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Revolutionizing Urine Metals Analysis with SampleSense

INTRODUCTION

Clinical laboratories need to rapidly and accurately analyze thousands of biological samples for trace metal contaminants by ICPMS. This requirement means laboratories must constantly look for new techniques to maintain high sample throughput requirements. Many clinical labs have taken advantage of the *FAST* technology introduced by ESI in 2006. The *FAST* is an automated sample introduction system for ICP and ICPMS which increases instrument efficiency up to five-fold by reducing time otherwise wasted performing sample flush, read delay, and wash. In addition, *FAST* system includes a chemically inert, metal free valve that reduces contamination and carryover regardless of matrix.

SampleSense *FAST* is the most recent advancement in *FAST* technology. SampleSense couples an autosampler with an inert valve having integrated optical sensors to automatically detect the presence of a non-segmented liquid sample. Upon detection, the sensed sample is injected to the ICPMS nebulizer and the ICPMS analysis is triggered. Sample throughput is improved, sample consumption per analysis is reduced, and errors otherwise caused by empty sample tubes or missing sample tubes are eliminated. Un-sensed samples are not triggered for analysis and ICPMS QC software can be configured to identify and report un-sensed samples, saving the operator from the time-consuming task of trying to understand ICPMS data generated from non-sample events.

SampleSense eliminates valve timing parameters, method adjustments to account for timing differences associated with variations in sample viscosity or even long-term instrument hardware variables that can affect analysis timing such as a sample line that accidentally becomes kinked. With SampleSense, throughput is further enhanced and the presence of the sample at the instrument valve is positively determined prior to sample injection, adding a higher level of authentication for patient results.

INSTRUMENTATION

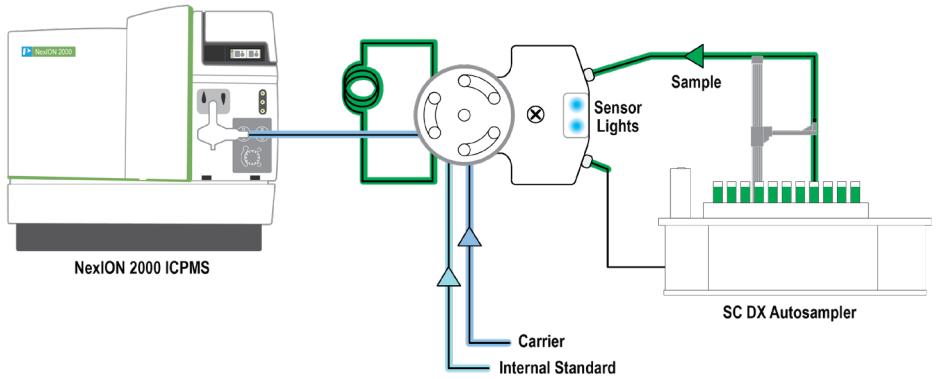

Figure 1. Illustration of the SampleSense Valve being loaded with sample on the NexION 2000 ICPMS. The Sensor lights (in blue) are indicating that sample has been loaded into the SampleSense valve. The sample is then injected and the analysis automatically triggered.

A NexION 2000 and the *FAST* with SampleSense valve (Figure 1) were used to evaluate the analysis of urine samples. In this experiment, ~ 1 L of anonymous urine was collected, spiked and analyzed in the same manner a laboratory would analyze patient samples. The calibration standards were matrix matched using ESI's Clinical Matrix and NYDOH proficiency testing samples were used as quality control samples. Multiple analyses were performed to demonstrate long term accuracy and precision. The instrument and method parameters can be found in Table 1.

Table 1. Instrument and method parameters.

Instrumentation:	NexION 2000 ICPMS + *FAST* with SampleSense
Elements Monitored:	Be, Sr, Mo, Sn, Sb, Cs, Ba, Gd, W, Pt, Tl, Bi, U, Pb, Cr, Al, Cu, Zn, Co, Ni, As, Mn, Cd
Analysis Modes:	Standard mode and KED mode (helium) based on ESI's urine clinical method (p/n: FI-CLIN-Urine)
Sample Preparation:	1:10 urine dilution with 2% HNO_3 (v/v)
Sample Volume:	1 mL sample loop
Standards Preparation:	ESI's urine metals clinical standards (p/n:M1-CLIN-U-A-100 & M1-CLIN-U-B-100) ESI's synthetic clinical matrix (p/n: CLIN-0500)
Rinse 1	0.1% Triton X
Rinse 2	5% HNO_3

RESULTS

Calibration

The method used in these experiments measures 23 elements. The calibration curves for a few of the elements (Be, Pb, and As) measured can be found in Fig. 2. The calibration standards were matrix-matched with a synthetic clinical matrix which mimics blood, serum, plasma, or urine but has been purified of the elements most commonly tested for in clinical panels (p/n: CLIN-0500, Elemental Scientific).

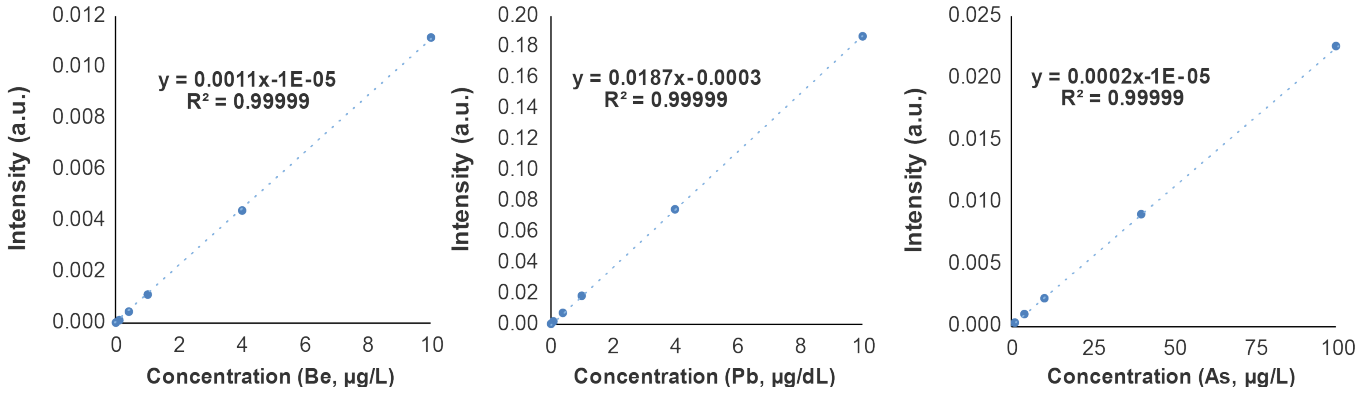

Figure 2. Example calibration curves for Be, Pb, and As from the urine metals method using SampleSense.

Precision

Figure 3 shows the normalized results for spiked urine samples from one of the three analyses. The precision for these 90 samples varied between 0.5 – 2.8 %RSD, with the average precision for the 23 elements being 1.5 %RSD (Table 2).

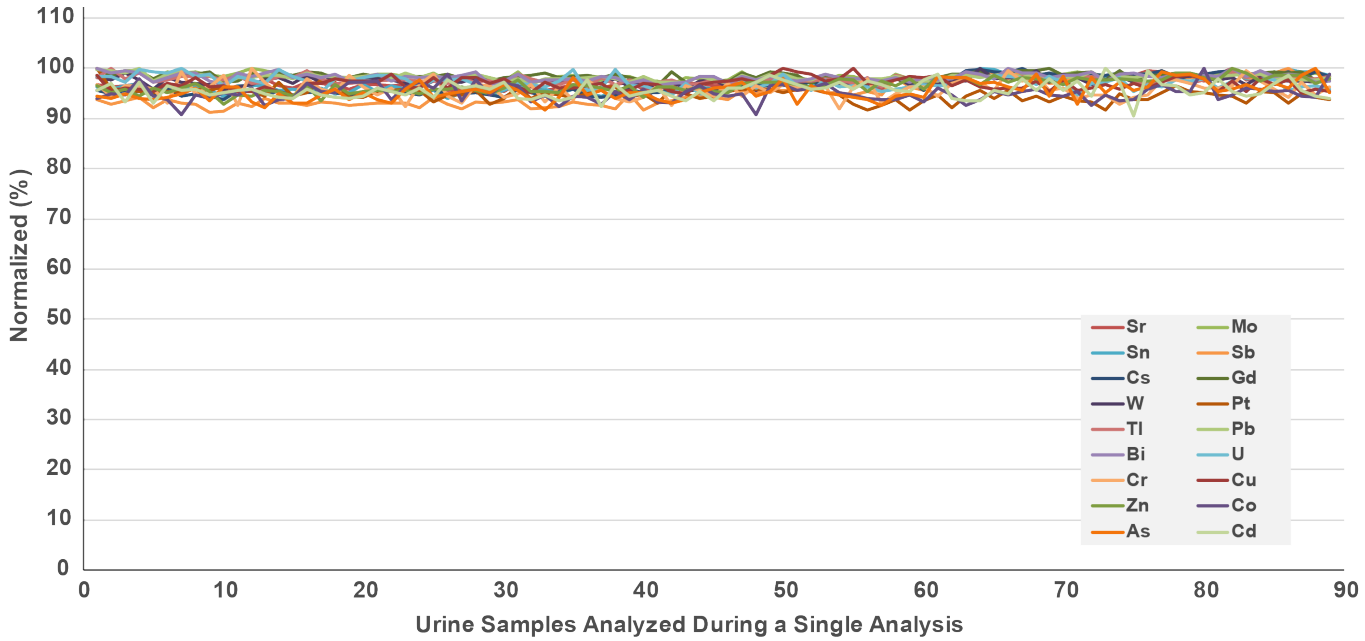

Figure 3. Normalized multi-element stability for spiked urine pool samples.

Table 2. Precision during a single analytical run for the analysis of spiked urine pool samples using *FAST* with SampleSense.

	Standard Mode													
	µg/L													µg/dL
	9Be	88Sr	98Mo	118Sn	121Sb	133Cs	138Ba	158Gd	184W	195Pt	205Tl	209Bi	238U	208Pb
Average	10.3	702	340	29.6	8.23	26.7	20.7	9.53	5.96	2.41	4.25	9.56	0.473	9.97
SD	0.3	8	3	0.3	0.08	0.3	0.2	0.10	0.04	0.04	0.04	0.09	0.006	0.05
%RSD	2.5	1.1	0.9	0.9	1.0	1.1	0.9	1.1	0.7	1.5	0.9	0.9	1.3	0.5

	KED Mode								
	µg/L								
	27Al	52Cr	55Mn	59Co	60Ni	63Cu	66Zn	75As	114Cd
Average	113	11.0	10.3	8.70	12.5	20.0	642	142	9.86
SD	3	0.2	0.2	0.12	0.2	0.3	5	3	0.19
%RSD	2.8	1.7	2.2	1.4	1.7	1.3	0.8	2.0	2.0

Accuracy

The NYDOH runs a proficiency testing (PT) program that clinical labs from around the world can participate in each year. Samples from the 2018 PT study were analyzed to evaluate the accuracy of this urine metals method on the NexION 2000 ICPMS incorporating *FAST* with SampleSense. The reference values and ranges for the three PT samples measured can be found in Table 3. The measured values (averaged values, n=6) are in very good agreement with the target values listed for As, Ba, Be, Cd, Co, Cr, Mn, Pb, and U. Not all of the elements measured for had a listed target value, thus the complete results can be found in Table 4. The elements Gd and Bi did not exhibit measurable levels and therefore were omitted, whereas Sr, Mo, Sn, Sb, Cs, W, Pt, Tl, Cr, Al, Cu, Zn, Ni, and Mn all had detectable levels in these PT samples.

Table 3. SampleSense results from historical NYDOH proficiency testing samples.

		As	Ba	Be	Cd	Co	Cr	Mn	Pb (µg/dL)	U
UE 18-08	*Reference Value (µg/L)*	175	4.2	5.1	0.45	3.2	1.8	7.5	2.2	0.138
	Reference Range (µg/L)	140 - 210	3.2 - 5.2	4.1 - 6.1	0 - 1.45	1.7 - 4.7	0 - 4.8	5.6 - 9.4	1.2 - 3.2	0.108 - 0.168
	SampleSense-Measured Value (µg/L)	172	3.9	4.8	0.51	3.2	1.9	7.5	2.3	0.133
UE 18-10	*Reference Value (µg/L)*	81.7	0.9	0.76	3.63	0.73	6.6	0.80	13.5	0.042
	Reference Range (µg/L)	65.4 - 98.0	0 - 1.9	0 - 1.76	2.63 - 4.63	0 - 2.23	3.6 - 9.6	0.25 - 1.35	10.8 - 16.2	0.012 - 0.072
	SampleSense-Measured Value (µg/L)	77.9	0.9	0.73	3.56	0.70	6.7	0.79	13.6	0.042
UE 18-15	*Reference Value (µg/L)*	7.57	1.19	1.63	4.42	0.60	3.43	3.24	3.20	0.0300
	Reference Range (µg/L)	1.57 - 13.57	0.19 - 2.19	0.63 - 2.63	3.42 - 5.42	0 - 2.10	0.43 - 6.43	2.43 - 4.05	2.20 - 4.20	0.0007 - 0.0607
	SampleSense-Measured Value (µg/L)	7.09	1.13	1.59	4.61	0.52	3.42	3.13	3.21	0.0286

SampleSense - Measured values: represent the average of 6 results (n = 6).
NYDOH PT samples were used as starting and ending QC samples for 3 separate analyses.

Table 4. NYDOH PT testing results for elements without reference values.

		Al	Cs	Cu	Ni	Mo	Pt	Sb	Sn	Sr	Tl	W	Zn
UE 18-08	*Average*	19.1	2.89	90.2	8.49	15.1	3.72	1.39	1.28	18.2	3.96	0.141	543
	SD	1.5	0.05	2.7	0.25	0.2	0.04	0.02	0.02	0.2	0.11	0.006	15
UE 18-10	*Average*	16.4	9.29	26.2	7.14	153	0.188	0.228	0.946	379	1.07	0.420	714
	SD	3.4	0.30	1.1	0.50	3	0.004	0.007	0.033	14	0.05	0.009	23
UE 18-15	*Average*	13.0	7.22	13.6	5.41	204	0.461	0.729	5.37	96.3	0.267	0.169	697
	SD	2.1	0.21	0.5	0.30	3	0.004	0.022	0.19	0.6	0.035	0.013	23

Average, SD = represent the average or standard deviation from 6 results (n = 6).
NYDOH PT samples were used as starting and ending QC samples for 3 separate analyses.
Gd and Bi are not listed above, these were not detected in the NYDOH PT samples tested.

SUMMARY

- The SampleSense valve eliminates the need for method timing parameters.
- Changes in sample loop volumes (e.g. 1 mL to 2 mL sample loop) requires no method modifications.
- Intelligent Sample Verification Technology (ISV) provides:
  - Urine samples with different viscosities are all injected with optimized loading conditions
  - Monitors and logs any sample loading issues (i.e. missing samples or QC solutions, capped vials, bubbles present in sample loop).
- Matrix matched calibration curves demonstrated very good linearity using ESI's Clinical Matrix.
- Very good accuracy was reported for 2018 NYDOH PT urine samples, which were supplemented as reference samples.
- Urine samples measured during an analytical run demonstrated good precision (≤ 2.8 %RSDs).
- Multiple analyses were performed, which resulted in 1140 blanks, standards, and urine pool samples being analyzed successfully with **ZERO** sample loading errors.

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