VDSP Overview and Meeting Agenda

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for the
Vitamin D Standardization Program (VDSP)
Meeting Agenda

- Importance of standardized laboratory measurement of vitamin D
- VDSP system to promote standardization
- Impact of standardization
- Working together to promote standardization
VDSP Goal

Promote the standardized laboratory measurement of total 25-hydroxyvitamin D – a measure of vitamin D status – in order to improve clinical and public health practice worldwide.

*Note:* 25-hydroxyvitamin D is abbreviated as 25(OH)D
Nutritional Forms of Vitamin D

Molecular Formula:     \( \text{C}_{27}\text{H}_{44}\text{O} \)                       \( \text{C}_{28}\text{H}_{44}\text{O} \)
Molecular Weight:       384.6 g/mole               396.65 g/mole

Vitamin D3 or 
Cholecalciferol

Vitamin D2 or 
Ergocalciferol

Molecular Formula:  \( \text{C}_{27}\text{H}_{44}\text{O} \)  \( \text{C}_{28}\text{H}_{44}\text{O} \)
Molecular Weight:  384.6 g/mole               396.65 g/mole
Structural Forms for 25(OH)D

The two primary metabolites of interest differ only in the side chains.

25-hydroxyvitamin D2
Molecular Formula: $C_{28}H_{44}O_2$
Molecular Weight: 412.65 g/mole

25-hydroxyvitamin D3
Molecular Formula: $C_{27}H_{44}O_2$
Molecular Weight: 400.63 g/mole
Total 25-Hydroxyvitamin D or 25(OH)D

- Total 25(OH)D is defined as
  \[ \text{Total } 25(\text{OH})D = 25(\text{OH})D_2 + 25(\text{OH})D_3 \]

- Units: \( \text{ng/mL or nmol/L} \) where:
  \[ \text{ng/mL} \times 2.5 \approx \text{nmol/L} \]

* Assumes that Vitamin D_2 and D_3 are of equal biological value.
A standardized laboratory measurement is one that is accurate and comparable over time, location, and laboratory procedure.
A standardized laboratory measurement of \texttt{25(OH)D} is one that is accurate and comparable to the \textit{NIST and Ghent Reference Measurement Procedures (RMPs)} over time, location, and laboratory procedure.
Standardization Does Not Require a Single Analytic Approach
Effects of Standardization

- Harmonization of laboratories and methods
- Laboratories report “true” value – based on NIST and Ghent RMPs*
- Standardization leads to more informed decision making by physicians, policy makers and others.

1. Standardize vitamin D measurement in national health surveys worldwide.

2. Promote standardized 25(OH)D measurement by:
   - Assay manufacturers
   - Clinical and research laboratories

3. Conduct an international research program devoted to:
   - Improving the laboratory measurement of 25(OH)D.
   - Documenting and studying differences in standardized 25(OH)D concentrations among national surveys worldwide.
VDSP Reference Measurement System Components

- NIST & Ghent RMPs
- NIST Standard Reference Materials (SRM)
- CDC Vitamin D Standardization-Certification Program
- Accuracy-Based Quality Assurance Programs
- Study designs for standardizing completed studies
Calibration Traceability Scheme*

* Adapted from: Myers G. Steroids 2008;73:1293-1296
Calibration Traceability Scheme*

Reference procedure (LC-IDMS or GC-IDMS) Reference Laboratories

Primary Calibrator

Calibration

Single Donor Samples

Calibration

Commutable SRM

Accuracy-Based PT/EQA

Commutable Samples

Assay Manufacturer

Clinical Laboratory

* Adapted from: Myers G. Steroids 2008;73:1293-1296
VDSP Research Agenda

- NIST methods development
- Biological value of 3-epi-25(OH)D3
- Reporting of 24R,25(OH)2D values by DEQAS
- Commutability study – 2\textsuperscript{nd} more extensive study
- Compare standardized national survey data
- Promote standardization of completed studies
Suggested Assay Performance Limits Based on Biological Variation*

<table>
<thead>
<tr>
<th>Measurements</th>
<th>CV (%)</th>
<th>Bias (%)</th>
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</thead>
<tbody>
<tr>
<td>Reference Labs</td>
<td>≤ 5%</td>
<td>≤ 1.7%</td>
</tr>
<tr>
<td>“Routine” Labs</td>
<td>≤ 10%</td>
<td>≤ 5%</td>
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</tbody>
</table>

Ask yourself?

• What’s your assay’s %CV? Is it ≤ 10%
• What’s your assay’s Bias? Is it ≤ 5%
References


Thank you!
Importance of Standardization in National Health Surveys

- Essential in setting, monitoring and updating evidence-based medical practice guidelines.
- Provide reference ranges
- Promote commercial standardization.
- The first step, however, is *Standardization*. 