ADVANCED INSTRUMENTS

Application Note

Optimizing Accuracy Performance of a Thermo Scientific Matrix WellMate Dispenser using the Artel MVS®



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ABSTRACT

This application note discusses an approach for optimizing pipetting accuracy of a stand-alone Thermo Scientific Matrix WellMate dispenser by using the Artel MVS measurement information. The MVS supports verifying both tip-by-tip precision and accuracy values for nearly all liquid handlers.[1,2] The focus of this paper is volume measurement and accuracy optimization. *This application note does not speak to the quality of volume transfer performance you should expect from any WellMate.* This application note will show that once volume transfer accuracy is known, it can be improved by simply tightening or loosening the adjustment screws within the 8-channel dispensing cartridge. In this study, a WellMate dispenser employing a standard 8-channel disposable cartridge was used to dispense aqueous dye solution from 5 – 350 µL. The "As Found" (initial, non-optimized) volume measurement values were used on a channel-by-channel basis to determine if the individual adjustment screws had to be tightened (to allow less liquid to be dispensed) or loosened (to allow more liquid to be dispensed). Within minutes, the volume transfer accuracy was dramatically improved for the entire volume range, i.e., the optimized measured volumes are referred to as "As Left," or post-optimization measurements. This example stresses that a laboratory can do more with the instrumentation that they have if there are processes for monitoring and optimizing the volume transfer performance. For instance, even bulk dispensers like the WellMate, which are typically used for non-critical dispenses, can be easily optimized to deliver important assay-specific target volumes with high accuracy.

INTRODUCTION

The use of bulk dispensers in the laboratory has become quite commonplace, especially for routine dispensing of buffers or other reagents into microplates. Additionally, as assays have become more miniaturized, there has been more emphasis on employing low-volume dispensers – especially for the ease of use and simplicity that these systems offer. More commonly, however, the performance of most dispensers goes widely unchecked, which is either due to lack of time, skill, or ease of implementing a QC methodology. This application note discusses how to improve the performance of a WellMate dispenser using the Artel MVS. The channel-by-channel performance metrics become quite important when trying to understand exactly how a dispenser is behaving, because not all channels behave the same way. Improving pipetting accuracy for the WellMate is a simple and effective process: (1) dispense target volumes and measure performance with the MVS; (2) determine if the individual adjustment screws need to be tightened or loosened on a channel-by-channel basis; (3) adjust the screws; (4) re-test; and (5) repeat as needed. For more information on the dispenser and adjustments, it is recommended to refer to the WellMate manual.[3]

MATERIALS

- Artel MVS, QualAssure solutions and Verification Plates
- Thermo Scientific Matrix WellMate with standard bore 8-tip cartridge and a 7/64-inch Allen wrench
- Optional: a pipette or liquid handler to pre-fill plates with MVS Diluent

PROCEDURE & RESULTS

A Biomek 96-tip NXp was employed to pre-fill each 96-well Verification Plate with Diluent before dispensing Aqueous QualAssure solutions with the WellMate. **Figure 1** depicts the fully primed WellMate and **Figure 2** shows a close-up of the disposable dispensing cartridge's adjustment screws, as well as the 7/64-inch Allen wrench used for adjustments.

The As Found performance was determined after each of the eight target volumes (5, 10, 25, 50, 100, 150, 200, and 350 µL) was dispensed into an Artel 96-well Verification Plate (12 reps per channel at each volume). This initial performance data showed that the system was running about 3-5% high at all test volumes with overall CVs within approximately 2% (**Table 1**). Upon observing that all test volumes were slightly over dispensed by the same relative amount, two target volumes (50 and 100 µL) were selected to compare results after performing multiple rounds of channel-by-channel screw adjustments. Since the rotation rate of the peristaltic pump cannot be manipulated and therefore remains at a constant rpm, simple modifications to each channel's adjustment screws allowed for optimizing each channel by: (1) tightening to decrease the amount of volume dispensed, or (2) loosening to allow more volume through. Using two mid-range target volumes, three rounds of adjustment screw modifications were performed (2 test volumes, 3 rounds of adjustments = 6 individual test plates in total).

During the optimization testing, only one adjustment screw per channel was manipulated during each round. **Table 2** shows the overall performance data from the three optimization rounds for the two target volumes. In some cases, however, an adjustment screw did not have to be adjusted. **Figure 3** shows the per channel performance at 100 µL during each optimization round – and note that the adjustment screw for channel 5 was only manipulated twice, not three times. Following the three rounds of adjustments, the overall As Left performance of the system was checked over the full volume range to show a relative accuracy improvement to be within 1% for all target volumes (**Table 3**). **Table 4** compares the As Found and As Left overall mean volume values for each target volume.



Figure 1. The 8-channel WellMate primed with aqueous dye for volume verification measurements.

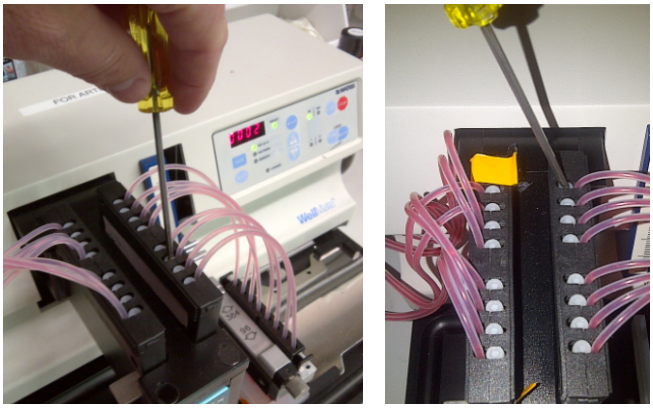


Figure 2. The individual adjustment screws can be tightened or loosened using a 7/64-inch Allen wrench. Because the peristaltic pump stays constant, tightening a screw, which 'pinches' the tubing, will decrease the amount of liquid dispensed and loosening a screw increases the amount of fluid dispensed into the microplate.

CONCLUSIONS & CONSIDERATIONS

In a few quick tests, the individual channels on a system that is typically employed as a bulk dispenser were optimized for accurate delivery over a volume range of 5 – 350 µL. In the work performed, some efforts were made to try to determine how much of a rotation of each adjustment screw impacted the dispensed volume. According to the manual, "each full revolution of the screw will adjust the volume level by approximately 8 mg for the ten shots dispensed (or 0.8 mg/dispense)"[3]. In the work performed here, it seemed that rotating and tightening one screw about 180 degrees (a half turn) resulted in approximately 0.2 - 0.4 µL less fluid to be dispensed (*this relationship was not analytically explored further and it might be different for different cartridges*).

There are a few things to consider before, and during, this type of optimization process:

- An iterative testing approach might be required to further improve accuracy.
- One should not adjust or optimize for accuracy without first knowing and ensuring that the dispensed volume precision is good and repeatable.
- As noted above, this application note does not speak to the quality of volume transfer performance you should expect from any WellMate. This application note focuses on the process of optimization only.
- The calibration process for screw adjustments may be dependent on the disposable dispensing cartridge. For instance, new vs used cartridges may have some slight differences in tubing, size of the channel opening, etc. It is recommended to periodically check the performance of any robotic method until a baseline performance level is established, where a frequency of performance assessment can be understood and scheduled.
- Because all target volumes were overdelivering in this case, optimizing the volumes for just two target volumes worked well. If there had been differences in relative accuracies across the volume range, i.e., some volumes running high and others low, the optimization process would not have been so simple. If this were the case, one approach would be to designate one cartridge for the higher volume range and, depending on performance, another 1-2 cartridges for the lower volume range (with each cartridge being optimized over its designated volume range as discussed above).

Table 1. Initial, As Found Overall Performance at Each Test Volume

Target Volume (µL)	Target Solution	Number of Reps per TIP	Mean Volume (µL)	Relative Inaccuracy (%)	Standard Deviation (µL)	CV %
350	Range HV	12	366.71	**4.77**	5.19	**1.42**
200	Range A	12	207.25	**3.63**	2.22	**1.07**
150	Range A	12	155.88	**3.92**	1.64	**1.05**
100	Range A	12	103.99	**3.99**	1.03	**0.99**
50	Range A	12	51.76	**3.53**	0.54	**1.05**
25	Range B	12	25.87	**3.47**	0.32	**1.24**
10	Range B	12	10.39	**3.94**	0.12	**1.17**
5	Range C	12	5.24	**4.88**	0.11	**2.10**

Table 2. Overall Relative Inaccuracy Following Each Optimization Round

Target Volume (µL)	As Found (%)	1st Round of Set Screw Adjustments (%)	2nd Round of Set Screw Adjustments (%)	3rd Round of Set Screw Adjustments (%)
100	**3.99**	**2.61**	**0.51**	**-0.25**
50	**3.53**	**2.44**	**-0.05**	**-0.01**

Table 3. As Left, Final Overall Performance

Target Volume (µL)	Target Solution	Number of Reps per TIP	Mean Volume (µL)	Relative Inaccuracy (%)	Standard Deviation (µL)	CV %
350	Range HV	12	350.50	**0.14**	1.74	**0.50**
200	Range A	12	199.99	**0.00**	0.59	**0.30**
150	Range A	12	149.58	**-0.28**	0.64	**0.43**
100	Range A	12	99.86	**-0.14**	0.41	**0.41**
50	Range A	12	49.74	**-0.53**	0.25	**0.50**
25	Range B	12	24.91	**-0.37**	0.17	**0.69**
10	Range B	12	10.00	**0.01**	0.05	**0.52**
5	Range C	12	5.02	**0.32**	0.08	**1.64**

Table 3. As Left, Final Overall Performance

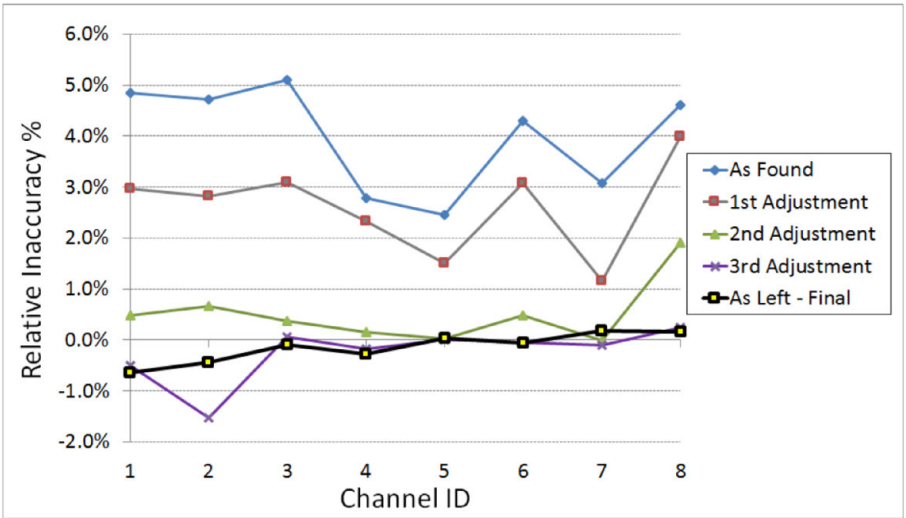


Table 3. As Left, Final Overall Performance

Target Volume (µL)	As Found Mean Volume (µL)	As Left (Final) Mean Volume (µL)
350	**366.71**	**350.50**
200	**207.25**	**199.99**
150	**155.88**	**149.58**
100	**103.99**	**99.86**
50	**51.76**	**49.74**
25	**25.87**	**24.91**
10	**10.39**	**10.00**
5	**5.24**	**5.02**

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