

# Multi-parameter Transmitters for Process Control in Pharmaceutical Manufacturing

## Applying on-line process control in process analytical technology

The FDA's Process Analytical Technology (PAT) initiative recognizes that a high quality, consistent and safe product is more likely to be assured through timely measurements of critical quality and performance attributes of raw and in-process materials and processes. If the design of the product is understood, the manufacture of the product is consistent, the input variables are controlled, and the impact of critical variables is known, then a predictable product can be manufactured. This process understanding is the key to PAT. To gain an understanding of process, data measurements are necessary to make process control decisions. This concept is especially critical for water production since water is the single most widely used material by every producer worldwide.

The PAT initiative is recognized and supported globally. The USP – the standards setting body for drug products and devices in the U.S. – has endorsed the use of on-line conductivity instrumentation in Chapter <645> Water Conductivity for product control and for additional process and system control, while warning of the challenges of off-line testing high purity waters from airborne and sampling contaminants. Similar cautions exist regarding off-line testing for USP <643> Total Organic Carbon.

## On-line process control using analytical transmitter-sensor combination

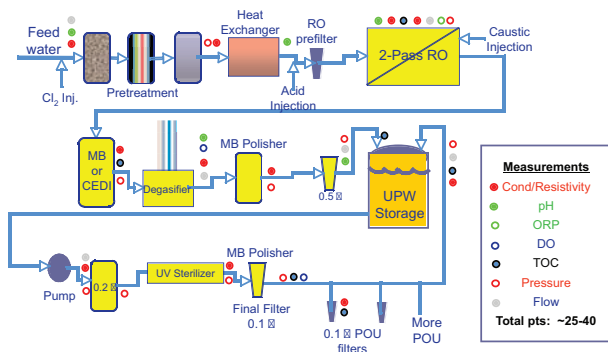
On-line process TOC sensors are designed as a transmitter-sensor combination. The transmitter is an instrument that measures the input/output conductivity and temperature measurements from the TOC sensor, processes them into a TOC measurement, and produces a reading. The output may be viewed on the transmitter display or transmitted via analog or digital signal to an external chart recorder, PLC, computer or similar recording device.

The advantage of using a multi-parameter transmitter is that the user may add other process parameters in addition to the TOC sensor. Measurement sensors such as conductivity, pH, oxidation reduction potential (ORP), dissolved oxygen or dissolved ozone, flow, pressure and tank level may be connected to the same transmitter, in addition to TOC sensor(s). With the use of patch cables, the transmitter may be located up to 300 feet (90 meters) from the sensor(s). In the case where the water system control panel is a distance from the sensor port, this concept allows the user to install the sensor at the sample port and the transmitter at the control panel.

## Water quality is critical for pharmaceutical manufacturers

All medicinal products have some Purified Water (PW) or Water For Injection (WFI) component in their manufacturing process, either directly as an ingredient or solvent, diluent, vehicle for transmission, reagent, or indirectly by cleaning contact. For drugs produced for U.S. consumption, the end-product testing related to water quality is known as United States Pharmacopeia (USP) <645> Water Conductivity, <643> Total Organic Carbon. There are related tests in international pharmacopeia (EP, JP).

The operator responsible for the water system (plant production or engineering) must monitor process analytics and physical measurements throughout the water system to measure and control water quality from the feed water to final distribution. Typically these in-process measurements include conductivity, TOC, dissolved ozone, pH, ORP, turbidity, flow rate, % rejection, tank level, temperature, pressure, and hardness. Such multiple measurements are made less complex by using a multi-parameter transmitter to monitor multiple sensor parameters simultaneously.



Water purification system

### Using a multi-parameter transmitter and Intelligent Sensor Management for major sensor parameters

Multi-parameter transmitters and intelligent digital sensors provide the tools necessary to take full advantage of the benefits of continuous on-line

measurement. Transmitters offer extra measurements, relays for valve control and early warning notification systems. Extra analog outputs are provided to transmit all necessary measurements. This allows the user to transmit multiple parameters such as

- Non-temperature-compensated conductivity measurements for compendial requirements
- Temperature-compensated conductivity measurements for process control
- Temperature
- TOC for compendial requirements and process control

Intelligent Sensor Management (ISM™) sensors provide enhanced measurement performance while communicating vital information for process management and control in real time. One configurable multi-parameter transmitter communicates directly with an ISM™ sensor via firmware handshake, and the transmitter automatically configures itself to measure that parameter. Critical points throughout a system are monitored and controlled on-line with data provided locally at point of use or remotely in a control room. In addition, attributes for specific USP, European Pharmacopeia (EP) and Japanese Pharmacopeia (JP), and alarms unique to the pharmaceutical industry, can be validated in a suitable multi-channel transmitter.

The multi-parameter feature allows the user to install, operate, calibrate and maintain a single transmitter, instead of using one transmitter for pH, another for conductivity, another for TOC, etc. The Plug-and-Measure feature of ISM sensors permits simple connection and automatic calibration of each sensor. Additional calibration and diagnostic data reside within the sensor's electronics to provide calibration histories, warnings, and sensor lifetime and hardware failure notifications.

The M800 multi-parameter transmitter platform covers all major measurement parameters in one instrument. As many as four separate inputs of measurement for conductivity, pH/ORP, dissolved oxygen, and dissolved ozone are possible, plus two additional channels for flow. ISM sensors display remaining sensor lifetime and time to next maintenance and calibration.

These enhanced diagnostics reduce unscheduled process downtime and improve process safety. Color-coded alarm management significantly improves quick access to critical sensor information. The unique diagnostics display (iMonitor), offers all this information on one easy-to-read screen. A large, high-resolution color touchscreen simplifies all transmitter operations.

The programmable display of up to eight measurement values or diagnostics data provides vital information on one screen, or up to eight screens, to suit requirements. Fully tailorable wizard set-up reaches any menu function in just three touches. This concept reduces training effort and configuration failures to a minimum. Transmitter configurations can be downloaded to a PC and uploaded to other M800 transmitters. This feature simplifies handling and reduces commissioning errors significantly.



Thornton 5000TOCe sensor



M800 multi-parameter transmitter

### Conclusion

With fewer personnel available in facilities operations, on-line analytical instrumentation becomes more critical. A practical, cost-effective solution to measure and control Pure Water, High Purity Water and Water For Injection for the pharmaceutical manufacturing process is to apply continuous on-line measurement systems with intelligent ISM sensors and a multi-parameter transmitter that produces continuous measurement results. In this way, the operator can monitor the entire water system for real-time process control, which is a key goal of the PAT initiative.

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AN-0129 Rev A 07/11