Validation of a Combined Analytical Method for Toxic Metals in Urine: Improving Laboratory Efficiency and Implications for Biomonitoring Use

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Introduction

Exposure to toxic metals is linked to adverse health outcomes[1]. Analyzing urine for toxic metals including Arsenic (As), Barium (Ba), Beryllium (Be), Cadmium (Cd), Lead (Pb), Thallium (Tl), Uranium (U), and Mercury (Hg) is a crucial step in monitoring exposures in the public and for emergency response testing. The NJ Department of Health Metals Laboratory has traditionally used separate analytical methods to test for the array of toxic metals in urine: Urine Metals (As, Ba, Be, Cd, Pb, Tl, U) and Urine Mercury. An improved method was developed to maximize efficiency through reduction of analysis time, laboratory costs, and labor. Here, we assess the applicability of this method to both emergency response and biomonitoring analyses and describe the validation of the combined method for testing metals in urine by inductively coupled plasma mass spectrometry.

Methodology

New method:

CDC Urine Methods
- DLS 3018.4-02, 3018A.3- 02 (Toxic metals: Ba, Be, Cd, Pb, Tl, U)
- DLS 3002.7-05 (Total arsenic)

NY DOH Urine Method
- LINC-412SOP (Mercury)

Combined Urine Method
(As, Ba, Be, Cd, Pb, Tl, U, Hg)

Key New Components:
-3% hydrochloric acid to the rinse to reduce mercury carryover/reduce rinse times
-ICPMS Intelligent Rinse during run
-Hg preservative solution of 20% sulfamic acid and 10% Triton X-100

Validation:
- Testing five historical CLIA-certified PT urine specimens of known metals content on three different runs.
- Analyzing previously tested biomonitoring samples at low, medium, and high concentrations using the combined method to compare) against the previous methods.

Parameters:
- Linearity ($R^2 > 0.990$)
- Accuracy (within known acceptable PT range)
- Precision (≤ 20% RSD)
- Analytical specificity (checking for interferences with <20% RSD

Results

Table 1. Accuracy and Precision for Emergency Response Range Samples*.
After analyzing five historical CLIA-certified PT urine samples, accuracy of the method showed the true values fell within the accepted PT range for each analyte and sample. Precision of the method showed all analytes were <20% RSD, with most showing <10% RSD.

PT Sample	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	True Value (ug/L)	Acceptance range (ug/L)	Average (ug/L)	Std Dev	% RSD
Hg	107	107	103	108	112	120	112	78.4-146	110	5.89	5.38
As	569	577	576	587	591	583	587	470-704	581	8.04	1.39
Ba	25.6	26.9	27.7	28.2	27.6	27.7	26.9	21.5-32.3	27.3	0.92	3.39
Be	19.7	21.0	20.1	20.1	19.5	19.5	19.9	15.9-23.9	20.0	0.57	2.84
Cd	6.52	6.68	6.89	6.66	6.73	6.74	6.43	5.43-7.43	6.70	0.121	1.80
Pb	3.10	3.01	3.08	3.02	3.02	3.09	3.11	2.11-4.11	3.05	0.0408	1.34
Tl	3.44	3.38	3.44	3.40	3.40	3.39	3.39	2.71-4.07	3.41	0.0256	0.752
U	0.731	0.678	0.721	0.725	0.703	0.707	0.691	0.553-0.829	0.711	0.0193	2.72

*Note: Table 2 only shows one of five Pt samples tested across 6 days for both accuracy and prevision.

Table 2. Relative Standard Deviation for Analytical Specificity.
All data for analytes from the combined method match the data from the separate methods with RSDs <20% at biomonitoring levels.

Analyte		Hg Urine (ug/L)	Combined Urine	RSD%
Hg	Low	0.756	0.810	4.88
	Medium	1.40	1.59	9.22
	High	4.18	3.93	4.33
		Multielement (ug/L)	**Combined Urine**	**RSD%**
As	Low	4.99	4.39	9.07
	Medium	14.1	16.1	9.11
	High	23.8	22.7	3.58
Ba	Low	0.851	0.975	9.57
	Medium	2.32	2.20	3.61
	High	4.52	3.80	12.2
Cd	Low	0.098	0.113	10.1
	Medium	0.341	0.328	2.75
	High	0.568	0.659	10.5
Pb	Low	0.438	0.343	17.2
	Medium	0.733	0.593	14.9
	High	1.06	0.849	15.9
Tl	Low	0.039	0.0384	1.10
	Medium	0.088	0.1026	10.8
	High	0.430	0.5102	12.0
U	Low	0.007	0.007	0.00
	Medium	0.013	0.025	12.3
	High	0.021	0.016	19.1

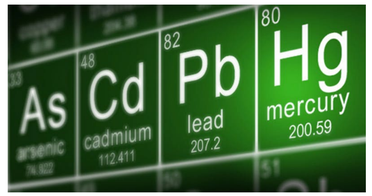
Note: All Be results are < detection limit for biomonitoring samples.

Table 3. Target Analytes' Reporting Limits

Hg	0.5
As	2
Ba	0.2
Be	0.1
Cd	0.08
Pb (ug/L)	0.1
Tl	0.04
U	0.005

Conclusions

- This new method can efficiently and accurately quantify all target analytes.
- The changes made to the rinse mixture allowed for a significant decrease in rinse times between samples and a 75% reduction in analysis time per sample.
- Addition of a Hg preservative, which is not part of the multielement urine methods, looks to not affect results at varying concentrations of each analyte.
- Our results highlight the value of continued method improvement to better facilitate public health laboratory analytics.
- The ability to precisely and accurately analyze CLIA-certified PT samples shows the method is equipped for emergency response testing.
- Analytical specificity of the data indicates this method is applicable for biomonitoring purposes to detect analytes at varying concentrations.



Future Direction
- Periodically reevaluate the method for efficiency and applicability as regulations are updated.

References

1. National Center for Health Statistics (NCHS). "2015-2016 Data Documentation, Codebook, and Frequencies." *Centers for Disease Control and Prevention*, June 2018, wwwn.cdc.gov/Nchs/Nhanes/2015-2016/UM_I.htm.

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