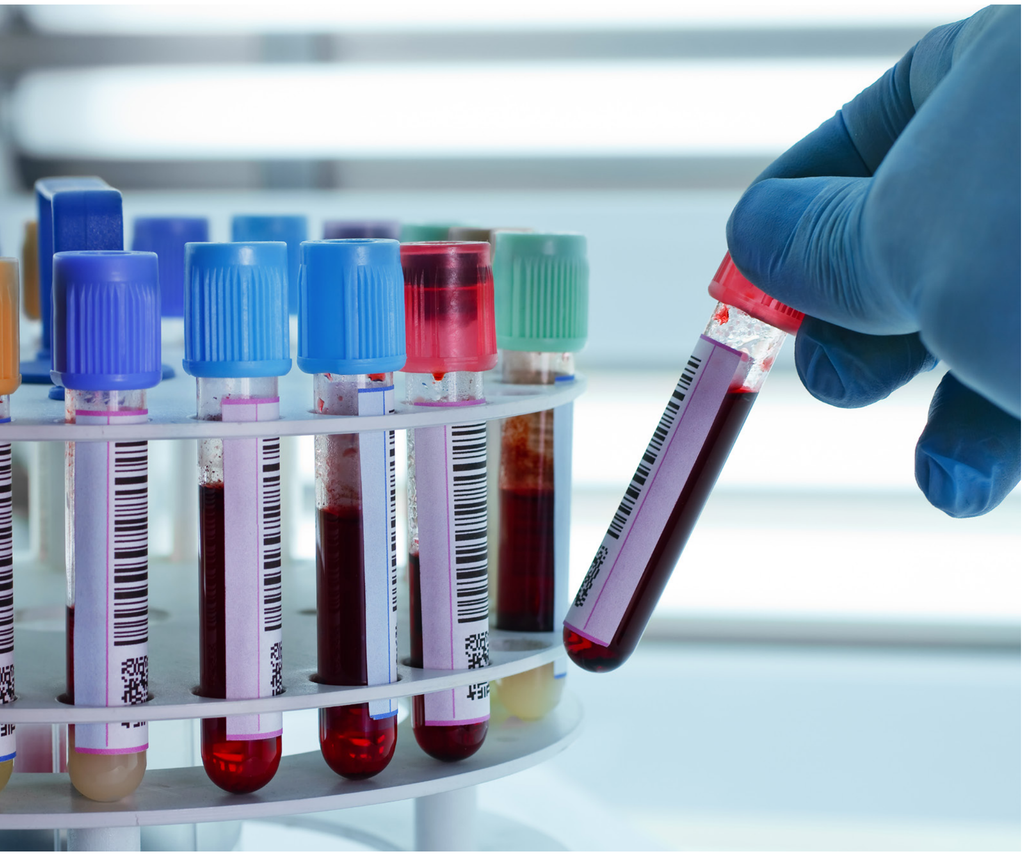

Challenge
Determination of up to 33 elements in the range of ng/L to g/L in samples with high matrix load and various interferences.

Solution
ICP-MS PlasmaQuant MS Q with patented 3D focusing of ions for high sensitivity and integrated collision reaction cell technology for targeted removal of interferences.

Intended audience
Clinical diagnostics laboratories, research, pharma.

Universal Sample Preparation of Clinical Samples by Alkaline Dilution for Determining up to 33 Elements Using ICP-MS

Introduction

The determination of trace elements in human samples has become a standard method in medical diagnostics. The most common applications are analyses of whole blood, serum, plasma, and urine for various elements. The information which can be obtained from the elemental concentration varies depending on the element and sample type. Essential trace elements such as copper, zinc, selenium, or iodine are mainly used as biomarkers. Certain diseases are known to cause deficiency or excess of certain trace elements, so if the concentration is outside the reference range, this could be a valuable indication for diagnosis. On the other hand, occupational medicine regularly analyzes clinical samples to monitor occupational exposure to toxic elements such as lead, chromium, cadmium, nickel, or mercury. Further possible applications include the monitoring of treatments (e.g., platinum determination after administration of platinum-based cytostatics) and implants (e.g., potential migration of titanium, chromium, or cobalt from implants into the human body). Due to the high number of elements and sometimes very low concentrations which must be determined in human samples, inductively coupled plasma-mass spectrometry (ICP-MS) is the method of choice for this application. Its main advantages are multi-element capability, which allows short measurement times and, thus, high sample throughput, and better sensitivity for most elements compared to other techniques for elemental analysis.

In particular, whole blood is a challenging matrix because it contains more cells and proteins than plasma or serum. If diluted with acidic solutions, which is the typical way of sample preparation for ICP-MS analysis, these cells and proteins often precipitate by denaturation, coagulation or due to protonation. Elements bound to or adsorbed by precipitated material are lost from the solution, compromising the analytical result.

Aspiration of precipitates can also cause blockages within the ICP-MS nebulizer. Therefore, best practice for the sample preparation of whole blood is dilution with alkali solution containing ammonia for breaking up cells and preventing protein precipitation. Furthermore, the complexing agent EDTA helps stabilizing elements which are typically unstable under alkali conditions. The surfactant Tergitol is used to improve cell lysis, stabilize proteins and lipids in solution and to improve the washout from the tubings system. It is a more ecofriendly surfactant than the commonly used Triton X, which is no longer permitted for use without official authorization due to European REACH regulation.
The presence of carbon has been shown to improve ionization efficiency for certain elements such as arsenic and selenium. Consequently, a varying carbon content between samples and standards could lead to biased results. Therefore, 2-propanol is added for increasing the carbon content of all solutions to equalize the differences in natural carbon.

The present work demonstrates that the alkali dilution approach is suitable for all four typical clinical matrices, so that the ICP-MS introduction system does not need to be changed from acidic to alkali conditions and vice versa when different types of matrices are to be analyzed. By using matrix calibrators, the matrix matched calibration is simplified as less calibration levels need to be prepared.

Materials and Methods

Samples and reagents

- Ultrapure water type I (>18.2 MΩ cm, ELGA Purelab®, Veolia Water Technologies Germany GmbH, Celle, Germany)
- Ammonia solution 25%, p.a. (Merck KGaA, Darmstadt, Germany)
- 2-Propanol, VLSI grade (Carl Roth GmbH + Co. KG, Karlsruhe, Germany)
- EDTA, 99–101% (Supelco, Merck KGaA, Darmstadt, Germany)
- Tergitol 15-S-9 (Sigma-Aldrich, Merck KGaA, Darmstadt, Germany)
- ClinCal® Calibrators Whole blood (Lot 1458), plasma (Lot 1177), serum (Lot 1318), urine (Lot 1489) (RECIPE Chemicals + Instruments GmbH, Munich, Germany)
- ClinChek® Whole blood Control Level I, III Lot 1299 (RECIPE Chemicals + Instruments GmbH, Munich, Germany)
- ClinChek® Plasma Control Level I, II Lot 1518 (RECIPE Chemicals + Instruments GmbH, Munich, Germany)
- ClinChek® Serum Control Level I, II Lots 2062(RECIPE Chemicals + Instruments GmbH, Munich, Germany)
- ClinChek® Urine Control Level I, II Lot 2170 (RECIPE Chemicals + Instruments GmbH, Munich, Germany)
- Seronorm™ Trace Elements Whole Blood L-2 Lot 1406264 (SERO AS, Billingstad, Norway)
- Seronorm™ Trace Elements Serum L-1 Lot 1309438, L-2 Lot 1309416 (SERO AS, Billingstad, Norway)
- Seronorm™ Trace Elements Urine L-1 Lot 1403080, L-2 Lot 1403081 (SERO AS, Billingstad, Norway)
- Single element standard solutions (Sc, Tb: TraceCert®, 1000 mg/L; Y: TraceCert®, 10000 mg/L; Rh, Ir: High-Purity Standards, 1000 mg/L)

Sample preparation

The lyophilized control materials were reconstituted with ultrapure water following the manufacturer's information. Reconstituted and fresh blood, plasma, and serum samples were diluted 20-fold prior to analysis with an alkali preparation solution consisting of 1% (*w*) ammonia, 0.5% (*V*) 2-propanol, 0.1 g/L EDTA, and 0.01% (*V*) Tergitol.

Reagent blank

Due to the number of chemicals used in the preparation solution and their high concentration, minimizing the contribution of impurities to the background elemental concentration of the preparation solution is crucial for sensitive and accurate measurements. Therefore, different products were tested for their contamination with all analytes. It was found that the contribution of different purity grades of ammonia and 2-propanol were negligible compared to the impurities introduced by EDTA. Surprisingly, the p.a. grade EDTA tested contained much lower traces of certain elements, e.g., Cr, Mn, Co, Cd, Pb than trace metals basis grade EDTA, though it was slightly more contaminated with others. Since this work focuses on a large list of elements, the p.a. grade EDTA was considered the best compromise, whereas for optimum analytical conditions for a certain element, the trace metals basis grade EDTA might be the better choice. Unfortunately, Tergitol 15-S-9 is not available in different purity grades.

Calibration

The lyophilized calibrators were reconstituted with ultrapure water following the manufacturer's information. Three calibration levels were prepared for each matrix by applying different dilution factors. The calibrators for blood and serum were diluted 200-, 100-, and 20-fold with the alkali preparation solution. The calibrator for plasma was diluted 500-, 200-, 100-, and 20-fold, and the calibrator for urine was diluted 4000-, 1000-, 200-, 100-, and 20-fold.
To correct for long-term drifts and matrix effects, an internal standard solution containing 20 µg/L Sc, Y, Rh, Tb, and Ir in alkali preparation solution was prepared.

Instrument settings

For the analysis a PlasmaQuant MS Q ICP-MS (Analytik Jena GmbH+Co. KG, Jena, Germany) was used. Further details on the configuration of the system are listed in Table 1.

Table 1: Instrument configuration

Parameter	Specification
Nebulizer	SeaSpray™ (0.4 mL/min)
Spray chamber	Scott double-pass, Peltier-cooled
Torch	Fassel-Torch with 2.4 mm injector
Cones	Nickel sampler und skimmer
Autosampler	ASX-560 (CETAC) with enclosure, HEPA filter and ASXpress Plus (CETAC) rapid sample introduction system
Sample loop	1.25 mL, 1.0 mm ID

The alkali preparation solution was used as the rinse solution of the autosampler and as the carrier solution of the rapid sample introduction system. The internal standard solution was added on-line to the sample solution via the peristaltic pump of the PlasmaQuant MS Q. Black/black PVC tubing (0.76 mm ID) was used for introducing the sample solution and orange/green PVC tubing (0.38 mm ID) was used for the internal standard solution.

Method parameters

The method parameters used are given in Table 2.

Table 2: General method parameters

Parameter	Specification
Plasma gas flow	9.0 L/min
Auxiliary gas flow	1.50 L/min
Sheath gas flow	0.00 L/min
Nebulizer gas flow	0.98 L/min
RF power	1.26 kW
Sampling depth	6.0 mm
Pump rate	15 rpm
iCRC gas, flow	Hydrogen – 200 mL/min (H_2) Helium – 120 mL/min (He120); 200 mL/min (He200)
Stabilization delay	30 s (H_2); 25 s (nG); 20 s (He120); 10 s (He200)*
Spray chamber temperature	3 °C
Skimmer bias (BOOST)	6 V (H_2)
Points per peak	1 (peak hopping)
Scans per replicate	5
Replicates	3

* The stabilization delay of the first measurement mode includes sample uptake. Between measurement modes, switching times of < 5 s can be chosen. To obtain the best measuring precision possible, longer stabilization delays were used achieving an average RSD of < 2%.
H_2 – Hydrogen mode; nG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

For eliminating matrix- and/or plasma-based polyatomic interferences, helium as a collision gas and hydrogen as a reaction gas were introduced into Analytik Jena's patented integrated collision reaction cell (iCRC). To achieve a maximum sensitivity and lowest limits of detection for elements measured in reaction mode, the patented BOOST technology was used. In BOOST mode, a positive voltage is applied to the back of the skimmer cone. This enables compensating the loss of sensitivity by collision of analytes with gas molecules in reaction gas mode with high flow rates. Isotopes which are not interfered by polyatomic interferences were measured in no gas mode. In total, four different measurement modes were used in this method: hydrogen, no gas, and two helium modes with flow rates of 120 mL/min and 200 mL/min, respectively.

Evaluation parameters

The choice of isotopes, measurement modes, and dwell times is shown in Table 3. For Pb, the sum of the isotopes ^{206}Pb, ^{207}Pb, ^{208}Pb was used to account for variability of isotopic abundances. For Hg, the sum of the isotopes ^{199}Hg, ^{200}Hg, ^{201}Hg und ^{202}Hg was used to achieve a higher sensitivity. This can be done because no interferences are expected on any of these isotopes.

For internal standards a dwell time of 20 ms in hydrogen- and no gas modes, and 50 ms in helium modes was chosen. The isotopes chosen were ^{45}Sc, ^{89}Y, ^{103}Rh, ^{159}Tb, and ^{193}Ir. Using the ASXPress Plus sample introduction system, a total measuring time of 2.5 min for all elements listed in Table 3 could be achieved including sample uptake, measurement, and rinsing.

Table 3: Element specific method parameters

Element	Isotope	Expected polyatomic interferences	Mode	Correction equation	Dwell time [ms]	Internal standard
Aluminum	^{27}Al	^{13}C^{14}N^{+}, ^{11}B^{16}O^{+}	He120		50	^{45}Sc
Antimony	^{121}Sb		NG		20	Interpolate
Arsenic	^{75}As	^{40}Ar^{35}Cl^{+}, ^{74}Ge^{1}H^{+}	H_2		50	^{89}Y
Barium	^{137}Ba		NG		20	Interpolate
Beryllium	^{9}Be		NG		100	^{45}Sc
Bismuth	^{209}Bi		NG		50	^{193}Ir
Cadmium	^{114}Cd		NG	- 0.0268 · ^{118}Sn	20	Interpolate
Calcium	^{44}Ca		H_2		20	^{45}Sc
Chromium	^{52}Cr	^{40}Ar^{12}C^{+}, ^{36}Ar^{16}O^{+}, ^{38}Ar^{14}N^{+}	H_2		50	^{89}Y
Cobalt	^{59}Co	^{24}Mg^{35}Cl^{+}, ^{43}Ca^{16}O^{+}, ^{45}Sc^{14}N^{+}	He120		50	Interpolate
Copper	^{65}Cu	^{40}Ar^{25}Mg^{+}	NG***		10	Interpolate
Copper (urine)	^{65}Cu	^{40}Ar^{25}Mg^{+}	He120		20	Interpolate
Gold	^{197}Au		NG		20	^{193}Ir
Iodine	^{127}I		NG		20	Interpolate
Iron	^{56}Fe	^{40}Ar^{16}O^{+}	H_2		20	^{89}Y
Iron (blood)	^{57}Fe	^{40}Ar^{16}O^{1}H^{+}, ^{40}Ca^{16}O^{1}H^{+}	NG***		2.5	Interpolate
Lead	$^{206-208}$Pb		NG		20 each**	^{193}Ir
Lithium	^{7}Li		NG		20	^{45}Sc
Magnesium	^{25}Mg	^{12}C^{13}C^{+}	NG***		5	^{45}Sc
Manganese	^{55}Mn	^{39}K^{16}O^{+}, ^{40}Ar^{15}N^{+}, ^{37}Cl^{18}O^{+}	He120		50	Interpolate
Mercury	$^{199-202}$Hg		NG		50 each*	^{193}Ir
Molybdenum	^{98}Mo		NG	- 0.1111 · ^{101}Ru	20	Interpolate
Nickel	^{60}Ni	^{24}Mg^{36}Ar^{+}, ^{44}Ca^{16}O^{+}, ^{23}Na^{37}Cl^{+}	He120		200	Interpolate
Palladium	^{108}Pd		NG	- 0.07031 · ^{111}Cd	20	Interpolate
Phosphorus	^{31}P	^{15}N^{16}O^{+}, ^{14}N^{16}O^{1}H^{+}	NG***		2.5	^{45}Sc
Platinum	^{195}Pt		nG		20	^{193}Ir
Potassium	^{39}K	^{38}Ar^{1}H^{+}, ^{23}Na^{16}O^{+}	NG***		5	^{45}Sc
Selenium	^{78}Se	^{40}Ar^{38}Ar^{+}, ^{40}Ca^{38}Ar^{+}	H_2	- 0.03043 · ^{83}Kr	50	^{89}Y

Silver	^{107}Ag		NG		20	Interpolate
Sodium	^{23}Na		NG		5	^{45}Sc
Thallium	^{205}Tl		NG		20	^{193}Ir
Tin	^{118}Sn		NG		20	Interpolate
Titanium	^{49}Ti	$^{31}P^{18}O^+$, $^{32}S^{16}O^1H^+$, $^{14}N^{35}Cl^+$, $^{12}C^{37}Cl^+$	He200		200	^{45}Sc
Vanadium	^{51}V	$^{35}Cl^{16}O^+$, $^{38}Ar^{13}C^+$, $^{40}Ar^{11}B^+$	He200		200	^{45}Sc
Zinc	^{66}Zn	$^{35}Cl^{31}P^+$	NG***		10	Interpolate
Zinc (urine)	^{66}Zn	$^{35}Cl^{31}P^+$	He120		20	Interpolate

* Sum of the isotopes ^{199}Hg, ^{200}Hg, ^{201}Hg und ^{202}Hg to obtain higher sensitivity
** Sum of the isotopes ^{206}Pb, ^{207}Pb, ^{208}Pb to account for variable isotopic abundances
*** Interferences are negligible due to high concentration of analyte (mg/L)
H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Results and Discussion

Calibration

Exemplary calibration curves and parameters of As, Cd, Mn, and V are shown in Figure 1. Correlation coefficients were > 0.999 for all isotopes with deviations of < 10% from the calibration curve for all calibration levels (%Error).

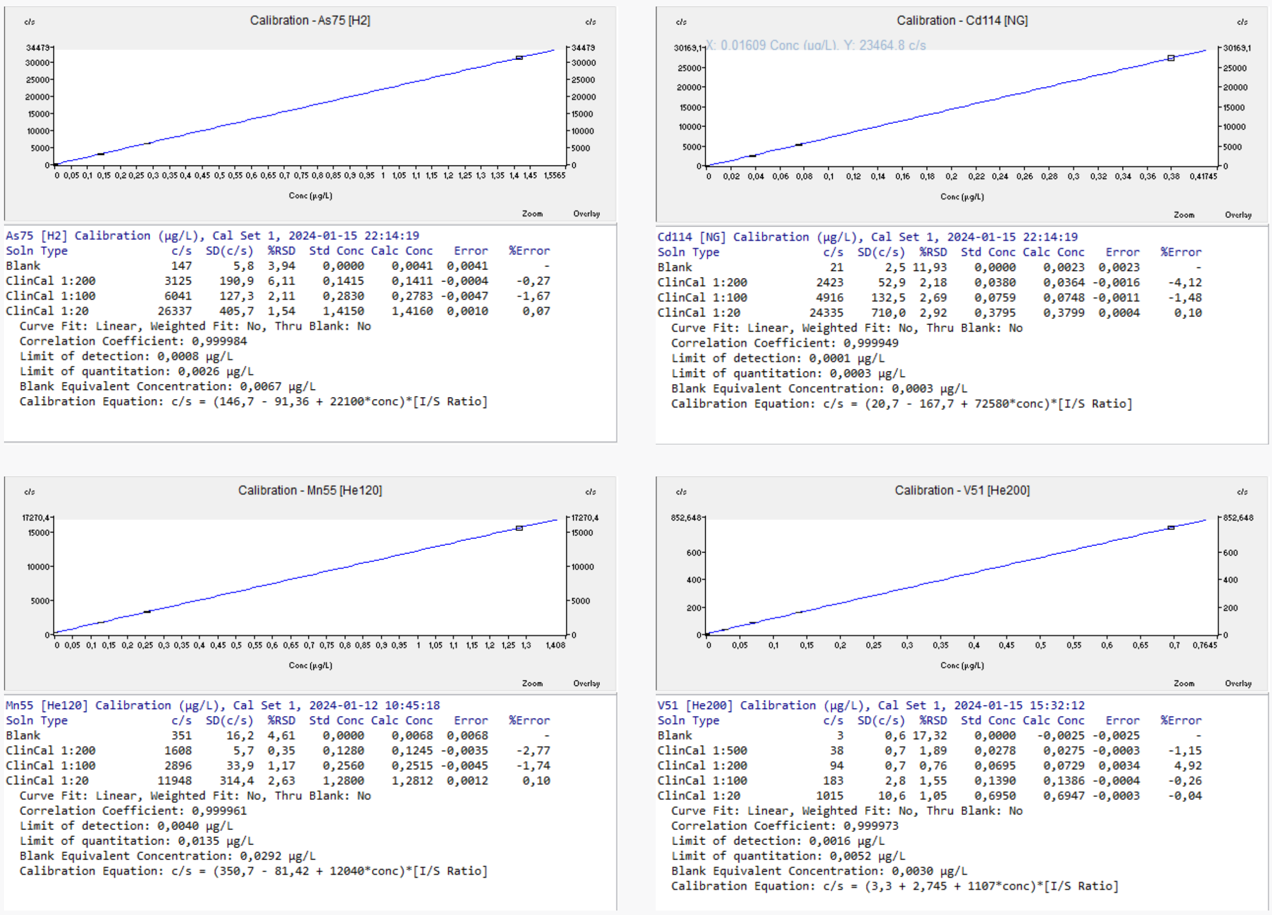

Figure 1: Calibration of As, Cd, Mn, and V by ICP-MS using matrix calibrators

Limits of detection and quantification

The instrumental limits of detection (LOD) and quantification (LOQ) of the calibration were determined using the blank and slope of the calibration curve in accordance with DIN 32645[1] and are shown in Table 4. The method detection and quantification limits (MDL, MQL) were calculated considering the dilution factor of the sample preparation.

Table 4: Limits of detection and quantification of the calibration (LOD, LOQ) and method (MDL, MQL) determined in accordance with DIN 32645[1]

Isotope [Mode]	Unit	LOD	LOQ	MDL	MQL
^{27}Al [He120]	µg/L	0.050	0.17	1.00	3.3
^{121}Sb [NG]	µg/L	0.00040	0.0013	0.0080	0.026
^{75}As [H_2]	µg/L	0.00080	0.0026	0.016	0.053
^{137}Ba [NG]	µg/L	0.0027	0.0089	0.054	0.18
^{9}Be [NG]	µg/L	0.00060	0.0020	0.012	0.040
^{209}Bi [NG]	µg/L	0.00030	0.0010	0.0060	0.020
^{114}Cd [NG]	µg/L	0.00011	0.00035	0.0021	0.0070
^{44}Ca [H_2]	mg/L	0.0077	0.025	0.15	0.51
^{52}Cr [H_2]	µg/L	0.0028	0.0092	0.056	0.18
^{59}Co [He120]	µg/L	0.00040	0.0013	0.0080	0.026
^{65}Cu [NG]	mg/L	0.0000048	0.000016	0.00010	0.00032
^{65}Cu [He120]	µg/L	0.028	0.092	0.56	1.8
^{197}Au [NG]	µg/L	0.0005	0.0017	0.010	0.033
^{127}I [NG]	µg/L	0.0021	0.0069	0.042	0.14
^{57}Fe [NG]	mg/L	0.017	0.055	0.33	1.1
^{56}Fe [H_2]	µg/L	0.0013	0.0043	0.026	0.086
$^{206-208}$Pb [NG]	µg/L	0.0007	0.0023	0.014	0.046
^{7}Li [NG]	mg/L	0.000010	0.000033	0.00020	0.00066
^{25}Mg [NG]	mg/L	0.00015	0.00050	0.0030	0.0099
^{55}Mn [He120]	µg/L	0.0040	0.013	0.080	0.26
$^{199-202}$Hg [NG]	µg/L	0.0031	0.010	0.062	0.20
^{98}Mo [NG]	µg/L	0.0015	0.0050	0.030	0.099
^{60}Ni [He120]	µg/L	0.0015	0.0050	0.030	0.099
^{108}Pd [NG]	µg/L	0.00020	0.00066	0.0040	0.013
^{31}P [NG]	mg/L	0.0061	0.020	0.12	0.40
^{195}Pt [NG]	µg/L	0.000068	0.00022	0.0014	0.0045
^{39}K [NG]	g/L	0.000068	0.00023	0.0014	0.0045
^{78}Se [H_2]	µg/L	0.0058	0.019	0.12	0.38
^{107}Ag [NG]	µg/L	0.00040	0.0013	0.0080	0.026
^{23}Na [NG]	g/L	0.000012	0.000039	0.00024	0.00079

^{205}Tl [NG]	µg/L	0.00014	0.00046	0.0028	0.0092
^{118}Sn [NG]	µg/L	0.00040	0.0013	0.0080	0.026
^{49}Ti [He180]	µg/L	0.10	0.34	2.0	6.7
^{51}V [He180]	µg/L	0.0016	0.0053	0.032	0.11
^{66}Zn [NG]	mg/L	0.000037	0.00012	0.00073	0.0024
^{66}Zn [He120]	µg/L	0.16	0.51	3.1	10

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Whole blood

The results of the analyzed whole blood reference materials are shown in Tables 5 and 6. Since Al, Ba, Be, Bi, Hg, I, Li, and V are not specified in the calibrator material, these elements could not be quantified using this calibrator-based method. In Seronorm™ Whole Blood L-2 (Lot 1406264), out of the 23 elements specified in the whole blood calibrator only concentrations of the elements As, Cd, Co, Cr, Cu, Mn, Mo, Ni, Pb, Se, Sn, Tl, and Zn are certified.

Table 5: Elemental concentrations and recoveries of ClinChek® Whole Blood Level I and II

Isotope [Mode]	Unit	ClinChek® Whole Blood Level I			ClinChek® Whole Blood Level II		
		Result	Control range	Recovery [%]	Result	Control range	Recovery [%]
^{75}As [H_2]	µg/L	3.16	–	105	9.46	7.66–11.5	99
^{114}Cd [NG]	µg/L	1.58	1.18–1.97	100	3.62	2.83–4.24	103
^{44}Ca [H_2]	mg/L	40.8	36.1–48.9	96	40.0	35.7–48.3	95
^{52}Cr [H_2]	µg/L	2.39	1.67–2.78	107	5.99	4.47–7.44	100
^{59}Co [He120]	µg/L	1.64	1.31–1.97	100	7.28	5.81–8.72	100
^{65}Cu [NG]	mg/L	0.731	0.590–0.885	99	1.16	0.934–1.40	100
^{57}Fe [NG]	mg/L	348	276–414	101	335	272–408	99
$^{206\text{-}208}$Pb [NG]	µg/L	37.1	30.1–45.2	99	95.4	76.5–115	100
^{25}Mg [NG]	mg/L	24.2	21.6–26.4	101	32.1	29.1–35.6	99
^{55}Mn [He120]	µg/L	7.67	6.32–9.48	97	15.1	11.7–17.6	104
^{98}Mo [NG]	µg/L	2.05	1.64–2.46	100	4.71	3.64–5.47	103
^{60}Ni [He120]	µg/L	2.01	1.58–2.63	96	4.51	3.62–5.43	100
^{108}Pd [NG]	µg/L	1.40	1.07–1.61	105	2.54	2.01–3.02	101
^{31}P [NG]	mg/L	324	262–394	99	315	259–388	97
^{195}Pt [NG]	µg/L	1.65	1.34–2.01	99	2.44	1.99–2.99	98
^{39}K [NG]	g/L	1.19	1.07–1.31	100	1.58	1.44–1.75	99
^{78}Se [H_2]	µg/L	84.5	66.5–99.7	102	159	127–191	100
^{107}Ag [NG]	µg/L	1.82	1.39–2.32	99	4.29	3.42–5.12	100
^{23}Na [NG]	g/L	1.95	1.73–2.11	102	1.89	1.70–2.08	100
^{205}Tl [NG]	µg/L	0.908	0.717–1.08	101	4.30	3.44–5.17	100
^{118}Sn [NG]	µg/L	1.74	1.51–2.26	93	4.34	3.76–5.64	92
^{66}Zn [NG]	mg/L	4.37	3.55–5.32	99	5.98	4.90–7.36	98

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Table 6: Elemental concentrations and recoveries of ClinChek® Whole Blood Level III and Seronorm™ Whole Blood L-2

Isotope [Mode]	Unit	ClinChek® Whole Blood Level III			Seronorm™ Whole Blood L-2		
		Result	Control range	Recovery [%]	Result	Control range	Recovery [%]
^{75}As [H_2]	µg/L	19.4	15.4–23.0	101	12.8	11.3–17.0	90
^{114}Cd [NG]	µg/L	7.24	5.63–8.44	103	4.90	4.00–6.02	98
^{44}Ca [H_2]	mg/L	41.0	35.9–48.5	97	-	-	-
^{52}Cr [H_2]	µg/L	11.0	8.88–13.3	99	10.9	8.5–12.8	102
^{59}Co [He120]	µg/L	13.3	10.7–16.0	100	5.01	4.13–6.22	97
^{65}Cu [NG]	mg/L	1.71	1.36–2.04	101	1.28	1.07–1.60	95
^{57}Fe [NG]	mg/L	341	274–411	100	-	-	-
$^{206\text{-}208}$Pb [NG]	µg/L	260	208–312	100	337	269–405	100
^{25}Mg [NG]	mg/L	40.9	37.0–45.3	99	-	-	-
^{55}Mn [He120]	µg/L	21.8	17.4–26.1	100	31.4	25.1–37.7	100
^{98}Mo [NG]	µg/L	8.82	7.06–10.6	100	5.08	4.24–6.37	96
^{60}Ni [He120]	µg/L	12.8	10.2–15.2	100	15.1	12.7–19.1	95
^{108}Pd [NG]	µg/L	5.33	4.32–6.47	99	-	-	-
^{31}P [NG]	mg/L	327	263–394	100	-	-	-
^{195}Pt [NG]	µg/L	4.85	3.94–5.92	98	-	-	-
^{39}K [NG]	g/L	2.04	1.82–2.22	101	-	-	-
^{78}Se [H_2]	µg/L	214	161–242	106	164	128–193	102
^{107}Ag [NG]	µg/L	8.57	6.8–10.2	101	-	-	-
^{23}Na [NG]	g/L	1.84	1.70–2.08	98	-	-	-
^{205}Tl [NG]	µg/L	8.60	6.9–10.3	100	10.5	8.1–12.2	103
^{118}Sn [NG]	µg/L	8.93	7.56–11.3	95	5.30	4.19–6.30	101
^{66}Zn [NG]	mg/L	7.82	6.27–9.41	100	7.0	5.7–8.5	99

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Urine

The results of the analyzed urine reference materials are shown in Tables 7 and 8. Since Au is not specified in the calibrator material, this element could not be quantified using this calibrator-based method. In Seronorm™ Urine L-1 (Lot 1403080) and L-2 (Lot 1403081), concentrations of the elements Ag, Ba, Pd, and Pt are not certified.

Table 7: Elemental concentrations and recoveries of ClinChek® Urine Level I and II

Isotope [Mode]	Unit	ClinChek® Urine Level I			ClinChek® Urine Level II		
		Result	Control range	Recovery [%]	Result	Control range	Recovery [%]
^{27}Al [He120]	µg/L	32.0	26.7–40.0	96	84.7	65.8–98.7	103
^{121}Sb [NG]	µg/L	6.08	4.88–7.31	100	49.8	40.5–60.7	99
^{75}As [H_2]	µg/L	17.1	13.6–20.3	101	52.1	40.8–61.2	102
^{137}Ba [NG]	µg/L	11.1	8.77–13.2	101	50.4	40.3–60.5	100
^{9}Be [NG]	µg/L	0.058	0.041–0.085	93	0.228	0.171–0.285	100
^{114}Cd [NG]	µg/L	2.53	2.05–3.08	99	14.7	11.8–17.7	100
^{52}Cr [H_2]	µg/L	4.14	3.26–4.90	102	10.1	8.01–12.0	101
^{59}Co [He120]	µg/L	2.04	1.64–2.46	99	9.90	7.84–11.8	101
^{65}Cu [He120]	µg/L	59.0	46.6–69.9	101	115	92.2–138	100
^{127}I [NG]	µg/L	115	92.2–138	100	520	413–619	101
^{56}Fe [H_2]	µg/L	41.0	32.5–48.8	101	223	178–267	100
$^{206\text{-}208}$Pb [NG]	µg/L	26.0	21.1–31.6	98	51.6	41.3–62.0	100
^{25}Mg [NG]	mg/L	18.4	14.9–22.3	99	45.8	36.6–54.9	100
^{55}Mn [He120]	µg/L	4.08	3.27–4.90	100	9.65	7.99–12.0	97
$^{199\text{-}202}$Hg [NG]	µg/L	2.23	1.15–2.68	116	15.8	9.05–18.8	113
^{98}Mo [NG]	µg/L	20.0	16.2–24.3	99	94.1	75.5–113	100
^{60}Ni [He120]	µg/L	3.21	2.60–3.90	99	14.5	11.7–17.5	99
^{108}Pd [NG]	µg/L	1.30	0.911–1.69	100	8.79	6.10–10.2	108
^{195}Pt [NG]	µg/L	0.038	0.025–0.053	98	0.114	0.086–0.143	100
^{78}Se [H_2]	µg/L	29.0	21.8–36.3	100	81.6	65.4–98.1	100
^{107}Ag [NG]	µg/L	1.36	0.944–1.75	100	5.32	3.99–6.65	100
^{205}Tl [NG]	µg/L	7.26	5.90–8.85	98	19.4	15.5–23.3	100
^{118}Sn [NG]	µg/L	5.21	4.13–6.19	101	10.1	8.06–12.1	100
^{51}V [He200]	µg/L	20.7	16.8–25.2	98	50.5	41.3–62.0	98
^{66}Zn [He120]	mg/L	0.191	0.156–0.234	98	0.592	0.478–0.717	99

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Table 8: Elemental concentrations and recoveries of Seronorm™ Urine L-1 and L-2

Isotope [Mode]	Unit	Seronorm™ Urine L-1			Seronorm™ Urine L-2		
		Result	Control range	Recovery [%]	Result	Control range	Recovery [%]
^{27}Al [He120]	µg/L	11.3	5.5–16.6	102	124	85–128	115
^{121}Sb [NG]	µg/L	9.0	5.0–9.4	126	103	72–133	100
^{75}As [H_2]	µg/L	156	126–190	99	258	209–314	99
^{9}Be [NG]	µg/L	-	-	-	5.3	4.1–6.2	102
^{114}Cd [NG]	µg/L	0.20	0.12–0.27	107	4.8	3.9–5.8	98
^{52}Cr [H_2]	µg/L	10.1	7.6–11.4	106	29.8	24–36.1	99
^{59}Co [He120]	µg/L	0.80	0.64–0.97	99	9.8	8.1–12.2	97
^{65}Cu [He120]	µg/L	21	16–24	104	57.6	44.9–67.6	102
^{127}I [NG]	µg/L	105	84–126	100	309	237–356	104
^{56}Fe [H_2]	µg/L	11.9	9.8–14.7	97	-	–	-
$^{206-208}$Pb [NG]	µg/L	0.72	0.36–1.08	100	81.2	64–96.2	101
^{25}Mg [NG]	mg/L	76.6	61.3–92.2	100	-	–	-
^{55}Mn [He120]	µg/L	1.35	1.10–1.66	98	9.7	7.4–11.2	104
$^{199-202}$Hg [NG]	µg/L	0.097	0.077–0.116	101	45.0	35.2–52.9	102
^{98}Mo [NG]	µg/L	47.1	37.6–56.6	100	-	-	-
^{60}Ni [He120]	µg/L	1.59	1.27–1.92	99	39.4	32.5–48.8	97
^{78}Se [H_2]	µg/L	15.7	12.6–19.0	99	70.2	57.3–86.1	98
^{205}Tl [NG]	µg/L	0.15	0.12–0.17	109	8.8	6.87–10.33	102
^{118}Sn [NG]	µg/L	0.33	0.26–0.39	102	48.4	38.6–58.1	100
^{51}V [He200]	µg/L	0.87	0.66–0.99	104	24.9	20.7–31.2	96
^{66}Zn [He120]	mg/L	0.353	0.277–0.417	102	1.292	1.023–1.538	101

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Plasma

The results of the analyzed plasma reference materials are shown in Table 9. Since Au, Ba, Be, Fe, Li, Mo, and Ti are not specified in the calibrator material, these elements could not be quantified using this calibrator-based method.

Table 9: Elemental concentrations and recoveries of ClinChek® Plasma Level I and II

Isotope [Mode]	Unit	ClinChek® Plasma Level I			ClinChek® Plasma Level II		
		Result	Control range	Recovery [%]	Result	Control range	Recovery [%]
^{27}Al [He120]	µg/L	9.91	7.60–14.1	91	46.2	36.6–60.9	95
^{121}Sb [NG]	µg/L	1.28	0.982–1.64	98	4.75	3.82–5.73	100
^{75}As [H_2]	µg/L	9.70	6.80–12.6	100	44.7	35.8–53.7	100
^{209}Bi [NG]	µg/L	0.931	0.745–1.12	100	4.48	3.45–5.17	104
^{114}Cd [NG]	µg/L	2.49	1.71–3.18	102	11.0	8.81–13.2	100
^{52}Cr [H_2]	µg/L	3.33	2.25–4.18	103	10.5	8.46–12.7	99
^{59}Co [He120]	µg/L	2.07	1.66–2.49	100	9.41	7.38–11.1	102
^{65}Cu [NG]	mg/L	0.731	0.621–0.840	100	1.27	1.07–1.45	101
^{127}I [NG]	µg/L	48.7	39.3–59.0	99	104	82.8–124	100
^{25}Mg [NG]	mg/L	15.8	13.8–16.9	103	28.4	25.9–31.7	99
^{55}Mn [He120]	µg/L	4.54	3.56–5.34	102	15.7	12.2–18.3	103
$^{199-202}$Hg [NG]	µg/L	2.07	1.51–2.52	102	9.49	7.44–11.2	102
^{60}Ni [He120]	µg/L	6.79	4.73–8.79	100	13.9	11.1–16.7	100
^{108}Pd [NG]	µg/L	1.91	1.53–2.55	94	7.52	6.16–9.24	98
^{195}Pt [NG]	µg/L	1.72	1.41–2.12	98	6.90	5.50–8.25	100
^{78}Se [H_2]	µg/L	75.5	56.8–85.1	106	119	93.5–140	102
^{107}Ag [NG]	µg/L	1.90	1.52–2.29	100	7.36	5.90–8.85	100
^{205}Tl [NG]	µg/L	5.26	4.20–6.29	100	10.4	8.25–12.4	101
^{118}Sn [NG]	µg/L	1.24	0.903–1.68	96	7.61	6.24–9.36	98
^{51}V [He200]	µg/L	1.23	0.747–1.39	115	9.35	7.88–11.8	95
^{66}Zn [NG]	mg/L	1.55	1.35–1.82	98	1.99	1.66–2.25	101

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Serum

The results of the analyzed urine reference materials are shown in Tables 10 and 11. In Seronorm™ Serum L-1 (Lot 1309438) and L-2 (Lot 1309416), only concentrations of the elements Al, Cr, Co, Cu, Fe, Hg, Li, Mg, Mn, Ni, Se, and Zn are certified.

Table 10: Elemental concentrations and recoveries of ClinChek® Serum Level I and II

Isotope [Mode]	Unit	ClinChek® Serum Level I			ClinChek® Serum Level II		
		Result	Control range	Recovery [%]	Result	Control range	Recovery [%]
^{27}Al [He120]	µg/L	16.7	11.4–21.1	103	60.6	44.7–74.6	102
^{121}Sb [NG]	µg/L	1.78	1.37–2.05	104	7.11	5.54–8.31	103
^{75}As [H_2]	µg/L	9.38	7.58–11.4	99	18.4	15.4–23.2	95
^{137}Ba [NG]	µg/L	23.9	19.6–29.5	98	60.8	49.1–73.7	99
^{9}Be [NG]	µg/L	2.06	1.45–2.42	106	9.47	7.31–12.2	97
^{209}Bi [NG]	µg/L	1.39	1.08–1.79	96	5.66	4.15–6.92	102
^{114}Cd [NG]	µg/L	1.93	1.56–2.35	98	5.74	4.75–7.13	97
^{52}Cr [H_2]	µg/L	1.44	1.18–1.97	91	4.93	4.73–7.10	83
^{59}Co [He120]	µg/L	1.99	1.60–2.41	99	5.44	4.53–6.79	96
^{65}Cu [NG]	mg/L	0.744	0.632–0.855	100	1.42	1.19–1.61	101
^{197}Au [NG]	µg/L	102	72.2–120	106	497	376–565	106
^{127}I [NG]	µg/L	38.0	32.5–48.8	94	72.6	62.9–94.3	92
^{56}Fe [H_2]	mg/L	0.844	0.730–0.988	98	1.58	1.26–1.71	107
^{7}Li [NG]	mg/L	3.57	3.19–4.32	95	7.26	6.44–8.71	96
^{25}Mg [NG]	mg/L	15.4	14.4–17.6	97	21.4	19.6–24.0	98
^{55}Mn [He120]	µg/L	2.29	1.81–3.01	95	5.76	4.99–7.49	92
$^{199-202}$Hg [NG]	µg/L	2.07	1.58–2.63	99	7.99	6.41–9.61	100
^{98}Mo [NG]	µg/L	1.72	1.36–2.27	95	5.82	4.62–6.92	101
^{60}Ni [He120]	µg/L	1.82	1.43–2.38	96	6.04	4.84–7.27	100
^{108}Pd [NG]	µg/L	4.99	3.86–5.78	104	20.4	15.6–23.4	104
^{195}Pt [NG]	mg/L	0.278	0.214–0.322	104	0.927	0.712–1.07	104
^{78}Se [H_2]	µg/L	59.9	46.1–69.2	104	107	83.7–126	102
^{107}Ag [NG]	µg/L	4.98	3.85–5.77	104	20.1	15.5–23.3	103
^{205}Tl [NG]	µg/L	1.94	1.52–2.29	102	7.93	6.18–9.27	103
^{118}Sn [NG]	µg/L	1.96	1.62–2.43	96	9.26	7.57–11.4	98
^{49}Ti [He200]	µg/L	12.3	6.90–12.8	125	39.3	28.1–46.8	105
^{51}V [He200]	µg/L	2.07	1.47–2.45	106	8.24	6.13–9.19	108
^{66}Zn [NG]	mg/L	1.15	1.04–1.40	95	1.62	1.45–1.96	95

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Table 11: Elemental concentrations and recoveries of Seronorm™ Serum L-1 and L-2

Isotope [Mode]	Unit	Seronorm™ Serum L-1			Seronorm™ Serum L-2		
		Result	Control range	Recovery [%]	Result	Control range	Recovery [%]
^{27}Al [He120]	µg/L	46.8	36.9–55.4	101	123	94–141	105
^{52}Cr [H_2]	µg/L	2.39	1.30–3.05	110	5.5	4.0–7.5	96
^{59}Co [He120]	µg/L	1.15	0.67–1.57	102	3.04	2.13–3.97	100
^{65}Cu [NG]	mg/L	1.100	0.999–1.176	101	1.877	1.700–2.000	101
^{56}Fe [H_2]	mg/L	1.50	1.17–1.77	102	2.24	1.72–2.58	104
^{7}Li [NG]	mg/L	5.242	4.202–6.320	100	9.677	7.739–11.639	100
^{25}Mg [NG]	mg/L	18.5	13.4–20.1	110	37.1	27.1–40.7	109
^{55}Mn [He120]	µg/L	10.1	7.9–11.9	102	15.1	11.6–17.4	104
$^{199-202}$Hg [NG]	µg/L	1.10	0.53–1.60	103	2.05	1.44–2.67	100
^{60}Ni [He120]	µg/L	5.56	3.38–7.90	99	9.8	7.9–11.9	109
^{78}Se [H_2]	µg/L	88	76–99	101	133	120–157	96
^{66}Zn [NG]	mg/L	1.173	0.952–1.242	107	1.742	1.404–1.831	108

H_2 – Hydrogen mode; NG – no gas; He120 – Helium mode 120 mL/min; He200 – Helium mode 200 mL/min

Summary

Achieving recoveries between 90% and 110% for the majority of the 33 investigated elements in all four body fluid matrices demonstrates the superior performance of the PlasmaQuant MS Q ICP-MS in the field of clinical diagnostics. Using the patented integrated collision reaction cell (iCRC), polyatomic interferences on even strongly interfered isotopes could be eliminated. With the patented ion mirror ReflexION for 90° deflection and 3D focusing of the ion beam, high sensitivity could be achieved allowing low method limits of detection in the ng/L range in both no gas and iCRC measurement modes.

The accuracy, sensitivity, and robustness of the PlasmaQuant MS Q is combined with exceptionally low running costs considering a total argon consumption of only 11.5 L/min for a measurement time of 2.5 minutes per sample for 33 elements using a volume of less than 70 µL of the original sample.

Figure 2: PlasmaQuant MS Q

Recommended device configuration

Table 12: Overview of devices, accessories, and consumables

Article	Article number	Description
Initial configuration		
PlasmaQuant MS Q	818-08011-2	ICP-MS with integrated collision reaction cell
Hydrogen generator	810-88026-0	Generator producing H_2 on-demand from ultrapure water
Autosampler ASX-560	810-88015-0	Autosampler with up to 370 positions
ASXPress Plus for PlasmaQuant MS	810-88017-0	Rapid introduction system with 7-port valve for ICP-MS
Starter Kit PQMS STANDARD	810-88518-0	Kit of sample introduction system for aqueous samples
Enclosure ENC-560 DC for ASX-560	810-88063-0	Dust protection cover for autosampler
HEPA filter for enclosure ENC-560 DC	810-88064-0	For using the enclosure in combination with exhaust
SeaSpray™ nebulizer	418-88092-0	For aqueous samples with high matrix load
Sample loop 1.25 mL for ASXPress Plus	418-88172-0	Inner diameter 1 mm
Consumables		
Consumables kit ICP-MS all inclusive	810-88117-0	For PlasmaQuant MS Q
Consumables kit autosampler	810-88126-0	For ASX-560 autosampler
Consumables kit valve	810-88127-0	For ASXPress Plus rapid sample introduction system
Maintenance kit hydrogen generator	810-88421-0	For hydrogen generator

References

[1] DIN 32645:2008-11, *Chemical analysis – Decision limit, detection limit and determination limit under repeatability conditions – Terms, methods, evaluation.*

Headquarters
Analytik Jena GmbH+Co. KG
Konrad-Zuse-Strasse 1
07745 Jena · Germany

Phone +49 3641 77 70
Fax +49 3641 77 9279

info@analytik-jena.com
www.analytik-jena.com

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