CDC’s Clinical Standardization Programs to improve accuracy and reliability of hormone tests

Hubert W. Vesper, Ph.D.
Director, Clinical Standardization Programs
Division of Laboratory Sciences
CDC’s Clinical Standardization Programs help laboratories and manufacturers to improve and maintain the accuracy and reliability of laboratory tests.
CDC improves patient care and public health by ensuring laboratory measurements are accurate and reliable

**Goal**
Improve diagnosis, treatment, and prevention of selected diseases by standardizing clinical laboratory measurements

**Objective**
Create measurement results that are traceable to one accuracy basis and thus are comparable across methods, location, and over time

**Standardization** is a process in which the accuracy, and other relevant analytical performance parameters of an assay are improved and maintained to meet certain clinical needs

A standardized laboratory test has demonstrated through a thorough, independent assessment that its analytical performance meets relevant analytical performance goals
CDC’s Clinical Standardization Programs improve and maintain accurate and reliable disease biomarker measurements for new and established assays

<table>
<thead>
<tr>
<th>Program Name</th>
<th>Biomarker</th>
<th>Program Focus</th>
<th>Main Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol Reference Method Laboratory Network (CRMLN)</td>
<td>Total Cholesterol, Total Glycerides, HDL-Cholesterol, LDL-Cholesterol</td>
<td>Improve and Maintain Accuracy and Reliability</td>
<td>Assay Manufacturers and Laboratories with LDTs</td>
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<tr>
<td>Hormones Standardization Program (HoSt)</td>
<td>Testosterone, Estradiol, Thyroxine (2019), Triiodothyronine (2019)</td>
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<tr>
<td>Vitamin D Standardization Certification Program (VDSCP)</td>
<td>Total 25-hydroxyvitamin D</td>
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<tr>
<td>Lipids Standardization Program (LSP)</td>
<td>Total Cholesterol, Total Glycerides, HDL-Cholesterol, Apo Lipoprotein A-I, Apo Lipoprotein B</td>
<td>Monitor Accuracy and Reliability During Routine Testing</td>
<td>Clinical and Research Laboratories</td>
</tr>
<tr>
<td>Accuracy-based Monitoring Program (AMP)</td>
<td>Testosterone, Estradiol, Total 25-hydroxyvitamin D</td>
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</table>
CDC’s Clinical Standardization Programs provide unique services at every step in the standardization process.

<table>
<thead>
<tr>
<th>Standardization Steps</th>
<th>Standardization Elements and Activities</th>
<th>CDC’s Program Components</th>
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</thead>
<tbody>
<tr>
<td>Develop and Maintain Reference System</td>
<td>Reference Methods and Reference Materials</td>
<td>Hormones and Lipids Reference Laboratories</td>
</tr>
<tr>
<td>Establish Metrological Traceability</td>
<td>Calibration and Analytical Performance Assessment of LDTs and Manufacturers</td>
<td>Standardization Laboratory (HoSt, VDSCP, CRMLN)</td>
</tr>
<tr>
<td>Verify “End-User” Test Performance</td>
<td>Performance Verification of Testing in Patient Care and Research</td>
<td>Monitoring Laboratory (LSP, AMP, ab-EQA/PT)</td>
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CDC operates reference methods for key disease biomarkers

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Accuracy</th>
<th>Precision</th>
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<tbody>
<tr>
<td>Total Cholesterol</td>
<td>±1.0%</td>
<td>≤1%</td>
</tr>
<tr>
<td>LDL-Cholesterol</td>
<td>≤2%</td>
<td>≤1.5%</td>
</tr>
<tr>
<td>HDL-Cholesterol</td>
<td>≤1.0 mg/dL</td>
<td>≤1 SD</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≤2.5%</td>
<td>≤2.5%</td>
</tr>
<tr>
<td>Total 25-Hydroxyvitamin D</td>
<td>±1.7%</td>
<td>≤5.0%</td>
</tr>
<tr>
<td>Testosterone</td>
<td>±2.1%</td>
<td>≤2.7%</td>
</tr>
<tr>
<td>Estradiol</td>
<td>±2.8%</td>
<td>≤5.7%</td>
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</tbody>
</table>
CDC is developing new reference methods and harmonization programs

- Thyroid stimulating hormone
- Thyroid hormones
- Parathyroid hormones
Testosterone tests standardized by CDC showed better accuracy than non-standardized tests in 2018.
Estradiol measurements of participants in the CDC Hormones Standardization Program improve over time.
CDC Hormones Standardization Program for testosterone improved patient care through standardization of tests and development standardized reference intervals
Mean bias (calibration bias) is not always a major contributor to measurement inaccuracy

Proportion of calibration bias, sample-specific effects, and imprecision contributing to inaccurate estradiol measurements in 3 participants of an interlaboratory comparison study
CDC’s Clinical Standardization Programs use individual donor samples to better detect and address measurement bias caused by sample-specific factors.

Mean bias and individual sample bias from 40 samples measured by 20 CDC-VDSCP participants.

Diamonds: Mean Bias
Circles: Individual sample bias
The bias of some testosterone assays appears to be associated with SHBG concentrations in the sample.

Individual sample mean bias by SHBG concentration observed with one participant.

- CDC Hormone Standardization Program is screening all sera for SHBG.
Initial study suggests that some assays have no association between moderately increased biotin levels and measurement bias.

Percent difference in measurement bias between unspiked and biotin-spiked sera determined in 20 participants.

- CDC Clinical Standardization Program is screening all sera for biotin.

Sera used in CDC’s Clinical Standardization Programs have biotin concentrations of < 1 ng/mL.
CDC is continuously addressing needs and requests from its stakeholders by expanding its standardization program activities.

| Reference methods and materials development          | • PTH  
|                                                    | • Free and total T4  
|                                                    | • Glucose  
|                                                    | • Creatinine  
| Standardization and harmonization programs in development | • PTH  
|                                                    | • Thyroid function tests (Free and total T4 and TSH)  
|                                                    | • Free testosterone  
|                                                    | • Binding proteins  
| Accuracy-based Monitoring Program (AMP) for clinical and research laboratories | Available for vitamin D and testosterone  

Partnership for the Accurate Testing of Hormones (PATH) supports and promotes standardized hormone tests for better healthcare and research.

**PATH is a stakeholder organization**

- Consists of clinical, medical and public health organizations
- Promotes accurate tests and appropriate use of hormone tests through
  - Education
  - Advocacy
  - Technical Support

www.hormoneassays.org

**PATH Members**

- American Association for Clinical Chemistry
- American Society for Bone and Mineral Research
- American Thyroid Association
- American Urological Association
- Androgen Excess/PCOS Society
- Association of Public Health Laboratories
- Centers for Disease Control and Prevention
- College of American Pathologists
- Endocrine Society
- International Andrology Society
- Laboratory Corporation of America
- National Institute of Health/NICHD
- North American Menopause Society
- Pediatric Endocrine Society
- Quest Diagnostics
- Siemens Healthineers
CDC’s Clinical Standardization Programs improve the accuracy and reliability of clinical tests and enables correct and consistent diagnosis, treatment and prevention of key chronic diseases

- show measurable improvements in accuracy with tests used in research and patient care
- address calibration accuracy and sample-specific bias
- provide new accuracy-based monitoring programs designed for clinical and research laboratories
- expand to include new high priority analytes
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**CDC Standardization Team**

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Sam Caudill, PhD  
Otoe Sugahara, BS  
Ashley Ribera, BS  
Fidelia Pokuah, MPH

Komal Dahya, BS  
Krista Poynter, BS  
Lynn Collins, BS  
Nasim Khoshnam, MS  
Shahzad Momin, BS  
Deanne Lazarre, BS  
Tiancheng Edwards, BS  
Brandon Laughlin, MS  
Bianca Smith, BS  
Douglas Wirtz, BS

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**Organizations**

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Partnership for the Accurate Testing of Hormones  
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The Endocrine Society  
CDC Foundation
Thank you!

For further information, please contact standardization@cdc.gov or visit www.cdc.gov/labstandards/vdscp.html

Hubert W. Vesper, PhD
Director, Clinical Standardization Programs
hvesper@cdc.gov

For more information, contact NCEH/ATSDR
1-800-CDC-INFO (232-4636)
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