Development of a standard reference material for vitamin D in serum\textsuperscript{1–4}

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ABSTRACT

The most widely used indicator of vitamin D status is the measurement of 25-hydroxyvitamin D [25(OH)D] in either serum or plasma. Several studies have reported discrepancies between the results of assays used to measure 25(OH)D, however, which calls into question the ability of 25(OH)D assays to reflect accurately the vitamin D status of individuals. The National Institute of Standards and Technology has been working with the National Institutes of Health’s Office of Dietary Supplements to develop a standard reference material for circulating vitamin D analysis. This standard reference material will provide a material with stable, well-defined levels of the analytes of interest. Investigators will be able to use the standard reference material to validate new analytic methods as they are developed and to assign values to in-house quality-control materials. Am J Clin Nutr 2008; 88(suppl):511S–2S.

STANDARD REFERENCE MATERIAL FOR VITAMIN D

The prevalence of vitamin D deficiency or insufficiency in the general population is an issue of concern. The most widely used indicator of vitamin D status is the measurement of 25-hydroxyvitamin D [25(OH)D] in either serum or plasma. Because circulating 25(OH)D can arise from hydroxylation of either vitamin D\textsubscript{2} or vitamin D\textsubscript{3}, measurement of total 25(OH)D [both 25(OH)D\textsubscript{2} and 25(OH)D\textsubscript{3}] is essential for accurate assessment of vitamin D status (1).

Several studies, including interlaboratory comparisons, have reported discrepancies between the results of assays used to measure 25(OH)D (2, 3). Data from the Vitamin D External Quality Assessment Scheme have also illustrated assay-specific results (4). Although it is difficult to point to a particular cause for these discrepancies, some of the aspects of 25(OH)D measurements that researchers have considered include the assays’ ability to respond equally to 25(OH)D\textsubscript{2} and 25(OH)D\textsubscript{3}, preparation of calibrants, and the recovery of 25(OH)D from spiked samples (5). In addition, a recently discovered metabolite, 3-epi-25-hydroxyvitamin D [3-epi-25(OH)D\textsubscript{3}], which might be present in samples from infants, can pose problems for certain assays (6).

The current level of variability in 25(OH)D measurements calls into question the ability of 25(OH)D assays to reflect accurately the vitamin D status of individuals. In addition, the lack of agreement in assay results obtained by different methods might complicate the ability to define optimal levels of circulating 25(OH)D (3). For these reasons, investigators have called for international standardization of vitamin D measurements.

The National Institute of Standards and Technology (NIST) has been working with the National Institutes of Health’s Office of Dietary Supplements to develop a standard reference material (SRM) for circulating vitamin D analysis. NIST has a long history of providing SRMs for the clinical chemistry community to support accuracy in clinical laboratory measurements.

The reference material currently in development at NIST, SRM 972 Vitamin D in Human Serum, consists of 4 pools of fresh-frozen serum. Each pool has a different level of 25(OH)D\textsubscript{2}, 25(OH)D\textsubscript{3}, or both. One pool also contains 3-epi-25(OH)D\textsubscript{3}. NIST designed the SRM to pose similar analytic challenges to those encountered in patient samples. NIST will assign values for each of the analytes through measurements at NIST and collaborating laboratories. NIST will perform its measurements by isotope-dilution liquid chromatography-mass spectrometry and tandem mass spectrometry methodology. The certificate of analysis for SRM 972 will include values for 25(OH)D\textsubscript{2}, 25(OH)D\textsubscript{3}, and 3-epi-25(OH)D\textsubscript{3}. NIST anticipates official release of SRM 972 in 2008.

This new SRM is not intended to characterize any particular analytic method as superior to another. Instead, NIST designed the SRM to serve as a reproducible point of comparison. The SRM will provide a material with stable, well-defined levels of the analytes of interest. Investigators can use the SRM to validate new analytic methods as they are developed and to assign values to in-house quality-control materials. In addition, the new SRM can serve as an adjunct to

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\textsuperscript{2}Presented at the National Institutes of Health conference “Vitamin D and Health in the 21st Century: an Update,” held in Bethesda, MD, September 5–6, 2007.

\textsuperscript{3}Certain commercial equipment, instruments, or materials are identified in this report to specify adequately the experimental procedure. Such identification does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that the materials or equipment specified are necessarily the best available for the purpose.

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existing quality assurance programs, such as the Vitamin D External Quality Assessment Scheme, for vitamin D measurements.

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REFERENCES