

Microbial Detection



THORNTON

Leading Pure Water Analytics

7000RMS Microbial Detection Analyzer

Continuous, real-time analysis

Results in seconds

No sample preparation

No reagents required

Process/batch sampling modes



Continuous At-Line Microbial Monitoring For Pharmaceutical Waters

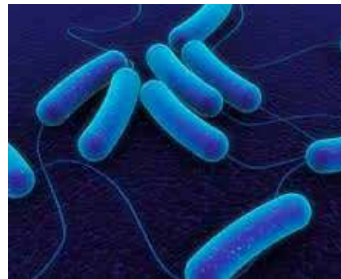
METTLER TOLEDO

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)

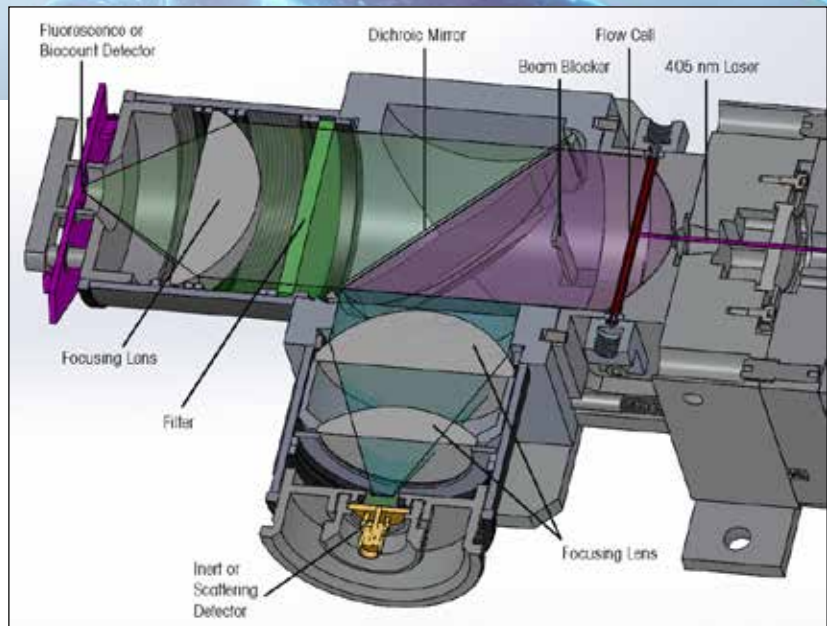
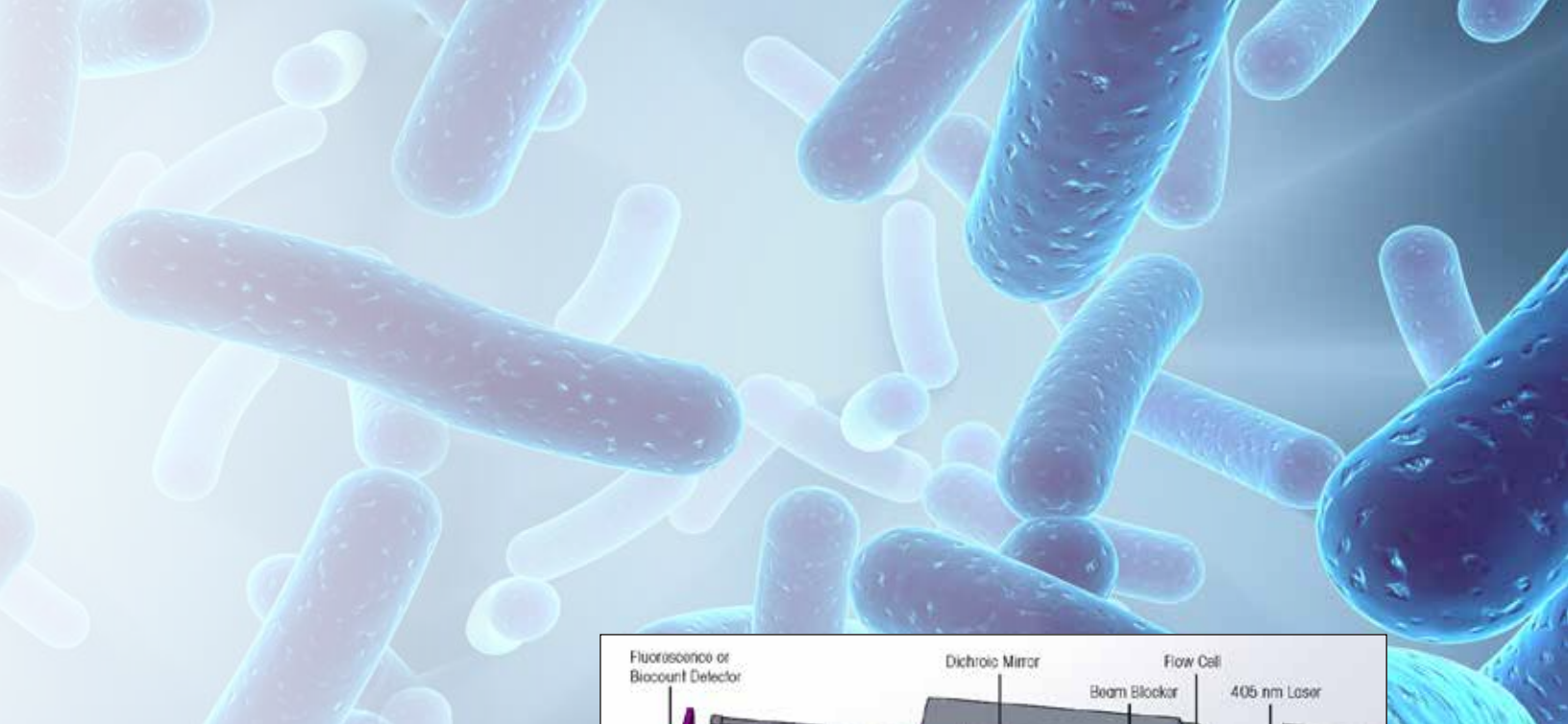
Real-time Microbial Detection
Results every two seconds

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



Cross-section drawing of the optical detection system

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.

7000RMS

Lower Operating Costs, Reduce Risk

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.”¹

- 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

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7000RMS Installation Options

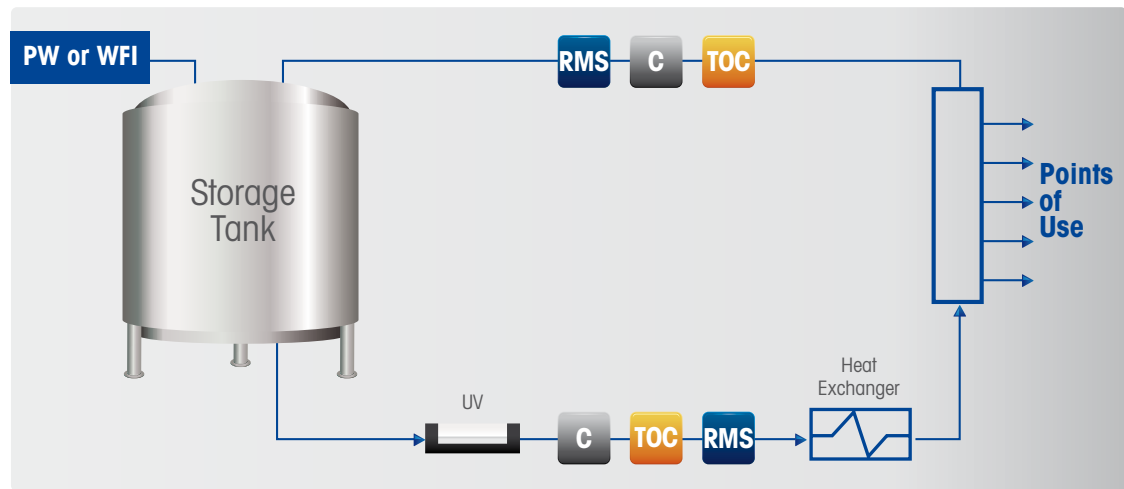
Flexible Options for the Entire Loop

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.

Return Loop Control

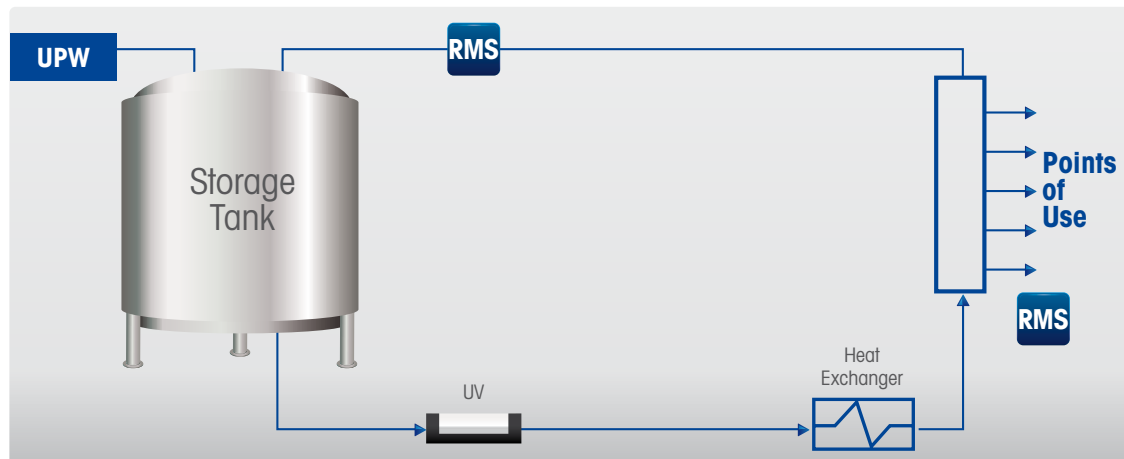


Measurement Points | **C** Conductivity **TOC** TOC **RMS** 7000RMS

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.

Point of Use Monitoring



- ✓ Main Water Loop
- ✓ Sub Loops
- ✓ Points of Use

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 Up to 8.2ft (2.5 meters) SJ cord length provided standard
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

Description	Order Number
7000RMS Microbial Detection Analyzer	58 045 001

METTLER TOLEDO provides performance, calibration and maintenance services for all 7000RMS Analyzers.

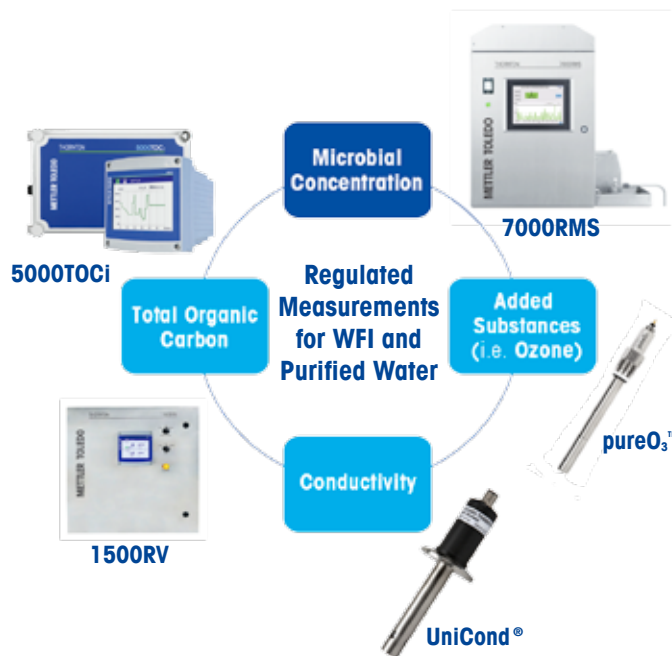
Validation Support Services are available upon request.



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.



www.mt.com

For more information

METTLER TOLEDO Group

Process Analytics Division

Local contact: www.mt.com/contacts

Subject to technical changes

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