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References

Masato Maekawa1*
Terumi Taniguchi1
Hitomi Higashi1
Haruhiko Sugimura2
Kokichi Sugano3
Takashi Kanno1

1 Department of Laboratory Medicine
2 First Department of Pathology
Hamamatsu University School of Medicine
Hamamatsu, Japan
3 Oncogene Research Unit
Cancer Prevention Unit
Tochigi Cancer Center
Research Institute
Utsunomiya, Japan

*Address correspondence to this author at: Department of Laboratory Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-3192, Japan. Fax 81-53-435-2794; e-mail mmaekawa@hama-med.ac.jp.
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Increased Selenium Concentrations in Seronorm Trace Elements Serum (Level 2)

To the Editor:
Selenium is an essential trace element in humans, the majority of it occurring in selenoproteins. These proteins have several known physiologic functions; they are important antioxidants, maintain normal thyroid function, and are thought to play a role in inhibiting tumor growth (1). There has been considerable interest in studying selenoproteins in serum because the selenium concentrations reported for many populations are less than those required for optimum activity of selenoenzymes. This may have both long- and short-term consequences for human health (1).

Recently we evaluated magnetic sector inductively coupled plasma mass spectrometry (ICP-MS) methods for determination of selenium in human serum (2). Quality-control protocols should play an important part in any study examining the concentrations of trace elements in clinical samples (3). As part of our quality-assurance program, external reference samples were analyzed extensively over a 12-month period.

The purpose of this note is to alert the wider clinical and analytical community that the reported selenium target concentration for Seronorm™ Trace Elements Serum (Level 2) may be in error, at least within some batches. We consistently measured increased selenium concentrations in this sample, using two different sample preparation techniques in combination with magnetic sector ICP-MS; these results were confirmed by independent analyses at two other leading laboratories.

The reference samples analyzed were Seronorm Trace Elements Serum, Levels 1 (MI0181) and 2 (NO0371) with stated (mean ± 2 SD) selenium concentrations of 83 ± 6 and 136 ± 9 µg/L, respectively. Fifteen vials of Level 1 and 12 vials of Level 2 were analyzed, all with the same reference (201504 and 203105) and lot numbers (MI0181 and NO0371).

At the University of Tasmania, selenium concentrations were measured by an ELEMENT magnetic sector ICP-MS (Finnigan) (2). The isotope 82Se was monitored using the highest instrumental resolution available (m/Δm ~7500), samples diluted 1 + 9, indium as internal standard; ethanol and nitric acid added (both to 5 mL/L); and quantification by external calibration. Samples were also prepared for analysis after microwave digestion (Milestone MLS-1200) in the presence of nitric acid (2).

Microwave-digested samples were analyzed for selenium by electrothermal atomic absorption spectroscopy (ET-AAS; Perkin-Elmer 5100 PC Atomic Absorption Spectrometer; method of standard additions) at the Ecochemistry Laboratory, Applied Ecology Research Group, University of Canberra, Australia (4). The Seronorm samples were also analyzed by dynamic reaction cell (DRC)-ICP-MS (Perkin-Elmer Sciex) at the Laboratory of Analytical Chemistry,
Table 1. Measured selenium concentrations in Seronorm Trace Elements Serum Levels 1 and 2.

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Level 1</th>
<th>Level 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stated Seronorm target: ICP-MS&lt;sup&gt;a&lt;/sup&gt;</td>
<td>83 (6)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>136 (9)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stated Seronorm target: ET-AAS&lt;sup&gt;d&lt;/sup&gt;</td>
<td>81 (3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>129 (8)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ethanol addition method&lt;sup&gt;d&lt;/sup&gt;</td>
<td>82&lt;sup&gt;d&lt;/sup&gt;Se</td>
<td>83 (5)</td>
</tr>
<tr>
<td>Microwave digestion method&lt;sup&gt;d&lt;/sup&gt;</td>
<td>82&lt;sup&gt;d&lt;/sup&gt;Se</td>
<td>88 (3)</td>
</tr>
<tr>
<td>Confirmatory ET-AAS&lt;sup&gt;e&lt;/sup&gt;</td>
<td>82&lt;sup&gt;d&lt;/sup&gt;Se</td>
<td>88 (9)</td>
</tr>
<tr>
<td>Confirmatory DRC-ICP-MS&lt;sup&gt;f&lt;/sup&gt;</td>
<td>77&lt;sup&gt;d&lt;/sup&gt;Se</td>
<td>86 (3)</td>
</tr>
<tr>
<td></td>
<td>80&lt;sup&gt;d&lt;/sup&gt;Se</td>
<td>84 (2)</td>
</tr>
<tr>
<td></td>
<td>82&lt;sup&gt;d&lt;/sup&gt;Se</td>
<td>87 (2)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values supplied by the manufacturer, as measured by magnetic sector ICP-MS and ET-AAS.

<sup>b</sup> Values for stated Seronorm target are the mean (2 SD).

<sup>c</sup> Analysis by magnetic sector ICP-MS at the University of Tasmania, in high resolution mode (m/Δm ~7500), using 82<sup>d</sup>Se with indium as internal standard. Samples were diluted 1 + 9, with ethanol and nitric acid addition (5 mL/L). Values shown are from five analytical replicates.

<sup>d</sup> Analysis by magnetic sector ICP-MS at the University of Tasmania, in high resolution mode (m/Δm ~7500), using 82<sup>d</sup>Se with indium as internal standard. Samples were digested 1:1 with nitric acid before dilution (1 + 9; final nitric acid concentration, ~100 mL/L). Values shown are from five analytical replicates.

<sup>e</sup> Analysis by ETAAS at the University of Canberra with Zeeman background correction, after sample microwave digestion (method as for d above). Values shown are from two analytical replicates.

<sup>f</sup> Analysis by DRC-ICP-MS at Ghent University, using 77<sup>d</sup>Se, 80<sup>d</sup>Se, and 82<sup>d</sup>Se isotopes with yttrium internal standard. Samples were diluted 1 + 24 with 10 mL/L nitric acid. Values shown are from five analytical replicates.

Ghent University, Belgium. 77<sup>d</sup>Se, 80<sup>d</sup>Se, and 82<sup>d</sup>Se were the isotopes monitored by this technique (reaction gas, CO; sample diluted 1 + 24; yttrium internal standard; quantification by standard addition) (3). Representative selenium concentrations measured in Seronorm Level 1 and 2 serum samples are shown in Table 1. Considering the Level 1 sample, all values from the three analytical techniques agreed (within quoted uncertainty ranges) with the stated target value. Mean (SD) selenium concentrations for the Level 2 sample, however, were consistently higher than the target values: 161 (4) µg/L by magnetic sector ICP-MS, 152 (5) µg/L by DRC-ICP-MS, and 166 (17) µg/L by ET-AAS vs the suggested target value of 136 µg/L.

A mean (SD) selenium concentration of 168 (17) µg/L was also obtained by magnetic sector ICP-MS analysis after microwave digestion of serum samples.

On the basis of our findings we propose that the selenium concentration in these batches of Seronorm Level 2 Trace Elements Serum may be inaccurate. We believe that a value of 150–165 µg/L may more closely reflect the true selenium concentration in these batches. We wish to make clear that we have no reason to doubt the quality of the initial certification process or the quality of the initial calibrating laboratories. Rather, we suggest that unknown factors such as aging, contamination, or changed manufacturing practices have caused these batches of this reference sample to differ from those originally prepared and evaluated.

References

Editor’s Note: Attempts to obtain comment from the manufacturer were unsuccessful.

Urinary Methylmalonic Acid Test May Have Greater Value than the Total Homocysteine Assay for Screening Elderly Individuals for Cobalamin Deficiency

To the Editor:
I read with interest the review on recommendations about total homocysteine (tHcy) determinations (1). In this review, the authors recommend screening individuals (>75 years) for cobalamin (vitamin B<sub>12</sub>) deficiency, using upper limits for tHcy of 16 µmol/L (folate-supplemented) and 20 µmol/L (nonsupplemented). Use of the tHcy test for screening, however, may miss a large...