

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

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4 Stanislas GRASSIN-DELYLE,<sup>a,b</sup> Marie MARTIN,<sup>a,c</sup> Ons HAMZAOUI,<sup>a</sup> Elodie LAMY<sup>a</sup>,  
5 Christophe JAYLE,<sup>e</sup> Edouard SAGE,<sup>f</sup> Isabelle ETTING,<sup>a,c</sup> Philippe DEVILLIER,<sup>b,d</sup> Jean-Claude  
6 ALVAREZ<sup>a,c</sup>

7

8 <sup>a</sup> Plateforme de spectrométrie de masse MasSpecLab, INSERM UMR 1173, UFR des Sciences de  
9 la Santé Simone Veil, Université Versailles Saint Quentin, Université Paris Saclay, Montigny le  
10 Bretonneux, France

11 <sup>b</sup> Département des maladies respiratoires, Hôpital Foch, Suresnes, France

12 <sup>c</sup> Laboratoire de toxicologie, Hôpital Raymond Poincaré, AP-HP, Garches, France

13 <sup>d</sup> Laboratoire de pharmacologie UPRES EA220, Université Versailles Saint Quentin, Université  
14 Paris Saclay, Hôpital Foch, Suresnes, France

15 <sup>e</sup> Chirurgie thoracique et cardiaque, CHU de Poitiers, INSERM 1082, Université de Poitiers,  
16 Poitiers, France

17 <sup>f</sup> Service de chirurgie thoracique, Hôpital Foch, Suresnes, France

18

19 Corresponding author: Stanislas GRASSIN-DELYLE  
20 INSERM UMR 1173  
21 UFR des Sciences de la Santé Simone Veil  
22 2 avenue de la source de la Bièvre  
23 78180 Montigny le Bretonneux, France  
24 E-mail address: stanislas.grassin-delyle@uvsq.fr  
25 Phone: + 33.1.70.42.94.22.

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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

## 46 1. INTRODUCTION

47 Inductively coupled plasma mass spectrometry (ICP-MS) is used widely to analyze trace and ultra-  
48 trace elements in biological matrices. Human exposure to elements released from toxics, drugs and  
49 implanted medical devices is conventionally monitored by assaying serum, blood, and urine.  
50 However, tissue or hair samples often provide additional useful information. For instance, toxic  
51 elements can enter the lungs through the inhalation of smoke or contaminated air. Furthermore,  
52 elements absorbed by the digestive and/or pulmonary tract can find their way into the bloodstream  
53 and become distributed throughout and incorporated into the body's various tissues - including the  
54 hair. Hence, measurements in hair can reflect the body's cumulative exposure to the various  
55 elements. Lastly, some elements may be deposited directly on the hair by external contamination [1-  
56 4].

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

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

78

## 79 **2. MATERIALS AND METHODS**

### 80 **2.1. Chemicals and reagents**

81 Analytical and internal standards were purchased from LGC Standards (Molsheim, France). ICP-  
82 MS-grade nitric acid, hydrochloric acid, hydrogen peroxide and Triton X100 were obtained from  
83 Fisher Scientific (Illkirch, France). Whole blood, urine and hair quality control (QC) samples were  
84 supplied by Centre de Toxicologie du Québec (Québec, Canada). Ultrapure deionized water  
85 (18m $\Omega$ ) was obtained from a water station (Purelab Flex, Elga Labwater, Antony, France). Argon  
86 5.0 was purchased from Messer (Puteaux, France).

87

### 88 **2.2. Working and calibration standard solutions**

89 Working and calibration standard solutions were prepared by diluting 1000  $\mu\text{g}\cdot\text{mL}^{-1}$  or (for Cu, Fe,  
90 Rb, and Zn) 10000  $\mu\text{g}\cdot\text{mL}^{-1}$  single-element standard solutions. Three sets of 15 calibration standards  
91 were prepared: the first set contained all the elements (except those detailed thereafter) in 5% HNO<sub>3</sub>  
92 in metal-free plastic tubes, the second contained Sb, Hf, Au, Pt, and Ru in 20% HCl in metal-free  
93 plastic tubes, and the third contained Hg only in borosilicate tubes. The chosen standard  
94 concentrations were based on those published previously for human samples. Hence, the calibration  
95 range differed from one element to another: Gouille *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  $-20^{\circ}\text{C}$ , 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  $40^{\circ}\text{C}$ .

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  $\mu\text{g}/\text{mL}$  gallium and iridium, and  
114 100  $\mu\text{g}/\text{mL}$  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  $220^{\circ}\text{C}$  over 15 min, followed maintenance at  $220^{\circ}\text{C}$  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.

135

## 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.

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

152

### 153 **2.6. Analysis of clinical trial samples**

154 To confirm its suitability for clinical samples, the method developed here was used to measure  
155 elements in whole blood, hair and lung samples from 25 patients participating in a clinical trial  
156 (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



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

183

### 184 **3.3. Validation of the method**

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

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

200

### 201 **3.4. Analysis of clinical trial samples**

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

204

#### 205 **4. CONCLUSION**

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

212

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214 None

215

#### 216 **6. DISCLOSURE OF CONFLICTS OF INTEREST**

217 The authors declare no conflicts of interest.

218

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223 Paris).

224

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	$0.25 \pm 0.04$	$-0.00062 \pm 0.00053$	$0.9963 \pm 0.0029$

## ICP-MS method for human samples

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]	9.0	1.5	1.8 [1.6-2.0]	13.4
		4.2 [3.9-4.5]	13.3		1.8 [1.2-2.1]	14.8
		4.2 [4.0-4.6]	9.6		1.6 [1.5-1.8]	13.6
Sn	0.21	0.22 [0.20-0.24]	3.5	0.020	0.018 [0.016-0.020]	9.0
		0.24 [0.24-0.25]	13.7		0.017 [0.016-0.019]	5.2
		0.25 [0.24-0.25]	5.9		0.017 [0.016-0.020]	8.7
Te	0.21	0.21 [0.19-0.22]	4.5	0.032	0.032 [0.031-0.034]	6.1
		0.22 [0.21-0.24]	9.7		0.032 [0.029-0.035]	9.8
		0.21 [0.20-0.22]	5.4		0.029 [0.028-0.033]	6.6
Th	0.00040	0.00038 [0.00036-0.00042]	6.5	0.0013	0.0015 [0.0015-0.0016]	4.8
		0.00042 [0.0004-0.00043]	14		0.0015 [0.0014-0.0017]	6.9
		0.00037 [0.00033-0.00042]	7.9		0.00145 [0.0014-0.0015]	5.1
Tl	0.12	0.11 [0.10-0.11]	5.6	0.048	0.041 [0.040-0.042]	3.6
		0.11 [0.10-0.12]	8.3		0.044 [0.041-0.046]	7.5
		0.11 [0.11-0.12]	6.0		0.041 [0.040-0.044]	4.2
U	0.0044	0.0037 [0.0036-0.0038]	4.1	0.0020	0.0017 [0.0016-0.0020]	7.3
		0.0039 [0.0036-0.0042]	6.5		0.0018 [0.0016-0.0019]	4.2
		0.0037 [0.0036-0.0038]	4.4		0.0017 [0.0016-0.0019]	7.0
V	0.35	0.41 [0.37-0.42]	3.4	0.12	0.13 [0.13-0.14]	6.4
		0.37 [0.37-0.39]	12.5		0.13 [0.12-0.15]	3.6
		0.36 [0.35-0.37]	5.5		0.13 [0.12-0.14]	6.1
Zn	8.8	8.9 [8.5-11.2]	11.8	16.8	18.8 [15.6-22.0]	12.5
		9.2 [8.0-10.0]	6.4		19.3 [17.4-23.0]	4.0
		9.4 [8.3-10.9]	11.3		18.9 [17.2-20.0]	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	2.4 [2.3-2.4]	2.0	7.5	7.8 [7.3-8.8]	10.9				
		0.45 [0.44-0.47]							2.6 [2.5-2.6]	14	7.9 [6.2-8.2]	10.7
		0.46 [0.45-0.47]							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	0.29 [0.26-0.30]	11.5	0.75	0.86 [0.79-0.93]	9.9				
		0.086 [0.078-0.092]							0.31 [0.22-0.33]	1.8	0.90 [0.71-1.00]	1.1
		0.075 [0.069-0.087]							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	0.23 [0.20-0.30]	9.9	0.75	0.80 [0.78-0.84]	3.9				
		0.068 [0.067-0.071]							0.25 [0.24-0.26]	8.3	0.79 [0.77-0.80]	11.5
		0.069 [0.060-0.070]							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 [1.2-1.3]	3.2	3.8	3.9 [3.8-4.0]	4.0				
		0.41 [0.40-0.42]							1.3 [1.2-1.3]	4.0	3.9 [3.6-4.2]	5.6
		0.40 [0.39-0.40]							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	0.12 [0.11-0.13]	4.2	0.38	0.41 [0.38-0.44]	4.9				
		0.041 [0.037-0.043]							0.12 [0.12-0.13]	14.0	0.39 [0.38-0.40]	9.8
		0.042 [0.042-0.046]							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	0.27 [0.26-0.27]	2.6	0.75	0.73 [0.72-0.75]	3.0				
		0.078 [0.076-0.079]							0.26 [0.25-0.26]	9.6	0.73 [0.69-0.76]	8.4
		0.076 [0.075-0.078]							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 [2.3-2.5]	2.9	7.5	7.0 [6.8-7.2]	3.8				
		0.74 [0.72-0.76]							2.4 [2.3-2.4]	5.0	7.0 [6.6-7.4]	4.6
		0.72 [0.71-0.73]							2.4 [2.2-2.4]	3.2	7.2 [6.9-7.5]	3.9

## ICP-MS method for human samples

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



## ICP-MS method for human samples

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

## ICP-MS method for human samples

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.





