

Industry: Pharmaceutical**Products:** Contacting Conductivity Process Liquid Analyzer

Background

The United States Pharmacopoeia (USP) and European Pharmacopoeia (EP) standards require total organic carbon (TOC) to be monitored in water used in pharmaceutical manufacturing. Compliance with these standards is a requirement for companies that market pharmaceuticals in the United States. The standards are contained in the USP monograph (article).

The USP specifies qualifications for sterility and packaging methods by pharmaceutical water category. The two basic types of water preparation are water for injection (WFI) and purified water (PW). The analytical standards for these two types of water are similar in most ways. Differences are that WFI is subject to stricter bacterial count standards and must also pass the bacterial endotoxin test. Descriptions for most of the preparation methods are similar, as well; however, WFI preparation must incorporate distillation or double pass reverse osmosis. Descriptions of the various methodologies used in the preparation of USP water applies equally to PW and WFI.

PW is obtained by distillation, ion-exchange treatment, reverse osmosis, or other suitable process. It is prepared from water that complies with the drinking water regulations of the U.S. Environmental Protection Agency (EPA). It contains no added substances. WFI is purified by distillation or reverse osmosis.

Since these waters are used as ingredients in either dose form or bulk pharmaceuticals, 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.

The fundamental objectives of the USP are:

- I. To maintain or improve the existing water quality
- II. Improvement of the reliability of the measured values utilizing modern analytic instruments
- III. Reduction of the number of samples
- IV. Authorization of the in-line measuring method

USP 23 and 24

Before 1996, the quality of the pharmaceutical waters was determined by several off-line, laboratory tests that are now considered to be antiquated. The USP monograph 23 (and currently 24) replaced these tests with an on-line conductivity measurement as the initial marker. While PW only needs to meet a TOC limit, the WFI has to meet bacterial tests in addition to the TOC and conductivity limits. This application note focuses on the USP requirements for conductivity only. This change to an on-line conductivity measurement was done to:

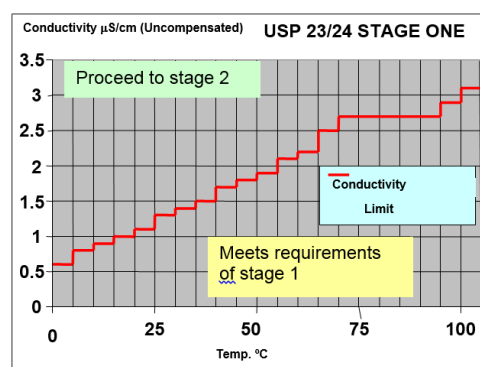
- Improve the reliability of the testing by using modern instrumentation
- Provide immediate alarms and options for quality control
- Eliminate sample collection and handling errors
- Reduce the cost of testing.

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

Stage One: Use in-line or grab sample methods to measure conductivity and water temperature. This conductivity reading must not be temperature compensated. Compare these readings to the Stage I graph shown below. If the conductivity is below the limit stated for that temperature, the water meets the requirements. If above the limit, proceed to Stage Two.

Advantages to in-line measurement are:

- I. Uses real-time information for conductivity and temperature
- II. Immediate limit value alarm
- III. Data output for recording and documentation of the water quality
- IV. Simple and reasonably-priced measurement
- V. Avoids errors due to sampling, handling, and transport



Stage Two: Take a grab sample and measure the conductivity after equalization with atmosphere and temperature normalization to 25°C. If the water conductivity is below 2.1 μS then Stage Three is needed.

Stage Three: If Stage Two is exceeded, measure the pH of the grab sample and check conductivity against the results in table I of conductivity vs. pH. If the sample is within the limits, it passes. If it does not, the water is deemed unacceptable for PW or WFI use.

Solution

Yokogawa's conductivity transmitters and converters possess USP functions that make this seemingly complex and troublesome requirement pain-free and automatic. In the FLXA two-wire conductivity transmitter, the USP23/24 Stage One table is pre-programmed. 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.

Yokogawa's conductivity converters offer additional USP features. They can display and transmit the uncompensated conductivity for USP compliance and the NaCl temperature-compensated measurement, which is valuable for process control. Alarms on these units can be dedicated as USP "warning" alarms with user-defined safety margins. These "warning" alarms will inform the operator that the water is trending toward the USP limit so that preemptive corrective action can be taken.

Product Recommendations

Conductivity Measurement System:

Process Liquid Analyzer:

2-wire FLXA202 Contacting Conductivity Analyzer

4-wire FLXA402 Contacting Conductivity Analyzer

Sensor Selection:

Analog and Digital SMART sensors are available. Analog options allow users to interface with a system that has been used historically. SENCOM™ technology allows sensors to transmit and receive data when connected to a transmitter/analyzer or any PC. The

SMART digital sensors maintain specific measurement and calibration data on an integrated circuit that is an integral part of the sensor for easy plug and play solutions. The data management software optimizes sensor performance for enhanced reliability and process safety.

Option #1:

SC42-SP34 Large-Bore Conductivity Sensor (fittings available for flow-through, insertion, or immersion installations)

Option #2:

SC4A Conductivity Sensor (fittings available for insertion, sanitary, or retractable installations.)



Digital SMART Option:

The reusable smart adapter, SA11, offers full measuring parameter functionality of analog sensors equipped with a Variopin connector and Yokogawa ID chip. The SA11 automatically recognizes the installed sensor and prepares the proper configuration.



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YOKOGAWA ELECTRIC CORPORATION

World Headquarters

9-32, Nakacho 2-chome, Musashino-shi, Tokyo 180-8750, JAPAN

<http://www.yokogawa.com/an/>



Represented
by:



Ph: 612-861-1749

www.arjaynet.com

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