

# Method development for ultra-trace quantification and isotope ratio measurement of uranium in urine

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## HSL – background

The Health and Safety Laboratory (HSL) is the UK's leading industrial health and safety facility with over 30 years of research experience covering a variety of sectors. Operating as an agency of the Health and Safety Executive (HSE), it provides scientific and technical services to protect people's health and safety by ensuring that risks are properly controlled. HSL's expertise encompasses a wide range of topics from fire/explosion hazards and safety engineering, to occupational and environmental health and human factors. HSL is designated as a WHO (World Health Organisation) Collaborating Centre for occupational health and safety research and its expertise is offered to public and private sector organisations.

## HSL – biological monitoring and analysis

One of HSL's specialist groups manages environmental and biological monitoring and analysis. This ranges from sampling and identification of infectious, toxic and allergenic micro-organisms, molecular biology and setting up mobile laboratory facilities through to human metabolism studies and the analysis of health effects arising from toxic substances and physical agents. This involves measuring individual exposure to organic chemicals, pesticides and trace elements in biological samples. Typical projects encompass single investigations and large-scale surveys of exposure to chemical, biological or physical hazards aimed at using

and developing early markers of organ damage to assess the biological, psychological and physiological changes caused by these external stressors.

Many jobs involve using chemicals that can be harmful to health if not properly controlled. For some chemicals, biological monitoring can be used to indicate how good control is and how much of the chemical has entered the body. It is a way of assessing exposure and health risks and involves measuring the chemical or its breakdown products in urine, blood or breath.

## Importance of biological monitoring

The Health and Safety Executive (HSE) has introduced Biological Monitoring Guidance Values (BMGVs) into their publication Guidance Note EH40 – *Occupational Exposure Limits*.<sup>1</sup> These guidance values are intended to assist in the interpretation of biological monitoring results with respect to occupational exposure.

There are two types of guidance values:

**Health guidance values:** they are set at a level at which there is no indication from the scientific evidence available that the substance being measured is likely to be injurious to health. These are often "biological equivalents" of occupational exposure limits.

**Benchmark guidance values:** these are practicable, achievable levels set at the 90th percentile of available biological monitoring results collected from a repre-

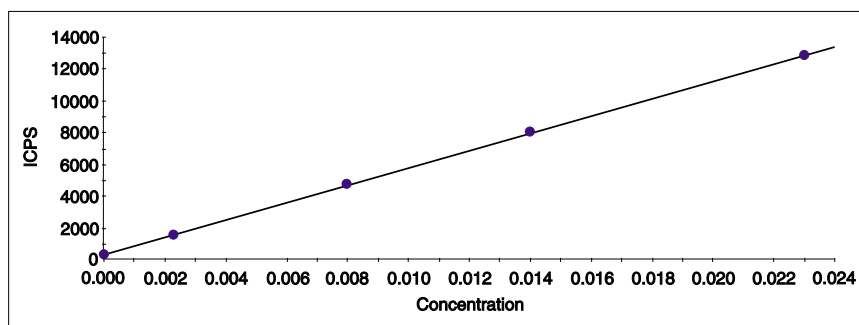
sentative sample of workplaces with good occupational hygiene practices. They are not health based. In the UK, there are currently 13 chemicals with BMGVs proposed by HSE. These are listed in EH40. Each one has an information sheet outlining the monitoring method to be used and other details. These information sheets can be supplied by HSL, on behalf of HSE, on request.

Internationally, the American Conference of Governmental Industrial Hygienists<sup>2</sup> has set guidance values for 38 substances in the US, and the Deutsche Forschungsgemeinschaft<sup>3</sup> in Germany has introduced values for 63 chemicals. HSL is able to use these values and other authoritative sources to provide additional help with the interpretation of results.

## Determination of uranium in urine

Enriched uranium (i.e. enriched in <sup>235</sup>U) is required as a fuel for nuclear power stations. In the enriched uranium manufacturing process (usually based on gas centrifugation of UF<sub>6</sub>), both enriched and depleted uranium are produced. The depleted uranium so formed (a dense and hard material) has been used as a counterweight material (particularly in aircraft, although more modern aircraft now use tungsten-based materials) and, more significantly, as a major component in the penetrators of armour-piercing shells. Neither natural nor depleted uranium are highly radioactive (the half-lives for the decay processes

$^{238}\text{U} \rightarrow ^{234}\text{Th} + \text{alpha particle}$  and  $^{235}\text{U} \rightarrow ^{231}\text{Th} + \text{alpha particle}$  are  $4.5 \times 10^9$  and  $7.0 \times 10^8$  years, respectively), so for the general public, health effects from radiation exposure are relatively low. However, like other heavy metals, such as cadmium, uranium is known to be toxic to the kidneys, where it is transported to before excretion in the urine (this is why urine, rather than blood, is analysed to determine uranium exposure). Consequently, primarily as a result of the use of depleted uranium-based penetrators in shells in the Gulf War and Balkan conflicts, interest in (and concern about) the possible environmental consequences and health impact of this material has been growing in recent years. It is for this reason that HSL has an interest in developing a method for ultra-trace quantification and isotope ratio measurement of uranium in urine.



**Figure 1.**  $^{238}\text{U}$  calibration ICP-MS (0 to 23  $\text{pg mL}^{-1}$ ).

**Table 1.** Average concentrations measured for sample groups A, B and C.

Sample identity	Average concentration ( $n = 10$ ) ( $\text{pg mL}^{-1}$ )	Uranium level spiked ( $\text{pg mL}^{-1}$ )	Spike recovery (%)
Group A	$7.3 \pm 1.3$	0	—
Group B	$15.9 \pm 1.1$	9.5	91
Group C	$98.5 \pm 1.7$	95	96

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**Table 2.**  $^{235}\text{U}/^{238}\text{U}$  isotope ratio measurements in 2% (v/v) nitric acid and 1 : 10 diluted urine.

8 pg mL <sup>-1</sup> U in nitric acid	Time	$^{235}\text{U}/^{238}\text{U}$	1 : 10 diluted urine (95 pg mL <sup>-1</sup> U before dilution)	Time	$^{235}\text{U}/^{238}\text{U}$
1	12:56:15	0.00283	1	19:08:54	0.00276
2	12:57:46	0.00275	2	19:10:25	0.00291
3	12:59:18	0.00279	3	19:11:57	0.00285
4	13:00:49	0.00273	4	19:13:29	0.00288
5	13:02:21	0.00296	5	19:15:00	0.00279
Mean		0.00281	Mean		0.00284
SD		0.00009	SD		0.00006
%RSD		3.26	%RSD		2.23

### Instrument selection for depleted uranium determination in urine

In order to develop such a method it was necessary for HSL to purchase an ICP-MS capable of measuring isotopes of uranium at low parts per trillion (pg mL<sup>-1</sup>) levels.

Prior to purchase, HSL sought to evaluate the performance of several ICP-MS instruments. This involved measuring total uranium concentration and isotope ratios of  $^{235}\text{U}$  and  $^{238}\text{U}$  of 30 urine samples. These samples were subdivided into three groups, as outlined below:  
 Group A: 10 blank urine samples  
 Group B: 10 samples of blank urine spiked with 9.5 pg mL<sup>-1</sup> of U  
 Group C: 10 samples of blank urine spiked with 95 pg mL<sup>-1</sup> of U

### Instrument performance evaluation

For the analysis, the urine samples were diluted 1 : 10 with 1% HNO<sub>3</sub> and spiked with  $^{175}\text{Lu}$  as the internal standard. Calibration solutions were prepared from blank to 23 pg mL<sup>-1</sup> U and spiked with the Lu internal standard. Both  $^{235}\text{U}$  and  $^{238}\text{U}$  were measured so that quantitative results and isotope ratio measurements could be recorded. The calibration obtained for  $^{238}\text{U}$  is shown in Figure 1. The results were obtained using an X Series ICP-MS from Thermo Electron Corporation.

Figure 1 shows the high sensitivity and low background (equivalent to

0.6 pg mL<sup>-1</sup> U) achieved for  $^{238}\text{U}$  and demonstrates the performance that was necessary to achieve the uranium detection limits required by HSL. The average concentrations found for the three groups of samples supplied (A, B and C as described above) are shown in Table 1. These results are based on the  $^{238}\text{U}$  data and have been blank subtracted and corrected for the 1 : 10 dilution applied before analysis.

By optimising the data acquisition parameters for  $^{235}\text{U}$  and  $^{238}\text{U}$ , acceptable isotope ratio precision – enough to confidently detect differences between natural and depleted uranium at pg mL<sup>-1</sup> levels in urine – could be achieved for the  $^{235}\text{U}/^{238}\text{U}$  ratio (Table 2). This is clearly illustrated by the fact that the  $^{235}\text{U}/^{238}\text{U}$  ratios measured for uranium in the nitric acid and diluted urine matrices were found to be significantly lower (i.e. depleted in  $^{235}\text{U}$ ) than the natural  $^{235}\text{U}/^{238}\text{U}$  ratio of  $0.007253 \pm 0.000002$ . This is not unexpected, since commercial uranium solutions used for elemental analysis are usually produced from uranium starting materials depleted in  $^{235}\text{U}$ .

### Conclusions

The results obtained demonstrate the performance of the X Series ICP-MS for trace uranium determination in urine. On the basis of the data obtained from this and other experiments and the fulfillment of other required criteria, HSL elected to purchase a quadrupole ICP-MS instrument.

The instrument's sensitivity, flexibility and ease of use will enable HSL to carry out enhanced analyses for both routine and research applications for a broad spectrum of elements in different clinical samples. This will ultimately improve the biological monitoring capability of HSL, as elements such as selenium, chromium and vanadium will be analysed for the first time at HSL using the collision cell interference attenuation technology option of the instrument. Through the combination of the spectrometer's sensitivity enhancement options and optimised clinical sample introduction apparatus it is easier to analyse elements such as platinum, which previously relied on flow-injection sample introduction to achieve the necessary limits of detection.

### References

1. Guidance Note EH40/00 Occupational Exposure Limits, ISBN 0 7176 1730 0. HSE Books, PO Box 1999, Sudbury, Suffolk CO10 2WA. UK.
2. American Conference of Governmental Industrial Hygienists, <http://www.acgih.org/>
3. Deutsche Forschungsgemeinschaft (DFG) (Ed.), List of MAK and BAT Values 2003, Maximum Concentrations and Biological Tolerance Values at the Workplace. Report 39 MAK-Values-List (DFG), 1. Edition November 2003, Wiley-VCH, Weinheim.