

Convenient Conductivity Calibration to Meet Pharmacopeia Regulations

Pharmacopeias require that conductivity measurement systems be periodically calibrated to ensure their precision. The range of accessories and time required, and complexities involved in system calibration can lead to operator error, inaccurate calibration, and imprecise measurements. A cutting-edge conductivity measurement and calibration system greatly simplifies the calibration process, ensures accuracy, and is in full compliance with global pharmacopeia standards.



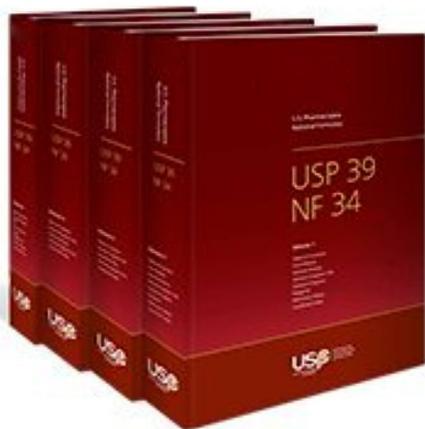
Introduction

Obtaining accurate conductivity measurements for establishing the level of water purity relies on a number of factors, including the use of high quality sensors, precise determination of sample temperature (as temperature affects water conductivity), and assurance that the measuring system is calibrated correctly.

Global pharmacopeias require that conductivity measurement systems are periodically calibrated if they are used to measure regulated pharmaceutical waters and other compendial fluids. These global pharmacopeias mandate conductivity measuring circuit verification independent of the conductivity sensing element, which can be a complicated procedure.

In order to meet prescribed pharmacopeial conductivity calibration requirements, a water system owner or service provider must have precision traceable resistors or a decade box which can simulate a resistance (conductivity) and temperature measurement, and are certified and traceable to a national standard. In addition, certified and traceable calibration liquid standards are necessary to complete the calibration of the sensor's cell constant. This array of calibration tools can be awkward to use and requires substantial operator training. Further, the calibration process itself is time consuming and open to a variety of errors that can result in incorrect calibration and, therefore, inaccurate conductivity measurements.

Current regulations for calibration and specific procedures are reviewed in this paper. The common calibration method is compared with a state-of-the-art procedure using a digital calibration system that significantly simplifies the process, and also meets global pharmacopeia requirements.



Global pharmacopeia instrument requirements

Calibration of a conductivity measurement system's electronics is required to ensure the system can accurately measure temperature and a resistance. Calibration of the electronics is accomplished by replacing the conductivity/temperature sensor with National Institute of Standards and Technology, or equivalent national authority traceable precision resistors, to give a predictable instrument response.

As advanced conductivity systems have multiple measurement circuits to cover their extended range, each range on the measurement system requires separate calibration prior to use, or at least calibration of the circuit that is to be used during operation. The frequency of re-calibration is dependent on instrument design, frequency of use, etc. However, some older instruments have multiple ranges, yet they are equipped only with a single calibration adjustment, so every time the range to be measured changes, re-calibration may be required, making calibration of the electronics more complex.

Of particular importance when calibrating conductivity measurement systems, is accurate verification of the sensor's cell constant. This is a factor that represents the geometrical properties of the conductivity sensor and it must be known within $\pm 2\%$. The cell constant can be verified directly by using a solution of known or traceable conductivity, or indirectly by comparing the instrument reading taken with the conductivity sensor in question to readings from a conductivity sensor of known or traceable cell constant.

Excluding the conductivity sensor cell constant accuracy, the instrument resistance measurement accuracy must be $\pm 0.1 \mu\text{S}/\text{cm}$. Accuracy of the temperature measurement must be $\pm 2^\circ\text{C}$.

In order to increase the measurement accuracy for the conductivity ranges used (which can be very wide), and to ensure complete calibration of the equipment, global pharmacopeia recommend that periodic verification of the entire equipment be performed. An accepted calibration period is once per year but many owners calibrate every six months. To better understand the intricacies of these procedures, system requirements and calibration processes are summarized below.

Conductivity calibration and performance requirements

"On-line conductivity testing provides real-time measurements and opportunities for real-time process control, decision, and intervention. Precaution should be taken while collecting water samples for off-line conductivity measurements. The sample may be affected by the sampling method, the sampling container, and environmental factors such as ambient carbon dioxide concentration and organic vapors." USP <645>.



Instrument (meter, transmitter or measurement circuit) requirements

- The temperature measurement circuit should be verified.
- Uncompensated conductivity or resistivity must be reported.
- The instrument display must have a minimum resolution of 0.1 $\mu\text{S}/\text{cm}$. Resolution of 1 $\mu\text{S}/\text{cm}$ is unacceptable.
- Instrument performance must be verified to $\pm 0.1 \mu\text{S}/\text{cm}$ by replacing the sensor with a traceable precision (0.1%) resistor. For example, a 100 k Ω resistor with a 0.1 cm^{-1} cell constant should display $1.0 \pm 0.1 \mu\text{S}/\text{cm}$.

Conductivity sensor requirements

- Temperature must be accurate to $\pm 2 \text{ }^\circ\text{C}$.
- The conductivity sensor cell constant must be accurate and known to $\pm 2\%$.
- The sensor must be calibrated in a liquid standard solution of known conductivity. This can take several approaches:
 - Procure liquid standard solutions from NIST or from another reliable chemical supplier.
 - Prepare solutions to a specific conductivity such as ASTM method D1125.
 - Use any solution and determine its conductivity with a traceable reference conductivity measurement system.

Sequence of calibration with conventional instrumentation

The following is the typical sequence of calibration of the measuring circuit electronics, sensor temperature element and sensor cell constant with conventional instrumentation.

1. Instrument electronics calibration

General procedure:

1. Detach the sensor from the instrument.
2. Attach "traceable temperature simulators" (precision resistors) to the instrument in place of the sensor.
3. Compare the measured temperature to the traceable temperature.
4. If necessary, adjust the instrument reading for temperature using the instrument's firmware.
5. Attach "traceable resistance simulators" (precision resistors) to simulate a conductivity measurement.
6. Compare the measured conductivity to the traceable conductivity.
7. If necessary, adjust the instrument reading for conductivity using the instrument's firmware.

The instrument can be calibrated separately at the supplier's factory, at the end user location or in a metrology lab. When calibrating, follow protocols provided by the supplier and use recommended measurement values. Calibrate all necessary measurement circuits. Most instruments have multiple measurement circuits to obtain measurements across a broad conductivity range.

2. Temperature sensor calibration

General procedure:

1. Use a calibrated instrument (any calibrated instrument which meets previously stated specifications is acceptable for performing a calibration); however, using the actual instrument included in the current calibration process is preferred.
2. Using the actual sensor cable length is preferred to minimize variable cable resistance.
3. Connect the sensor to the instrument.
4. Using a reference temperature system (a second temperature sensor), compare the measured temperature to the reference temperature.
5. Use a temperature bath other medium to fix the water temperature.
6. The temperature sensor must be within ± 2 °C, if it is outside the range, an adjustment must be made.
7. Determine whether to calibrate in ice water or heated water.
8. If necessary, adjust the temperature using the temperature instrument's firmware. This adjustment is made to determine a new calibration factor(s).

If necessary, enter the new calibration factor(s) into the instrument's firmware.

3. Cell constant calibration methods

The following methods may be used to verify or calibrate conductivity sensor cell value.

Verify or calibrate conductivity in a liquid standard solution with certified conductivity value.

Purchased liquid standard solutions: Liquid standard conductivity solutions may be purchased from a reliable supplier that provides traceability of the solution.

- Select a liquid calibration standard solution carefully. The conductivity of a purchased solution <1 $\mu\text{S}/\text{cm}$ will be vulnerable to contamination and unpredictable effects CO_2 from the atmosphere.

Prepared liquid standard solutions:

- A liquid standard solution may be chemically prepared in a laboratory to a specific conductivity.
- Use ASTM D1125 standard solution D to prepare a liquid standard solution with a conductivity of 146.93 $\mu\text{S}/\text{cm}$.

Verify or calibrate against another calibrated conductivity sensor (cell):

- This method is accepted by the United State Pharmacopeia (USP) and encouraged by the European Pharmacopeia (EP).
- This procedure is performed in-line with a reference sensor used for comparison and the sensor under calibration. This method permits the calibration of the sensor in water of the quality in which it normally operates and measures. This method also eliminates the risk of removing the sensor from the system and the potential of contaminating the system and the sensor.

Return conductivity sensor to the manufacturer for calibration and certification:

- Use a manufacturer of conductivity instruments and sensors with a validated and traceable process for performing a conductivity and temperature calibration, that produces a traceable certificate to support the calibration performed.
- It is a common and accepted practice for sensors and instruments to be returned to the supplier for calibration and certification.

A better solution for measurement and calibration

As can be seen from the above descriptions, calibration of conventional conductivity systems is far from straightforward. To provide a more accurate and user-friendly conductivity measurement and calibration system, METTLER TOLEDO Thornton has developed a range of convenient conductivity sensors, instruments, and accessories.

UniCond conductivity sensors

UniCond™ sensors contain both the physical sensor and the measuring circuit in a single, compact unit. The main advantage with an integrated sensor and measuring circuit is that the wiring distance from the sensor's electrodes to the measuring circuit is reduced to less than 5 cm (2 in.) and is fixed in place without using connectors or terminals. This is in contrast to traditional installations which must handle various lengths of analog signal cable, typically from 5 to 50 m from sensor to transmitter with terminations on at least one end.



UniCond Sanitary Sensor

With the very short and fixed analog signal wiring inside UniCond sensors, the issues of cable capacitance and resistance are eliminated. Not only does this prevent errors at low conductivity where AC leakage through cable capacitance is a problem, it also allows much closer control over measurement parameters. With much improved handling of polarization effects, UniCond sensors have a greatly extended upper range. UniCond sensors feature METTLER TOLEDO's Intelligent Sensor Management (ISM™) technology. ISM was developed to simplify analytical sensor operations and improve sensor performance. It achieves this through a variety of capabilities.

Plug and Measure: UniCond sensors carry their own identification and calibration data. When connected to an ISM transmitter, this data is automatically uploaded and the transmitter configures itself automatically without any operator intervention.

Predictive diagnostics tools: These tools continually monitor sensor exposure to conditions that could result in the need for maintenance.

Digital signal: Traditional measurement systems send an analog signal to a transmitter, which converts the signal into a displayed value. Analog signals are prone to electrical interference and can degrade over long cable runs. ISM sensors convert the analog measurement into a digital signal. The digital signal is highly robust and remains stable even over long cable runs.



M800 and M300 transmitters

ISM transmitters are versatile in operation and easy to use. ISM's Plug and Measure feature provides rapid, error-free measurement from start up. The transmitters convenient multi-channel, multi-parameter capability enables several sensors to be measured from the same instrument for convenience in display and providing computed variables. Computed variables can include % rejection to indicate reverse osmosis performance or deionization capacity to predict exhaustion of ion exchange resin. Parameters of pH, ORP, dissolved oxygen, ozone, TOC and flow can be monitored along with conductivity on the same transmitter.

UniCond calibrator

The UniCond calibrator eliminates the complexity of calibrating with individual resistors, one or more decade boxes, and verification of the temperature circuit; all of which are difficult to manage on site. The Calibrator includes precision traceable resistors for the necessary ranges. It simultaneously connects to the UniCond sensor, cable, and ISM transmitter for a fast, reproducible, and certified system calibration without removing the sensor from the process. The well-documented procedure is further simplified with menu-driven firmware that also allows cell constant and temperature factor adjustment for a complete system calibration or verification.



UniCond Calibrator

The UniCond calibrator enables in-line calibration of all the measurement circuits to ensure the measurement system is in compliance with global pharmacopeia standards without having to remove the sensor from the process.

Pharma waters verifiers

Thornton Pharma Waters Verifiers offer a convenient method of verifying the accuracy of the conductivity measuring circuits in UniCond sensors and the M800 and M300 transmitters. This can be done without additional equipment and within the conductivity range of pharmaceutical waters such as Water for Injection (WFI) and Purified Water (PW).

When a conductivity measuring circuit requires calibration, the entire measuring range of the circuit must be calibrated. Thus, several calibration points along the measuring range are strategically selected to optimize the accuracy of the full range. State-of-the-art circuit designs, such as the ones used on the UniCond sensors, have a wide dynamic range that extends from very low to very high conductivity. However, pharmacopeia standards such as USP <645> require very low conductivity water, between 0.6 and 3.1 µS/cm. The Pharma Waters Verifiers verify several points within the operating pharmaceutical water range.

The pharma waters verifiers provide the opportunity to verify a specific conductivity range that is more appropriate for today's pharmaceutical water systems. The Verifiers also allow for system verification in between the normal calibration times.



Pharma Waters Verifiers

Calibration procedure for UniCond system

UniCond electronics calibration

General procedure:

1. Detach the UniCond from its cable.
2. Attach the UniCond sensor to one end of the "Y" connector on the UniCond calibrator.
3. Attached the other end of the "Y" connector to the previously disconnected cable.
4. Compare the measured temperature to the traceable temperature.
5. Access the transmitter's electronic calibration menu
6. Compare the measured values to the traceable values listed on the UniCond calibrator.
7. If necessary, adjust the reading using the transmitter firmware.

For cell constant and cell temperature calibration, follow the steps previously described in sections 2 and 3.

Conclusion

Calibrating conductivity measurement systems to satisfy pharmacopeial requirements can be a complex, time consuming process. In addition, operator error can result in a conductivity system reporting inaccurate measurements. It is therefore important that accessories for sensor calibration are simple to use while also providing assurance that global pharmacopeia regulations are being met.

METTLER TOLEDO Thornton has developed a leading-edge conductivity measurement system with unique calibration and verification tools that, as shown, greatly simplify the calibration process. All components of the measuring and calibration system are provided with traceable certification from the factory as new and for any returns for calibration. The features of Intelligent Sensor Management technology significantly enhance system performance and ease of operation.

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