Semi-automated liquid handling: Mitigating analyst-to-analyst variability in QC bioassays

Stuart Dunn; Labcorp, Harrogate, UK

Overview

- Cell-based potency assays (bioassays) can be complex to execute, often requiring hundreds of pipetting steps.
- Transfer of such methods into a quality control (QC) environment requires significant training, with varying levels of success dependent on analyst experience and technique.
- Complex methods developed by a single person can lead to robustness issues when other analysts are involved.
- Assigning cause to manual pipetting errors is difficult, making troubleshooting anomalous results challenging during analytical investigations.
- Can the VIAFLO 96, a semi-automated liquid handler (Integra Biosciences), offer a potential solution to reduce operator error and facilitate method training and transfer in QC bioassays?

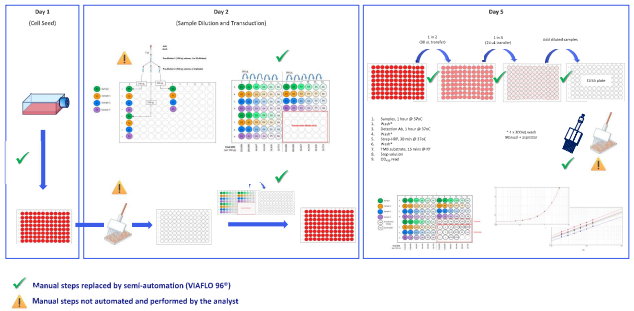
Integra VIAFLO®

- Supports 96- and 384-well plate setup
- Performs whole plate transfers and serial dilutions
- Small footprint; fits into a standard biological safety cabinet
- Programs (volume/speed/mix etc.) set up and stored in the pipette head like a conventional electronic pipette
- Minimal software validation required in the QC environment

Integra VIAFLO 96

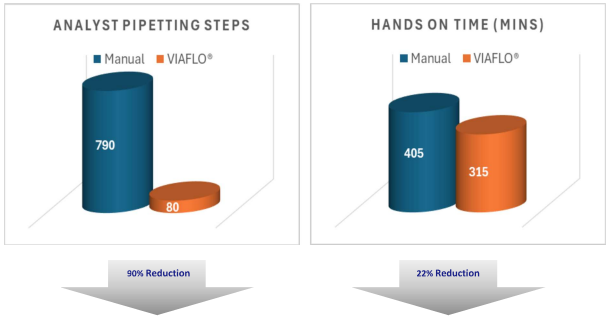
Evaluation

- A 5-day bioassay was selected to evaluate the VIAFLO 96 performance, as it had been found difficult to train out.

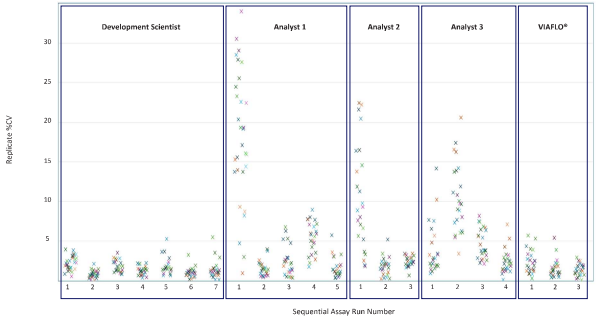


Results

- The automation steps for the 5-day method were relatively easy to set up by the development scientist and were completed within 10 days, requiring little optimisation.
- Running the method required the analyst to change tip boxes, load tips and load plates/ reservoirs manually.
- There was a:
  - Reduction in direct pipetting by the analyst from 790 to 80 steps; a **90% reduction**.
  - Reduction in analyst hands-on time by 2 hours from the 7 hours required in the fully manual method; a **22% reduction**.



- Replicate variability was shown to be superior to 3 separate analysts that attempted to train in the method.
- Replicate variability matched that of the assay developer when tested on 3 separate occasions.



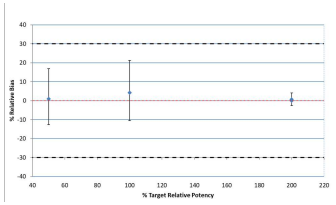
Performance

- Performance was assessed across 3 target potency levels of 50%, 100% and 200%.
- Acceptable accuracy, intermediate precision and dilutional linearity was achieved.

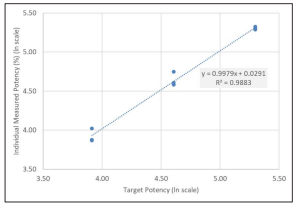
Intermediate Precision

Target Potency (%)	Run No.	Relative Potency (%)	Relative Potency (ln scale)	%GCV
50	1	48	3.87	9
	2	48	3.88	
	3	56	4.02	
100	1	100	4.61	9
	2	98	4.58	
	3	116	4.75	
200	1	198	5.29	2
	2	206	5.33	
	3	200	5.30	

Accuracy



Linearity



Summary

- We successfully completed a trial using the Integra VIAFLO® to show the potential to reduce analyst hands-on time and improve consistency in performance for a gene therapy transduction potency assay that was difficult to train out.
- The trial significantly reduced operator-required pipetting steps by 90%, thus reducing operator fatigue and potential error.
- Total assay time required to complete versus full manual pipetting was reduced by over 20%.
- The Integra VIAFLO® offers a viable solution to semi-automating cell-based assays in a QC laboratory.
- Minimal software validation is required, a process that is burdensome in a Good Manufacturing Practice (GMP) setting.
- Once developed, such semi-automated methods would be easier to train out.

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