Standardization of the ADVIA Centaur Vitamin D Total Assay

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Summary
With the availability of the Vitamin D Standardization Program (VDSP), manufacturers are now able to align their assays to an accepted reference standard in 25(OH)vitamin D testing. The objectives of this study were to examine the ADVIA Centaur® Vitamin D Total assay’s alignment to the 25(OH)vitamin D Reference Measurement Procedure (RMP), and how that alignment compares to the calibration prior to the RMP alignment and to existing patient results.

Background
Vitamin D is a steroid hormone involved in the intestinal absorption of calcium and the regulation of calcium homeostasis. Aiding renal absorption of calcium, vitamin D is essential for the formation and maintenance of strong, healthy bones. In recent years, the number of commercially available vitamin D assays has increased, and due to the lack of a universal standard, different manufacturers’ vitamin D assays and protocols on different LC-MS/MS instruments yield varying results.

The VDSP is an initiative of the NIH Office of Dietary Supplements (NIH ODS) and a collaboration with the National Institute of Standards and Technology (NIST), the CDC, and Ghent University that was launched under the coordination of Christopher Sempos, PhD, NIH ODS, to standardize 25(OH)vitamin D measurement across methods and manufacturers. The NIST Reference Measurement Procedure (RMP) is the primary reference method for the measurement of total 25(OH)vitamin D, i.e., 25(OH)vitamin D₃, 25(OH)vitamin D₄, and 3-epi-25(OH)vitamin D₃. There is also a second method—isotope dilution liquid chromatography mass spectrometry (ID-LC/MS/MS)—from Dr. Linda Thienpont at Ghent University that is traceable to the NIST RMP.

The VDSP samples consist of 50 unique patient specimens ranging in vitamin D concentration from 5.04 to 60 ng/mL. The ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment is standardized to the Ghent University 25(OH)vitamin D RMP by directly value-assigning 10 serum pools with increasing concentrations of 25(OH)vitamin D₃ directly from the VDSP sample concentration using multiple lots of ADVIA Centaur Vitamin D Total reagents and calibrators on multiple ADVIA Centaur systems.

Study Design
Centre Hospitalier Universitaire (CHU) is a university hospital in Nice, France, that performs 14,450 vitamin D tests annually using the DiaSorin LIAISON system. The objective of the study was to evaluate the ADVIA Centaur Vitamin D Total assay traceable to the 25(OH)vitamin D RMP in a French population compared to the DiaSorin LIAISON system.

Results
Figure 1 demonstrates the alignment of the revised ADVIA Centaur Vitamin D Total assay with the 25(OH)vitamin D RMP. For 122 samples in the range of 7.8 to 148.1 ng/mL, the slope between the ADVIA Centaur Vitamin D Total assay and the ID-LC/MS/MS 25(OH)vitamin D RMP was 0.93; intercept was 2.89 ng/mL with a correlation coefficient of 0.99.

Figure 1: ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment.
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Figure 2 compares the 25(OH)vitamin D alignment to the calibration prior to the 25(OH)vitamin D RMP alignment using the 200 remnant samples from CHU. This adjustment is a result of value-assigning 10 serum pools with increasing concentrations of 25(OH)vitamin D directly from the samples with ID-LC/MS/MS 25(OH)vitamin D RMP concentrations using multiple lots of ADVIA Centaur Vitamin D Total reagents and calibrators on multiple ADVIA Centaur systems. The impact of the 25(OH)vitamin D RMP alignment is not equivalent across the range of the assay, as shown in Table 1. Samples in the lower and higher range of the assay will decrease in vitamin D total values, while samples in the middle range will increase.

Table 1: Expected difference in ADVIA Centaur Vitamin D Total patient values based on 25(OH)vitamin D RMP alignment.

<table>
<thead>
<tr>
<th>Range (ng/mL)</th>
<th>Expected Difference (ng/mL)</th>
<th>Average Bias %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>-1.5</td>
<td>-15.1%</td>
</tr>
<tr>
<td>15–30</td>
<td>2.1</td>
<td>9.8%</td>
</tr>
<tr>
<td>30–50</td>
<td>-1.2</td>
<td>-2.6%</td>
</tr>
<tr>
<td>&gt;50</td>
<td>-10.0</td>
<td>-13.6%</td>
</tr>
</tbody>
</table>

Figure 2: ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment compared to ADVIA Centaur Vitamin D Total prior to RMP alignment.

In Figure 3, the ADVIA Centaur Vitamin D Total assay with the 25(OH)vitamin D RMP and prior to the 25(OH)vitamin D RMP are compared to the DiaSorin LIAISON from CHU. For the ADVIA Centaur assay the difference between points is shown based on the alignment to the 25(OH)vitamin D RMP. For individual patient samples in the low and high end, values are reduced as a result of the 25(OH)vitamin D alignment. Compared to DiaSorin LIAISON the ADVIA Centaur Vitamin D Total assay without the 25(OH)vitamin D RMP has better agreement than the ADVIA Centaur Vitamin D Total assay with the 25(OH)vitamin D RMP.

Figure 3: ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment compared to DiaSorin LIAISON.

Conclusion

Vitamin D standardization is a necessary requirement to create the anchor vitamin D values laboratories need, and it is important that laboratories and clinicians know how their vitamin D assay is standardized. The study described in this document demonstrates the alignment of the ADVIA Centaur Vitamin D Total assay to the 25(OH)vitamin D RMP and its impact on patient results. Alignment to the 25(OH)vitamin D RMP is an important step for all manufacturers, and as with any standardization program, it will take time before the industry is aligned.

References:
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