CDC Accuracy-Based Monitoring Program (CDC AMP)

Participant Protocols for the following analytes offered in CDC AMP:

Serum Total Testosterone (TT)

Serum Total 25-hydroxyvitamin D (VD)

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GOAL

The objective of the CDC Accuracy-based Monitoring Program (CDC AMP) is to assist participants who perform routine measurements in patient care and research with maintaining and documenting high quality laboratory measurements by monitoring and evaluating the analytical accuracy and precision of their assay over time.

PRINCIPLE

The CDC AMP monitors total testosterone (TT) and total 25-hydroxyvitamin D (VD) measurements of the participating assay and compares the results to the reference values established by the CDC reference measurement procedure (RMP). Measurement bias and imprecision are assessed each quarter using predefined criteria and detailed evaluation reports are provided. Documents indicating Successful Participation or Recognition of Participation are also provided.

PROTOCOL

Safety

Consider all serum specimens potentially positive for infectious agents including HIV and the hepatitis B virus. Hepatitis B vaccination series are recommended for all analysts working with whole blood and/or plasma. Universal precautions should be observed; wear protective gloves, laboratory coats, and safety glasses during all steps of this method. Any residual sample material should be discarded by autoclaving after analysis is completed. Place disposable plastic, glass, and paper (pipette tips, auto sampler vials, gloves, etc.) that contact serum in a biohazard autoclave bag and keep these bags in appropriate containers until sealed and autoclaved. Wipe down all work surfaces with appropriate disinfectants when work is finished.

Participation

Participation in the CDC AMP is voluntary. Laboratories may enroll in the CDC AMP for one or more analytes offered; See appendix A for analytes that are currently available. Registration forms can be provided upon request by contacting standardization@cdc.gov.

Materials

The materials used to assess the analytical accuracy and precision of laboratory tests in the CDC AMP are sera obtained following the updated C37 protocol[1]. Sera prepared according to this protocol have been shown to be commutable in previous studies and were found suitable for use in trueness control and calibration[2].

All materials are shipped on dry ice, unless otherwise requested, and should be immediately stored at or below -70° C upon receipt.

Each participant will receive one box per enrolled assay that contains samples for all four quarters (1 year). Each vial contains at least 0.4 mL of serum. Vials are arranged in order of analysis in each box (12 positions for each quarter), as shown in FIGURE 1. Do not mix vials or run them out of the specified order. If samples are inadvertently mixed, please refer to the list of vials provided with the shipment or contact standardization@cdc.gov.

		1	2	3	4	5	6	7	8	9
Q1	A	1 January	2 January	3 January	4 January	5 February	6 February	7 February	8 February	9 March
	B	10 March	11 March	12 March						
Q2	C	1 April	2 April	3 April	4 April	5 May	6 May	7 May	8 May	9 June
	D	10 June	11 June	12 June						
Q3	E	1 July	2 July	3 July	4 July	5 August	6 August	7 August	8 August	9 September
	F	10 September	11 September	12 September						
Q4	G	1 October	2 October	3 October	4 October	5 November	6 November	7 November	8 November	9 December
	H	10 December	11 December	12 December						
	I									

Figure 1: CDC AMP Sample Box Orientation

Procedure

Participants are to analyze **4 consecutive samples in duplicate per month over 1 to 4 runs** along with regular patient and/or study samples. Sample IDs should be confirmed with the sample list in the data submission template provided by the CDC prior to analysis.

Ensure that the CDC AMP samples are completely thawed and homogenized prior to analysis. Do not vortex or shake vigorously. CDC AMP samples should be placed in random intervals along with study samples or patient samples in each run.

Participants should follow their laboratories' standard operating procedures for analysis. The same quality control/assurance procedures used for patient or study samples should be applied to the CDC AMP samples.

Performance is evaluated on a quarterly basis with 12 samples per quarter.

- 1st Quarter (Q1): January 1- March 31
- 2nd Quarter (Q2): April 1 – June 30
- 3rd Quarter (Q3): July 1- September 30
- 4th Quarter (Q4): October 1- December 31

Data Submission

Each participant must complete the data submission form provided by the CDC AMP which includes assay characteristics (instrumentation, calibrators, and reagents), and data results. Individual measurements are to be reported in appropriate units for each analyte (see Appendix A). All data must be submitted to the CDC AMP via email (standardization@cdc.gov) before the last day of each quarter.

Reference Values

Reference values are assigned to the sera by the CDC RMPs, which use ID-LC-MS/MS and certified primary standards as calibrators[3,4]. These sera are traceable to SI units as described in ISO 17511[5]. The CDC RMPs have been verified through comparison studies with the National Institute for Standards and Technology (NIST) and/or the University of Ghent. These methods including CDC RMPs are recognized by the Joint Committee for Traceability in Laboratory Medicine (JCTLM) as higher-order RMPs.

Data Evaluation

Bias and imprecision of the measurements are assessed using established protocols. Data evaluation reports and documents indicating Successful Participation or Recognition of Participation are provided to the participant quarterly. The acceptable overall mean bias of ±12.02% and ±15.60% for TT and VD respectively, is based on biological variability data and is used as the evaluation criteria[6,7] (See APPENDIX A). Precision evaluation uses all results from each run and is performed following procedures previously published[8]. The list of CDC AMP participants meeting criteria may be listed on the CDC CSP website.

REFERENCES

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4. Mineva EM, Schleicher RL, Chaudhary-Webb M, Maw KL, Botelho JC, Vesper HW, Pfeiffer CM. A Candidate Reference Measurement Procedure for Quantifying Serum Concentrations of 25-Hydroxyvitamin D3 and 25-Hydroxyvitamin D2 Using Isotope-Dilution Liquid Chromatography-Tandem Mass Spectrometry. Anal Bioanal Chem. 407:19 (2015).
5. European Committee of Standardization, International Organization for Standardization. In vitro diagnostic medical devices - Measurement of quantities in samples of biological origin - Metrological traceability of values assigned to calibrators and control materials (ISO/DIS 17511). Brussels. 2000.
6. Yun YM, Botelho JC, Chandler DW, Katayev A, Roberts WL, Stanczyk FZ, Vesper HW, Nakamoto JM, Garibaldi L, Clarke NJ, Fitzgerald RL. Performance Criteria for Testosterone Measurement Based on Biological Variation in Adult Males: Recommendations from PATH. Clinical Chemistry 58(12): 1703-1710, (2012).
7. Stöckl D, Sluss PM, Thienpont LM. Specifications for trueness and precision of a reference measurement system for serum/plasma 25-hydroxyvitamin D analysis. 408:8-13 (2009)
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APPENDIX A-CURRENT CDC AMP ANALYTES, MEAN BIAS CRITERIA, AND REPORTING UNITS

Analyte	Units	%B Allow*
Total Testosterone (TT)	ng/dL	±12.02
Total 25-hydroxyvitamin D (VD)	nmol/L	±15.60

* %B Allow-Criteria derived from data on biological variability[6,7].

**Precision evaluation uses all results from each run and is performed following procedures previously published[8].