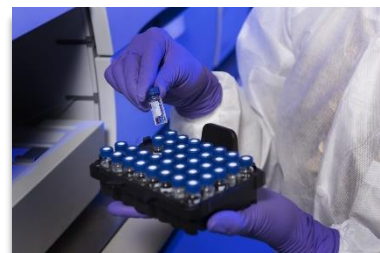




CDC CLINICAL STANDARDIZATION PROGRAMS UPDATE

CDC Clinical Standardization Programs (CSP) ensure analytical accuracy and precision across measurement systems, laboratories, and over time. The programs provide services to laboratories, manufacturers of diagnostic products, and organizations involved in proficiency testing/external quality assessment schemes.



DID YOU KNOW?

CLSI C37-A is no longer a Consensus Guideline; a new guidance document is in place now

Manufacturers of *in vitro* diagnostic medical devices, PT/EQA providers, clinical laboratories, research and calibration laboratories need commutable reference materials that can be used for calibration or trueness control.

The Clinical and Laboratory Standards Institute (CLSI) guideline C37-A, published in 1999, provided guidance to prepare commutable pooled serum reference materials. This guideline was used to create materials for a broad range of measurands. Based on the experiences obtained with this protocol, an update of the guidelines was required. In 2018, CLSI decided not to revise or update C37-A and has placed it in an archived status. This means that C37-A is no longer considered a consensus guideline.

To address the required updates, CDC convened a team of experts and created an updated protocol that was published in the journal *Clinical Chemistry and Laboratory Medicine* (***“An updated protocol based on CLSI document C37 for preparation of off-the-clot serum from individual units for use alone or to prepare commutable pooled serum reference materials”***, Danilenko U, Vesper H, Myers G, Clapshaw P, Camara J and Miller G. *Clin Chem Lab Med.* 2019 doi:10.1515/cclm-2019-0732).

The updated protocol provides step-by-step guidance for the collection of individual serum units, processing of units, qualifying the units for use in a pool and frozen storage of aliquots of pooled sera to manufacture frozen serum pools. Guidance on how to perform quality control of the final product and suggestions on documentation are also provided.

Manufacturers of commutable serum are now following this newly updated protocol. Therefore, we suggest referencing the above cited publication when referring to the procedure used to obtain commutable serum.

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Of Special Interest

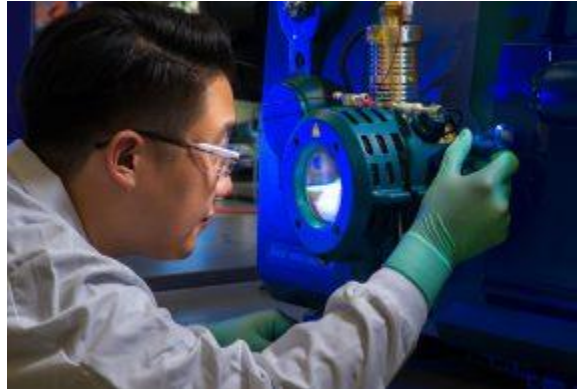
CDC CSP Update will provide information on:

- Hormone Standardization Programs (CDC HoSt)
- Vitamin D Standardization-Certification Program (CDC VDSCP)
- Thyroid Standardization Program
- Cholesterol Reference Method Laboratory Network (CRMLN)
- Lipids Standardization Program (CDC LSP)
- Accuracy-based Monitoring Programs (CDC AMP)
- New Programs and Services for Biomarker Measurements
- Latest List of Newly Certified Participants for CDC HoSt, VDSCP, AMP and LSP

CDC CSP Spotlight

Main activities led by the CDC CSP:

- Develops metrological reference methods and uses them to assign reference values to calibrators and trueness controls
- Provides sera with reference values to participants for assessing analytical bias, imprecision and sensitivity
- Evaluates routine assays for their analytical performance using established protocols and analytical performance criteria
- Issues certificates to participants meeting analytical performance criteria



CSP is conducting a commutability study of WHO/NIBSC 07/202 material for sTfR

Iron deficiency is the leading cause of anemia and affects >2 billion people worldwide. In 2004, a Joint WHO/CDC Technical Consultation recommended the measurement of serum ferritin and soluble transferrin receptor (sTfR) to assess the iron status of populations. However, the measurement of sTfR presents challenges due to a lack of assay standardization, as demonstrated by an inter-measurement procedure bias range of 132% for sTfR.

One of CDC CSP objectives is to assist with establishing high quality reference materials that can be used for calibration or trueness control. This year, CSP will conduct a study that aims to fully evaluate the commutability of a recombinant sTfR reference material released by the WHO/NIBSC in 2009 called 07/202. The study will also evaluate the commutability of differently prepared serum-based materials from 2 independent manufacturers. By identifying a commutable reference material for sTfR, assay manufacturers can then use that reference material to harmonize across different measurement procedures, thus ensuring that the results obtained for any patient sample will have equivalent results irrespective of the measurement procedure used. Agreement between results across different clinical measurement procedures is critical for the correct diagnosis and treatment of patients.

The design of the 2020 sTfR commutability study is based on the findings of a previous study conducted by the CDC in 2013. The 2020 sTfR commutability study will be completed in collaboration with major assay manufacturers and samples will be measured across several different commercially available measurement procedures. The study includes 20 individual donor serum samples that span the healthy sTfR range (1.65 – 5.40 mg/L) and that exceed this range, thus indicating iron deficiency.

The 2020 sTfR commutability study data will be analyzed according to the new **2018 IFCC Working Group's "Recommendations for Assessing Commutability"**. Materials will be considered commutable if they behave like patient samples. The impact of recalibration of the measurement procedures to the WHO 07/202 reference material will be determined by evaluating the inter-measurement procedure bias range before and after instrument recalibration. Ultimately, if established as commutable, the use of these materials as calibrators across sTfR measurement procedures will help decrease inter-assay variability and will help improve the diagnosis and treatment of patients with iron deficiency.

CDC CSP Available Programs and Services

CDC CSP improves the diagnosis, treatment, and prevention of diseases through accurate and reliable laboratory measurements. The programs and services provided by CDC CSP also assist laboratories and assay manufacturers with investigations of potential sources of bias and other imprecision.

<i>CDC CSP assists laboratories and assay developers with calibration and assessment of assay performance</i>	
Program	Analytes
Hormone Standardization (HoSt) Programs	Total Testosterone, Estradiol, Free Thyroxine (New)
Vitamin D Standardization-Certification Program (VDSCP)	Total 25-hydroxyvitamin D
Cholesterol Reference Method Laboratory Network (CRMLN)	Total Cholesterol, Total Glycerides, HDL-C, LDL-C

<i>CDC CSP enables laboratories and investigators to continuously monitor the accuracy of measurements in patient care and research studies over time</i>	
Program	Analytes
CDC Lipid Standardization Programs (LSP)	Total Cholesterol, Total Glycerides, HDL-Cholesterol, Apolipoprotein AI, Apolipoprotein B, (New): Lp(a), Non-HDL
CDC Accuracy-based Monitoring Programs (AMP)	Total 25-hydroxyvitamin D, Total Testosterone in Males, Total Testosterone in Females

<i>Method Verification of Samples and Analytes</i>
CDC offers up to 120 different samples for more detailed method verification and characterization for Total 25-hydroxyvitamin D, Total Testosterone and Estradiol. We also offer orientation values of additional steroid hormones (17 α -Hydroxyprogesterone, 17-OHP Androstenedione, Progesterone, Testosterone, Estrone, 17 β -Estradiol, Estrone sulfate, and Dehydroepiandrosterone sulfate) and 24,25-Dihydroxyvitamin D. Customization is available upon request.

CDC CSP: What's New for 2020

- **Free Thyroxine (FT4) Certification Program:** CDC has established a FT4 reference measurement procedure and is ensuring its accuracy through the IFCC reference laboratories network for FT4. The CDC Thyroid Standardization Program is scheduled to start in Summer 2020.
- **Glucose Standardization Program:** CDC has established reference measurement procedure (RMP) for Glucose in serum that will be used to assign target values to serum and EQA/PT materials.
- **Reference Method for Parathyroid Hormone (PTH):** CDC is finalizing work to develop a PTH reference measurement procedure by mass spectrometry. This method quantifies intact PTH (iPTH) and fragments. CDC plans to launch PTH standardization program in fall 2020.
- **Total Glycerides Certification by CRMLN:** CRMLN member laboratories are accepting applications for participation in Total Glycerides assay certification. Please contact one of the CRMLN member laboratories to schedule certification. https://www.cdc.gov/labstandards/pdf/crmln/CRMLN_Analytical_Services_List-508.pdf
- **Lipoprotein a (Lp-a):** CSP will have a pilot program for the standardization of Lp(a) using target values assigned by CDC mass spectrometry method.
- **Lipids Standardization Program Certification for Non-HDL Cholesterol:** The CDC Lipid Standardization Program (CDC LSP) now offers non-HDL assay certification. To enroll, contact cdclsp@cdc.gov for more information.

***Contact us for more information: Standardization@cdc.gov

Continuous Participation in Certification is Critical to Patient Care and Public Health!

Continuous evaluation and certification help to ensure that your assay's performance is consistently of high quality.

Certified Participant(s) List for CDC HoSt and VDSCP

A complete list of certified assays for **VDSCP** and **HoSt** can be viewed at:

https://www.cdc.gov/labstandards/hs_certified_participants.html (website updated quarterly).

Certified Participant(s) List for Cholesterol Reference Method Laboratory Network

Certified Manufacturers: https://www.cdc.gov/labstandards/crmln_certified_manufacturers.html

Certified Clinical Laboratories: https://www.cdc.gov/labstandards/crmln_certified_laboratories.html

Participants Meeting CDC AMP Criteria (2019)

Quarter	AMP Participant	Analyte(s)
Q1	Quest Diagnostics - Chantilly, VA	Total Testosterone in Female; Total Testosterone in Male
Q2	Quest Diagnostics - Chantilly, VA	Total Testosterone in Female; Total Testosterone in Male
	Boston Children's Hospital - Boston, MA	Total Testosterone in Female; Total Testosterone in Male; Total 25-Hydroxyvitamin D (VD)
	Pennington Biomedical Research Center - Baton Rouge	Total 25-Hydroxyvitamin D (VD)
Q3	Quest Diagnostics - Chantilly, VA	Total Testosterone in Female; Total Testosterone in Male
	Boston Children's Hospital - Boston, MA	Total Testosterone in Female; Total Testosterone in Male; Total 25-Hydroxyvitamin D (VD)

CSP Stakeholder Engagement

CDC CSP continues its engagement and collaboration in projects to support standardization and harmonization efforts through partnerships with national and international stakeholders. These activities include, for example, engagement with stakeholders on identifying priority analytes, development of reference measurement procedures and materials, and reference values assignments for projects to improve the accuracy and reliability of clinical assays used in patient care, public health and research. Additionally, CSP is providing technical assistance and consultation to other standardization programs and PT/EQA providers.

CDC CSP is providing technical assistance and support to stakeholders such as:

- **International Federation of Clinical Chemistry and Laboratory Medicine (IFCC):** Committees for Standardization of Thyroid Function Tests (C-STFT) and Bone Metabolism (C-BM), Working Groups on Apolipoproteins by Mass Spectrometry and Commutability
- **US College of American Pathologists (CAP):** Accuracy-based Surveys Committee
- **International Organization for Standardization (ISO):** ISO Technical Committee 212 (Clinical Laboratory Testing and in vitro diagnostic test systems), Working Group 2 (Reference Systems)
- **American Association for Clinical Chemistry (AACC):** Universal Sample Bank for Troponin
- **Partnership for the Accurate Testing of Hormones (PATH)**
- **Joint Committee for Traceability in Laboratory Medicine (JCTLM)**
- **US National Glycohemoglobin Standardization Program (NGSP)**
- **Clinical and Laboratory Standards Institute (CLSI)**
- **Metrological Institutes:** National Institute of Standards and Technology (NIST), Laboratoire National de métrologie et d'essais (LNE), National Institute for Biological Standards and Control (NIBSC)

Upcoming Events

CDC Standardization Programs will be present at upcoming meetings/events.

Join us to learn more about our programs and services, and to discuss our work in person:

- an update on the status of assay standardization for lipids, testosterone, estradiol and 25-hydroxyvitamin D
- information on changes to the current program and introduce new products and services to better demonstrate measurement accuracy and performance to other organizations and agencies
- outline plans for introducing new analytes such as free thyroxine (free T4), PTH and Glucose

March 28-31, 2020 – Endocrine Society's Annual Meeting, [ENDO 2020](#), San Francisco, California, USA

CDC Sessions:

- 03/29/2020, 09:00am-9:50am PST, *Room 311*
CDC Clinical Standardization Programs Forum: CDC Hormones Standardization Programs

Posters:

- 03/28/2020, 01:00pm - 3:00pm, ENDOExpo P24 - *Steroid Biology and Action Improving the Diagnosis, Treatment, and Prevention of Endocrine Diseases Through Accurate and Reliable Laboratory Measurements with CDC's Clinical Standardization Programs*
- 03/30/2020, 01:00pm - 3:00pm, ENDOExpo P71 – *Healthcare and Delivery Improving the Accuracy and Reliability of Free Thyroxine (FT4) Measurements Through the CDC Clinical Standardization Programs (CSP)*

March 29 - April 3, 2020 - **Mass Spectrometry Applications to the Clinical Lab** ([MSACL 2020](#)), Palm Springs, CA

- 03/31/2020, 08:00-9:00 pm PST., *Room 1*
CDC Clinical Standardization Programs Forum: Overview of ongoing & new CDC's Standardization Programs

May 24-28, 2020 – International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) [WorldLab Seoul 2020](#)

CDC Sessions:

- 05/27/2020, 02:30pm-4:00pm: CDC Clinical Standardization Forum
- 05/28/2020, 09:00am - 09:30am: CDC Clinical Standardization Programs for Clinical Laboratory Results
Speaker: Hubert Vesper (US)

May 31 – June 4, 2020 - [American Society of Mass Spectrometry Annual Conference](#), Houston, Texas

CDC Workshop:

- The Multidimensional Clinical Space – From Discovery to Practice in Screening and Diagnostics

July 26-30, 2020 – **AACC Annual Scientific Meeting & Clinical Lab Expo 2020**, Chicago, IL

CDC Clinical Standardization Programs will provide presentations during CDC forum and brown bag sessions at the [AACC Annual Meeting](#), *Details TBD*

CDC CSP wishes all members and program participants, a very happy New Year!

We hope to continue to hear from you on program participation, as well as suggestions for new priority items and interests.

For more information or to enroll in our Standardization Programs, contact us at:

CDC AMP/HoSt and VDSCP: Standardization@cdc.gov

LSP and CRMLN: cdclsp@cdc.gov

Website: <https://www.cdc.gov/labstandards/index.html>

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry. Use of trade names is for identification only and does not imply endorsement by the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry, the Public Health Service, or the U.S. Department of Health and Human Services.