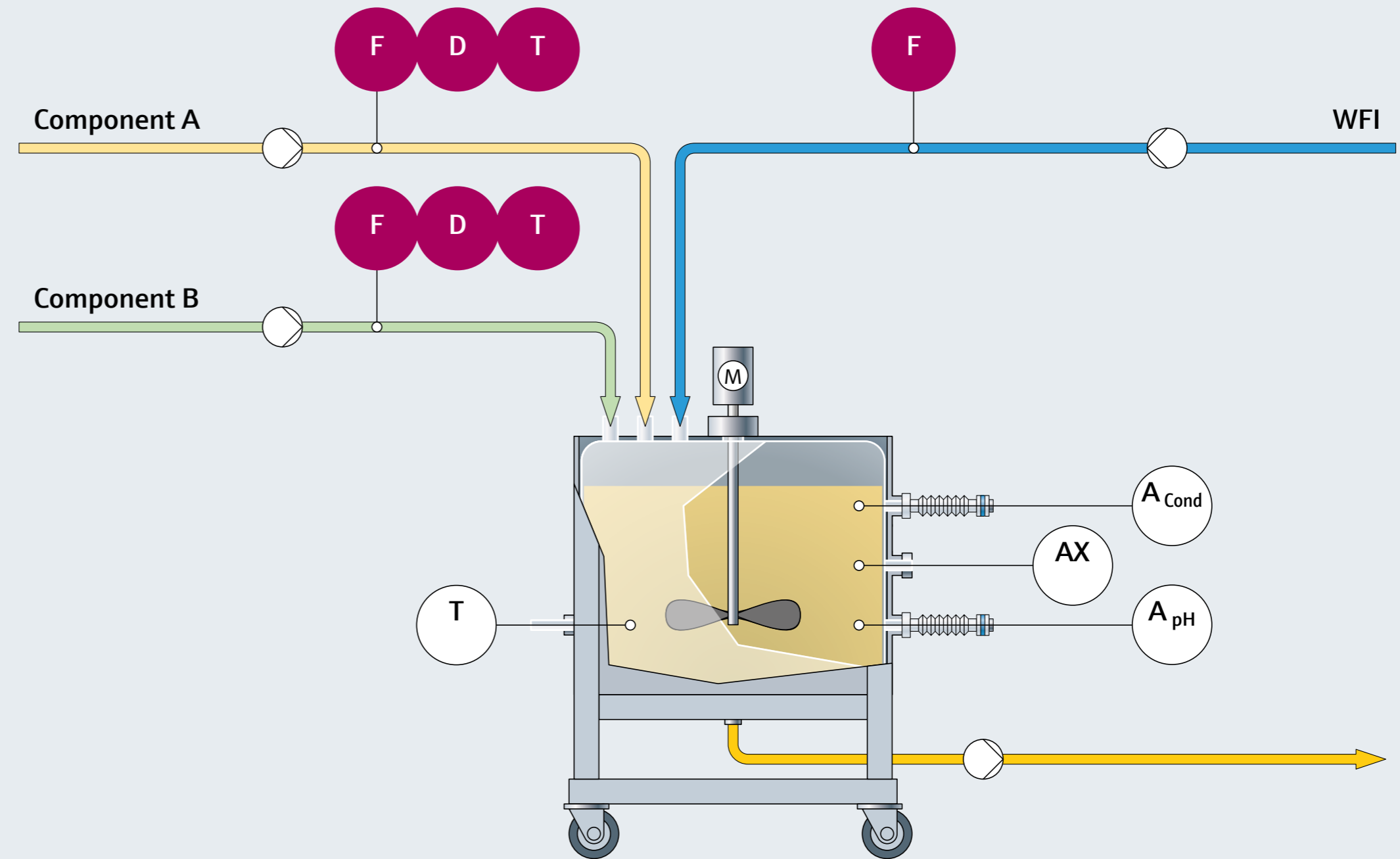
Promass U 500 meets the requirements listed with excellence thanks to its measuring performance using direct mass flow measurement. In addition, the device offers high scaling of the flow ranges and excellent reproducibility across all four available nominal diameters, which are held by the same base unit. Promass U 500 also fulfills all industry requirements (ASME BPE, BPOG, FDA, cGMP, USP Class VI, TSE/BSE, 3.1) and enables density measurement in real time.



# Single-use media preparation

The goal of media preparation is to provide the broth in which microorganisms or cell cultures have the best conditions for cell growth and protein expression. Purified water, nutrients, buffers and other components are added and heat-sterilized. Temperature-sensitive components are passed through sterile filters.

The supply of water for injection (WFI) as well as components A and B each require a precise flow measurement which enables precise measurement over large flow ranges. In addition, the instrumentation for WFI and the composition of components must be suitable for the measurement of changing liquids without having to readjust the parameters.



### Your challenge

**Medium:** Low conductivity, different compositions of components

**Process temperature:** 5 to 50 °C (41 to 120 °F)

**Density:** 0.8 to 1.25 g/cm<sup>3</sup>

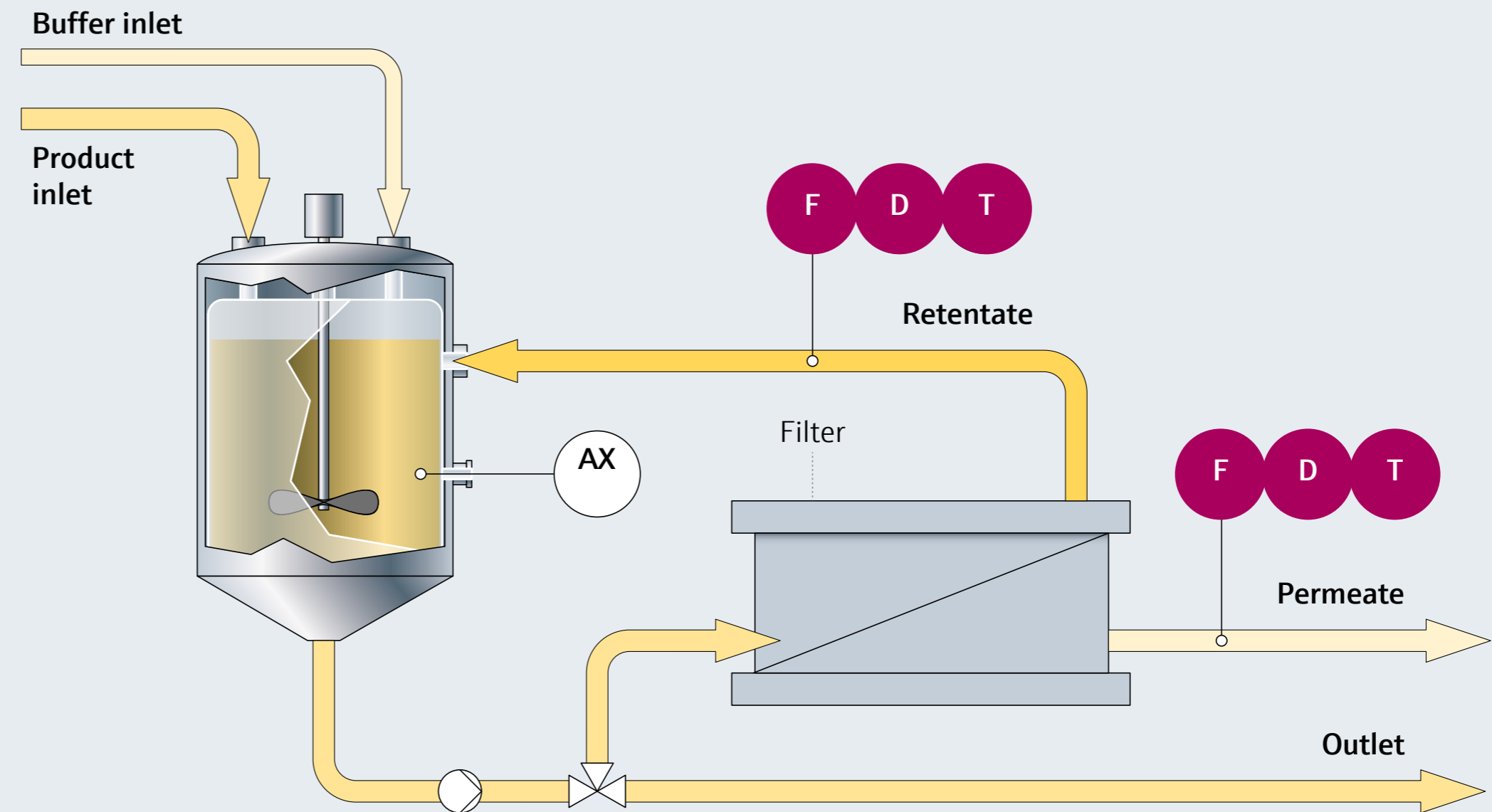
### Our answer

Promass U 500 fulfills the required ASME BPE standard in this process offers the necessary high repeatability over a large flow range and enables precise dosing of the smallest quantities. Thanks to the Coriolis measuring principle, accurate and simple recording of nonconductive fluids as well as an additional temperature and density measurement are also possible in real time.

# Single-use concentration

Tangential flow filtration (TFF) is one of the most important downstream processes in upstream and downstream processing in order to separate cells or build-ups from the fermentation broth, or to clean and concentrate the target protein.

Flow measurement is required for retentate flow and permeate flow. This is necessary to prevent filter clogging and damage to the product by high shear rates while the liquid density increases. For optimal cleaning or concentration, it is important to control the permeate flow in order to maintain a constant transmembrane pressure.



## Your challenge

**Medium:** Highly viscous product, possible clogging

**Process temperature:** 5 to 50 °C (41 to 120 °F)

**Density:** 0.8 to 1.25 g/cm<sup>3</sup>

## Our answer

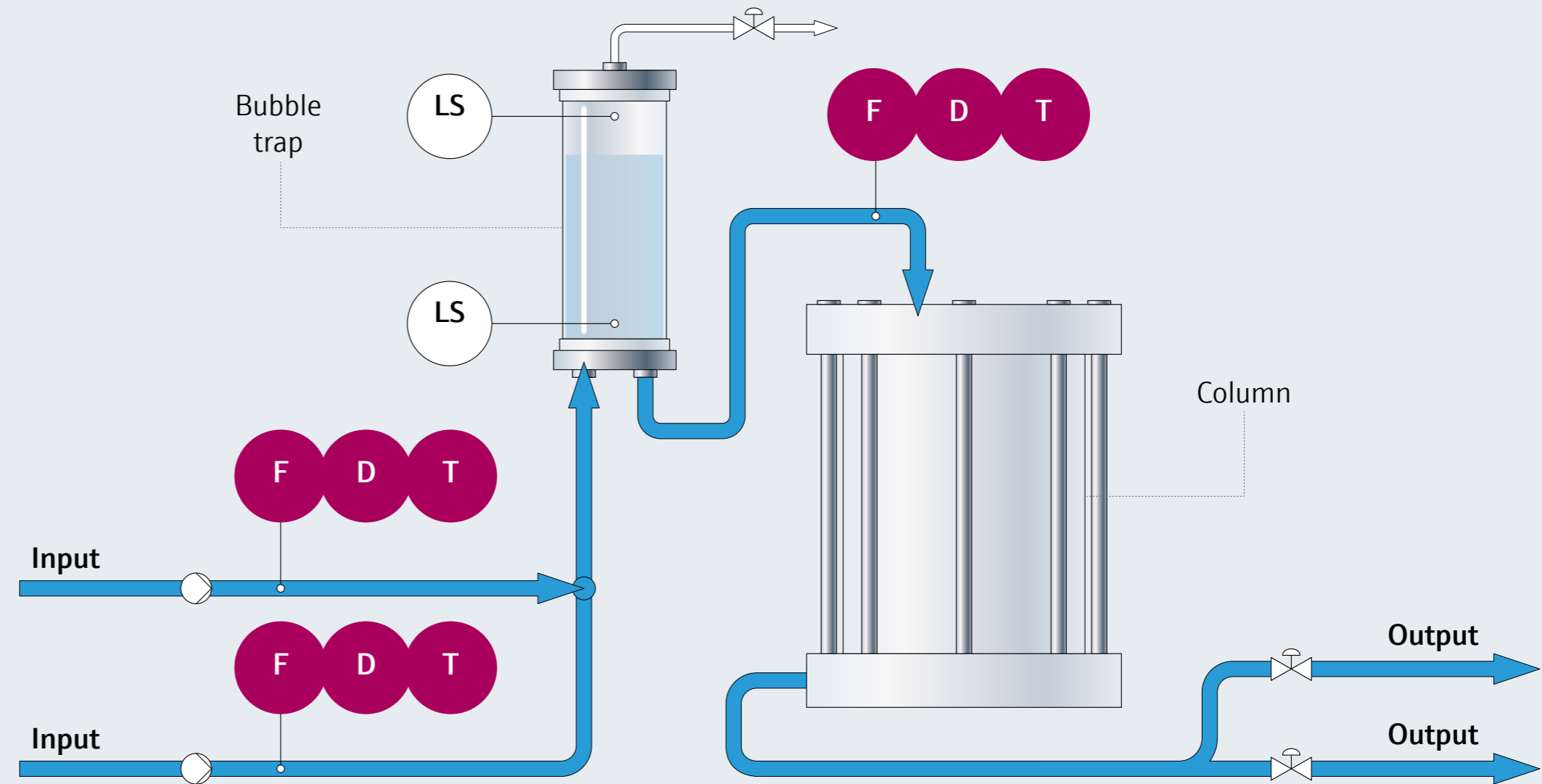
The necessary high reproducibility over large flow ranges is no problem for Promass U 500, which can be used for a flow rate from 0.12 to 75 liters per minute. Thanks to the multivariable measurement functions, precise density and temperature measurement is possible in real time. The Coriolis device also measures the flow of nonconductive as well as other, changing liquids without readjustment.



# Single-use chromatography process

Column chromatography is used to separate proteins from the complex mixture of the fermentation broth. Measurement of the mobile phase flow, which is composed of the water for injection (WFI) and concentrated buffer, takes place at the inlet upstream of the bubble trap.

Precise monitoring of the mobile flow rate is essential for proper separation of target proteins and maintaining the desired gradients. Upstream of the column, the control of the linear flow velocity as well as temperature and density are monitored in order to ensure precise chromatographic separation.



### Your challenge

**Medium:** Buffer solutions

**Process temperature:** 5 to 50 °C (41 to 120 °F)

**Density:** 0.8 to 1.25 g/cm<sup>3</sup>

### Our answer


Measuring changing liquids without having to readjust in between is no problem for Promass U 500, which also easily handles the requirement for high reproducibility over large flow ranges and the option of dosing small quantities. WFI, which is not or only slightly conductive, can also be measured precisely with the Coriolis measuring device.

# Technical data

## Overview

Promass U 500 boasts various functions and features which bring clear advantages for biopharmaceutical single-use applications.

Find more information about the technical data of the sensor, disposable component and transmitter on the following pages.

The Promass U 500 measuring system meets EMC requirements in accordance with IEC/EN 61326. It is compliant with the requirements of the EU and ACMA guidelines and is labeled with the **CE** or  symbol.



# Promass U base unit

## Sensor

The base unit of Promass U 500 is available as an insertion version for front panel mounting as well as a tabletop version in its own housing. Both versions hold all four available nominal diameters. More details on the technical data can be found on this page.



<b>Nominal diameters</b>	DN 04 (1/8"), DN 06 (1/4"), DN 15 (1/2"), DN 25 (1")
<b>Flow rate</b>	0.12 to 75 l/min
<b>Process pressure</b>	6 bar (87 psi)
<b>Process temperature</b>	3 to 60 °C (37.4 to 140 °F)
<b>Ambient temperature</b>	5 to 40 °C (41 to 104 °F)
<b>Degree of protection</b>	IP54, with open housing IP20
<b>Max. measured error</b>	<ul style="list-style-type: none"> <li>■ Mass flow and volume flow (liquids): ±0.5 % o.r.</li> <li>■ Repeatability: Mass flow and volume flow (liquids) ±0.25 % o.r.</li> <li>■ Temperature: ±2.5 °C (±4.5 °F)</li> <li>■ Density: Base accuracy (liquids): ±0.01 g/cm<sup>3</sup></li> <li>■ Repeatability: ±0.005 g/cm<sup>3</sup></li> <li>■ Temperature: ±0.125 °C (±0.225 °F)</li> </ul>
<b>Operable flow range</b>	Over 1000:1
<b>Materials</b>	Stainless steel 1.4409
<b>Compliance</b>	cGMP, FDA, ASME BPE, BPOG, USP Class VI, TSE/BSE, 3.1

Subject to modifications and amendments



# Promass U disposable component

## Disposable measuring tube

The disposable measuring tube is available in four nominal diameters and can be used for a flow rate of 0.12 to 75 liters per minute. Read more about the technical data on this page.



<b>Nominal diameters</b>	DN 04 (1/8"), DN 06 (1/4"), DN 15 (1/2"), DN 25 (1")
<b>Flow</b>	0.12 to 75 l/min
<b>Process pressure</b>	6 bar (87 psi)
<b>Process temperature</b>	3 to 60 °C (37.4 to 140 °F)
<b>Max. measured error</b>	<ul style="list-style-type: none"><li>■ Mass flow and volume flow: (liquids) ±0.5 % o.r.</li><li>■ Temperature: ±2.5 °C (±4.5 °F)</li><li>■ Density: base accuracy (liquids): ±0.01 g/cm<sup>3</sup></li><li>■ Repeatability: ±0.005 g/cm<sup>3</sup></li></ul>
<b>Operable flow range</b>	Over 1000:1
<b>Materials</b>	<ul style="list-style-type: none"><li>■ Measuring tube: stainless steel 1.4435 (316L)</li><li>■ Process connections: Makrolon RX1805 polycarbonate</li></ul>
<b>Compliance</b>	cGMP, FDA, ASME BPE, BPOG, USP Class VI, TSE/BSE, 3.1

Subject to modifications and amendments



# Proline 500

## Transmitter

The Proline 500 transmitter is available with an aluminum housing and Touch Control. Read more about the technical data on this page.



<b>Display</b>	4-line, backlit display with Touch Control (external operation)
<b>Operation</b>	<ul style="list-style-type: none"> <li>Web server (WLAN)</li> <li>On-site display</li> </ul>
<b>Materials</b>	Aluminum
<b>Energy supply with wide-range power supply</b>	<ul style="list-style-type: none"> <li>DC 24 V</li> <li>AC 24 V (50/60 Hz)</li> <li>AC 100–240 V (50/60 Hz)</li> </ul> <ul style="list-style-type: none"> <li>Operating tools such as FieldCare from Endress+Hauser</li> <li>HART handheld terminal</li> </ul>
<b>Ambient temperature</b>	Standard: -20 to 60 °C (-4 to 140 °F)
<b>Outputs</b>	Port 1 (communication): current output (4–20 mA, HART) or digital communication via Modbus RS485, PROFINET (Ethernet-APL/SPE)
<b>Communication</b>	Port 2/3 – freely configurable I/O modules: <ul style="list-style-type: none"> <li>Current output (4–20 mA)</li> <li>Pulse/frequency/switch output</li> <li>Pulse output (phase-shifted)</li> <li>Relay output</li> <li>Current input (4–20 mA)</li> <li>Status input</li> </ul>
<b>Approvals</b>	Non-hazardous area: CSA C/US; GP, EAC; UKCA
<b>Degree of protection</b>	IP66/67, Type 4X enclosure, suitable for contamination level 4 <ul style="list-style-type: none"> <li>With open housing: IP20, Type 1 enclosure, suitable for contamination level 2</li> <li>Display module: IP20, Type 1 enclosure, suitable for contamination level 2</li> </ul>

Subject to modifications and amendments

# First-class and simple

High-precision flow measurement with Proline Promass U 500 for biopharmaceutical single-use applications.

The Coriolis measuring device offers unmatched measuring performance, enables a cGMP-compliant production and boasts multivariable measurement functions (mass flow, density and temperature). Furthermore, Promass U 500 meets the requirements for high reproducibility over large flow ranges and has the option of dosing small quantities.

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