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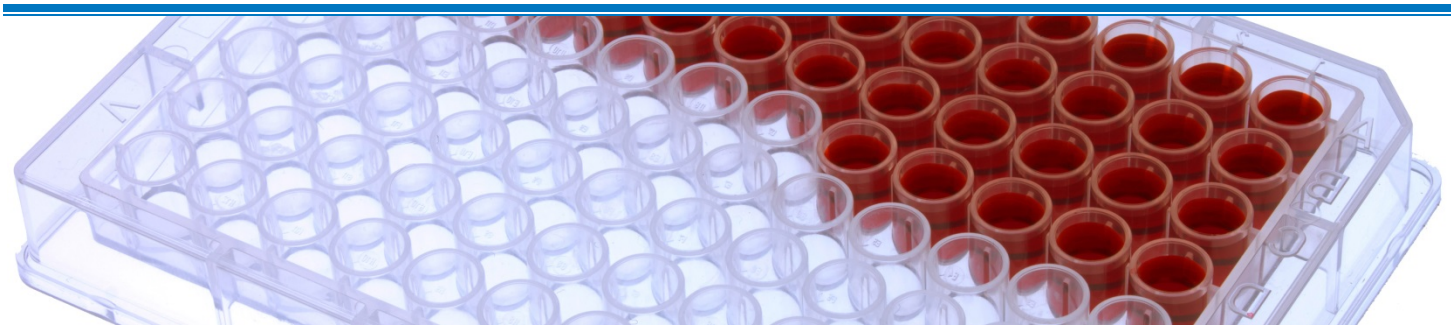
14306 Industrial Rd
Omaha, NE 68144 USA
+1.402.733.2829
cetac.com

Application Note



Comparison of the CETAC MVX-7100 Micro-Volume Workstation with an Established Laboratory Method for the Assessment of Lead, Mercury, and Arsenic in Human Whole Blood

Hope Adzitso[1], Sarah A. Hackenmueller[2], Daniel Ricks[1], Christian L. Law[1], Frederick G. Strathmann[3,4]

[1]ARUP Laboratories, Salt Lake City UT, 84108

[2]Department of Pathology and Laboratory Medicine, University of Wisconsin-Madison, Madison WI, 53705

[3]Department of Pathology, University of Utah, [4]ARUP Institute for Clinical and Experimental Pathology, Salt Lake City UT, 84108

INTRODUCTION

Conventional autosamplers used in clinical ICP-MS are largely based on the needs of non-clinical environments. Their disadvantages are numerous and include high sample volume consumption, large dead volumes resulting in wasted sample, and the inability to integrate easily with high throughput formats such as 96 and 384 well plates. Further, use of a low-volume autosampler allows for a reduction in reagents translating into an overall reduction in costs.

Figure 1. MVX -7100 µL Workstation

METHODS

Use of clinical samples

This project and its protocols were approved by the University of Utah Institutional Review Board (IRB #00007275).

Instrumentation

The established laboratory method uses a Perkin Elmer 9000 (lead, mercury, cadmium, arsenic screen) and a Perkin Elmer DRC II (arsenic hydride confirmation). Standard addition was used for calibration with no weighting and the origin ignored. A representative pool sample was analyzed and subtracted out by the PerkinElmer software to correct for the unfortified fraction of each element in the pool.

The MVX-7100 method was conducted using an Agilent 7700x (Agilent Technologies, Santa Clara, CA). Lead and mercury were analyzed in standard mode while arsenic was analyzed using the Octopole Reaction System at 4.5L/min of helium gas. Standard addition was used for calibration with 1/x weighting and the origin ignored. No calibration or reagent blank was used in the data analysis and the low standard was set as the internal standard reference file.

Working calibrator preparation

Four concentrations of calibrators were prepared containing mercury, lead and arsenic. Goat whole blood was fortified with an amount of each analyte from stock solutions (Inorganic Ventures, Christiansburg, VA) to obtain the concentrations listed in Table 1.

Quality control preparation

Four concentrations of quality control materials were prepared containing each element at the concentrations listed in
Table 2. Goat blood was fortified with each analyte from stock solutions stock solutions (Inorganic Ventures, Christiansburg, VA) using a separate lot from the calibrator stocks. Established values listed are from 20 separate days of results.

Sample preparation for CETAC ASX-510 HS autosampler

For the ASX-510 HS method, 100µL of sample was mixed with 100µL of 1% nitric acid and diluted to a total volume of 5 mL with diluent (0.5% nitric acid and 0.05% Triton X-100) to which yttrium, gallium, beryllium and iridium had been added to serve as internal standards.

Sample preparation for CETAC MVX-7100

For the MVX-7100 method, 20µL of sample was mixed with 20µL of 1% nitric acid and diluted to a final volume of 1mL in a polypropylene vial or 96-well plate using either an acidic diluent as described above or an alkaline diluent (1.75% EDTA, 0.1% Triton X-100, 1% NH_4OH) to which 1.5 ng/mL of indium was added to serve as the internal standard.

Table 1. Calibrator target concentrations.

	As (µg/L)	Hg (µg/L)	Pb (µg/dL)
Standard 1	10	2.5	2
Standard 2	50	5	10
Standard 3	100	15	20
Standard 4	250	80	50

Table 2. Target concentrations for the quality control materials

	As (µg/L)	Hg (µg/L)	Pb (µg/dL)
QC1	11	3	5
QC2	45	14	10
QC3	70	44	20
QC4	200	83	50

RESULTS

Carryover

Carryover was assessed using the calculated concentration observed from a low concentration sample preceded by the highest calibrator as follows:

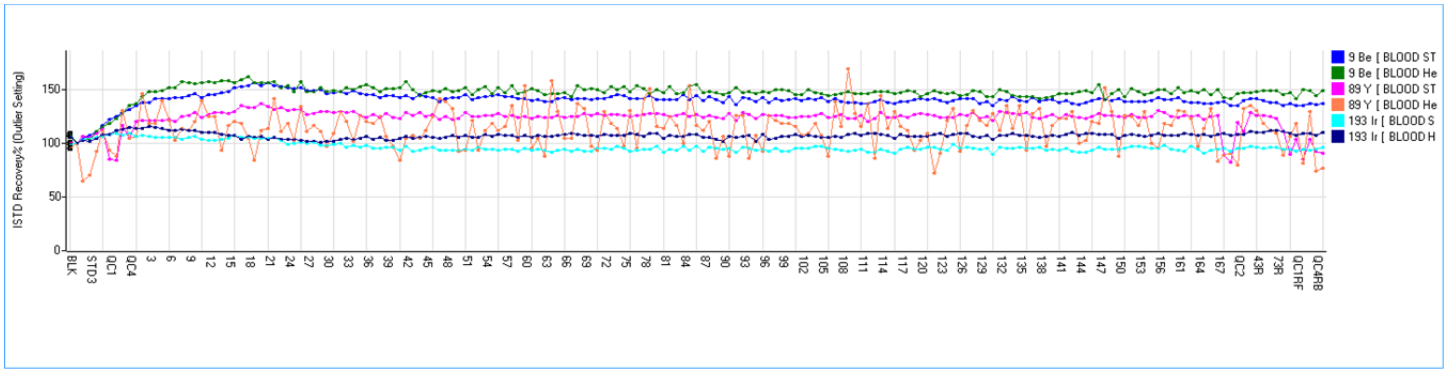
H1, H2, L1, L2, H1, H2, L1, L2, H1, H2, L1, L2 with $[(_{Avg}L2 - _{Avg}L1) / _{Avg}H1] \times 100 = \%$ carryover

Results are summarized in Table 3.

Table 3. Sequential carryover observed with the ASX-510 HS and MVX-7100 autosamplers.

Autosampler	Element	Percent Carryover
ASX-510 HS	Pb	< 0.02%
	Hg	< 0.02%
	As	< 0.02%
MVX-7100	Pb	< 0.01%
	Hg	< 0.01%
	As	< 0.01%

A



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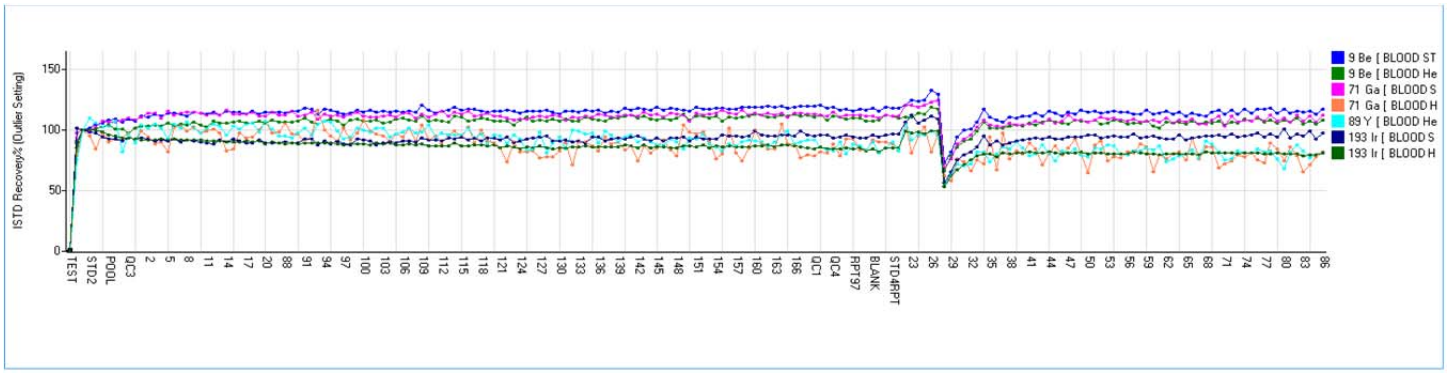

Figure 2. Internal standard stability plot for two separate batches. (A) 178 patient samples analyzed in total. Internal standards included beryllium, yttrium, and iridium in standard and helium modes. (B) Identical analysis to that above, however, the run was paused (noted as a collective drop in internal standard) and restarted to complete analysis.

Patient and quality control comparison

For three separate comparison studies, all quality control results were within established ranges and met laboratory criteria for run validation. Quality control samples were included at the beginning and the end of the analytical batch.

Patient comparisons demonstrated acceptable agreement with Deming regression statistics of < 10% proportional bias (slope) and < 5% constant bias (y-intercept).

Run stability

Stability of the system was assessed by visualization of the internal standard plot for beryllium, yttrium and iridium in both standard and helium modes (Figure 2). The MVX-7100 system demonstrated acceptable variation. The poor reproducibility seen for yttrium in helium mode was not a function of the MVX-7100 as no other internal standard followed the same trend indicating sub-optimal performance and a requirement for further optimization of yttrium in helium mode.

CONCLUSIONS

The results from the method using the MVX-7100 low volume autosampler were comparable to the established method currently in use. Of note, 5 times less patient sample was required as was 5x less diluent. The estimated reduction in reagent costs was estimated to be 16% per sample. In addition, use of the MVX-7100 allows a higher capacity workflow to be developed with the addition of liquid handlers and 96 or 384 well-based preparations.