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# **A high-resolution ICP-MS method for the determination of 38 inorganic elements in human whole blood, urine, hair and tissues after microwave digestion**

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27 **ABSTRACT**

28

29 Inductively coupled plasma-mass spectrometry (ICP-MS) is currently the reference method for the  
30 determination of inorganic elements, and has many applications in healthcare and the environmental  
31 field. The objective of the present study was to develop and validate a high-resolution ICP-MS  
32 method for the simultaneous quantification of 38 elements in samples of human whole blood, urine,  
33 hair and tissues after microwave mineralization. The samples were incubated with nitric acid,  
34 hydrogen peroxide and internal standards prior to microwave mineralization for 25 minutes. The  
35 analysis was performed with an Element XR ICP-MS and validated using commercial reference  
36 standards (whole blood, urine, and hair) and in-house quality control samples. The 38 elements  
37 were detected in low-, medium- or high-resolution mode, depending on interferences and  
38 sensitivity. The lower and upper limits of quantification were adjusted for each element. The  
39 method was linear for all elements (correlation coefficient  $>0.996$ ), and the inter- and intraday  
40 precision values (coefficient of variation) were below 15%. Samples from a clinical trial were used  
41 to confirm the high-resolution ICP-MS method's suitability for the assessment of patient samples.

42

43 **Keywords:** Inductively coupled plasma-sector field mass spectrometry; human blood; human hair;  
44 human urine, human tissue; microwave digestion; elements

45

## 1. INTRODUCTION

Inductively coupled plasma mass spectrometry (ICP-MS) is used widely to analyze trace and ultra-trace elements in biological matrices. Human exposure to elements released from toxics, drugs and implanted medical devices is conventionally monitored by assaying serum, blood, and urine. However, tissue or hair samples often provide additional useful information. For instance, toxic elements can enter the lungs through the inhalation of smoke or contaminated air. Furthermore, elements absorbed by the digestive and/or pulmonary tract can find their way into the bloodstream and become distributed throughout and incorporated into the body's various tissues - including the hair. Hence, measurements in hair can reflect the body's cumulative exposure to the various elements. Lastly, some elements may be deposited directly on the hair by external contamination [1-4].

The limits of detection (LOD) associated with conventional quadrupole ICP-MS mean that the technique is not ideal for the simultaneous quantification of several trace elements in human blood or serum samples [5]. Inductively coupled plasma - sector field mass spectrometry (ICP-SFMS) has greater sensitivity and resolving power; this produces LOD in the pM range [6] and enables useful performance over a broad concentration range. The use of ICP-MS to assay trace elements in human samples (with or without prior mineralization) has already been reported. For example, ICP-MS with an octopole-based collision/reaction cell has been used to quantify 37 trace elements in human blood [7]. After acid sample dilution, high-resolution ICP-MS has been applied to the determination of 20 to 42 elements in human urine and serum; the concentrations were similar to those observed in non-occupationally exposed populations [6, 8]. Methods for the ICP-SFMS quantification of 4 to 8 abundant elements in human blood and/or serum after microwave digestion have also been reported [9, 10]. Microwave digestion was shown to enhance the recovery of elements and to be more reproducible and accurate than wet or dry digestion procedures [11, 12]. However, all the methods reported to date have various shortcomings: (i) they can only detect a

small number of elements simultaneously; (ii) for some elements, the LOD is above the concentration found in clinical samples; (iii) analyses are restricted to blood and serum samples (i.e. hair and other human tissues could not be assessed); and (iv) microwave digestion is not applied. The objective of the present study was to develop and validate a method for the simultaneous quantitation of 38 trace elements in human tissues, urine and whole blood samples, following microwave mineralization. The method's suitability for the analysis of clinical samples was also demonstrated.

## 2. MATERIALS AND METHODS

### 2.1. Chemicals and reagents

Analytical and internal standards were purchased from LGC Standards (Molsheim, France). ICP-MS-grade nitric acid, hydrochloric acid, hydrogen peroxide and Triton X100 were obtained from Fisher Scientific (Illkirch, France). Whole blood, urine and hair quality control (QC) samples were supplied by Centre de Toxicologie du Québec (Québec, Canada). Ultrapure deionized water (18mΩ) was obtained from a water station (Purelab Flex, Elga Labwater, Antony, France). Argon 5.0 was purchased from Messer (Puteaux, France).

### 2.2. Working and calibration standard solutions

Working and calibration standard solutions were prepared by diluting 1000 µg.mL<sup>-1</sup> or (for Cu, Fe, Rb, and Zn) 10000 µg.mL<sup>-1</sup> single-element standard solutions. Three sets of 15 calibration standards were prepared: the first set contained all the elements (except those detailed thereafter) in 5% HNO<sub>3</sub> in metal-free plastic tubes, the second contained Sb, Hf, Au, Pt, and Ru in 20% HCl in metal-free plastic tubes, and the third contained Hg only in borosilicate tubes. The chosen standard concentrations were based on those published previously for human samples. Hence, the calibration range differed from one element to another: Goulle *et al.* and Cesbron *et al.* reported elemental

96 concentrations in whole blood, plasma, urine and hair samples from a population of healthy  
97 volunteers in France [3, 13]; Heitland and Koster reported on the concentrations of 37 trace  
98 elements in blood samples from inhabitants of northern Germany [7]; Schultze *et al.* described  
99 whole blood and serum concentrations of metals in a Swedish population-based sample [14];  
100 Alimonti *et al.* and Minoia *et al.* reported concentrations of metals in blood, serum or urine samples  
101 from healthy adults living in Rome [15] or Lombardy [16]. To prepare the calibration curve, 10  $\mu$ L  
102 of each calibration standard solution were added to 190  $\mu$ L of deionized water. Quality control  
103 samples were stored at -20°C, whereas calibration standard stock and working solutions were stored  
104 at room temperature.

105

### 106 **2.3. Sample preparation**

107 Whole blood, urine and tissue samples were processed directly, whereas hair samples were washed  
108 first to eliminate any external contamination (using the method developed by the International  
109 Atomic Energy Agency, with some modifications [17-19]). The strand of hairs was washed once  
110 with 0.1% Triton X100, three times with deionized water and then once with acetone, prior to  
111 drying in an oven at 40°C.

112 Next, 200  $\mu$ L of urine, whole blood or plasma, 15 mg of lung tissue, or 10 mg of hair were added to  
113 quartz tubes containing 10  $\mu$ L of the internal standard solution (10  $\mu$ g/mL gallium and iridium, and  
114 100  $\mu$ g/mL indium and scandium). Two hundred microliters of nitric acid and 200  $\mu$ L of hydrogen  
115 peroxide were then added. The tubes were capped, transferred to the microwave reaction chamber  
116 (Ultrawave, Milestone, Sorisole, Italy) and then microwaved at 1500 W (heating from ambient  
117 temperature to 220°C over 15 min, followed maintenance at 220°C for 10 min) at a pressure of 110  
118 bar. After the samples had cooled, they were transferred to 15 mL polypropylene tubes and made up  
119 to a volume of 6 ml with deionized water.

120

## 121    **2.4. Instrumentation and the analytical procedure**

122    The samples were handled using an ASX-520 autosampler (CETAC technologies, Omaha, NE,  
123    USA), a PFA-ST microflow nebulizer, and a PC<sup>3</sup> Peltier-cooled cyclonic quartz chamber (both  
124    from Elemental Scientific Instruments, Ltd, Birmingham, UK) maintained at +2°C. A demountable  
125    quartz torch with a quartz injector (internal diameter: 1.75 mm), a platinum sampler, and skimmer  
126    cones were used (Elemental Scientific Instruments, Ltd). The ICP-MS instrument was an Element  
127    XR (ThermoFisher, Les Ulis, France) controlled with Element ICP-MS software (v3.1.2.242). The  
128    operating conditions (torch position, lenses, gas flows and detector voltage) were optimized daily in  
129    low-, medium- and high-resolution modes, using a 100 ppt tuning solution (ThermoFisher). This  
130    yielded oxide levels ( $^{238}\text{U}^{16}\text{O}/^{238}\text{U}$ ) below 10%, and a resolution of around 4000 and 10000 in the  
131    medium- and high-resolution modes, respectively. Mass calibration was performed as required. The  
132    main ICP-MS detection parameters are shown in Supplementary Table 1. The parameters used to  
133    detect the elements of interest and their internal standards are summarized in Supplementary Table  
134    2.

## 136    **2.5. Validation of the ICP-MS method**

137    The ICP-MS method was validated using reference standards (at two different concentrations) for  
138    whole blood, urine, and hair. Since theoretical concentrations were not available for all 38 elements  
139    in the matrix, a set of in-house QC samples at three concentrations (containing the elements spiked  
140    into blank water) were also analysed. To assess intra- and interday performance levels, all QC  
141    samples were analysed on three different days as six replicates. Calibration curves included a  
142    sample blank, a zero sample, and 7 to 15 calibration standards (depending on the element) over a  
143    preselected concentration range for each element (based on the literature data for the different  
144    matrices [3, 7, 13-16]). The intensity of each element in the sample blank was subtracted from the  
145    intensity measured in each sample.

For each element, the ratio between the peak area and the peak area of the corresponding internal standard was plotted against the concentration; the relationship was then probed in a regression analysis. The correlation coefficient was analysed for each calibration curve. The precision was defined as the coefficient of variation (CV), which was determined for each QC and had to be less than  $\pm 15\%$ . The lower limit of quantification (LLOQ) was defined as the calibration standard that gave a signal intensity of at least ten times the standard deviation recorded for sample blanks.

## **2.6. Analysis of clinical trial samples**

To confirm its suitability for clinical samples, the method developed here was used to measure elements in whole blood, hair and lung samples from 25 patients participating in a clinical trial (designed to assess the role of trace elements in lung cancer; NCT01949181).

### 157 3. RESULTS AND DISCUSSION

#### 158 3.1. Sample preparation

159 A variety of vessels and reagent mixtures were tested for microwave mineralization. Disposable  
160 borosilicate glassware contaminated samples with several elements, whereas quartz tubes provided  
161 reproducible results and low levels of contamination (results not shown). The composition of the  
162 mineralization mixture was also optimized by comparing 100, 200 or 400  $\mu\text{L}$   $\text{HNO}_3$  in the presence  
163 of absence of 100 or 200  $\mu\text{L}$  of  $\text{H}_2\text{O}_2$  for the mineralization of 200  $\mu\text{L}$  of sample matrix. The  
164 composition with 200  $\mu\text{L}$   $\text{HNO}_3$  and 200  $\mu\text{L}$   $\text{H}_2\text{O}_2$  yielded the most complete digestion (with the  
165 absence of particulate matter and a sufficient amount of sample) and so was used for the subsequent  
166 experiments. This digestion method was found to be appropriate for all samples: whole blood,  
167 urine, hair, or lung tissue. In contrast to conventional dilution methods, the microwave  
168 mineralization method destroys organic molecules in the matrix; this avoids the formation of  
169 deposits on the cones, reduces fouling of the instrument, and therefore increases the sensitivity.

170

#### 171 3.2. ICP-MS analysis

172 Most elements were detected in low-resolution mode. However, polyatomic or isobaric  
173 interferences (due to the environment or the sample preparation) occurred for some other elements.  
174 Hence, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn and Tl had to be detected in medium-resolution mode, and  
175 Ge, As, Se and Pd had to be detected in high-resolution mode [6]. Although a higher resolution  
176 improved the method's specificity, the transmission was about 10% in medium-resolution mode and  
177 1.5% in high-resolution; this decreased the sensitivity. However, our method was sensitive enough  
178 to detect all the elements at the required concentrations.

179 We also optimized the number of runs and passes, which therefore modified the sample volume and  
180 the sensitivity. With our final acquisition parameters (2 runs, 2 passes, and the sample parameters

described in Supplementary Table 2), the total run time was 3.8 min per sample, and the sample volume was 2 mL.

### 3.3. Validation of the method

The LLOQ and calibration curve were selected to cover the range of concentrations described in human whole blood, urine or hair samples [3, 7, 13-16]. The LLOQ and ULOQ for each element are given in Table 1. Some of the elements analyzed here (such as U, Ru and Hf) are not at all abundant in human samples (i.e. pM concentrations), while others (such as Cu and Zn) are quite abundant ( $\mu$ M concentrations). Hence, the dynamic range was different for each element (from 1.3- to 7.0-log), with LLOQ ranging from 0.1 pM (Hf) to 10  $\mu$ M (Zn). The regression was linear for all elements other than  $^{205}\text{Tl}$ , for which quadratic regression was used. The correlation coefficient for calibration curves (analyzed on 6 different days) ranged from 0.9963 to 0.9999. For each element, the LLOQ, ULOQ, number of calibration standards, and the calibration curve's slope, y-intercept and correlation coefficient are shown in Table 1.

The measured concentrations and precision for the intraday and interday analysis of external QC samples (whole blood, urine and hair) and internal QC samples are detailed in Tables 2-5. The intraday, interday or total precision was always below 15%. The method developed here was therefore highly precise for the determination of all 38 tested elements over a wide range of concentrations and in all matrices.

### 3.4. Analysis of clinical trial samples

The results for samples from 25 clinical trial participants are shown in the Figure. The method was suitable for the analysis of clinical samples of whole blood, hair or lung tissue.

#### 4. CONCLUSION

Here, we describe a method for the quantification of metals and metalloids in human samples of whole blood, urine, hair and tissues. The method has a number of advantages over previously described methods: the simultaneous analysis of 38 elements, microwave mineralization, high sensitivity, high precision, and a broad dynamic range that can be customized for each element. Furthermore, the method was found to be suitable for the analysis of human samples from clinical trial participants over the whole concentration range reported in these matrices.

#### 5. ACKNOWLEDGEMENTS

None

#### 6. DISCLOSURE OF CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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225 **8. TABLES**

226

**Table 1:** Limits of quantification and characteristics of the calibration curve for each element ( $n = 6$ , values are quoted as the mean  $\pm$  standard deviation).

Element	LLOQ ( $\mu\text{M}$ )	ULOQ ( $\mu\text{M}$ )	Range of the calibration curve (Log)	Number of calibration standards	Slope of the calibration curve	y-intercept of the calibration curve	Correlation coefficient for the calibration curve
Ag	0.015	10	2.8	10	$0.92 \pm 0.09$	$0.010 \pm 0.015$	$0.9994 \pm 0.0007$
As	0.01	1	2.0	7	$0.09 \pm 0.01$	$-0.0015 \pm 0.0033$	$0.9987 \pm 0.0016$
Au	0.01	1	2.0	10	$0.72 \pm 0.05$	$0.0014 \pm 0.0034$	$0.9972 \pm 0.0028$
Ba	0.002	5	3.4	8	$0.47 \pm 0.03$	$-0.0032 \pm 0.0103$	$0.9987 \pm 0.0009$
Be	0.01	0.5	1.7	7	$0.01 \pm 0.0008$	$-0.000005 \pm 0.00001$	$0.9990 \pm 0.0013$
Bi	0.004	1	2.4	8	$4.2 \pm 0.5$	$0.0016 \pm 0.017$	$0.9988 \pm 0.0023$
Cd	0.005	10	3.3	11	$0.17 \pm 0.01$	$-0.0036 \pm 0.0026$	$0.9995 \pm 0.0005$
Ce	0.0002	1	3.7	9	$3.1 \pm 0.3$	$0.00035 \pm 0.0009$	$0.9998 \pm 0.0003$
Co	0.001	20	4.3	12	$3.0 \pm 1.0$	$0.12 \pm 0.11$	$0.9993 \pm 0.0005$
Cr	0.02	10	2.7	8	$2.3 \pm 0.8$	$0.025 \pm 0.023$	$0.9999 \pm 0.0002$
Cs	0.002	1	2.7	8	$3.16 \pm 0.17$	$0.0052 \pm 0.0081$	$0.9996 \pm 0.0005$
Cu	5	200	1.6	15	$2.0 \pm 0.7$	$0.058 \pm 1.89$	$0.9986 \pm 0.0011$
Fe	1	500	2.7	15	$3.1 \pm 1.1$	$3.1 \pm 2.0$	$0.9997 \pm 0.0002$
Ge	0.01	1	2.0	7	$0.21 \pm 0.02$	$-0.0011 \pm 0.0012$	$0.9991 \pm 0.0005$
Hf	0.0000001	1	7.0	15	$1.0 \pm 0.1$	$-0.0052 \pm 0.0032$	$0.9983 \pm 0.0012$
Hg	0.025	10	2.6	11	$0.2 \pm 0.01$	$0.0020 \pm 0.0026$	$0.9996 \pm 0.0003$
La	0.00005	1	4.3	11	$32.5 \pm 3.0$	$-0.0089 \pm 0.0030$	$0.9998 \pm 0.0002$
Mn	0.05	2	1.6	10	$3.5 \pm 1.2$	$0.0041 \pm 0.018$	$0.9996 \pm 0.0002$
Mo	0.005	1.5	2.5	11	$0.24 \pm 0.02$	$-0.0007 \pm 0.0002$	$0.9994 \pm 0.0002$
Ni	0.05	50	3.0	15	$0.76 \pm 0.27$	$0.041 \pm 0.041$	$0.9998 \pm 0.0001$
Pb	0.025	5	2.3	7	$3.0 \pm 0.7$	$-0.038 \pm 0.096$	$0.9991 \pm 0.0010$
Pd	0.005	0.5	2.0	7	$0.25 \pm 0.04$	$-0.00062 \pm 0.00053$	$0.9963 \pm 0.0029$

Pt	0.001	0.1	2.0	10	$0.76 \pm 0.02$	$-0.00006 \pm 0.0002$	$0.9997 \pm 0.0002$
Rb	0.1	50	2.7	10	$1.2 \pm 0.1$	$0.85 \pm 0.42$	$0.9996 \pm 0.0018$
Ru	0.000001	0.01	4.0	13	$0.40 \pm 0.03$	$0.00002 \pm 0.000007$	$0.9994 \pm 0.0010$
Sb	0.00001	0.1	4.0	10	$0.52 \pm 0.05$	$-0.0001 \pm 0.0005$	$0.9975 \pm 0.0011$
Se	0.1	10	2.0	11	$0.02 \pm 0.003$	$-0.021 \pm 0.029$	$0.9989 \pm 0.0010$
Sn	0.005	1	2.3	11	$0.70 \pm 0.04$	$-0.0019 \pm 0.0005$	$0.9994 \pm 0.0004$
Sr	0.1	10	2.0	7	$1.79 \pm 0.11$	$0.012 \pm 0.046$	$0.9997 \pm 0.0002$
Te	0.001	0.05	1.7	7	$0.03 \pm 0.003$	$-0.000004 \pm 0.000009$	$0.9991 \pm 0.0008$
Th	0.00025	0.01	1.6	7	$3.9 \pm 0.3$	$-0.00004 \pm 0.0001$	$0.9981 \pm 0.0012$
Ti	0.038	10	2.4	7	$0.17 \pm 0.003$	$0.0013 \pm 0.0038$	$0.9998 \pm 0.0002$
Tl	0.00025	0.05	2.3	7		Quadratic regression	
U	0.000001	0.001	3.0	15	$49.6 \pm 3.3$	$-0.00002 \pm 0.00008$	$0.9995 \pm 0.0003$
V	0.02	1.5	1.9	9	$2.2 \pm 0.8$	$-0.026 \pm 0.097$	$0.9996 \pm 0.0003$
W	0.0004	1	3.4	8	$1.0 \pm 0.2$	$-0.00007 \pm 0.0019$	$0.9999 \pm 0.0001$
Zn	10	200	1.3	7	$0.27 \pm 0.10$	$0.066 \pm 0.20$	$0.9990 \pm 0.0007$
Zr	0.00001	0.1	4.0	15	$0.90 \pm 0.06$	$-0.0013 \pm 0.0019$	$0.9968 \pm 0.0019$

**Table 2:** Validation data for whole blood QC samples. Measured concentrations are presented for three different days as the median [range] ( $\mu\text{M}$ ) from six replicate samples. The values of the CVs correspond to the intraday, interday and total CVs, respectively.

Blood level 1: QM-B-Q1505				Blood level 2: QM-B-Q1506		
	Theoretical concentration	Measured concentration	CV (%)	Theoretical concentration	Measured concentration	CV (%)
Ag	0.022	0.023 [0.022-0.024]	5.1	0.061	0.062 [0.057-0.065]	6.9
		0.024 [0.023-0.025]	14.9		0.063 [0.062-0.078]	7.9
		0.022 [0.019-0.023]	7.1		0.063 [0.058-0.066]	7.0
As	0.036	0.044 [0.037-0.047]	8.8	0.21	0.24 [0.20-0.29]	12.2
		0.044 [0.037-0.050]	7.4		0.23 [0.21-0.25]	7.9
		0.041 [0.038-0.042]	8.7		0.24 [0.21-0.27]	11.8
Ba	0.026	0.048 [0.046-0.049]	6.5	0.058	0.076 [0.075-0.079]	2.6
		0.042 [0.040-0.048]	13.6		0.082 [0.078-0.085]	9.4
		0.043 [0.041-0.049]	7.7		0.078 [0.077-0.080]	4.1
Be	0.30	0.45 [0.44-0.48]	4.6	1.9	2.8 [2.7-2.9]	4.2
		0.42 [0.38-0.45]	13.0		2.8 [2.6-2.8]	7.2
		0.42 [0.39-0.43]	6.3		2.7 [2.3-2.8]	4.6
Bi	0.013	0.013 [0.011-0.016]	9.3	0.034	0.035 [0.026-0.039]	14.4
		0.014 [0.014-0.015]	14.2		0.038 [0.035-0.044]	14.5
		0.013 [0.012-0.014]	10.0		0.035 [0.030-0.047]	14.4
Cd	0.053	0.061 [0.057-0.066]	5.7	0.12	0.13 [0.13-0.14]	4.8
		0.061 [0.052-0.066]	9.3		0.13 [0.12-0.14]	4.5
		0.057 [0.055-0.058]	6.3		0.13 [0.12-0.14]	4.8
Co	0.019	0.018 [0.017-0.019]	6.9	0.035	0.035 [0.033-0.037]	6.3
		0.021 [0.018-0.022]	14.6		0.032 [0.031-0.034]	11.0
		0.020 [0.017-0.022]	8.3		0.034 [0.030-0.039]	7.0

Cr	0.096	0.090 [0.066-0.102]	14.4	0.11	0.10 [0.09-0.10]	7.8
		0.094 [0.076-0.106]	12.0		0.11 [0.10-0.12]	14.2
		0.086 [0.079-0.108]	14.1		0.10 [0.10-0.12]	8.9
Cu	12.8	12.2 [11.8-12.7]	9.5	47.8	40.0 [38.2-40.9]	2.6
		13.1 [8.7-13.8]	15.0		39.3 [38.1-39.8]	2.6
		11.0 [10.8-11.3]	10.3		40.2 [38.2-41.3]	2.6
Hg	0.030	0.038 [0.036-0.041]	3.7	0.008	0.010 [0.009-0.011]	12.1
		0.036 [0.035-0.037]	9.3		0.010 [0.009-0.011]	0.9
		0.039 [0.038-0.039]	4.8		0.010 [0.008-0.012]	11.0
Mn	0.28	0.28 [0.26-0.30]	6.5	0.41	0.40 [0.38-0.43]	4.5
		0.27 [0.26-0.30]	6.0		0.39 [0.37-0.41]	6.4
		0.26 [0.25-0.31]	6.4		0.41 [0.37-0.44]	4.8
Mo	0.031	0.075 [0.056-0.086]	12.3	0.051	0.090 [0.071-0.093]	12.6
		0.076 [0.067-0.079]	14.7		0.077 [0.062-0.093]	13.8
		0.063 [0.056-0.082]	12.7		0.086 [0.065-0.089]	12.8
Ni	<LLOQ	NA	NA	0.18	0.15 [0.14-0.22]	11.9
					0.16 [0.13-0.17]	10.5
					0.17 [0.17-0.18]	11.7
Pb	1.1	1.0 [0.9-1.1]	6.3	2.4	2.1 [1.9-2.3]	4.8
		1.0 [1.0-1.0]	3.6		2.1 [2.0-2.2]	3.2
		1.0 [0.9-1.0]	6.1		2.0 [1.9-2.2]	4.6
Pt	0.0021	0.0022 [0.0019-0.0023]	9.4	0.012	0.014 [0.013-0.015]	3.6
		0.0020 [0.0019-0.0026]	12.7		0.014 [0.013-0.014]	5.2
		0.0020 [0.0018-0.0020]	9.9		0.013 [0.013-0.014]	3.9
Sb	0.029	0.033 [0.031-0.036]	9.7	0.11	0.13 [0.12-0.13]	2.0
		0.035 [0.023-0.037]	6.5		0.12 [0.12-0.13]	6.8
		0.032 [0.031-0.033]	9.3		0.13 [0.12-0.13]	3.0

Se	2.2	2.2 [2.1-2.5]	10.2	2.9	3.1 [2.7-3.5]	11.3
		2.5 [2.1-2.7]	12.5		2.7 [2.5-3.4]	13.6
		2.7 [2.2-2.8]	10.5		3.1 [2.7-3.5]	11.6
Sn	0.029	0.032 [0.027-0.037]	14.9	0.17	0.15 [0.14-0.16]	6.3
		0.032 [0.021-0.038]	6.9		0.16 [0.13-0.18]	4.5
		0.032 [0.029-0.038]	14.2		0.16 [0.15-0.17]	6.1
Sr	1.0	1.2 [1.1-1.2]	3.0	3.2	3.6 [3.4-3.8]	3.2
		1.1 [1.1-1.2]	4.1		3.5 [3.4-3.6]	5.0
		1.2 [1.1-1.2]	3.2		3.5 [3.3-3.6]	3.5
Te	0.020	0.021 [0.020-0.022]	6.4	0.062	0.064 [0.059-0.066]	3.8
		0.021 [0.020-0.022]	6.3		0.066 [0.064-0.069]	11.5
		0.019 [0.019-0.023]	6.4		0.069 [0.066-0.073]	5.3
Th	0.0029	0.0032 [0.0030-0.0035]	3.7	0.0086	0.0101 [0.0091-0.0103]	3.4
		0.0033 [0.0032-0.0033]	1.6		0.0100 [0.0098-0.0102]	2.3
		0.0033 [0.0032-0.0033]	3.5		0.0100 [0.0096-0.0102]	3.3
Tl	0.017	0.016 [0.016-0.017]	2.7	0.038	0.034 [0.031-0.036]	3.9
		0.015 [0.015-0.016]	8.3		0.036 [0.035-0.038]	7.8
		0.017 [0.016-0.017]	3.8		0.036 [0.034-0.036]	4.5
U	0.0020	0.0020 [0.0019-0.0021]	5.8	0.0035	0.0035 [0.0034-0.0039]	4.7
		0.0018 [0.0017-0.0018]	12.8		0.0038 [0.0035-0.0039]	13.9
		0.0019 [0.0018-0.0023]	7.0		0.0034 [0.0033-0.0035]	6.6
V	0.024	0.036 [0.030-0.040]	6.4	0.052	0.059 [0.055-0.064]	5.3
		0.038 [0.037-0.041]	10.4		0.058 [0.054-0.060]	4.9
		0.039 [0.036-0.040]	7.0		0.060 [0.055-0.064]	5.3
Zn	97	112 [106-117]	4.8	166	176 [156-182]	5.2
		113 [101-118]	11.5		178 [170-189]	7.8
		101 [99-107]	6.1		186 [165-193]	5.6

**Table 3:** Validation data for urine QC samples. The measured concentrations are presented for the three different days as the median [range] ( $\mu\text{M}$ ) from 6 replicate samples. The values of the CVs correspond to the intraday, interday and total CVs, respectively.

Urine level 1: QM-U-Q1503				Urine level 2: QM-U-Q1504		
	Theoretical concentration	Measured concentration	CV (%)	Theoretical concentration	Measured concentration	CV (%)
Ag	0.051	0.045 [0.040-0.047] 0.049 [0.047-0.051] 0.047 [0.040-0.049]	5.8 12.8 7.1	< LLOQ	NA	NA
As	1.3	1.4 [1.2-1.5] 1.5 [1.4-1.5] 1.4 [1.3-1.6]	7.7 8.8 7.8	0.67	0.77 [0.72-0.81] 0.74 [0.64-0.84] 0.67 [0.63-0.76]	9.0 14.5 9.9
Ba	0.031	0.047 [0.045-0.051] 0.046 [0.042-0.048] 0.053 [0.046-0.054]	6.3 12.6 7.4	0.012	0.038 [0.037-0.039] 0.033 [0.029-0.039] 0.031 [0.030-0.046]	13.8 14.6 13.9
Be	0.30	0.40 [0.39-0.44] 0.40 [0.39-0.41] 0.39 [0.37-0.44]	4.9 4.5 4.8	1.4	2.0 [1.8-2.0] 2.0 [1.8-2.1] 1.9 [1.7-2.0]	4.6 9.2 5.4
Bi	0.12	0.11 [0.10-0.13] 0.12 [0.09-0.13] 0.10 [0.09-0.14]	14.7 11.8 14.3	0.025	0.031 [0.027-0.031] 0.026 [0.025-0.036] 0.031 [0.024-0.031]	11.4 5.7 10.9
Cd	0.14	0.16 [0.15-0.16] 0.15 [0.15-0.16] 0.15 [0.15-0.16]	2.4 2.7 2.5	0.026	0.022 [0.021-0.028] 0.023 [0.022-0.031] 0.027 [0.019-0.029]	14.9 10.8 14.4
Co	0.14	0.15 [0.13-0.16] 0.14 [0.13-0.15] 0.15 [0.15-0.16]	5.0 11.4 6.1	0.035	0.035 [0.034-0.042] 0.039 [0.038-0.043] 0.039 [0.035-0.040]	6.2 10.3 6.8

Cr	0.093	0.095 [0.081-0.106]	14.6	0.41	0.46 [0.44-0.47]	6.5
		0.087 [0.083-0.126]	13.8		0.44 [0.38-0.49]	14.7
		0.105 [0.079-0.118]	14.5		0.41 [0.39-0.43]	8.0
Cu	0.14	0.13 [0.13-0.14]	8.0	17.0	16.3 [16.1-16.6]	3.7
		0.14 [0.13-0.17]	14.9		17.6 [16.2-18.9]	10.6
		0.15 [0.14-0.18]	9.3		16.2 [15.9-17.3]	5.1
Hg	0.066	0.039 [0.031-0.040]	14.9	0.17	0.15 [0.15-0.17]	4.6
		0.030 [0.027-0.042]	14.7		0.15 [0.14-0.16]	6.4
		0.034 [0.028-0.041]	14.9		0.15 [0.15-0.17]	4.9
Mn	0.099	0.098 [0.084-0.110]	6.8	0.049	0.049 [0.045-0.054]	7.1
		0.096 [0.093-0.103]	12.9		0.054 [0.045-0.059]	10.0
		0.089 [0.085-0.093]	7.8		0.053 [0.051-0.054]	7.5
Mo	0.63	0.72 [0.67-0.76]	4.8	2.9	3.3 [3.2-3.4]	3.8
		0.70 [0.63-0.73]	6.2		3.3 [3.1-3.5]	9.3
		0.68 [0.67-0.71]	5.0		3.1 [2.9-3.3]	4.8
Ni	0.27	0.27 [0.23-0.36]	12.2	0.18	0.14 [0.13-0.20]	11.5
		0.29 [0.26-0.37]	9.5		0.16 [0.13-0.17]	3.7
		0.31 [0.29-0.32]	11.9		0.16 [0.15-0.16]	10.8
Pb	0.34	0.31 [0.30-0.32]	7.0	0.80	0.64 [0.61-0.68]	3.6
		0.30 [0.24-0.33]	5.0		0.67 [0.65-0.71]	9.3
		0.30 [0.29-0.34]	6.8		0.63 [0.60-0.65]	4.6
Pt	0.0056	0.0051 [0.0050-0.0054]	4.9	0.010	0.009 [0.008-0.009]	4.3
		0.0056 [0.0050-0.0057]	10.2		0.010 [0.009-0.010]	14.9
		0.0055 [0.0053-0.0060]	5.8		0.010 [0.010-0.011]	6.5
Sb	0.015	0.016 [0.014-0.016]	6.5	0.056	0.063 [0.060-0.066]	6.5
		0.017 [0.016-0.019]	14.3		0.057 [0.050-0.060]	14.9
		0.017 [0.016-0.019]	7.8		0.057 [0.056-0.065]	8.0

Se	3.9	4.6 [4.1-5.3] 4.2 [3.9-4.5] 4.2 [4.0-4.6]	9.0 13.3 9.6	1.5	1.8 [1.6-2.0] 1.8 [1.2-2.1] 1.6 [1.5-1.8]	13.4 14.8 13.6
Sn	0.21	0.22 [0.20-0.24] 0.24 [0.24-0.25] 0.25 [0.24-0.25]	3.5 13.7 5.9	0.020	0.018 [0.016-0.020] 0.017 [0.016-0.019] 0.017 [0.016-0.020]	9.0 5.2 8.7
Te	0.21	0.21 [0.19-0.22] 0.22 [0.21-0.24] 0.21 [0.20-0.22]	4.5 9.7 5.4	0.032	0.032 [0.031-0.034] 0.032 [0.029-0.035] 0.029 [0.028-0.033]	6.1 9.8 6.6
Th	0.00040	0.00038 [0.00036-0.00042] 0.00042 [0.0004-0.00043] 0.00037 [0.00033-0.00042]	6.5 14 7.9	0.0013	0.0015 [0.0015-0.0016] 0.0015 [0.0014-0.0017] 0.00145 [0.0014-0.0015]	4.8 6.9 5.1
Tl	0.12	0.11 [0.10-0.11] 0.11 [0.10-0.12] 0.11 [0.11-0.12]	5.6 8.3 6.0	0.048	0.041 [0.040-0.042] 0.044 [0.041-0.046] 0.041 [0.040-0.044]	3.6 7.5 4.2
U	0.0044	0.0037 [0.0036-0.0038] 0.0039 [0.0036-0.0042] 0.0037 [0.0036-0.0038]	4.1 6.5 4.4	0.0020	0.0017 [0.0016-0.0020] 0.0018 [0.0016-0.0019] 0.0017 [0.0016-0.0019]	7.3 4.2 7.0
V	0.35	0.41 [0.37-0.42] 0.37 [0.37-0.39] 0.36 [0.35-0.37]	3.4 12.5 5.5	0.12	0.13 [0.13-0.14] 0.13 [0.12-0.15] 0.13 [0.12-0.14]	6.4 3.6 6.1
Zn	8.8	8.9 [8.5-11.2] 9.2 [8.0-10.0] 9.4 [8.3-10.9]	11.8 6.4 11.3	16.8	18.8 [15.6-22.0] 19.3 [17.4-23.0] 18.9 [17.2-20.0]	12.5 4.0 11.8

**Table 4:** Validation data for hair QC samples. The measured concentrations are presented for the three different days as the median [range] ( $\mu\text{mol/g}$ ) from 6 replicate samples. The values of the CVs correspond to the intraday, interday and total CVs, respectively.

Hair level 1: QM-H-Q1315				Hair level 2: QM-H-Q1406		
	Theoretical concentration	Measured concentration	CV (%)	Theoretical concentration	Measured concentration	CV (%)
Ag	0.014	0.016 [0.016-0.017]	5.0	0.0029	0.0032 [0.0032-0.0033]	1.9
		0.016 [0.014-0.017]	5.2		0.0033 [0.0032-0.0034]	11.3
		0.016 [0.015-0.016]	5.1		0.0030 [0.0030-0.0031]	4.3
As	0.0081	0.0088 [0.0085-0.0098]	7.0	0.0080	0.0090 [0.0084-0.0091]	2.9
		0.0089 [0.0085-0.0106]	8.0		0.0080 [0.0076-0.0084]	14.6
		0.0085 [0.0082-0.0093]	7.1		0.0080 [0.0078-0.0082]	5.7
Ba	0.13	0.14 [0.14-0.14]	4.3	0.020	0.020 [0.019-0.021]	3.6
		0.13 [0.12-0.14]	14.5		0.019 [0.019-0.02]	5.2
		0.12 [0.12-0.13]	6.4		0.002 [0.019-0.021]	3.8
Be	0.045	0.054 [0.043-0.056]	8.7	0.027	0.031 [0.029-0.033]	3.6
		0.049 [0.047-0.055]	9.8		0.027 [0.027-0.028]	13.8
		0.047 [0.044-0.049]	8.8		0.029 [0.028-0.031]	5.9
Bi	0.0078	0.0087 [0.0086-0.0090]	3.1	0.0029	0.0032 [0.0031-0.0035]	4.2
		0.0080 [0.0077-0.0084]	14.6		0.0029 [0.0028-0.0031]	12.0
		0.0078 [0.0076-0.0082]	6.0		0.0031 [0.0030-0.0032]	5.7
Cd	0.018	0.019 [0.019-0.020]	3.9	0.014	0.014 [0.014-0.015]	3.0
		0.018 [0.017-0.002]	11.9		0.014 [0.014-0.015]	3.5
		0.017 [0.017-0.019]	5.5		0.014 [0.014-0.015]	3.1
Co	0.046	0.039 [0.038-0.041]	4.9	0.042	0.037 [0.036-0.038]	2.1
		0.040 [0.039-0.040]	1.5		0.037 [0.036-0.038]	0.8
		0.039 [0.036-0.045]	4.6		0.037 [0.035-0.038]	2.0

Cr	0.0087	0.0095 [0.0077-0.0096]	7.1	0.037	0.035 [0.034-0.036]	4.9
		0.0089 [0.0085-0.0094]	13.0		0.034 [0.029-0.035]	10.9
		0.0097 [0.0090-0.0104]	8.0		0.035 [0.035-0.036]	6.0
Cu	0.29	0.25 [0.24-0.26]	3.2	0.94	0.80 [0.79-0.82]	1.1
		0.25 [0.24-0.26]	3.1		0.80 [0.79-0.80]	0.9
		0.26 [0.24-0.26]	3.2		0.79 [0.79-0.81]	1.1
Hg	0.010	0.012 [0.011-0.013]	4.3	0.019	0.020 [0.020-0.021]	2.5
		0.011 [0.010-0.011]	13.8		0.020 [0.020-0.021]	3.8
		0.010 [0.010-0.011]	6.2		0.021 [0.020-0.022]	2.7
Mn	0.084	0.072 [0.069-0.073]	4.3	0.10	0.085 [0.084-0.086]	1.2
		0.074 [0.071-0.078]	5.6		0.085 [0.083-0.086]	1.3
		0.070 [0.067-0.078]	4.4		0.085 [0.085-0.087]	1.2
Mo	0.0087	0.0100 [0.0100-0.0110]	5.3	0.0038	0.0037 [0.0035-0.0039]	8.4
		0.0093 [0.0085-0.0099]	13.9		0.0036 [0.0043-0.0041]	13.8
		0.0091 [0.0084-0.0094]	6.9		0.0041 [0.0035-0.0046]	9.2
Ni	0.022	0.020 [0.018-0.02]	3.1	0.12	0.111 [0.109-0.114]	2.0
		0.018 [0.018-0.02]	4.0		0.111 [0.108-0.112]	1.9
		0.019 [0.019-0.02]	3.2		0.111 [0.105-0.112]	2.0
Pb	0.0074	0.0080 [0.0079-0.0082]	3.5	0.015	0.015 [0.014-0.015]	2.5
		0.0075 [0.0071-0.0080]	9.2		0.014 [0.013-0.014]	7.0
		0.0076 [0.0074-0.0082]	4.6		0.015 [0.014-0.015]	3.3
Pt	0.000087	0.000096 [0.000094-0.000098]	4.9	0.0012	0.0012 [0.0011-0.0012]	2.0
		0.000087 [0.000080-0.000093]	14.6		0.0011 [0.0011-0.0012]	8.6
		0.000087 [0.000082-0.000091]	6.8		0.0012 [0.0012-0.0013]	3.5
Sb	0.0076	0.0089 [0.0079-0.0092]	5.9	0.010	0.011 [0.010-0.011]	5.1
		0.0085 [0.0078-0.0093]	7.0		0.010 [0.010-0.011]	7.8
		0.0081 [0.0080-0.0088]	6.0		0.010 [0.010-0.011]	5.5

Se	0.038	0.041 [0.039-0.045]	5.6	0.013	0.012 [0.012-0.015]	5.7
		0.041 [0.039-0.046]	5.5		0.012 [0.012-0.012]	14.8
		0.044 [0.043-0.046]	5.6		0.014 [0.013-0.014]	7.5
Sn	0.050	0.069 [0.067-0.072]	4.7	0.052	0.073 [0.069-0.077]	3.2
		0.066 [0.062-0.069]	11.8		0.071 [0.070-0.073]	5.9
		0.063 [0.059-0.068]	6.0		0.074 [0.072-0.078]	3.6
Te	0.0042	0.0048 [0.0047-0.0048]	4.9	0.0055	0.0062 [0.0061-0.0063]	2.3
		0.0045 [0.0040-0.0048]	14.4		0.0058 [0.0056-0.0061]	10.5
		0.0041 [0.0041-0.0046]	6.7		0.0057 [0.0056-0.0060]	4.2
Th	0.011	0.017 [0.016-0.018]	5.4	0.023	0.029 [0.027-0.031]	2.8
		0.016 [0.015-0.017]	13.6		0.030 [0.030-0.031]	7.8
		0.016 [0.015-0.017]	6.9		0.029 [0.028-0.029]	3.7
Tl	0.0011	0.0012 [0.0011-0.0012]	4.4	0.00045	0.00049 [0.00047-0.00049]	1.9
		0.0011 [0.0010-0.0012]	13.6		0.00047 [0.00046-0.00048]	5.1
		0.0011 [0.0010-0.0011]	6.4		0.00047 [0.00046-0.00047]	2.5
U	0.0021	0.0025 [0.0023-0.0025]	5.0	0.0015	0.0016 [0.0016-0.0017]	2.3
		0.0024 [0.0023-0.0026]	9.0		0.0016 [0.0016-0.0017]	0.3
		0.0023 [0.0021-0.0025]	5.6		0.0016 [0.0016-0.0017]	2.1
V	0.024	0.020 [0.020-0.021]	4.5	0.014	0.012 [0.012-0.013]	5.4
		0.020 [0.020-0.022]	1.6		0.012 [0.011-0.014]	1.1
		0.019 [0.019-0.022]	4.2		0.012 [0.012-0.012]	5.1
Zn	3.4	3.7 [3.6-3.9]	2.8	4.9	5.0 [4.9-5.1]	3.3
		3.8 [3.6-4.0]	3.5		4.9 [4.8-5.2]	5.5
		3.7 [3.6-3.7]	2.9		5.2 [4.8-5.4]	3.6

**Table 5:** Validation data for internal QC samples. The measured concentrations are presented for the three different days as the median [range] ( $\mu\text{M}$ ) from 6 replicate samples. The values of the CVs correspond to the intraday, interday and total CVs, respectively.

Internal QC level 1				Internal QC level 2			Internal QC level 3		
	Theoretical concentration	Measured concentration	CV (%)	Theoretical concentration	Measured concentration	CV (%)	Theoretical concentration	Measured concentration	CV (%)
Ag	0.75	0.47 [0.47-0.48]	1.7	2.5	2.4 [2.3-2.4]	2.0	7.5	7.8 [7.3-8.8]	10.9
		0.45 [0.44-0.47]	6.1		2.6 [2.5-2.6]	14		7.9 [6.2-8.2]	10.7
		0.46 [0.45-0.47]	2.7		2.7 [2.6-2.7]	5.3		7.1 [6.0-7.9]	10.9
As	0.075	0.083 [0.077-0.095]	7.8	0.25	0.29 [0.26-0.30]	11.5	0.75	0.86 [0.79-0.93]	9.9
		0.086 [0.078-0.092]	14.6		0.31 [0.22-0.33]	1.8		0.90 [0.71-1.00]	1.1
		0.075 [0.069-0.087]	9.0		0.29 [0.25-0.31]	10.8		0.87 [0.76-0.91]	9.2
Au	0.075	0.073 [0.068-0.075]	4.0	0.25	0.23 [0.20-0.30]	9.9	0.75	0.80 [0.78-0.84]	3.9
		0.068 [0.067-0.071]	10.5		0.25 [0.24-0.26]	8.3		0.79 [0.77-0.80]	11.5
		0.069 [0.060-0.070]	5.2		0.26 [0.22-0.26]	9.7		0.72 [0.68-0.80]	5.5
Ba	0.38	0.40 [0.38-0.41]	2.8	1.3	1.3 [1.2-1.3]	3.2	3.8	3.9 [3.8-4.0]	4.0
		0.41 [0.40-0.42]	5.3		1.3 [1.2-1.3]	4.0		3.9 [3.6-4.2]	5.6
		0.40 [0.39-0.40]	3.2		1.3 [1.2-1.3]	3.3		4.0 [3.9-4.3]	4.2
Be	0.038	0.039 [0.036-0.041]	4.7	0.13	0.12 [0.11-0.13]	4.2	0.38	0.41 [0.38-0.44]	4.9
		0.041 [0.037-0.043]	12.5		0.12 [0.12-0.13]	14.0		0.39 [0.38-0.40]	9.8
		0.042 [0.042-0.046]	6.2		0.13 [0.13-0.13]	6.2		0.37 [0.35-0.40]	5.7
Bi	0.075	0.080 [0.079-0.083]	1.5	0.25	0.27 [0.26-0.27]	2.6	0.75	0.73 [0.72-0.75]	3.0
		0.078 [0.076-0.079]	6.6		0.26 [0.25-0.26]	9.6		0.73 [0.69-0.76]	8.4
		0.076 [0.075-0.078]	2.7		0.25 [0.23-0.25]	4.1		0.77 [0.76-0.80]	4.0
Cd	0.75	0.75 [0.72-0.77]	1.9	2.5	2.5 [2.3-2.5]	2.9	7.5	7.0 [6.8-7.2]	3.8
		0.74 [0.72-0.76]	5.5		2.4 [2.3-2.4]	5.0		7.0 [6.6-7.4]	4.6
		0.72 [0.71-0.73]	2.6		2.4 [2.2-2.4]	3.2		7.2 [6.9-7.5]	3.9

Ce	0.075	0.075 [0.074-0.077]	1.5	0.25	0.26 [0.25-0.27]	4.2	0.75	0.78 [0.73-0.83]	3.7
		0.077 [0.075-0.078]	2.1		0.26 [0.26-0.29]	8.1		0.79 [0.78-0.81]	3.1
		0.075 [0.074-0.077]	1.6		0.26 [0.24-0.26]	4.8		0.79 [0.76-0.83]	3.6
Co	1.5	1.6 [1.6-1.7]	1.8	5.0	5.6 [5.4-5.7]	2.4	15.0	16.3 [15.0-17.4]	4.2
		1.7 [1.7-1.8]	8.4		5.6 [5.6-5.8]	1.9		16.1 [15.5-16.9]	6.2
		1.7 [1.7-1.8]	3.3		5.7 [5.5-5.9]	2.3		16.9 [16.4-17.4]	4.5
Cr	0.75	0.72 [0.71-0.74]	2.1	2.5	2.4 [2.4-2.5]	2.4	7.5	7.3 [7.1-7.6]	4.1
		0.76 [0.73-0.78]	11.1		2.5 [2.5-2.6]	5.0		7.5 [6.9-8.0]	3.2
		0.78 [0.76-0.82]	4.3		2.6 [2.5-2.6]	2.8		7.4 [7.1-7.5]	4.0
Cs	0.075	0.087 [0.080-0.088]	3.7	0.25	0.29 [0.26-0.30]	3.4	0.75	0.82 [0.79-0.88]	3.1
		0.088 [0.080-0.090]	1.3		0.28 [0.28-0.29]	5.5		0.85 [0.84-0.87]	5.0
		0.085 [0.084-0.086]	3.5		0.28 [0.26-0.28]	3.7		0.86 [0.81-0.90]	3.4
Cu	15.0	15.8 [15.4-15.9]	1.9	50	53 [53-56]	2.3	150	158 [150-163]	4.0
		16.9 [16.4-17.6]	11.7		53 [52-55]	2.6		157 [143-165]	4.3
		17.1 [16.9-17.6]	4.4		53 [51-54]	2.4		160 [156-165]	4.1
Fe	37.5	39.0 [37.2-40.1]	2.2	125	130 [128-135]	2.2	375	366 [329-391]	5.2
		40.1 [39.1-41.8]	6.8		131 [130-138]	2.7		342 [316-360]	10.2
		41.1 [40.3-41.7]	3.1		133 [130-139]	2.2		365 [357-386]	6.1
Ge	0.075	0.082 [0.070-0.095]	7.6	0.25	0.27 [0.26-0.29]	4.3	0.75	0.84 [0.69-1.00]	9.9
		0.086 [0.080-0.090]	5.1		0.29 [0.28-0.29]	9.1		0.87 [0.69-0.97]	3.0
		0.082 [0.078-0.088]	7.2		0.29 [0.26-0.30]	5.1		0.86 [0.75-0.89]	9.3
Hf	0.075	0.092 [0.062-0.096]	9.5	0.25	0.29 [0.23-0.33]	12.8	0.75	0.82 [0.74-0.90]	5.4
		0.086 [0.080-0.091]	3.7		0.29 [0.22-0.29]	5.0		0.84 [0.75-0.86]	4.2
		0.084 [0.077-0.088]	9.0		0.29 [0.22-0.29]	12.2		0.85 [0.82-0.90]	5.3
Hg	0.75	0.87 [0.83-0.87]	1.6	2.5	2.9 [2.8-2.9]	1.2	7.5	7.4 [7.0-7.4]	4
		0.84 [0.82-0.85]	3.6		2.9 [2.8-2.9]	14.9		7.6 [7.0-8.0]	5.5
		0.85 [0.83-0.86]	2.0		2.6 [2.5-2.6]	5.2		7.5 [7.3-7.9]	4.2

La	0.075	0.069 [0.068-0.072]	1.6	0.25	0.24 [0.23-0.25]	3.1	0.75	0.73 [0.71-0.74]	4.1
		0.071 [0.068-0.072]	1.9		0.25 [0.24-0.26]	6.4		0.71 [0.67-0.76]	5.2
		0.070 [0.068-0.071]	1.7		0.24 [0.22-0.24]	3.7		0.75 [0.70-0.78]	4.2
Mn	0.15	0.17 [0.15-0.18]	6.1	0.50	0.58 [0.52-0.60]	4.5	1.5	1.7 [1.6-1.8]	2.7
		0.17 [0.16-0.18]	5.1		0.58 [0.52-0.60]	2.1		1.7 [1.7-1.8]	1.9
		0.17 [0.16-0.18]	6.0		0.57 [0.56-0.60]	4.3		1.7 [1.7-1.8]	2.6
Mo	0.11	0.11 [0.10-0.11]	3.7	0.38	0.35 [0.32-0.37]	3.7	1.1	1.1 [1.0-1.2]	4.5
		0.11 [0.11-0.12]	7.7		0.35 [0.34-0.36]	0.9		1.1 [1.0-1.1]	1.8
		0.11 [0.11-0.11]	4.4		0.35 [0.34-0.36]	3.5		1.1 [1.0-1.2]	4.3
Ni	3.8	3.7 [3.7-3.8]	1.6	12.5	12.6 [12.4-13.1]	2.5	37.5	36.4 [35.7-38.0]	3.9
		3.8 [3.7-3.9]	7.7		12.3 [12.2-12.9]	6.5		39.2 [36.1-41.4]	7.2
		4.0 [3.9-4.0]	3.0		13.1 [12.5-13.6]	3.2		38.5 [37.4-39.5]	4.4
Pb	0.38	0.38 [0.38-0.39]	1.5	1.3	1.2 [1.1-1.2]	2.6	3.8	3.4 [3.3-3.5]	3.5
		0.35 [0.34-0.36]	13.3		1.2 [1.1-1.2]	2.3		3.5 [3.3-3.7]	10.3
		0.35 [0.34-0.36]	4.8		1.2 [1.1-1.2]	2.5		3.2 [3.1-3.4]	4.8
Pd	0.033	0.028 [0.026-0.031]	6.7	0.11	0.10 [0.09-0.10]	6.0	0.38	0.32 [0.30-0.37]	9.6
		0.028 [0.026-0.030]	10.1		0.10 [0.09-0.10]	5.7		0.34 [0.29-0.38]	5.1
		0.030 [0.028-0.034]	7.2		0.10 [0.09-0.11]	6.0		0.31 [0.29-0.39]	9.2
Pt	0.0075	0.0085 [0.0082-0.0086]	1.8	0.025	0.029 [0.028-0.029]	2.2	0.075	0.083 [0.079-0.089]	3.5
		0.0086 [0.0083-0.0088]	2.5		0.029 [0.028-0.029]	3.5		0.083 [0.082-0.083]	1.3
		0.0086 [0.0085-0.0088]	1.9		0.028 [0.027-0.029]	2.4		0.083 [0.081-0.087]	3.3
Rb	3.8	4.0 [3.8-4.2]	2.7	12.5	14.3 [13.7-14.4]	2.9	37.5	35.0 [32.0-36.9]	4.9
		4.0 [3.8-4.1]	6.0		12.8 [12.5-13.4]	14.0		33.5 [32.3-34.4]	5.1
		4.2 [4.1-4.3]	3.3		14.5 [13.5-14.7]	5.5		33.8 [30.0-35.1]	4.9
Ru	0.00075	0.00082 [0.00081-0.00085]	2.3	0.0025	0.0024 [0.0024-0.0025]	3.2	0.0075	0.0077 [0.0073-0.0084]	4.0
		0.00076 [0.00072-0.00077]	14.8		0.0025 [0.0025-0.0026]	5.6		0.0080 [0.0077-0.008]	2.8
		0.00073 [0.00071-0.00076]	5.5		0.0025 [0.0023-0.0026]	3.6		0.0077 [0.0074-0.0081]	3.9

Se	0.75	0.94 [0.86-1.00]	4.2	2.5	2.9 [2.7-3.1]	4.4	7.5	9.1 [8.1-9.7]	5.5
		0.97 [0.92-1.01]	5.9		3.1 [2.8-3.1]	7.4		8.9 [8.6-9.6]	10.1
		0.93 [0.88-0.98]	4.4		2.9 [2.7-3.1]	4.9		8.4 [7.9-8.7]	6.3
Sr	0.75	0.78 [0.77-0.81]	1.7	2.5	2.7 [2.6-2.8]	3.5	7.5	8.4 [7.8-8.9]	4.0
		0.81 [0.79-0.83]	4.6		2.8 [2.7-2.9]	4.6		8.4 [8.3-8.6]	3.8
		0.81 [0.80-0.83]	2.2		2.8 [2.6-2.8]	3.6		8.1 [7.8-8.7]	3.9
Te	0.0038	0.0043 [0.0038-0.0047]	8.6	0.013	0.014 [0.013-0.016]	6.2	0.038	0.046 [0.038-0.047]	7.7
		0.0044 [0.0037-0.0045]	0.7		0.014 [0.013-0.015]	1.1		0.043 [0.037-0.045]	3.3
		0.0041 [0.0038-0.0049]	8.1		0.014 [0.013-0.015]	5.8		0.042 [0.041-0.045]	7.3
Th	0.00075	0.00081 [0.00077-0.00085]	2.9	0.0025	0.0029 [0.0025-0.0029]	5.4	0.0075	0.0078 [0.0077-0.0078]	3.6
		0.00074 [0.00073-0.00076]	14.3		0.0027 [0.0026-0.0027]	8.8		0.0080 [0.0075-0.0086]	5.3
		0.00073 [0.0007-0.00076]	5.6		0.0026 [0.0024-0.0028]	5.9		0.0076 [0.0075-0.0082]	3.9
Ti	0.75	0.74 [0.73-0.75]	2.0	2.5	2.5 [2.4-2.6]	3.0	7.5	7.3 [7.2-7.4]	3.5
		0.74 [0.73-0.76]	3.2		2.5 [2.4-2.5]	5.0		7.3 [6.8-7.8]	2.8
		0.72 [0.71-0.75]	2.1		2.4 [2.3-2.5]	3.3		7.4 [7.4-7.6]	3.4
Tl	0.0038	0.0038 [0.0036-0.0040]	3.4	0.013	0.013 [0.013-0.014]	3.8	0.038	0.042 [0.040-0.045]	4.3
		0.0043 [0.0042-0.0043]	15		0.015 [0.013-0.015]	9.1		0.043 [0.042-0.044]	2.8
		0.0042 [0.0039-0.0044]	6.2		0.014 [0.014-0.015]	4.8		0.043 [0.039-0.045]	4.1
U	0.000075	0.000073 [0.000066-0.000079]	6.5	0.00025	0.00027 [0.00027-0.00031]	5.2	0.00075	0.00078 [0.00073-0.00082]	3.8
		0.000070 [0.000066-0.000072]	9.9		0.00026 [0.00025-0.00028]	12.3		0.00078 [0.00078-0.00080]	11.8
		0.000076 [0.000068-0.000085]	7.0		0.00026 [0.00025-0.00027]	6.4		0.00085 [0.00081-0.00089]	5.4
V	0.11	0.12 [0.12-0.13]	4.1	0.38	0.38 [0.37-0.43]	4.2	1.1	1.2 [1.1-1.2]	4.2
		0.13 [0.12-0.13]	6.3		0.40 [0.39-0.41]	3.9		1.2 [1.1-1.3]	6.3
		0.13 [0.12-0.13]	4.4		0.41 [0.39-0.42]	4.2		1.1 [1.1-1.2]	4.5
W	0.075	0.078 [0.076-0.079]	1.6	0.25	0.26 [0.25-0.27]	2.1	0.75	0.71 [0.71-0.72]	3.2
		0.076 [0.075-0.078]	4.9		0.25 [0.24-0.25]	7.8		0.73 [0.68-0.76]	7.5
		0.075 [0.073-0.076]	2.2		0.25 [0.24-0.25]	3.3		0.76 [0.74-0.79]	3.9

				ICP-MS method for human samples					
Zn	15.0	13.6 [13.0-13.9]	2.3	50	47 [46-50]	3.1	150	144 [132-153]	4.4
		15.0 [14.7-15.6]	14.8		48 [48-51]	3.4		147 [137-153]	5.9
		15.0 [14.5-15.2]	5.5		48 [46-50]	3.2		147 [145-155]	4.6
Zr	0.0075	0.0085 [0.0079-0.0090]	10.0	0.025	0.038 [0.037-0.04]	3.3	0.075	0.076 [0.07-0.079]	7.0
		0.0091 [0.0071-0.0097]	1.7		0.038 [0.038-0.041]	2.0		0.078 [0.069-0.085]	8.6
		0.0090 [0.0075-0.0093]	9.4		0.039 [0.036-0.04]	3.2		0.080 [0.076-0.086]	7.2

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## 10. FIGURE LEGENDS

**Figure 1:** Concentrations of elements in (A) whole blood ( $\mu\text{M}$ ), (B) hair ( $\mu\text{mol/g}$ ) and (C) lung tissue ( $\mu\text{mol/g}$ ) samples from 25 participants in a lung cancer clinical trial. The whiskers indicate the range of values, and the horizontal line indicates the mean.



