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White Paper

# Standardization of the ADVIA Centaur Vitamin D Total Assay

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## Summary

With the availability of the Vitamin D Standardization Program (VDSP),<sup>1,2</sup> 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.<sup>3,4</sup> 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 D<sub>2</sub>, 25(OH)vitamin D<sub>3</sub>, and 3-epi-25(OH)vitamin D<sub>3</sub>. 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<sub>3</sub> 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 Measurement 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 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.

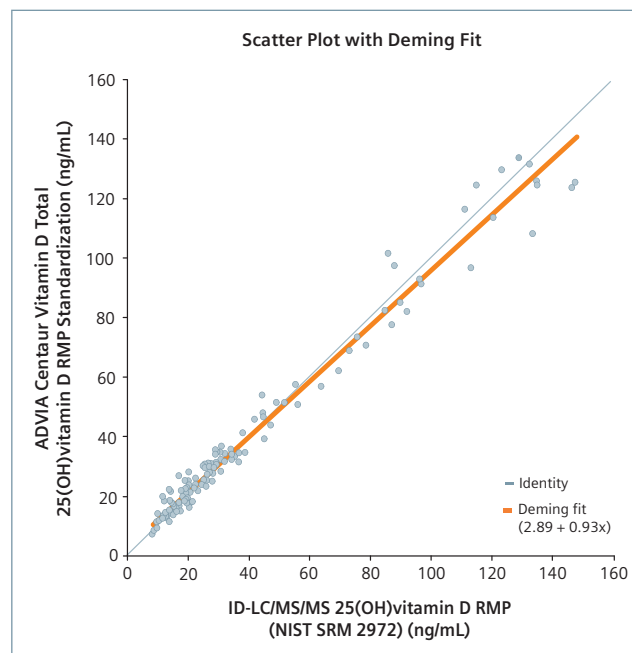
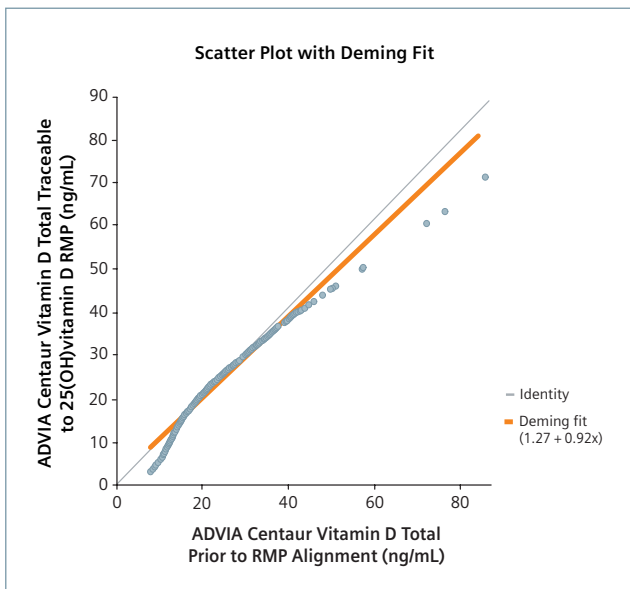


Figure 1: ADVIA Centaur Vitamin D Total assay with 25(OH)vitamin D RMP alignment.

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<sub>3</sub> 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.

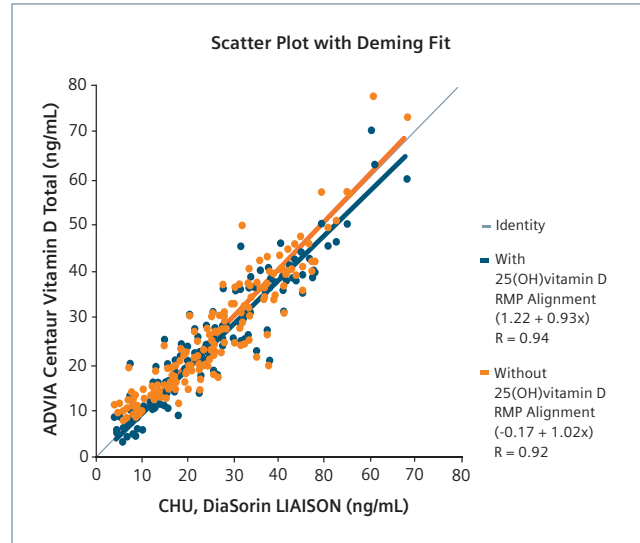
**Table 1:** Expected difference in ADVIA Centaur Vitamin D Total patient values based on 25(OH)vitamin D RMP alignment.

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.

### References:

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