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White Paper

Standardization of the ADVIA Centaur Vitamin D Total Assay*

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Answers for life.

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Summary

With the availability of the Vitamin D Standardization Program (VDSP),[1,2] manufacturers are now able to align their assays to a truth 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 Method 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.[3,4] 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 Method Procedure (RMP) is the primary reference method for the measurement of total 25(OH)vitamin D, i.e., 25(OH)vitamin D_2, 25(OH)vitamin D_3, and 3-epi-25(OH)vitamin D_3. 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 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 D_3 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.

A total of 200 remnant frozen clinical samples collected in March 2013 were supplied by Dr. Patricia Panaia-Ferrari, CHU, Nice, France, with known 25(OH)vitamin D values as determined by the DiaSorin LIAISON. These DiaSorin LIAISON 25(OH)vitamin D values were generated using fresh samples according to the manufacturer's instructions. Samples were sent to Siemens Healthcare Diagnostics (Tarrytown, New York, USA) for measurement using the ADVIA Centaur Vitamin D Total assay, with standardization either traceable or not traceable to the 25(OH)vitamin D Reference Method Procedure (RMP).

Results

Figure 1 demonstrates the alignment of the revised ADVIA Centaur Vitamin D Total assay with the 25(OH)vitamin D RMP. For 177 samples in the range of 5.0 to 100.0 ng/mL, the slope between the ADVIA Centaur Vitamin D Total assay and the ID-LC/MS/MS 25(OH)vitamin D RMP was 0.99; intercept was 0.53 ng/mL with a correlation coefficient of 0.96.

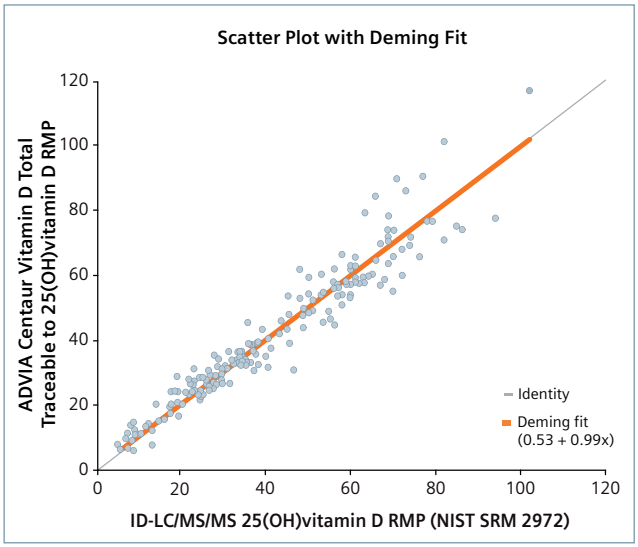

Figure 1: ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment.

* This version of the ADVIA Centaur Vitamin D Total assay is not available for sale in the U.S. Product availability may vary from country to country and is subject to varying regulatory requirements. In development on the ADVIA Centaur CP System.

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_3 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.

Range (ng/mL)	Expected Difference (ng/mL)	Average Bias %
<15	-1.5	-15.1%
15–30	2.1	9.8%
30–50	-1.2	-2.6%
>50	-10.0	-13.6%

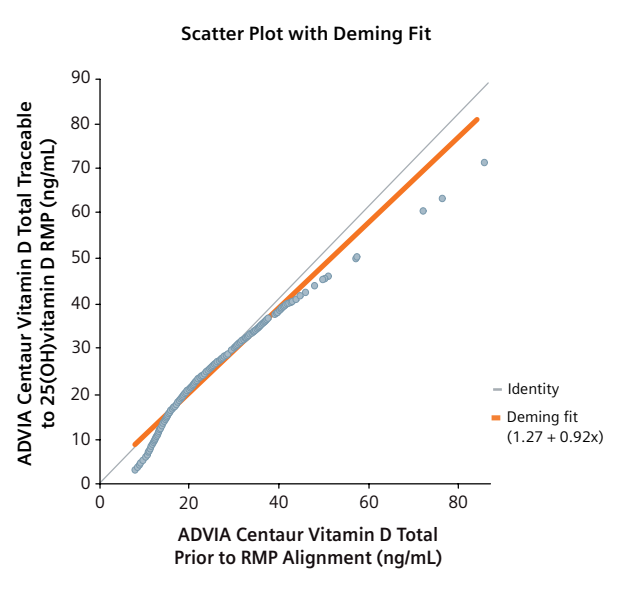

Figure 2: ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment compared to ADVIA Centaur Vitamin D Total prior to RMP alignment.

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.

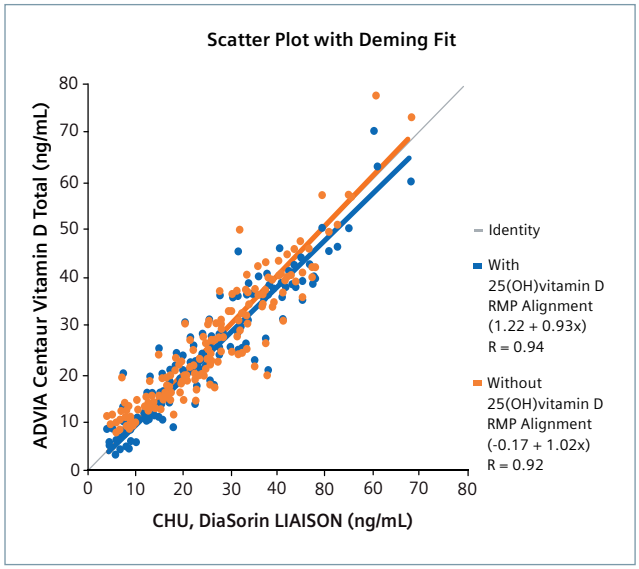

Figure 3: ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment compared to DiaSorin LIAISON.

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.

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