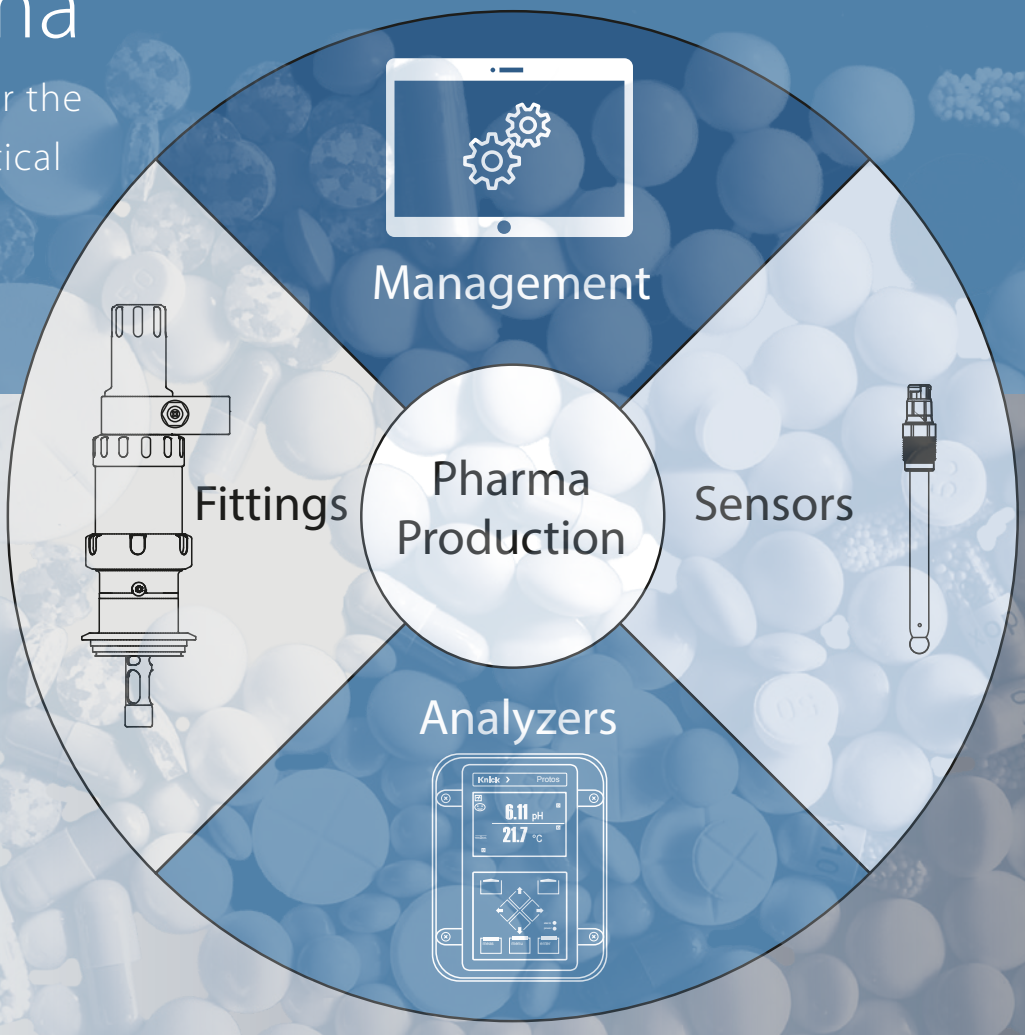
The Art of Measuring. Knick

Industry Information

Pharma

Solutions for the Pharmaceutical Industry



Solutions for the Pharma

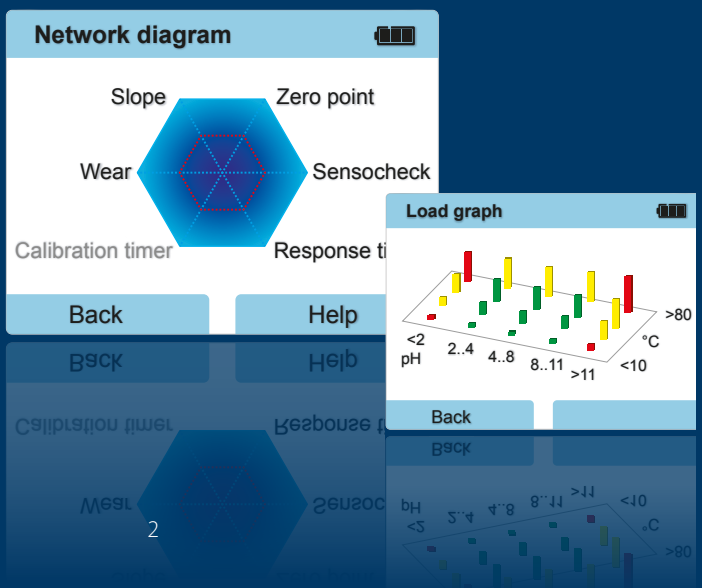
The most common critical parameters of pharmaceutical processes are pH, oxygen and conductivity. Measurement deviations can have a large impact on the final production result.

The pharmaceutical industry has therefore adapted tools for continuously improving measurement reliability, knowledge and data acquisition. Summarized under the term "Process Analytical Technology (PAT)".

Sensors

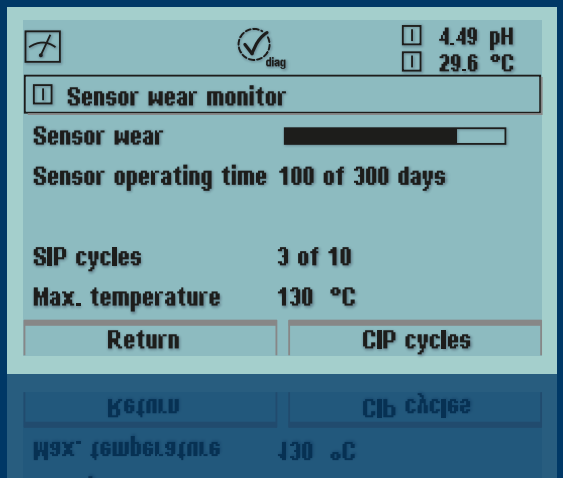
Sensors

As a minimum, pharmaceutical sensors must be sterilizable (SIP) and cleanable in place (CIP). To get worthwhile information on their everyday performance, sensors are ideally equipped with a chip that stores relevant quality parameters. Knick Memosens sensors offer this information in an easy to read sensor radar chart (graphic)



The sensor radar chart – available in numerous Knick analyzers – is an ideal tool to monitor and control the sensor performance in real time. The radar chart supports the operator in making maintenance decisions and helps to improve the lifetime of the sensor and to reduce operational costs. An additional "load graph" displays the exposure of the sensor depending on pH and temperature.

Last but not least, Knick offers pharmaceutical certifications with its sensors. These certifications include FDA, USP88, ATEX and others.



Industry

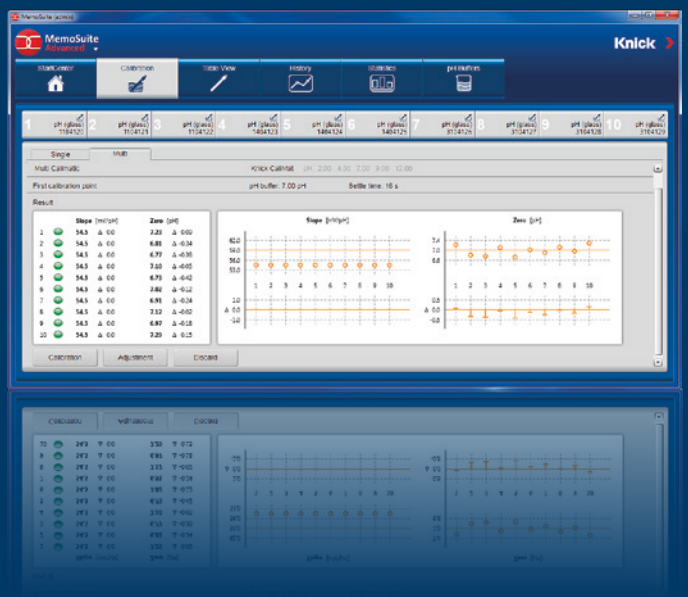
	Laboratory (QC/QA)	Pilot Plant	Production Process
Sensors	SE 102, SE 202, SE 340	SE 555, SE 605, SE 740	SE 555, SE 605, SE 680, SE 740
Management	Portavo / MemoSuite	MemoSuite	MemoSuite
Transmitters	Portavo	MemoRail	Protos
Fittings		Static Fittings	Automatic Systems

Typical process definition in pharmaceutical industry for R & D to industrial production process.

	Digital Sensor	Measurement	Material	Design	Certifications
	**SE 555**	pH pH/ORP	Glass Glass, Pt	CIP, SIP, Autoclavable	Cytotoxicity, ADI/TSE, FDA-approved O-ring, ATEX
	**SE 565**	ORP	Glass, Pt	CIP, SIP, Autoclavable	FDA-approved O-ring, ATEX
	**SE 546**	pH	PEEK, ISFET	SIP, Autoclavable	Cytotoxicity, FDA-approved O-ring, ATEX
	**SE 605H**	Conductivity	Stainless Steel, PEEK, EPDM	CIP, SIP, Autoclavable	FDA, USP Class VI, R_a < 0.4 µm, ATEX
	**SE 680**	Toroidal Conductivity	PEEK	CIP, SIP	FDA, USP<87>Grade 1, USP<88>classVI, EHEDG, ATEX
	**SE 706** **SE 707**	Oxygen Oxygen (Traces)	Stainless Steel, PTFE	CIP, SIP, Autoclavable	ADI/TSE, FDA + USP, ATEX
	**SE 740**	Optical Oxygen	Stainless Steel, Silicone	CIP, SIP	FDA, R_a < 0.4 µm, ADI/TSE

Solutions for the Pharma

Management



Sensor Management

A crucial requirement in any pharmaceutical environment is the ability to track any changes in the process or measurement and to make sure that data cannot be manipulated. To help customers achieve this, Memosens sensors can be easily connected to an asset management tool developed by Knick: MemoSuite Advanced.

MemoSuite Advanced offers the option to automatically calibrate up to 10 sensors, following GMP standards. This feature allows setting limits that must be met by the sensor during calibration. Failure to meet these limits results in the rejection of the sensor.

Industry

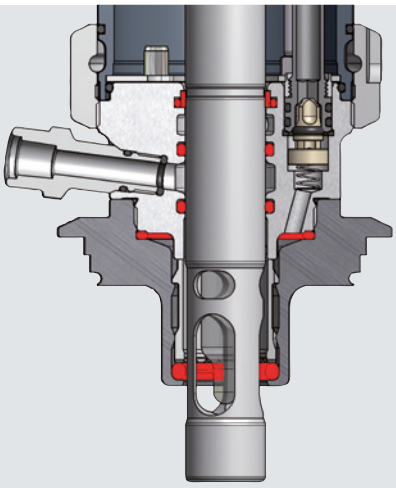
MemoSuite Advanced generates GMP calibration reports that can be automatically uploaded to any higher-level system.

Furthermore MemoSuite Advanced contains a database with all relevant sensor data. All relevant data of the sensor life cycle can be graphically displayed. MemoSuite Advanced is designed according to FDA 21 CFR Part 11, which assures that electronic data cannot be manipulated and electronic signatures are secure.

Solutions for the Pharma

ARI 106 H

ARI 106 H
for pH sensors
with pressurizable
liquid electrolyte



SensoGate WA 130 H, WA 131 H, WA 131 MH
lock-gate funtion

Fittings

Static and Retractable Fittings

Static and retractable fittings provide safety and convenience when the task is to measure pH, ORP, dissolved oxygen and conductivity. Especially for pharmaceutical applications, the ability to clean and sterilize are of utmost importance, as well as the availability of a wide range of materials.

The optimal choice for operation in the pharmaceutical industry without requirement of automation is the ARI106 H, an inexpensive and robust inline fitting for 12-mm sensors.

For extra safety and optimal – automatic – operation, Knick recommends SensoGate H retractable fittings. They are steam-sterilizable, validated for all wetted parts including the rinsing/calibration chamber.

Many "hygienic" fittings on the market have no lock-gate function with only one sealing to the process. This means that when the immersion tube is moved (in no matter what direction), the lower rinsing chamber and "inlet" and "outlet" are flooded with process medium until the next shut-off. The user is forced to use valves and apply elaborate rinsing and steam sterilization cycles to re-establish sterile conditions. SensoGate provides a patented 2-chamber system which safely seals off the process from "inlet" and "outlet". The customer only needs connections for steam and rinsing agents. The green gasket safely seals off the chamber when the probe is moved – in both directions. Afterwards, the process medium is safely removed from the rinsing chamber using rinse liquid and steam. This is supported by the patented flow body which increases the velocity of the rinsing agents at the inner surfaces.

Industry

SensoGate WA 130 H

SensoGate WA 131 H

SensoGate WA 131 MH

Recommended static and retractable fittings

Fitting	Type	Wetted materials	Design	Sensor type	Certifications
ARI 106 H	Inline	PEEK /1.4404 1.4435 / 1.4404 PVDF / 1.4404 PVDF / PVDF 1.4539 / 1.4404	CIP, SIP, Autoclavable	12 mm with PG 13.5 or 12 mm pressurizable, length: 120 ... 250 mm	Material traceability 3.1, surface roughness < 0.8/0.4 µm, FDA, USP<88> class VI
SensoGate WA130 H **SensoGate WA131 H** **SensoGate WA131 MH**	Inline retractable fitting (automatic or manual)	1.4404 / 1.4435	CIP, SIP, dairy pipe DN 50 ... 100, Ingold socket 25 mm, clamp 1.5 ... 3.5, Varivent DN 50 ... 80, BioControl DN 50, DN 65	12 mm with PG 13.5 or 12 mm pressurizable, length: 250 mm	ATEX, material traceability 3.1, surface roughness < 0.8/0.4 µm, inline steam sterilizability, FDA, USP<88> class VI

Solutions for the Pharma

MemoRail

Stratos

Protos

Portavo

Analyzers

Process Analyzers

A wide range of analyzers ensures that each application in the pharmaceutical process can be covered: Starting from the small and easy to install MemoRail for fermenters and cleaning machines to the robust, full-featured modular Protos for batch control applications. Additionally Knick offers Portavo, the only portable analyzers with Memosens technology.

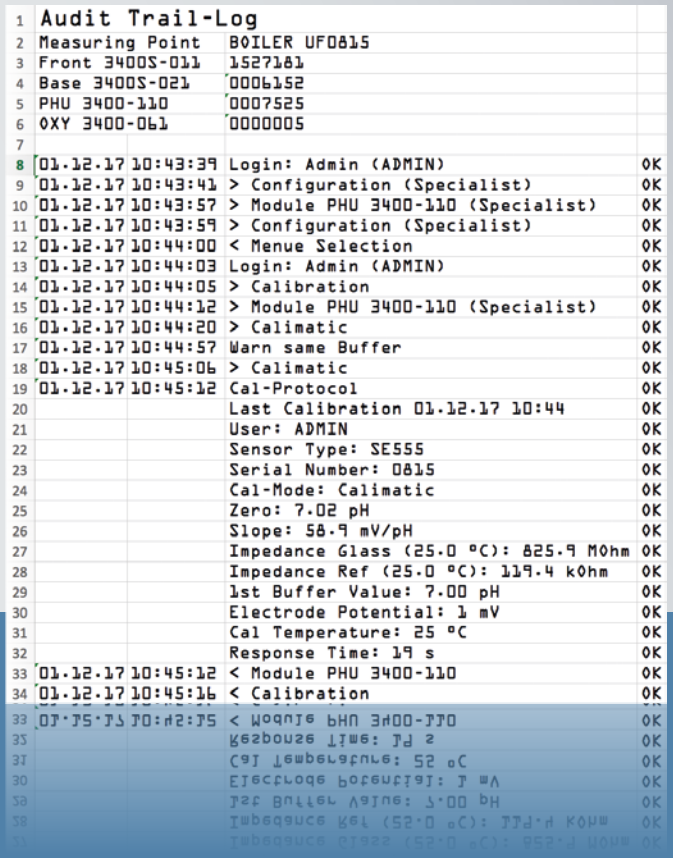
Again, data integrity is a main critical element in any pharmaceutical environment. This is why Knick has implemented the Audit Trail function in many of its analyzers. Audit trail is designed according to FDA 21 CFR Part 11 and guarantees that any change to the analyzer or its data is monitored, stored and traceable.

The analyzers, such as Protos, feature reliable backups and complete data recording in accordance with FDA regulation 21 CFR Part 11. This regulation is basically composed of "Electronic Records" and "Electronic Signature"; both parts interlock directly.

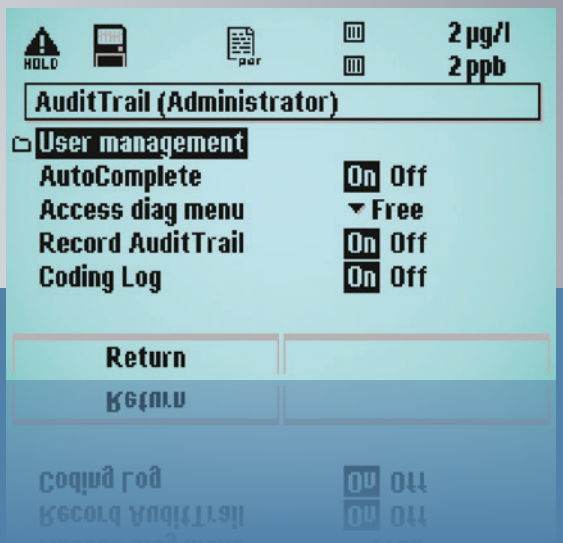
For every change in the menu of the analyzer, there is an exact recording of what was modified and who carried out this modification. For safety reasons, the Audit Trail is stored solely in a specially coded data memory by Knick. Readability from PC is not affected. This Audit Trail memory is ready equipped with a PC program that makes the logged Audit Trail data readable and can also decode them again in "log coding" mode. The data can easily be exported to other programs like for example Microsoft Excel.

As an extraordinary function, Knick analyzers offer a sensor radar chart for pH measurement.

Industry



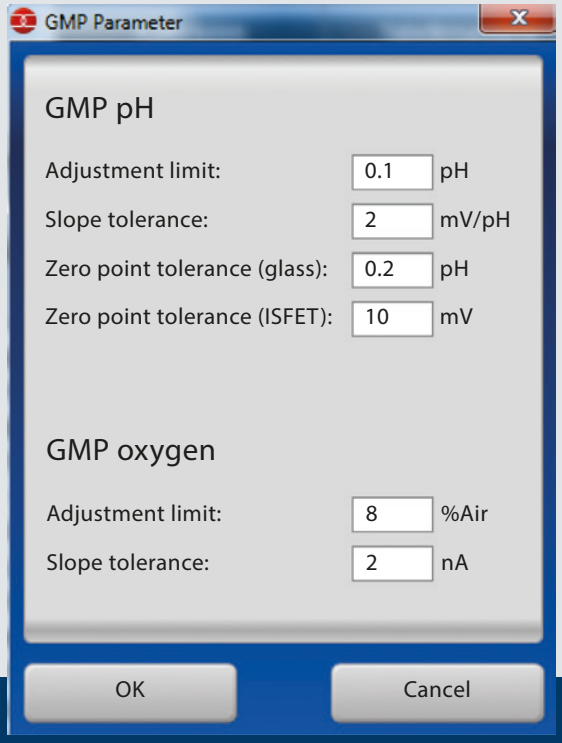
1	Audit Trail-Log					
2	Measuring Point		BOILER UFO815			
3	Front 3400S-011		1527181			
4	Base 3400S-021		0006152			
5	PHU 3400-110		0007525			
6	OXY 3400-061		0000005			
7						
8	01.12.17	10:43:39	Login: Admin (ADMIN)			OK
9	01.12.17	10:43:41	> Configuration (Specialist)			OK
10	01.12.17	10:43:57	> Module PHU 3400-110 (Specialist)			OK
11	01.12.17	10:43:59	> Configuration (Specialist)			OK
12	01.12.17	10:44:00	< Menue Selection			OK
13	01.12.17	10:44:03	Login: Admin (ADMIN)			OK
14	01.12.17	10:44:05	> Calibration			OK
15	01.12.17	10:44:12	> Module PHU 3400-110 (Specialist)			OK
16	01.12.17	10:44:20	> Calimatic			OK
17	01.12.17	10:44:57	Warn same Buffer			OK
18	01.12.17	10:45:06	> Calimatic			OK
19	01.12.17	10:45:12	Cal-Protocol			OK
20			Last Calibration 01.12.17 10:44			OK
21			User: ADMIN			OK
22			Sensor Type: SE555			OK
23			Serial Number: 0815			OK
24			Cal-Mode: Calimatic			OK
25			Zero: 7.02 pH			OK
26			Slope: 58.9 mV/pH			OK
27			Impedance Glass (25.0 °C): 825.9 MOhm			OK
28			Impedance Ref (25.0 °C): 119.4 kOhm			OK
29			1st Buffer Value: 7.00 pH			OK
30			Electrode Potential: 1 mV			OK
31			Cal Temperature: 25 °C			OK
32			Response Time: 19 s			OK
33	01.12.17	10:45:12	< Module PHU 3400-110			OK
34	01.12.17	10:45:16	< Calibration			OK

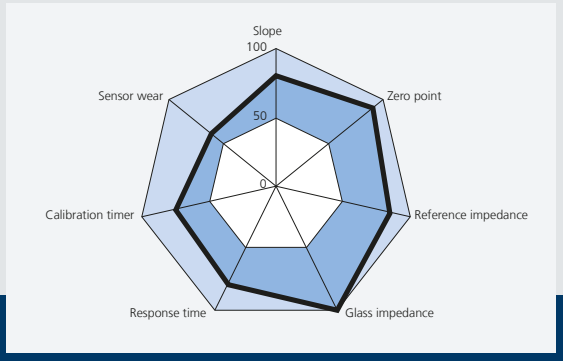


Recommended analyzers for pharmaceutical applications:

Device	Size	Output	Mounting	Memosens	Certifications	Audit Trail
MemoRail	12.5 mm	4 ... 20 mA	Cabinet (DIN rail)	Yes	ATEX (2), UL	No
MemoRail Modbus	17.5 mm	Modbus RTU	Cabinet (DIN rail)	Yes		No
Stratos (various versions)	148x148x117 mm	4 ... 20 mA, HART, FF, DP, PA	Wall, Pipe	Yes	ATEX (1), FM, CSA, NEPSI	Yes
Protos	213x163x160 mm	4 ... 20 mA, FF, PA	Wall, Pipe	Yes	ATEX (1), FM, CSA, NEPSI	Yes

Solutions for the Pharma





GMP Calibration

Manufacturing pharmaceutical products requires maximum accuracy for the acquisition of measured values. Failure effects must be eliminated as far as possible by calibrations / adjustments.

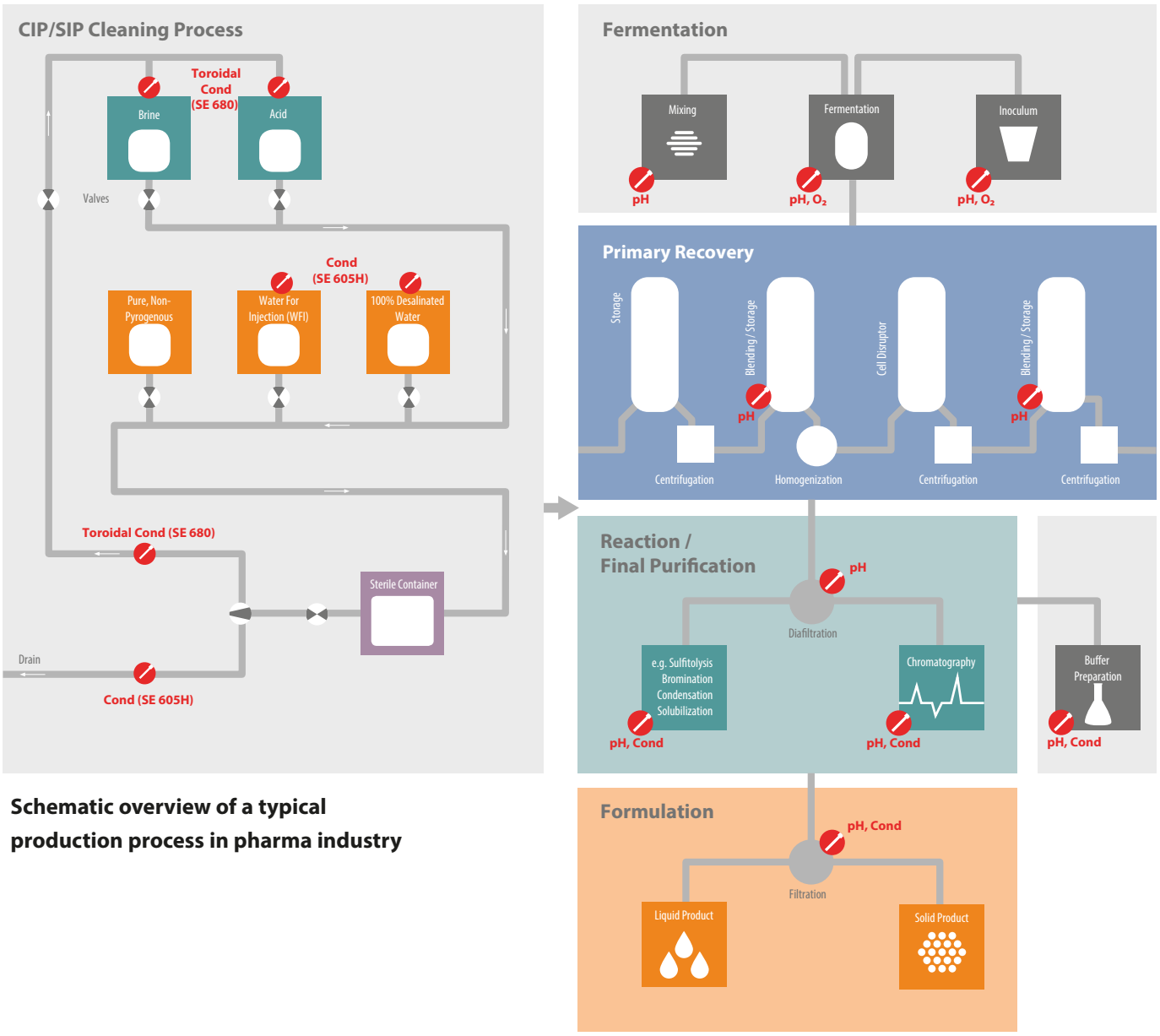
Limits (tolerances) can be specified for the parameters determined during a calibration. If after several calibrations the zero point or slope values lie outside the specified tolerances, this indicates that the sensor drift is inadmissibly high. A message will be generated and the sensor should be replaced. If the parameters lie within the specified tolerances, no adjustment will be made. This allows tracking the sensor parameters before and after a batch and thus ensuring consistent QM documentation of the production process.

Knick analyzers offer a sensor radar chart for pH measurement as a graphic representation of current sensor parameters – with slope, zero point, reference impedance, glass impedance, response time, calibration timer, and sensor wear.

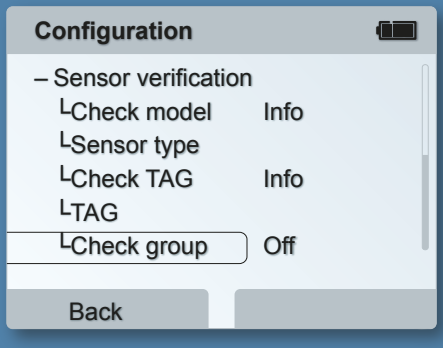
Cal SOP Calibration Procedure with Portavo

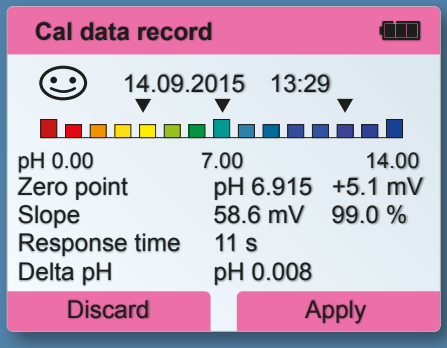
The Cal SOP calibration procedure sets new standards for use in the pharmaceutical sector. pH buffers can be individually selected for up to 3 calibration points. The third buffer acts as a verification buffer and allows users to define the maximum allowed deviation (delta pH). The system indicates deviations from the SOP tolerance and automatically suggests an "adjustment". This increases the safety of the SOP process. Also new are a multilevel user management with four user profiles and different access rights as well as a sensor verification feature, allowing sensors and devices to be directly associated. This guards against mistakes when operating the analyzer.

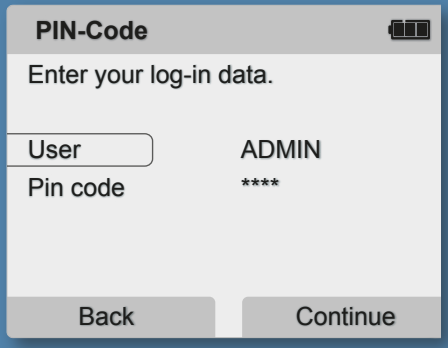
Industry



Schematic overview of a typical production process in pharma industry







Cal SOP Calibration Procedure with Portavo

Knick

Process Analytics

– Industrial transmitters

– Fittings

– Automatic cleaning and calibration systems

– Sensors

– Portables

– Laboratory meters

Knick
Elektronische Messgeräte
GmbH & Co. KG

Beuckestraße 22, 14163 Berlin
Telefon: +49 30 80191-0
Telefax: +49 30 80191-200
info@knick.de · www.knick.de

Knick
The Art of Measuring

Knick has been among the leading manufacturers of electronic measurement devices for process analysis for more than 70 years. Today, the company alignment is still focused on a high technical level and an intensely innovative orientation.

The current product range of Knick includes unique device series also for extremely difficult applications. As a system provider, Knick can guarantee expert analysis of your measurement requirements and provide qualified advice for complete measurement loops.

TP-194.000 Pharma EN0418