The Multichannel Verification System (Artel MVS®) by Advanced Instruments Delivers Equivalent Results to the Fluorescence Test Method Utilized by Beckman Coulter Life Sciences to Evaluate the Echo Acoustic Liquid Handler Systems

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Introduction

Beckman Coulter Life Sciences Echo acoustic liquid handlers are automated liquid handlers (ALHs) that use acoustic technology to provide contact-free transfer of liquids in increments of 2.5 nL or 25 nL depending on the model/series. The Echo is compatible with common solvents for biopharmaceutical applications including dimethyl sulfoxide (DMSO) and a variety of aqueous-based solutions. Beckman Coulter Life Sciences currently uses a fluorescence method to evaluate the accuracy and precision of systems. Beckman Coulter Life Science customers have asked for an in-house method to validate the performance of the Echo to save time and enable on-demand volume verification. Artel by Advanced Instruments provides a complete system, the Multichannel Verification System (Artel MVS®), that can be used for liquid handler evaluation at a customer site without the need to generate standard curves. The Artel MVS is also compliant with ISO 23783-2: Measurement procedures for the determination of volumetric performance. This study was designed to evaluate whether the Artel MVS and Beckman Coulter Life Sciences fluorescence test methods provide equivalent volume verification results at 25 nL and 250 nL on Series-525 and Series-655 for select aqueous and DMSO solutions. This work has demonstrated the equivalence of the Artel MVS test method compared to the fluorescence test method employed by Beckman Coulter Life Sciences, for the selected plate types described.

Methods & Materials

In this work, Beckman Coulter Life Sciences and Artel by Advanced Instruments collaborated to test Echo acoustic liquid handler-525 and Echo acoustic liquid handler-655 ALHs using the Beckman Coulter Life Sciences fluorescence method and the Artel MVS, which is a mobile system that can be used in any laboratory. Detailed method information for both methods can be found in the references. Briefly, Beckman Coulter Life Sciences fluids contain 0.15 mM fluorescein that is transferred into 384-well Greiner Bio-One 384-well µClear™ Bottom Polystyrene Microplates destination plates (Supplier: Greiner Bio-One 781096) and analyzed by laboratory personnel. The Artel MVS system is a commercial system that comes complete with aqueous or DMSO-based dye solutions (customized 70 % and 85 % DMSO solutions were manufactured to support this work), 384-well verification plates (black, optical-bottom microplates ARTEL MVS Part Number ARTEL MVS-245), shaker, an instrument with accompanying calibration plate, and software that is 21 CFR Part 11 compliance ready. Table 1 provides an outline of the testing plan.

A comparison of the two method specifications and calculated measurement uncertainty for each test volume evaluated in this study is provided in Table 2. A preliminary evaluation was performed to determine whether the performance of the Beckman Coulter Life Sciences Echo acoustic liquid handlers was adversely affected by the concentrations of Artel MVS test solutions compared to fluorescein test solutions. It was found that the Beckman Coulter Life Sciences Echo acoustic liquid handler performance was independent across the concentrations of solutions evaluated in this work (data not shown). It was also determined that mixing is an important parameter, and destination plates should be mixed before analysis as recommended in the Artel MVS software.

As the purpose of this collaboration between Beckman Coulter Life Sciences and Artel by Advanced Instruments was to evaluate whether the Beckman Coulter Life Sciences fluorescence test method and the Artel MVS method provide equivalent volume results for Beckman Coulter Life Sciences Echo acoustic liquid handlers, the % differences in volumes delivered were determined by Equation 1.

% difference=((X1-X2))/V **Equation 1**

where V equals the average test volume, X1 is the volume determined by the fluorescein test method and X2 is the volume determined by the MVS.

Considering the uncertainty (% inaccuracy) of each test method, the largest acceptable % difference at 25 nL would be 8.6 % and at 250 nL would be 7.0 %.

Table 1. Testing plan for Beckman Coulter Life Sciences Echo acoustic liquid handlers. Source plates polypropylene unless otherwise indicated. Target test volumes achieved with incremental dispenses were 25 nL and 250 nL.

Echo acoustic liquid handler System	Calibration
E-525 (25 nL)	384PP_AQ_BP
E-655 (2.5 nL)	384PP_AQ_GP3
E-655 (2.5 nL)	384PP_DMSO2

Table 2. Specifications for Artel MVS method [2] and Fluorescein [1] method in 384-well plates.

Method	ARTEL MVS	Fluorescein
Detection technique	Dual-dye absorbance spectroscopy	Single-dye fluorescence spectroscopy
Imprecision (% CV)	25 nL: 0.47 % 250 nL: 0.44 %	25 nL: 2 % 250 nL: 2 %
Uncertainty (% Inaccuracy)	25 nL: 3.64 % 250 nL: 2.04 %	25 nL: 5 % 250 nL: 5 %

Results

In all tests, the % CV was less than 5.0 % for 384-well plate reads, demonstrating acceptable precision of the Echo acoustic liquid handler systems with various solutions and plate types at both 25 nL and 250 nL (Figure 1).

In all 25 nL tests, the test volumes were within specification when testing with either method (Figure 2A).

In nearly all 250 nL tests, the test volumes were within specification when testing with either method (Figure 2B). On one system, the reported test volume was slightly out of specification for the fluorescein test method and just within specification for the MVS test method for the 250 nL test volume (Figure 2B). The % difference between the two test methods was 0.7 %, illustrating good agreement between the two test methods .

The % difference for 25 nL test volumes was less than 7.5 % and for the 250 nL test volumes less than 6.3 %, demonstrating agreement in the volumes determined by either method within the uncertainty of the respective methods.

Results-cont.

Figure 1. Precision of Fluorescein method and Artel MVS method for aqueous and DMSO liquids on Beckman Coulter Life Sciences Echo acoustic liquid handler-525 and Echo acoustic liquid handler-655. BP=buffer protein and GP=glycerol protein. 70, 85, and 100 refer to percent DMSO with water being the balance. Replicates (1, 2, 3) refer to the same test conducted on different Echo fixtures. In the case of BP,525-1 repeat, the same Echo instrument was tested as BP,525-1.

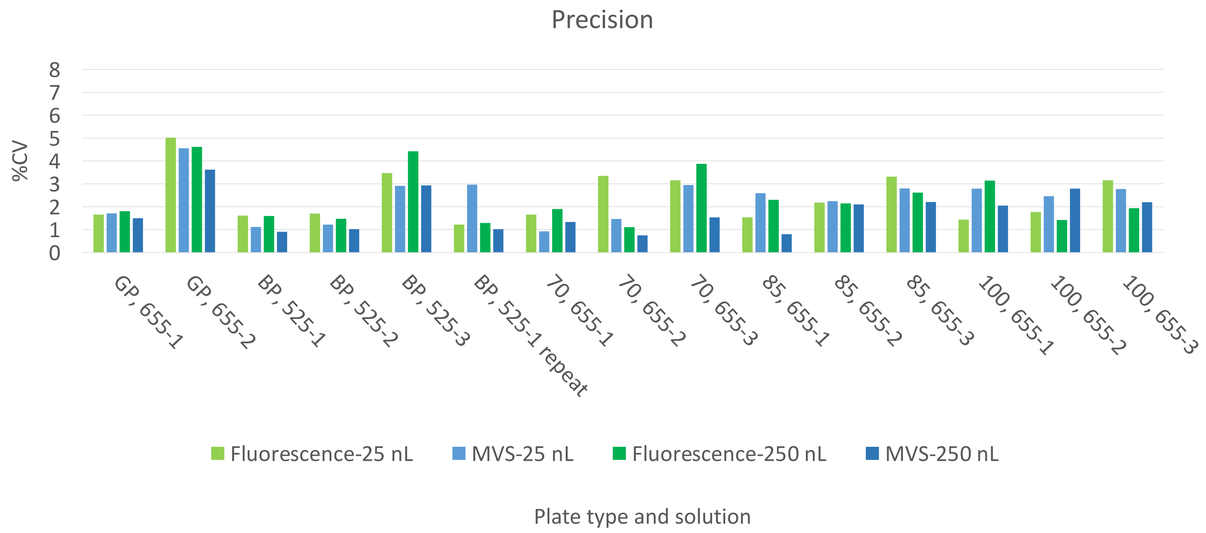
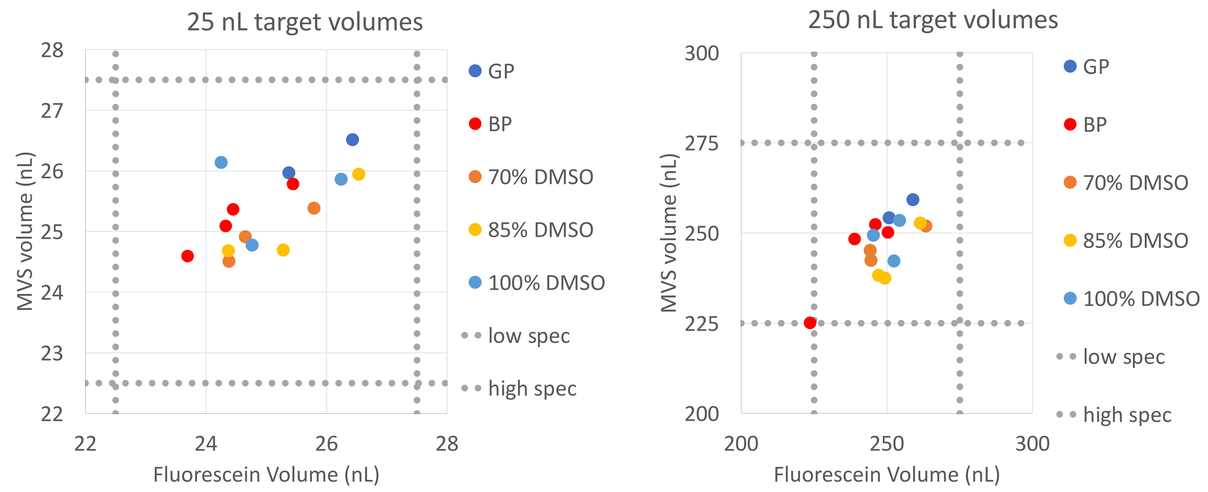


Figure 2. Accuracy of Fluorescein method and Artel MVS method for aqueous and DMSO liquids on Beckman Coulter Life Sciences Echo acoustic liquid handler-525 and Echo acoustic liquid handler-655. BP=buffer protein and GP=glycerol protein. 70, 80, and 100 refer to percent DMSO with water being the balance.



Conclusions

Beckman Coulter Life Sciences Echo acoustic liquid handler customers and engineers would like an alternative method for validating nanoliter volume delivery. The Artel MVS is a complete system for volume verification that is mobile, robust, and delivers results for a 384-well plate in under 10 minutes, enabling on-site repair and optimization of ALHs, reducing downtime and time for optimization. This work has demonstrated the equivalence of Artel MVS test method compared to the fluorescence test method employed by Beckman Coulter Life Sciences, for the selected plate types described. Note that certain Echo calibrations are not compatible with the Artel MVS system, and must be evaluated by other methods, if necessary. Thus, both test methods are acceptable for the evaluation of Echo acoustic liquid handler liquid handler accuracy and precision for select fluid calibrations. The Artel MVS system is also compliant with ISO 23783-2: Measurement procedures for the determination of volumetric performance. Contact Artel by Advanced Instruments for more information on the Artel MVS technology **www.aicompanies.com/discover-Artel-Artel MVS/.**

References

1. 1. Harris, D. et al. Debunking the Myth: Validation of Fluorescein for Testing the Precision of Nanoliter Dispensing. 2006 by The Association for Laboratory Automation. doi:10.1016/j.jala.2006.05.006.
2. 2. ISO 23783-2: Measurement procedures for the determination of volumetric performance.

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