

Application Bulletin 428/1 e

Automated conductivity measurement in low conducting water samples according to USP<645>

Branch

Water, wastewater, air, environmental protection; pharmaceutical industry

Keywords

USP 645; automation; DIS-COVER; conductivity; conductivity measurement; pH measurement; sterile water; low conductivity; stainless steel; temperature; temperature measurement; Thermostat; LL-Aquatrode plus; Stainless steel cell; branch 2; branch 4; 815; 906; 856; 6.0916.040; 6.0257.600

Summary

This Bulletin shows the possibility to automatically measure low conductivity of water samples according to USP 645. Especially sterile water samples, which are further used to prepare, e.g., injections, are measured according to this norm.

The USP<645> describes a three step analysis. The first step consists of measuring the conductivity and comparing it to a conductivity limit correlated to the measured temperature. If the limit is not met, the second step is carried out. Here, the sample is tempered to 25 ± 1 °C followed by a conductivity measurement. If the given conductivity limit of 2.1 $\mu\text{S/cm}$ is exceeded, the analysis will pass over to the third step in which the pH is measured. The measured conductivity of the second step is compared to given pH dependent limiting values.

Instruments

- Sample changer with two towers and swing heads
- Conductivity module
- DIS-COVER
- Titration vessel with thermostat jacket
- Thermostat
- Holder for titration vessel
- 50 mL buret for transfer
- 2 mL buret for addition of KCl sat.

Electrodes

Conductivity measuring cell (stainless steel), $c = 0.1 \text{ cm}^{-1}$	6.0916.040
LL-Aquatrode plus, U head $c(\text{KCl}) = 3 \text{ mol/L}$ as electrolyte	6.0257.600

Reagents

- KCl, puriss p.a., >99.5%

Solutions

$\beta(\text{KCl}) = \text{sat.}$	Approx. 90 g KCl is given into 250 mL deion. water. A small amount of KCl remains visible as deposit on the bottom of the flask.
Buffer pH 4	Metrohm: 6.2307.100
Buffer pH 7	Metrohm: 6.2307.110
Conductivity standard 100 $\mu\text{S/cm}$	Metrohm: 6.2324.010

Sample preparation

No sample preparation is required.

Calibration of conductivity measuring cell

According to USP the cell constant of the conductivity measuring cell must be known within 2%. This can be achieved by the calibration of the cell constant with conductivity standards which are traceable.

Analysis

250 mL sample is filled into the 250 mL beaker. The beaker is placed on the sample rack and covered with a Dis-Cover lid.

Calibration

Before each measurement series the cell constant of the conductivity measuring cell is calibrated using the 100 $\mu\text{S/cm}$ conductivity standard and the LL-Aquatrode plus is calibrated with buffer pH 4 and buffer pH 7.

1st step

The DIS-COVER lid is automatically removed from the beaker and the conductivity as well as the temperature is measured. It has to be taken care that the pH electrode is not dipped into the sample as otherwise the electrolyte of the pH electrode might influence the conductivity of the sample. If the conductivity was within the limit, the test is passed and the analysis is finished.

In case the conductivity is over the limit, the analysis continues with step 2. When the conductivity is even higher than 4.7 $\mu\text{S}/\text{cm}$ the analysis is stopped as the water must not be used as sterile water.

2nd step

To avoid cross-contamination 150 mL ultrapure water is dosed into the external vessel and aspirated. Afterwards 50 mL sample is pipetted into the external vessel for conditioning. After aspirating the 50 mL sample, further 150 mL sample is transferred and tempered to $25 \pm 0.5^\circ\text{C}$. When the temperature is reached the sample is stirred thoroughly for 5 min in order to saturate the sample with CO_2 . If the measured conductivity before and after these 5 minutes has a difference smaller than 0.1 $\mu\text{S}/\text{cm}$, the solution is saturated and the measured value after these 5 minutes is taken as end value. The test is passed if the conductivity of the sample is lower or equal to 2.1 $\mu\text{S}/\text{cm}$ and the analysis is finished.

If the conductivity is between 2.2 and 4.7 $\mu\text{S}/\text{cm}$, the analysis is continued with step 3. Higher conductivities than 4.7 $\mu\text{S}/\text{cm}$ are not accepted and the water does not pass the test.

3rd step

4.5 mL $\beta(\text{KCl}) = \text{sat.}$ is added to the sample in the external vessel and the pH of the water is measured. If the pH value is between 5.0 and 7.0 and the measured conductivity of step 2 is not higher as the listed value corresponding to the measured pH the test is passed. If not, the water must not be used as sterile water.

Parameters

pH calibration

Mode	CAL MEAS pH
Signal drift	2.0 mV/min
Min. waiting time	10 s
Max. waiting time	110 s
Measuring interval	2 s

Cell constant calibration

Mode	CAL Cond
Reference temp.	20 $^\circ\text{C}$
Conductivity	0.1 mS/cm
Temperature coeff.	2.11 $\%/^\circ\text{C}$
Signal drift	10 mS/min
Min. waiting time	10 s
Max. waiting time	52 s
Measuring interval	2.0 s

1st step: Conductivity measurement

Mode	MEAS Cond (Measurement with drift control)
Signal drift	0.001 mS/cm
Min. waiting time	10 s
Max. waiting time	52 s
Measuring interval	2 s
Stop meas. value	off
Reference temp.	off

2nd step: Conductivity measurement

Mode	MEAS Cond (Measurement with drift control)
Signal drift	0.001 mS/cm
Min. waiting time	10 s
Max. waiting time	1800 s
Measuring interval	2 s
Stop meas. value	off
Reference temp.	off

3rd step: pH measurement

Mode	MEAS pH (Measurement with drift control)
Signal drift	2 mV/min
Min. waiting time	10 s
Max. waiting time	110 s
Measuring interval	2 s
Stop meas. value	off

Calculation

No calculation is needed.

Example determination

1st step

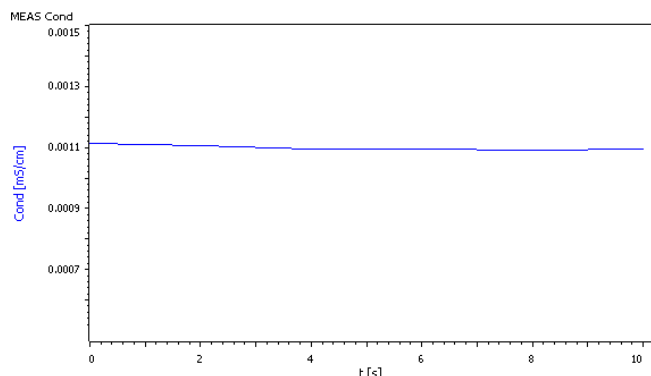


Figure 1: Conductivity measurement of ultrapure water.

2nd step

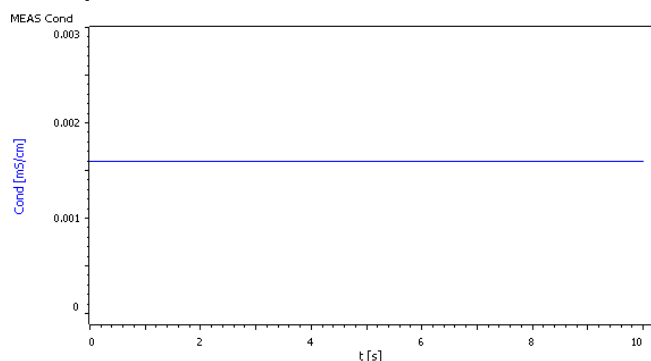


Figure 2: Conductivity measurement of deionized water.

3rd step

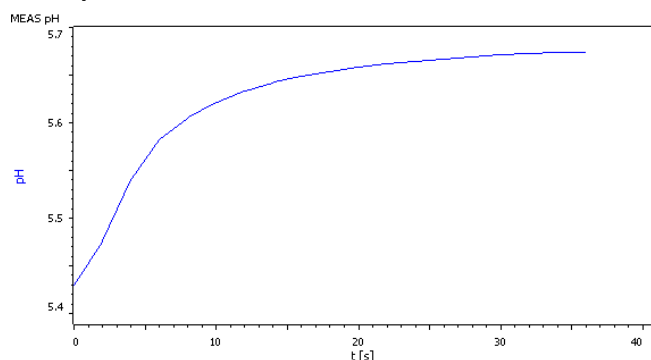


Figure 3: pH measurement of deionized water after addition of 0.45 mL β (KCl) = sat.

- The beaker has to be filled with 250 mL sample as otherwise the heights of the conductivity sensor and the pH electrode have to be adjusted manually for each measurement and to ensure that enough sample is present for the analysis.
- Over time the conductivity measuring cell ages and thus the cell constant may differ more than 2% from the one printed in the certificate. To re-determine the cell constant one of the following three approaches can be used.
 - Determination of the cell constant with one standard solution followed by the determination of the cell constant again with a different standard solution. The difference of the cell constants should be equal or less than 2%.
 - Determination of the cell constant with one standard solution and measurement of the conductivity of the second standard solution. The difference measured in the second standard solution should be less than 2% from the certified value.

Determination of the cell constant with one standard solution. Then comparison of the conductivity reading with the reading of a reference cell with traceable cell constant. The difference of the measured conductivity should be less than 2%.

References

- USP 37, <645> Water Conductivity

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Comments

- The conductivity measuring cell and the LL-Aquatrode plus are placed on different heights so that the pH electrode does not touch the sample during conductivity measurement.

Appendix

Photos of the setup



Figure 4: Overview of the whole system for water analysis consisting of a thermostat, a 867 pH module, a 856 conductivity module, an 815 Robotic USB Sample Processor XL, an LL-Aquatrode plus and a conductivity measuring cell. The left swing arm is used for analysis and the right one for the DIS-Cover



Figure 5: The pH electrode and the conductivity measuring cell are placed at different heights because the immersion of the electrode into the water may affect the conductivity. By considering this, the pH electrode is not immersed into the water during conductivity measurement.



Figure 6: Shows the holder 6.9920.261 for the external beaker and the positioning of the sensors at the external position while carrying out pH measurements.