

# APPLICATION NOTE

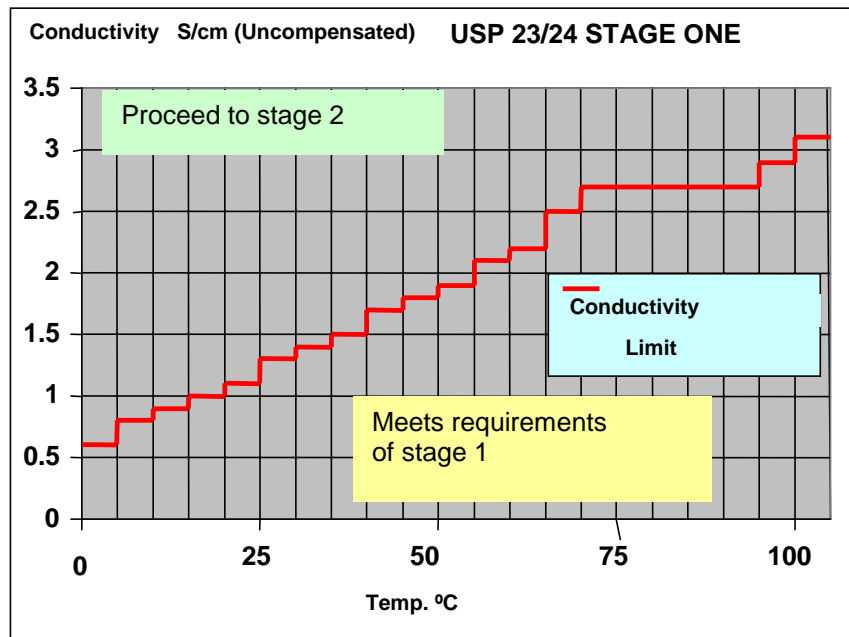
## Pharmaceutical Waters

### Introduction

United States Pharmacopoeia (USP) is the governing body responsible for issuing guidelines for the pharmaceutical industry. Implementing these guidelines is required for companies that bring drugs to the US market. This means that USP is important to all pharmaceutical companies, period. These guidelines are contained in the USP monograph (article). Among other functions, USP specifies standards of quality, purity, packaging, and labeling for a number of pharmaceutical waters including “Purified Water” (PW) and “Water for Injection” (WFI). These waters are used as ingredients in either dose form or bulk pharmaceuticals, so purity is critical. WFI is the purest grade of bulk water monographed by the USP, and is found in the manufacture of parenteral (injected), ophthalmic (eye drops), and inhalation products.

### USP 23, 24, and Beyond

Before 1996, the quality of these waters was determined by a number of off-line, “antiquated” laboratory tests. The USP monograph 23 replaced these tests with an on-line conductivity measurement as the initial marker. PW also has to meet a TOC limit, and WFI has to meet bacterial tests in addition to the TOC and conductivity limits. In this discussion, we will concentrate on the USP requirements for conductivity only. This change to an on-line conductivity



measurement was precipitated by many desires including improving the reliability of the testing by using modern instrumentation, providing immediate alarms and options for quality control, eliminating sample collection and handling errors, and reducing the cost of testing.

### Conductivity Requirements

The conductivity requirements mandated by USP are tiered in three stages:

**Stage One:** Use In-Line or grab sample methods to measure the conductivity and water temperature. This conductivity reading must not be temperature compensated. Compare these readings to the Stage 1 table of Conductivity vs. Temperature

(shown above). If the conductivity is below the limit stated for that temperature, the water meets the requirements. If the conductivity is above the limit, proceed to Stage Two.

**Stage Two:** Take a grab sample and measure conductivity after equalization with atmosphere and temperature normalization to 25 C. The water passes if conductivity is <2.1 S.

**Stage Three:** If Stage Two is exceeded, measure the pH of the grab sample and check conductivity against the Stage Three graph Conductivity vs. pH (not shown). If sample is within the limits, it passes. If it does not, the water is deemed unacceptable for PW or WFI use.

The last two stages require grab sample laboratory tests, so it is desired to never exceed the limits set in Stage 1. Yokogawa can help to ensure that these limits are not exceeded.

### The Solution

Yokogawa's conductivity transmitters and converters possess USP functions that make this seemingly complex and troublesome requirement pain free, and automatic. The SC202 two-wire conductivity transmitter has the USP Stage One table pre-programmed in its software. When enabled, the transmitter will send a FAIL signal when the water exceeds the USP limit. It also can display and transmit the uncompensated conductivity that USP mandates for compliance recording.

The SC402, DC402, and SC150 4-wire conductivity converters have additional USP features. These units have the ability to display and transmit the uncompensated conductivity for USP compliance, as well as the NaCl temperature compensated measurement, valuable for process control. The USP Stage One table is pre-programmed into these instruments, and a FAIL alarm will be given if the conductivity limits are exceeded. Alarms on these units can be dedicated as USP "warning" alarms with user defined safety margins. These "warning" alarms will inform the operator that his water is trending towards the USP limit, and will allow him to take preemptive corrective action.

### Summary

The USP functions built into Yokogawa's conductivity instruments provide an automated, trouble-free way for pharmaceutical companies to monitor and record their USP compliance. The four-wire converters possess this ability

without compromising the standard compensated measurement used for process control.

### Recommended Products:

#### Transmitters:

SC202 two-wire Conductivity Transmitter

#### Converters:

SC402 four-wire Conductivity Converter

DC402 four-wire Dual Channel Conductivity Converter

SC150 four-wire ¼ DIN Panel Mount Conductivity Converter

#### Sensors:

SC42-SP34 Large-Bore Conductivity Sensor (fittings available for Flow-Thru, Insertion, or Immersion installations)

SC4A Conductivity Sensor (fittings available for Insertion, Sanitary, or Retractable installations.)

