THORNTON

Leading Pure Water Analytics

"Does your Water Meet Global Pharmacopoeial Requirements?"

Quick Guide to Pharmaceutical Water Conductivity Requirements

Stage 1:	Conductivity vs. Temperature Tables
Stage 2:	Conductivity Limit
Stage 3:	Conductivity vs. pH Tables

USP requirements since
November 15, 1996 and
NEW EP requirements since July 1, 2004

METTLER TOLEDO

USP <645> Goals

Fundamental Goals of the changes to USP Purified Water and WFI

- Maintain/Improve existing water quality
- Improve the reliability of the testing (using modern instrumentation)
- Reduce the number of tests
- Make allowances for on-line, in-line testing

The Three-Stage Method for <645>

Stage 1: In-line Test:

A non-temperature compensated conductivity measurement corresponding to a measured temperature. If the conductivity does not exceed 1.3 µS/cm @ 25 °C (or tabulated values in Table A), ***the water meets <645> requirements.*** If not, go to Stage 2.

Stage 2: Lab Test:

Equilibrate a water sample with air. If the conductivity does not exceed 2.1 µS/cm at 25 °C, ***the water meets <645> requirements***. If not, go to Stage 3.

Stage 3: Lab Test:

Add saturated KCl to the previous sample and measure the pH. If the conductivity does not exceed the allowable level of conductivity (measured in Stage 2) at that pH, based on Table B, ***the water meets <645> requirements***. If the conductivity exceeds that limit, the water test fails.

In addition, there are requirements for the Instumentation & Sensor specified in <645>. See back page for details.

Advantages of on-line testing Stage 1:

- Real-time process information. Data may be logged, providing water history.
- Immediate alarms and options.
- Eliminates sample collection, handling and transportation errors, and costly OOS investigations.
- Easier and cost effective.
- In addition, temperature-compensated conductivity remains an excellent technique to observe water quality changes to process control.

What are the USP & EP Water Conductivity Requirements and how does it affect me?

• USP <645> became mandatory on November 15, 1996 and is continued in subsequent revisions. It is required for USP Purified Water & Water for Injection.

• Effective July 1, 2004, the European Pharmacopoeia (EP) has revised its conductivity requirements *for Aqua ad Iniectabilia (*WFI) and *Highly Purified Water*. ***These waters have the same 3-stage conductivity limit test required for USP Purified Water & WFI.*** This test requirement is harmonized with USP <645> Water Conductivity test.

• Effective July 1, 2004 , the EP has revised its requirements for *Aqua Purificata* (Purified Water). It is a single stage test. Measure the temperature and uncompensated conductivity. The conductivity limit is interpolated using the measured temperature and the next lower and higher temperature in Table C. If the measured conductivity does not exceed the conductivity limit, ***the water meets the EP requirements.*** Otherwise, the water conductivity test fails.

Table A
<645> Stage 1 Conductivity Limits as a Function of Temperature

Temperature (°C)	Stage 1 Conductivity Limit (µS/cm)
0	0.6
5	0.8
10	0.9
15	1.0
20	1.1
25	1.3
30	1.4
35	1.5
40	1.7
45	1.8
50	1.9
55	2.1
60	2.2
65	2.4
70	2.5
75	2.7
80	2.7
85	2.7
90	2.7
95	2.9
100	3.1

Table B
<645> Stage 3 Conductivity Limits as a Function of pH

pH	Stage 3 Conductivity Limit (µS/cm)
5.0	4.7
5.1	4.1
5.2	3.6
5.3	3.3
5.4	3.0
5.5	2.8
5.6	2.6
5.7	2.5
5.8	2.4
5.9	2.4
6.0	2.4
6.1	2.4
6.2	2.5
6.3	2.4
6.4	2.3
6.5	2.2
6.6	2.1
6.7	2.6
6.8	3.1
6.9	3.8
7.0	4.6

Table C
***Aqua Purificata* Conductivity Limits as a Function of Temperature**

Temperature (°C)	Conductivity Limit (µS/cm)
0	2.4
10	3.6
20	4.3
25	5.1
30	5.4
40	6.5
50	7.1
60	8.1
70	9.1
75	9.7
80	9.7
90	9.7
100	10.2

Meet USP, EP, and future JP Instrumentation Requirements for Purified Water, Highly Purified Water and Water for Injection using Thornton Instruments.

Specification:	USP & EP Requirements	Thornton 770MAX	Thornton 200 Series
Conductivity Sensor and Cell Constant Accuracy*	Verify cell constant within ±2% using a reference solution**, e.g. ASTM D1125 solution D (146.9 µS/cm) or other certified reference solution.	Smart Calibration of all sensors exceeds requirements: ± 1%. Conductivity Calibration traceable to ASTM D1125, D5391, and Ultrapure Water. Temperature calibration traceable to NIST.	Calibration of all sensors exceeds requirements: ± 1%. Conductivity Calibration traceable to ASTM D1125, D5391, and Ultrapure Water. Temperature calibration traceable to NIST.
Electrode Material	Suitable	316L SS & Titanium	
Conductivity Meter Calibration	NIST traceable 0.1% precision resistors in place of sensor. Traceable to national standard for EP.	• Smart Calibration • NIST traceable to 0.05% • Verification & Calibration for resistance & temperature • Recertification	• User Calibration • NIST traceable to 0.08% • Verification & calibration for resistance & temperature • Recertification
Instrument resolution	0.1µS/cm	0.001µS/cm	
Instrument accuracy @ 1.3 µS/cm	0.1µS/cm	(±0.3% of reading) ±0.004µS/cm	(±0.5% of reading) ±0.007µS/cm
Temperature compensation	Must be read uncompensated	Uncompensated & compensated	
Instrument dynamic range***	10^2	10^6	10^4

* For EP Purified Water system accuracy is 3% of reading plus 0.1µS/cm. ** For EP, must use solution less than 1500 µS/cm.
*** For operation and traceable calibration using a single sensor.

Thornton Inc. develops, manufactures and markets process control instrumentation to measure and monitor various parameters used to control pure and ultrapure water systems such as resistivity, conductivity, TOC, dissolved oxygen, flow, pressure, tank level, pH, ORP and temperature. Thornton is the recognized industry leader in the measurement of resistivity and conductivity, particularly in pure water. The ASTM "Standard Test Methods for Electrical Conductivity and Resistivity of Water" (D1125) was revised in 1995 based specifically on papers and recommendations from Thornton Inc. Thornton has been the principal consultant for conductivity to the USP and the Water Quality Committee of the Pharmaceutical Research and Manufacturers of America, and a staff associate is the Chairperson of the USP Pharmaceutical Water Expert Committee.

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