Continuous At-Line Microbial Monitoring
For Pharmaceutical Waters

7000RMS Microbial Detection Analyzer
- Continuous, real-time analysis
- Results in seconds
- No sample preparation
- No reagents required
- Process/batch sampling modes
7000RMS
Real-Time Microbial System

METTLER TOLEDO Thornton’s 7000RMS is an at-line analyzer for real-time measurement of microbial contamination (bioburden) in pharmaceutical water. Laser-based technology enables immediate detection and quantification of microorganisms directly from the water sample, overcoming limitations of time-consuming growth-based methods.

Measuring bioburden in Purified Water (PW) and Water for Injection (WFI) was dependent on time-consuming, error-prone culture-based lab methods. At-line microbial detection offers the potential to improve pharmaceutical water system operations, reduce costs, and ensure water quality.

Features

- **Convenient Touch Screen Display**
  with intuitive user interface

- **Greater Sensitivity**
  measurements down to 1 Auto Fluorescent Unit (AFU)

- **Real-time Microbial Detection**
  Results every two seconds

Benefits

- **Easy to Operate**
  7000RMS easily monitors at-line or grab samples for rapid detection

- **Rapid, reliable measurements**
  eliminates the variability and time consuming nature of traditional plate-count techniques

- **Real-time results are obtained for optimum control**
Principle of Operation

Microorganisms such as bacteria and fungi contain metabolites such as NADH and riboflavin to regulate growth and development. These metabolites fluoresce when exposed to light of certain wavelengths.

- A water sample, flowing at 30mL/min, is drawn into a flow cell in the 7000RMS where it is illuminated by a 405 nm laser.
- Particles, including microbes, in the flowing stream cause light to scatter.
- Forward-scattered (Mie) light is collected and analyzed.

- At the same time, the microorganism metabolites (NADH and riboflavin) are excited by the laser and release light energy as fluorescence.
- This fluorescence, of a certain wavelength range, is captured and analyzed.
- Algorithms within the 7000RMS combine fluorescence and particle signals to identify microorganisms, classifying them as Auto Fluorescent Units or AFU’s.
- The AFU count is displayed on the 7000RMS along with a trend chart showing a historical record of the detected AFU’s in the sample stream. Results can be displayed as frequently as every two seconds.
The 7000RMS detects microbial presence within seconds after the sample enters the analyzer. Measurements are continuously updated providing a real-time profile of your PW or WFI system. This real-time information enables the user to quickly divert contaminated water before it impacts other locations within the water system.

With no reagents, sample preparation, growth media, or incubation time requirements, the 7000RMS offers lower operating costs by reducing or even eliminating the need for routine plate counting. The 7000RMS reduces:

- Costs associated with plate counting
- Costs associated with false positive investigations
- Costs associated with delayed release of product while awaiting lab results

Managing Costs and Risk
Understanding the microbiological quality of pharmaceutical water prior to use and being able to react quickly to out-of-specification events reduces potential financial loss and regulatory risk.

- Water sampling for plate counting is often performed daily to weekly at multiple locations throughout the water system.
- Plate count results are not obtained for 5 to 7 days or longer.
- Estimates have shown that as much as 80% of positive results of plate counts are false-positives created by errors in manual, grab sampling.
- Costs to investigate these false-positive occurrences can have a significant negative financial impact on operations.
- Delays in product release while investigations are conducted can result in lost revenue and added costs.

“…the value of early detection should not be underestimated.”

“…Significant contamination of the water loop impacts multiple manufacturing areas and may affect a large number of batches if contamination is observed with several days delay” 1

1) Novel Concept for Online Water Bioburden Analysis: Key Considerations Applications and Business Benefits American Pharmaceuticals Review, July 2013
Pharmacopeia Guidelines
Alternative Microbial Methods

The General Information Chapter 1231 Water for Pharmaceutical Purposes, the United States Pharmacopeia (USP) has long supported on line, continuous monitoring of pharmaceutical waters so that historical in-process data is recorded to ensure the water system is in control and continues to produce water of acceptable quality.

Grab sampling provides incomplete information.

In USP 1231 compendial limits of 100 cfu/mL for Purified Water (PW) and 10 cfu/100 mL for Water for Injection (WFI) are the traditional microbial requirements for water quality. However, “water sampling protocols are limited in their ability to identify changes in ongoing water system performance making it difficult to provide ongoing trend analysis, as ‘grab’ samples can only provide a snapshot of the dynamic water system.”

- Continuous monitoring capability of the 7000RMS enables a more accurate and constant surveillance of water system status.
- At-line monitoring enables early indication of microbial excursions so that process and quality groups can ensure water used for manufacturing is in compliance and in control.

General Chapter 1223 Validation of Alternative Methods encourages selection, evaluation and use of technologies such as 7000RMS as alternatives to compendial methods. Chapter 1223 provides guidance and methods for the specification, qualification and implementation of alternative methods.

"Alternative methods and/or procedures may be used if they provide advantages in terms of accuracy, sensitivity, precision, selectivity, or adaptability to automation or computerized data reduction, or in other special circumstances." USP 1223

The USP 1223 and the EP (5.1.6) are informational documents for the validation of alternative microbiological methods, which detail validation procedures for different technologies and procedures. In addition, the FDA and the EMA (European Medicines Agency, which is the FDA equivalent) have also published guidelines for the deployment of alternative microbiological methods.

USP is a trademark of the United States Pharmacopeia

1) Novel Concept for Online Water Bioburden Analysis: Key Considerations Applications and Business Benefits
American Pharmaceuticals Review, July 2013
**Main Water Loop and Sub Loop Applications:**
The 7000RMS can be used throughout the PW and WFI purification system for monitoring microorganisms in the reverse-osmosis system, pure water storage, or distribution loops.

Like TOC and Conductivity, the 7000RMS can be placed at the main water loop and sub loops for supporting pharmacopeia regulatory control at the return loop. It can also be installed after the purification unit.

**Points of Use Applications:**
The 7000RMS can also be easily used to rapidly validate water at Points-of-Use, reducing sample analysis time and eliminating risk of sampling contamination and costs associated with plate counts.
7000RMS Analyzer
Specifications and Ordering Information

**General Specifications**

- **Sample flow rate**: 30mL/min
- **Biological detection limit**: 1 AFU (Auto Fluorescent Units)
- **Minimum detection size**: ≥ 0.5µm
- **Measurement range**: 0-10,000 total counts/mL
- **Data report interval**: 2 seconds (1mL)
- **Data communication**:
  - Ethernet - standard RJ 45 / Wi-Fi capable
  - SCADA connectivity via Modbus TCP
  - 2 analog output channels; 4-20mA standard, user software with configurable output ranges
- **Operational environment (non-condensing)**: Up to 37°C (98.6° F)

**Sample Water Requirements**

- **Sample temperature (non-condensing)**: 5-90°C (41-194° F)*
- **Online inlet pressure**: 0-7 bar (0-100 psig)

**Installation/Power/Enclosure**

- **Power**: 100-240VAC, 5A, 50-60 Hz
- **Physical dimensions (WxHxD)**: 22.2” (56.4cm) W x 24.25” (61.6cm) H x 12” (30.5cm) D
- **Monitoring location**: For continuous at-line monitoring panel, wall mounting tabs kit standard
- **Enclosure material**: Stainless steel
- **Weight**: 73.4 lbs (33.3 kg)

* Temperature above 45°C requires Sample Conditioning Coil (included)

**Ordering Information**

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<th>Description</th>
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<td>7000RMS Microbial Detection Analyzer</td>
<td>58 045 001</td>
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METTLER TOLEDO provides performance, calibration and maintenance services for all 7000RMS Analyzers.

Validation Support Services are available upon request.
METTLER TOLEDO Thornton, a leader in ultrapure and pure water analytics provider innovative analytical instruments and sensors for the parameters conductivity, TOC, pH, Microbial detection, dissolved oxygen and ozone.

As water is produced and consumed continuously, on-line testing enables the collection of real-time data which can be recorded and analyzed providing better process information and a complete water history. METTLER TOLEDO on-line sensors and analyzers provide simple, cost-effective measurement alternatives to off-line testing eliminating the errors associated with collecting, handling and transport of the water samples. METTLER TOLEDO on-line systems assure that critical water system measurements are available when you need them providing consistent, reliable process control.

METTLER TOLEDO Thornton provides complete on-line measurements for Pharmaceutical Water Systems.

5000TOCi Regulated Measurements for WFI and Purified Water
1500RV Conductivity
UniCond®
7000RMS Added Substances (i.e. Ozone)
pureO3™