Implementing an Instantaneous Microbial Detection System for Water on a Pharmaceutical Water Loop – A Case Study

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Introduction

Implementing a Rapid Microbiological Method (RMM) on a facility water loop that is capable of real-time, continuous particle and bioburden monitoring can provide a new level of information not possible with point samples and TOC monitors. Installing such a technology for evaluation on a regulated water loop, however, can be challenging due to its novelty, and the lack of end-user case studies on the assessment, use and benefit of these new technologies. This poster presents one such case study, highlighting the installation and evaluation of an instantaneous microbial detection system for water on a pharmaceutical purified water (PW) loop. The instantaneous bioburden monitor permits real-time detection and continuous monitoring of microbial contamination, enabling enhanced water loop bioburden monitoring, risk assessment, and a faster response to out-of-trend finding specification results. This case study includes background information on the technology, how potential risks of technology integration were addressed and mitigated, system installation and assessment.

Background

Bayer Animal Health

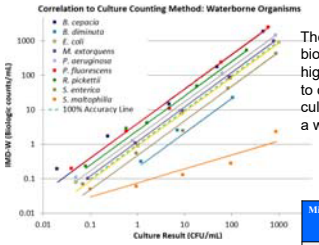
The evaluation of the IMD-W™ system was performed at the Bayer Animal Health facility in Shawnee, Kansas. At the Shawnee site a variety of products are manufactured, including sterile injectables, non-sterile liquids and pastes, solid tablets, soft chew tablets, and pour-on products. There are two water systems at the site, a Purified Water loop and a Water for Injection (WFI) loop. Bayer was interested in assessing the feasibility and utility of using new rapid microbiological technologies to supplement traditional testing and to support investigations using real-time data.

Instantaneous Microbial Detection Technology

IMD-W System

- Based on Laser-Induced Fluorescence (LIF)
- Detection of microbes in water without need for staining or reagents (no sample prep)
- Continuous operation and monitoring of inert and biologic particles in real-time
- Enhanced interferent (non-biologic) discrimination through advanced algorithms and use of two fluorescence detectors

Correlation to Culture Counting Method



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

R^2 Values

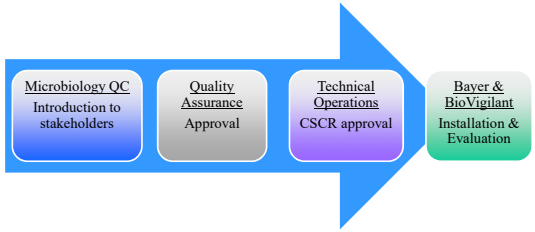
R^2 values are shown for the relationship between IMD-W biologic counts and culture CFU results. A value close to one shows a high level of correlation in the results from both methods.

Microorganism Tested	Coefficient of Determination (R^2)
B. cepacia	0.9998
B. diminuta	0.9982
E. coli	1.0000
M. extorquens	0.9994
P. aeruginosa	1.0000
P. fluorescens	1.0000
R. pickettii	1.0000
S. enterica	1.0000
S. maltophilia	0.9992

Case Study

RMM Evaluation and Installation Approval

The IMD-W system evaluation was sponsored within Bayer by Microbiology Quality Control who then gained support from Quality Assurance and Technical Operations to evaluate the technology on the facility's operational purified water (PW) loop. Once internal approval was obtained, Bayer worked closely with BioVigilant to evaluate the RMM technology.



Installation

The IMD-W system was installed on the Bayer PW loop by BioVigilant in collaboration with Bayer Technical Operations. A Critical System Change Request (CSCR) was required before IMD-W installation could occur on the loop. No issues were encountered during the installation process.

Testing Location Selection

The Bayer Animal Health facility includes both a PW and WFI loop. The PW loop was chosen for the evaluation to minimize risk of new technology integration on the WFI loop. The IMD-W system was installed near an in-line TOC monitor at the end of the PW loop, just before the return to the tank. The end-of-the-loop location was chosen due to it being the most representative location on the loop. By collecting data at this location, Bayer hoped to get a representative look at the health of the entire loop.

Evaluation

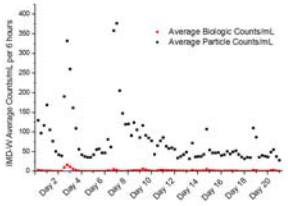
Goals of the evaluation were to familiarize Bayer with the technology, determine the system's ability to provide real-time and continuous information for trending loop health and assessing bioburden levels. Through the evaluation, Bayer hoped to develop an understanding of how the data could be evaluated against traditional loop data (CFUs).

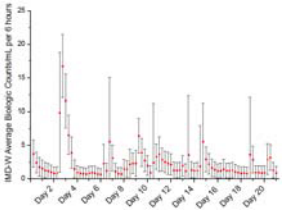
The IMD-W system was connected to the Bayer PW loop for approximately one month. The system was set up to monitor biologic and total particle counts continuously during this time. Minimal interaction with the IMD-W system was required.

Results and Conclusions

Continuous Monitoring Results

IMD-W total particle and biologic counts per 1mL, 10mL or 100mL analysis volume, as selected by the user, were reported by the system. IMD-W total particle and biologic count data per second was also available if more granularity in results was desired. The plot below shows IMD-W particle and biologic counts/mL averaged over every six-hour period for a 21-day continuous sample.





The plot above focuses upon the same biologic count data per 1mL, averaged every six hours with standard deviation bars. The increase in average biologic counts/mL seen on day three corresponds to an auto-sanitization process that was performed on the loop. Even during this increase, IMD-W biologic count/mL results were well below the maximum action level per USP<1231>.

This 21-day run gives a glimpse of biologic and particle count data specific to this PW loop. This data is useful in identifying baseline biologic count levels expected during normal, controlled operation of the water loop. Such baseline data is then utilized to set biologic count action and alert levels.

Technology Assessment

- Assessment required minimal operator intervention for **continuous online monitoring** and provided an advantage over traditional POU grab sampling.
  - Use of the system for POU sampling, as opposed to continuous online monitoring, would not present a labor efficiency due to the labor required to prepare samples.
- Reporting of discrete time-point values per 1mL created a substantial amount of data for evaluation. For ease of evaluation, reporting an average every six hours proved beneficial.
  - In everyday operation, the 100mL-analysis volume option would be selected, with data investigated at a higher resolution only if needed.
- The trended data provided by the IMD-W (e.g. averaged biological count data) would be useful for establishing a baseline against which water loop modifications and overall loop health can be assessed. Action and alert levels would be set based on baseline understanding of counts.
  - Evaluation data confirmed a sustained, low-level bioburden baseline of the PW loop.
- Obtaining a water-loop baseline using the IMD-W technology in continuous-sampling mode could be easily achieved with minimal maintenance, and would provide a real-time evaluation tool for identifying adverse trends.