Applicability of Bio-fluorescent Particle Counters for Monitoring of Water for Injection Systems

Bio-fluorescent particle counters (BFPCs), like BioVigilant's IMD-W™ Online Water Bioburden Analyzer, enable the continuous monitoring of total particle and bioburden levels in water for injection (WFI), purified water (PW), and controlled water systems. BFPC technology is based on bio-fluorescence detection and requires no sample preparation or staining. Also, BFPC systems continuously monitor and report total and bio-fluorescent particle counts in real time. This continuous data and feedback can be used to improve process understanding, more quickly assess the impact of process changes, and improve process control. Data is presented from a BFPC system installation on a highly controlled water system to show the applicability of this technology for monitoring water for injection (WFI) systems.

BFPC Background

BFPC systems can have an increased sensitivity as compared to the traditional culture-based method.[1] The technology uses the detection of intrinsic fluorescence and algorithms to analyze and categorize fluorescent particles as biologic (i.e. auto-fluorescence units "AFU") or inert. This method of detection is different from that used by the traditional culture-based method as it is not dependent upon an organism's ability to grow under established conditions. Furthermore, due to the potential for increased sensitivity and continuous (as opposed to intermittent) monitoring, BFPC systems often report a non-zero baseline of total particle and AFU counts. This baseline is dependent upon factors like physical particle load in, age of, sanitization method used in, and materials of construction of the water system. With non-zero, continuous results, BFPC systems are excellent trending tools used to rapidly signal a change in process control.[2,3]

BFPC Use on WFI Systems

Discussion has occurred on the applicability of BFPC systems for WFI applications. As mentioned, every water system has a unique fingerprint and level of baseline particle and AFU counts. Depending on the water system's baseline count levels, it may not be possible to assign statistical relevance to a single digit increase in AFU counts above this baseline. In addition, because AFU are not expected to be equivalent to CFU, guidance specified in CFU for alert and action levels may not be appropriate. This is a distinction understood by regulators. In the latest Annex 1 draft revision, *Table 2: Limits for microbial contamination during qualification* and *Table 7: Maximum action limits for viable particle contamination*, it is mentioned "if different or new technologies are used that present results in a manner different from CFU, the manufacturer should scientifically justify the limits applied and where possible correlate them to CFU."[4]

In a 2020 Process and Environmental Monitoring Methods (PEMM) working group meeting with the FDA Emerging Technology Team, it was mentioned that BFPC systems that report in units that do not directly correlate with the traditional method can still be acceptable as an alternative method.[5] In other words, there is support for technologies that report in units other than the CFU and communication that applied limits may not be the same as those used with the traditional method.

Another consideration is the intended application of the BFPC system. BFPC systems offer considerable value as trending tools used to indicate a change in process or control.

In this application, a change in trend instead of a small change in AFU counts is the focus.

Figure 1 contains BFPC data from an installation with very low particle and AFU counts. The reported data was from an IMD-W BFPC system and Rion KS-42B liquid particle counter installed side-by-side on a facility's highly purified water system with two upstream 50nm filters in series.

Baseline BFPC average count per milliliter values were very low at 0.01 particles per milliliter and 0.0003 AFU per milliliter. Furthermore, IMD-W average particles per milliliter and Rion average particles (≥ 0.2um in size) per milliliter, aligned at a value of 0.01 particles per milliliter.

In this example, counts per milliliter were averaged every six hours to provide results over an eight-day period. If an increased result had been observed, data could have been investigated at a higher resolution as BFPC systems report counts as often as every second.

In this installation, baseline particle and AFU count levels were very low. It is worth noting that this is not the case for all water systems.

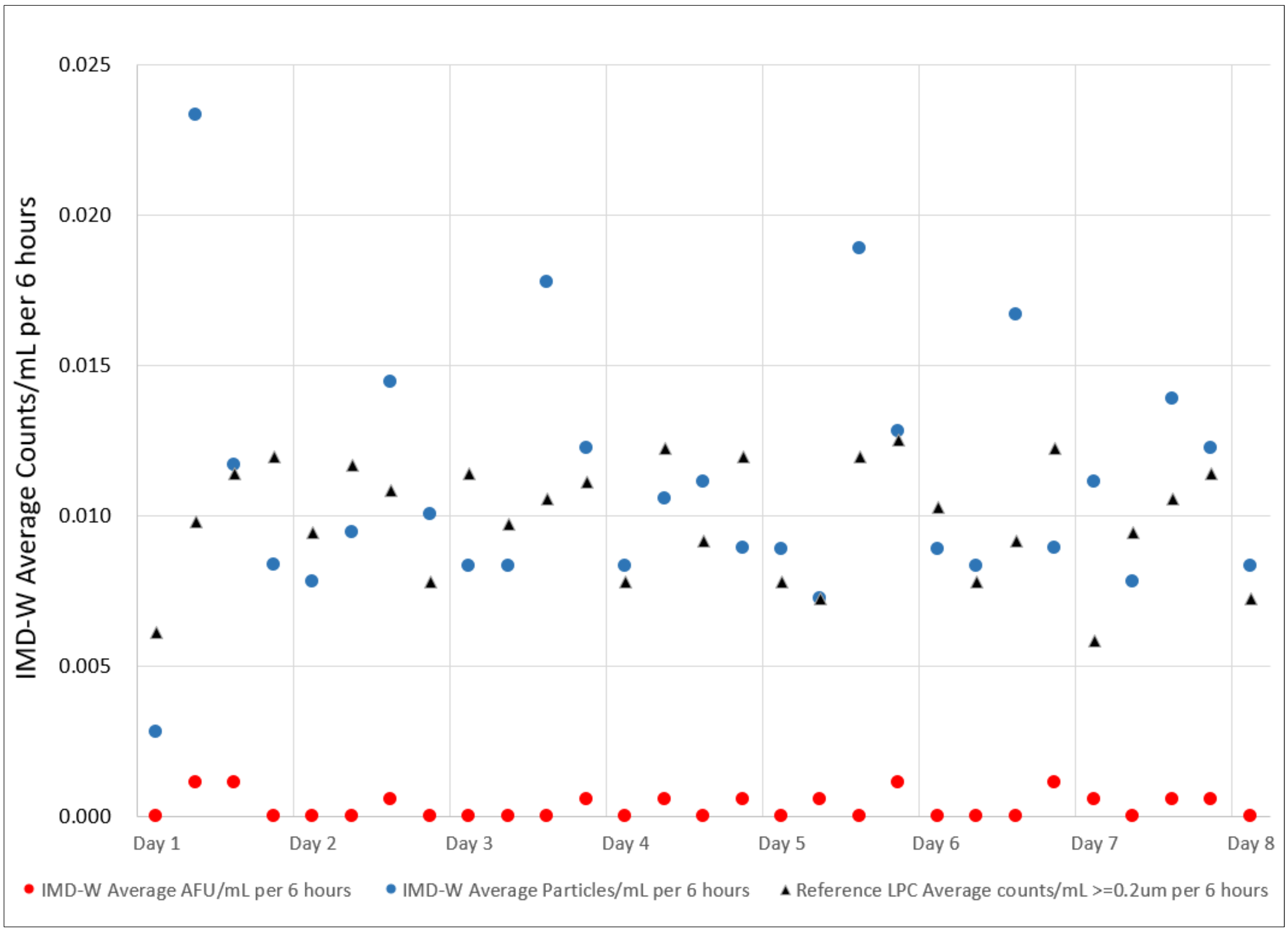

Figure 1*- IMD-W BFPC and reference liquid particle data obtained from a highly controlled, water system installation.*

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Conclusions

An understanding of baseline particle count levels and the intended application of a BFPC system are important when establishing a use case and setting internal expectations for the technology. Low baseline counts are possible with BFPC systems, but dependent upon the physical particle load within the water system monitored. Expectations of the BFPC system should be based on the enhanced abilities of the technology and its resulting data for the application selected. In the case of WFI systems, AFU counts may be higher than the target criteria applied when using the traditional method of less than 10 CFU per 100 milliliters. Because AFU are not equivalent to CFU, established alert and action levels should be based on AFU results obtained on the water system under test. Furthermore, BFPC systems are complementary tools to the traditional method. With continuous monitoring and high-resolution data reporting, BFPC systems are a data rich source that permit trending and a real-time assessment for process control. The applications and potential benefits of this technology should not be limited to the vision offered by the traditional method alone. BFPC systems are an enhancement to current monitoring techniques and deliver significant benefits to critical water utilities.

References

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