Knick

Process Analytics for BioPharma Industries

Knick – Partner of the Chemical and Pharmaceutical Industry since 1945.

Why Knick?

As a specialist for measurement and control technology, the owner-managed family company offers a high level of expertise and application knowledge in the field of liquid analysis in complex applications.

The in-house vertical range of manufacturing ensures product quality and flexibility with regard to customer-specific requirements.

Customer proximity and reliability characterize the company just as much as its innovative products and technologies, which are used today globally by well-known manufacturers in the chemical and pharmaceutical sectors.

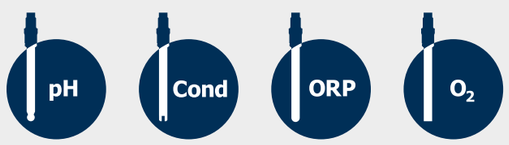
Process Analytics in Biotechnological and Pharmaceutical Industries

Biopharmaceutical manufacturing is generally characterized by the use of advanced technologies, harnessing of new scientific advances, and driven by a highly complex research and development enterprise.

The development of a novel active pharmaceutical ingredient typically requires large investments in time and capital to translate scientific discovery into new medicine and to build specialized manufacturing facilities and equipment, starting with the need to produce the initial supplies of an investigational compound for use in clinical trials prior to scale up to full-scale production upon FDA approval.

Knick Measuring Parameters:

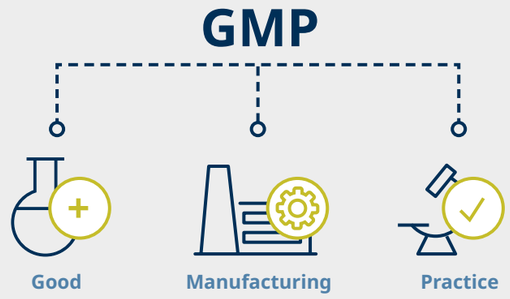
For decades, Knick has been advising and supporting companies worldwide on process analytics. Key competencies are the process-safe measurement of pH, ORP, conductivity and oxygen. In addition to sensors, Knick also offers innovative process analyzers, high-quality holders and fittings as well as unique cleaning and calibration systems.



Audit Trail Implemented

A seamless scale-up from R&D to GMP production requires documentation of any processes, changes, and deviations.

Therefore, all events are noted, documented, and transferred automatically in a safe way from the transmitter to the process control system (PCS) using the Audit Trail functionality. This way compliance with 21 CFR part 11 and EudraLex Vol. 4 Annex 11 is ensured.



Challenges Along the Way

Nowadays it is nearly impossible to fight rare or complex diseases without therapies developed by the biopharma industry. Animal, or insect cells, bacteria, and yeast are genetically modified to produce target molecules like recombinant proteins, vaccines, and many more.

Their manufacturing is a complex process due to the heterogeneity of the living organisms. Heterogeneity in the upstream process (USP) transfers to the subsequent product purification steps in downstream processes (DSP), too.

Some literature already describes how the application of the Process Analytical Technology (PAT) to these complex processes could enable significant improvement in upstream through the use of performance indicators. In downstream the application of PAT results in higher quality and purity of the final product.

It is universally acknowledged that to properly apply PAT, it is essential to move from the manual sampling and laboratory measurement procedures to automated control. As even minimal variations of process parameters have a major influence on the final product, controlling them in real-time minimizes the risk of lower yield and purity.

PAT Initiative of the FDA

The Process Analytical Technology (PAT) Initiative of the U.S: Food & Drug Administration (FDA) originates from a guidance published in 2004. The PAT initiative focus is to minimize risks to public health associated with pharmaceutical product manufacturing by enhancing the understanding and control of the manufacturing process to achieve Quality-by-Design (QbD).

PAT promotes a process which starts with the identification of each product's specific Critical Quality Attributes (CQAs), then proceeds with monitoring as often as possible the related Critical Process Parameters (CPPs) and of the Key Performance Indicators (KPIs), in order to automatically control them within pre-defined limits.

A Way Out

Automation throughout the upstream, downstream, and auxiliary processes helps to further reduce the risks of human errors, improves operational efficiency, and thus increases the safety and quality of the final product which benefits every patient.

Knick assists with commissioning, start-up installations, qualifications like IQ, OQ, as well as troubleshooting, and maintenance contracts in order to reduce our customers' workload, and ensure compliant and reliable measurements, and GMP compliant documentation.

cCare for Pharma
Fully Automated Maintenance System

**(R)evolution –
Automation of pH measuring loops with cCare for Pharma, the fully automated sensor maintenance system.**

**– cleaning
– calibration
– conservation**

Knick offers complete measurement loops from sensors to fully automatic sensor maintenance systems. Automated processes help to maximize standardization, avoid transcription errors, and increase compliance.

With the Knick cCare system major goals of FDA's PAT initiative are addressed:
- Standardization of calibration and cleaning processes for less variations, and deviations
- No more transcription errors leading to less batches lost
- Audit trail ensures compliance with the regulations

1

Transmitters
Central programming and operating unit of the system. Simple plain text operation and easy copying of settings. Expandable to fieldbus communication and operation with Memosens, digital, and analog electrodes.

2

Media connection with multifunction plug
Central supply of rinsing and calibration liquids in pre-assembled hoses. Quick, easy, and fail-safe installation via a multifunction plug, use of ball valves that reliably prevent media carryover and back-mixing.

3

Service switch
Central safety switch for immediate retraction of the sensor into the fitting. With warning signal function and active feedback on the actual position of the sensor.

4

Media adapter with containers and metering pumps
1-3 containers for cleaning and calibration solutions with wear-free pumps. Container capacity with 3.5 l buffer solution is sufficient for up to 140 calibrations. An additional cleaning or rinsing fluid can be supplied via the external valve in Unical.

5

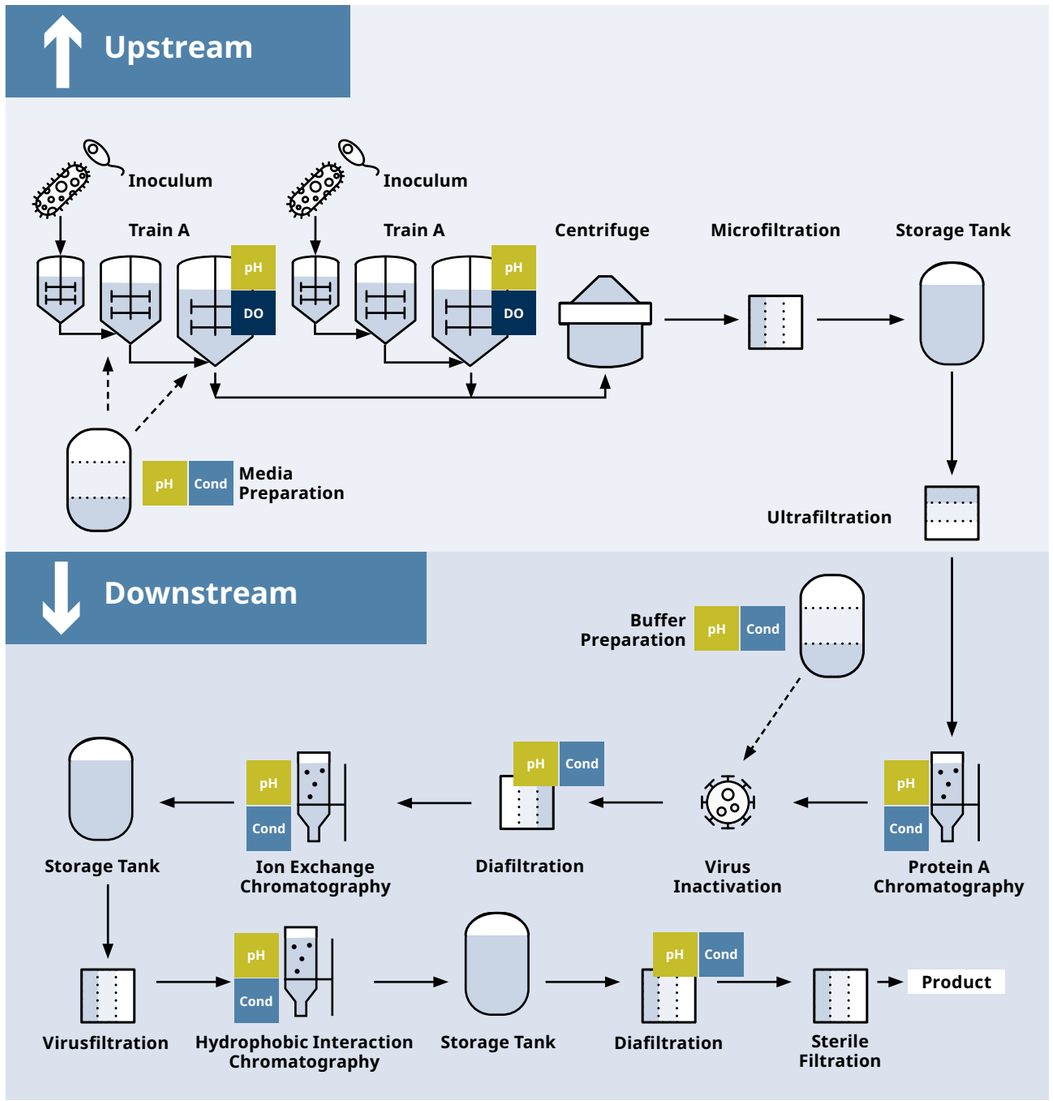
Retractable fittings
Fittings of the Ceramat or SensoGate series can be used. Modular systems available in various designs (materials, process connections, immersion length, etc.). Adaptable to any process application.

6

Controller
Electropneumatic function with service-friendly concept. Can be used directly in hazardous locations. Fully automatic, modular, low-wear and low-maintenance operation.

Biopharmaceutical Pathway
Solutions for every process step

Every process step of the biopharmaceutical pathway is important and requires specific measurement technology to control the critical process parameters for maximized yield, and reduced process deviations.



Pharma Solutions
Customized retractable fittings

Our well-thought-out fitting systems allow ideal solutions with regard to process connection, immersion depths and materials.

Thus, our retractable fittings meet all requirements due to process media, hygienic demands and installation situations. In addition, we can also customize fittings for our customers.

SensoGate WA130H
Process connection:
Clamp, beveled

SensoGate WA130H
Process connection:
Ingold (G 11/4)

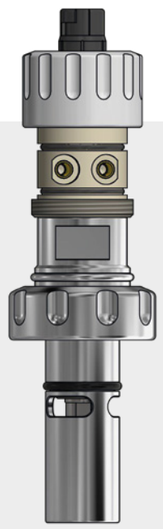
SensoGate WA131H
Process connection:
BioControl

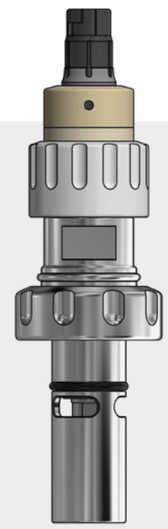
SensoGate WA131H
Process connection:
Varivent

USP <645> compliant

Verification for ultrapure water and Water for Injection.

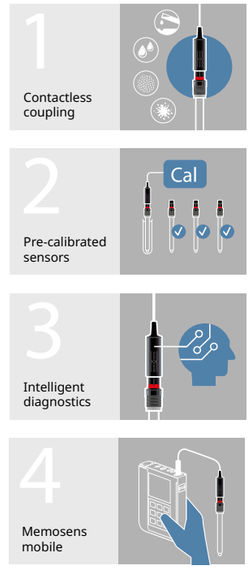
The special version of the SE605H sensor with CondCheck is used to check respectively verify the measured value. The check should be performed with a certified and traceable resistor which will be connected to the sensor via the plugs as can be seen in the drawing. The measuring chain does not have to be interrupted for the check.





Everything for complete and compliant (measurement) loops – Sensors, transmitters & fittings

MEMOSENS



Sensors

Robust sensors built for demanding applications like in upstream and downstream processing measure the value of the different media to provide maximum control of the processes.

In addition to analog, the sensors can also feature the digital Memosens design, which drastically reduces the susceptibility to errors in signal transmission, facilitates handling, and allows for more flexible maintenance.

Transmitters

Reliable transmitters (available in Ex and non-Ex) for display and data transfer of pH, conductivity and oxygen measured values for connection of Memosens, ISM and analog sensors.

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Fittings

Fittings are used to insert the sensors into the process in order to be able to determine the required measured values.

Various hygienic designs offer the greatest possible flexibility in terms of installation location and position, and (depending on the type of fitting) also allow sensor maintenance without shutting down the process.

Memosens is the waterproof and interference-free sensor coupling for liquid analysis that digitizes measurement data and stores calibration data.

Knick

Process Analytics

- Industrial Transmitters
- Fittings
- Automatic Cleaning & Calibration Systems
- Sensors
- Portables
- Laboratory Meters

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