Instantaneous Microbial Detection™ for Pharmaceutical Waters

IMD-W™ Instantaneous Microbial Detection System

BioVigilant®

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The IMD-W™ Instantaneous Microbial Detection™ system for pharmaceutical grade waters delivers a new tool for assessing and reacting to bioburden risks in real time.

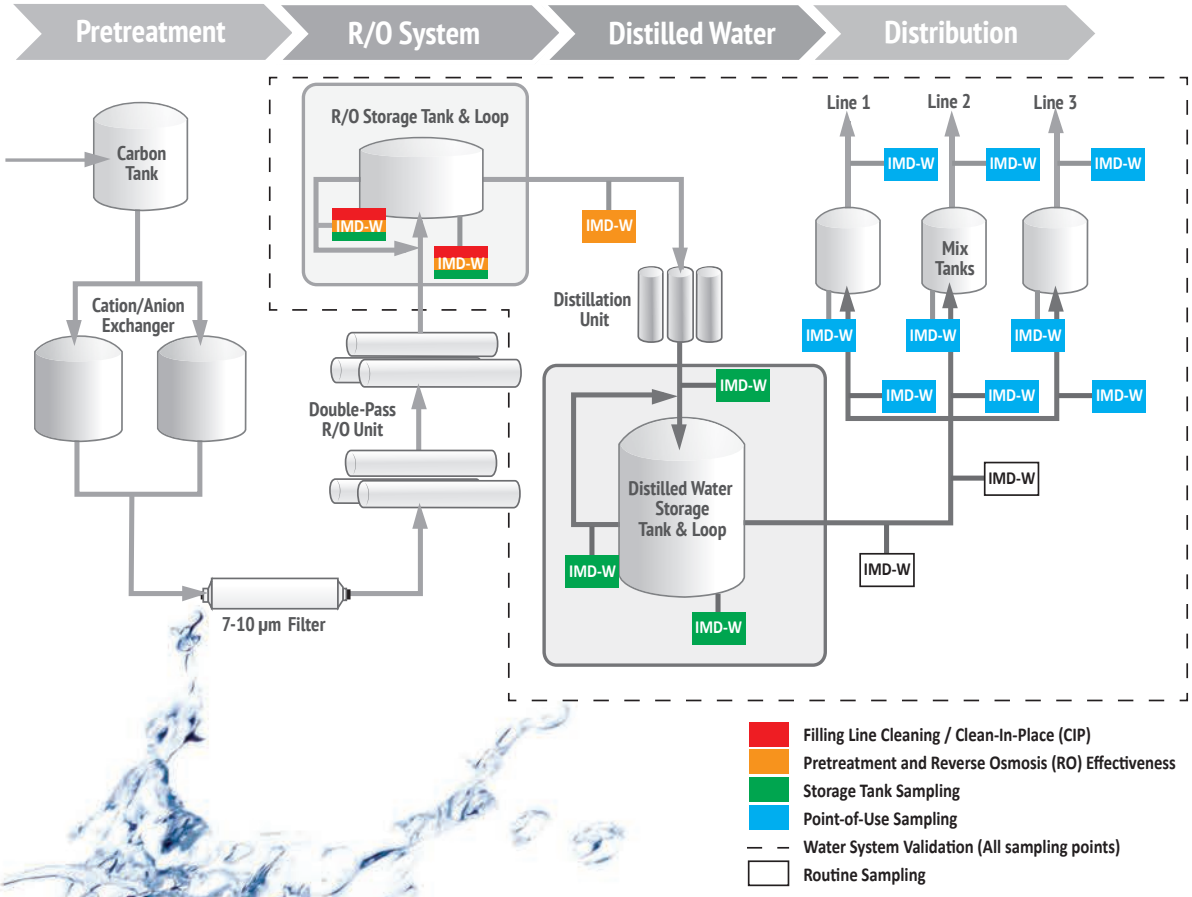
Water Sampling with the IMD-W System: One Method, Many Applications

Purified water has many uses throughout the biologics, pharmaceutical, and medical device industries - from cleaning equipment after manufacturing, to heating and cooling for sterilization and sanitization, to providing the base constituent of life-sustaining therapies. Because of the many uses for highly purified water, there are many ways to use the IMD-W system, an instantaneous microbial detection system for pharmaceutical grade waters.

Flexibility to Meet All of Your Application Needs: On-line, At-line, and In Laboratory

The IMD-W system has been designed specifically with flexibility of use in mind. The system may be used in a laboratory setting for the testing of individual samples, and also can be placed online for continuous monitoring.

General Pharmaceutical Water System Configuration



IMD-W Applications Examples

Filling Line Cleaning / Clean-In-Place (CIP)

Typically, the filling line conveyor belt and other ancillary equipment are considered product contact surfaces for the purposes of pharmaceutical, biologic, and medical device manufacturing and, for that reason, need to be as clean as the product itself. Residual API or sugars, for instance, may harbor microbial growth which could compromise sterility in the cleanroom. Therefore, water used for cleaning filling lines, conveyor belts, and other machinery should be rinsed down to bulk purified water levels with zero chemical residuals. The IMD-W system can facilitate the process by determining the water's microbial count prior to these cleaning processes, either by assessing grab samples from the clean water line, or for CIP processes, through direct online connection.

Pretreatment and Reverse Osmosis (RO) Effectiveness

Sampling of the purified water generation process, near or at the end of the pretreatment, is performed to confirm water quality inputs into Water-for-Injection (WFI) or Purified Water (PW) generation systems. Here, the IMD-W system can be used to monitor continuously the post-RO filtered water, much as online conductivity and TOC instruments are used. When combined, these data will help paint a picture of the pretreatment water generation process, support the development of schedules for critical system cleaning and sanitization, and lead to a better understanding of the microbial nature of that process throughout water production.

Storage Tank Sampling

Water within storage tanks usually is re-circulated to reduce the chances of microbial adhesion and biofilm formation. Even in these closed systems, changes may occur in not just the microbial quality of the water, but also in the integrity of redundant filters and gaskets. An IMD-W system can be very useful in monitoring these loops on a continuous basis to assure that microbial levels are low or to maintain a constant baseline. Potential contamination from gasket and filter changeouts may be monitored in real time, and the resulting data used to support the decision to bring a water generation system back into production. Finally, continuous monitoring of recirculating storage tanks allows for greater understanding of microbial proliferation in the system being monitored, if any exists. These data can provide a concrete rationale to justify water hold-time recommendations.

Point-of-Use Sampling

Sampling with an IMD-W system at the end of the WFI loop, prior to the redundant filtration, will confirm the overall fitness of the process, as well as quantify the system bioburden prior to point-of-use filtration. When IMD-W sampling is performed as part of an overall sampling plan, the data that is generated can provide an insightful snapshot into the prefiltration bioburden of a purified water generation process. When sampled continuously with an IMD-W system, the water generation process can be fully mapped out and understood, helping to support critical systems maintenance programs, filter changeout scheduling, and quality decisions related to the water.

Water System Validation

Validation of a purified water system typically is performed upon installation of the line, or when there are modifications to it. Every sample site is sampled, each day, for a period of a month or so during validation. This is a very work-intensive process using traditional methods, requiring those involved to wait each day for updated results from the past several days, and then to make adjustments to the line until counts are right. By using an IMD-W system, this iterative adjustment process can be greatly accelerated as a result of IMD-W's instantaneous microbial feedback on each water sample collected.

Routine Water Sampling

After water system validation has been completed, it is possible to reduce sampling requirements based upon schemes to monitor Critical Control Points (CCP) or through risk analyses of the validation data. In this situation, an online IMD-W system installed at each CCP can deliver continuous monitoring capability. Generated data can be sent to a central location and monitored remotely, much like data from online conductivity and TOC analyzers are managed. In this way, the IMD-W system can accelerate actions to mitigate risk and reduce investigation costs, driven by data collected in real time while offering a means to enhance process understanding.

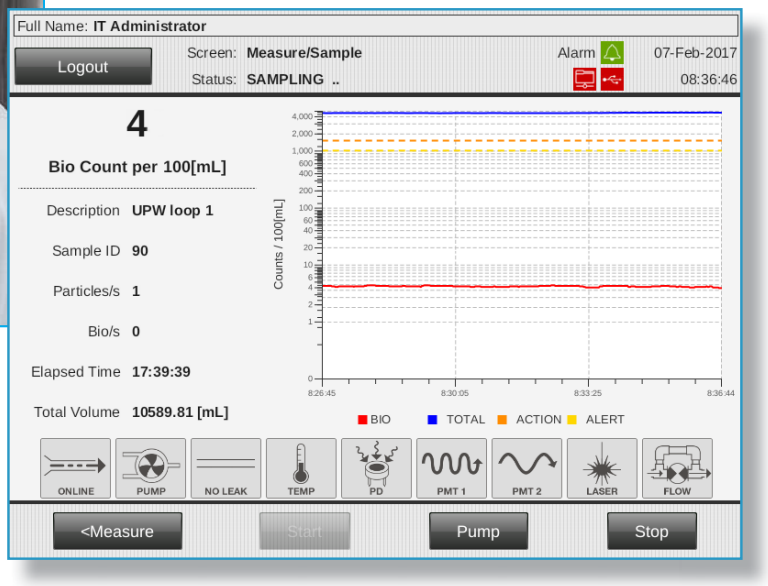
Benefits

- **Improved product quality**
- **Better risk management**
- **Enhanced process understanding**
- **Energy savings**
- **Improved resource allocation and labor efficiencies**

Features

- Real-time results without staining or reagents
- Detects particles and determines biologic status simultaneously
- Enhanced interferent discrimination
- Built-in purge and cleaning processes
- Automated system suitability routine
- 21 CFR Part 11 compliant
- Integrated touch screen user interface
- Data may be exported for offline analysis and storage
- Flexible communications interface for networking; can be controlled externally by common industrial control systems (e.g. SCADA, PLC)

User-friendly Interface



The IMD-W system's easy-to-read touch panel interface places all the critical real-time data and system controls right at your fingertips.

Industry-Driven Need

"The development and implementation of an online water bioburden analyzer (OWBA) offers the potential to improve pharmaceutical water system operations, reduce costs, and ensure water quality."

Excerpt from ***"Novel Concept for Online Water Bioburden Analysis: Key Considerations, Applications, and Business Benefits for Microbiological Risk Reduction"***

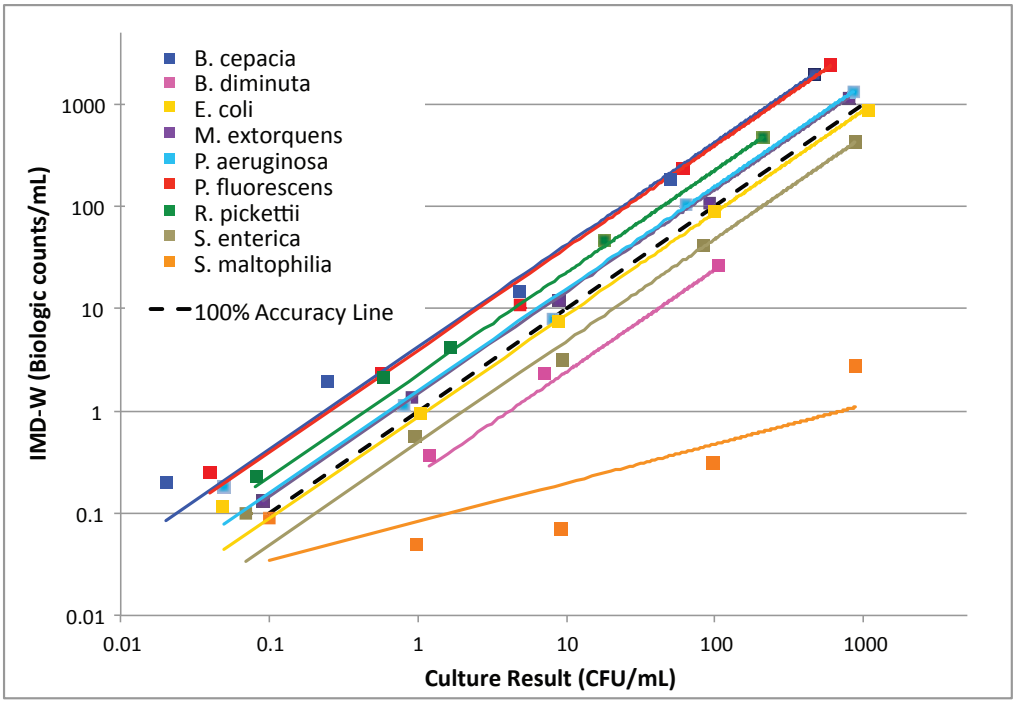
Authored by *OWBA industry workgroup comprised of members from Pfizer, Baxter, Merck, Novartis, Fresenius, Amgen and P&G*

American Pharmaceutical Review, May/June 2013 edition

Technical Specifications

Detection Method	Optical, Mie Scatter (particle detection) Optical, Auto-fluorescence (biologic status)
Detectors	(1) Photodiode, (2) PMTs
Minimum Detection Size	≥ 0.3 µm
Detection Limit	1 Bio-count
Measurement Mode	Continuous or At-line sampling for specified time or volume
Flow Rate	10 mL/min (Water Flow Rate), 5 mL/min (Measured Flow Rate)
Water Temperature	0 to 65°C (32 to 150°F) *higher temperatures when operated with external cooling solution*
Water Pressure	69 kPa to 690 kPa (10 psid to 100 psig)
User Interface	20.3-cm (8.0-inch) LCD touchscreen
Connectivity	10/100/1000 Base-T LAN, USB, Digital input, Digital output
Power Requirements	100-240 VAC, +10%/-15%, 1.0 A, 50-60 Hz
Power Consumption	60 Watts, max.
Vibration/shock	0.25 G, 5-300 Hz (1.0 G shipping)
Mounting Options	Wall, Rack, or Benchtop
Enclosure Material / Rating	Type 4 16-gauge mild steel, powder-coat finish / IP32
Dimensions	W: 47 x H: 46.4 x D: 31.75 cm. (W: 18.5 x H: 18.25 x D: 12.5 in.)
Weight	26 kg (57 lbs)

Correlation to Culture Counting Method: Waterborne Organisms



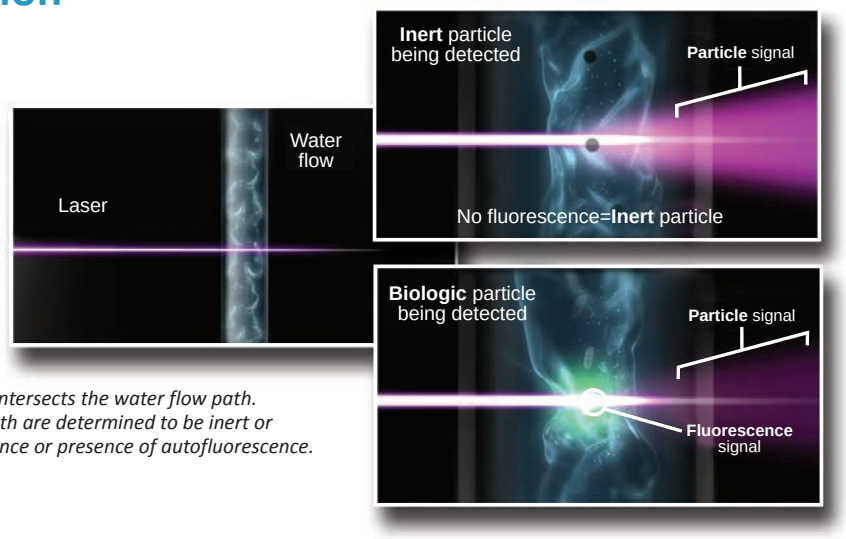
The IMD-W system's fluorescing particle counts show a high level of correlation to conventional CFU cultured counts across a wide dynamic range.

R^2 Values

Microorganism Tested	Coefficient of Determination (R^2)
Waterborne	
B. cepacia	0.9998
B. diminuta	0.9982
E. coli	1.0000
M. extorquens	0.9999
P. aeruginosa	0.9978
P. fluorescens	0.9989
R. pickettii	0.9993
S. enterica	0.9974
S. maltophilia	0.9370
Non-Waterborne	
A. brasiliensis	0.6764
B. subtilis	1.0000
C. albicans	0.9999
S. aureus	0.9991

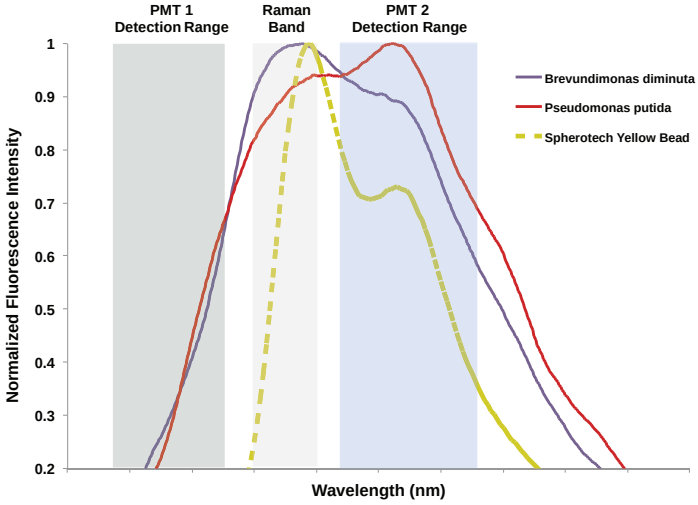
Coefficient of determination (R^2) values are shown for the relationship between IMD-W biologic counts and culture CFU results. A value close to one shows a high level of correlation in the results from both methods.

Principle of Operation



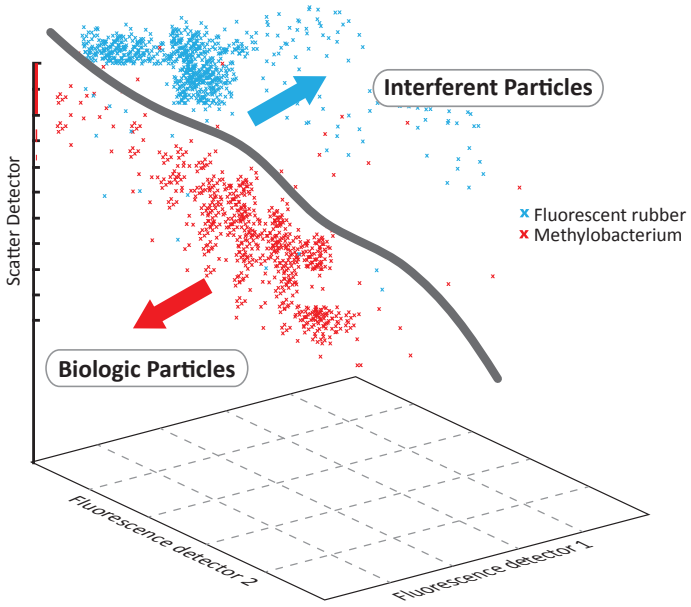
The IMD-W's 405nm laser intersects the water flow path. Particles within the flow path are determined to be inert or biologic, based on the absence or presence of autofluorescence.

IMD-W Detection Capabilities (Fluorescence Sensitivity)



Comparison of microbial and Spherotech Yellow Low Intensity (STY) bead fluorescence within the IMD-W detection range. STY is similar in size to microbes and exhibits a fluorescence spectrum and intensity when excited with 405nm on the same order of magnitude as microbes, making it a suitable general reference for size and fluorescence, and use as a one of a set of beads used for calibration.

Enhanced Interferent Discrimination



*The IMD-W system's advanced signal processing algorithm discriminates a biological particle by using **three** different signals.*

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