CDC Accuracy-Based Monitoring Program (CDC AMP)

Participant Protocols for the following analytes offered in CDC AMP:

Serum Total Testosterone in Males (TTM)

Serum Total Testosterone in Females (TTF)

Serum Total 25-hydroxyvitamin D (VD)

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GOAL

CDC Accuracy-based Monitoring Program (CDC AMP) helps participants performing routine measurements in patient care and research to maintain and document high quality laboratory measurements by monitoring and evaluating analytical accuracy and precision.

PRINCIPLE

CDC AMP provides blinded serum samples to participants. Participants measure one sample per week, in duplicate, along with regular patient or study samples for 12 weeks (1 quarter). Participants report measurement results for AMP samples to CDC. Evaluation of results is completed using data from all 12 weeks. CDC compares measurement results with the reference values established at the CDC Reference Laboratories. Measurement bias and imprecision over each quarter are assessed using established statistical procedures. Evaluation reports are provided to participants every quarter. Documents indicating Successful Participation or Recognition of Participation are also provided to the participants every quarter.

PROTOCOL

Safety

Consider all sera specimens potentially positive for infectious agents, including HIV and the hepatitis B virus. It is recommended that all analysts working with biological samples receive the hepatitis B vaccination. Observe universal precautions.

Participation

Participation in CDC AMP is voluntary. Participants may enroll in CDC AMP for one or more offered analytes. See appendix A for analytes that are currently available for CDC AMP. Enrollment forms can be requested by contacting standardization@cdc.gov.

Materials

The materials used in CDC AMP are sera obtained following the Clinical and Laboratory Standards Institute (CLSI) C37-A "Preparation and Validation of Commutable Frozen Human Serum" 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 studies[2].

Samples are shipped frozen and should be kept frozen after arrival. Each laboratory must provide adequate frozen storage at or below -70°C.

One box, with a total of 48 vials, is provided that includes CDC AMP samples for four quarters (1 year). Each vial contains at least 0.4 mL of serum. Vials are arranged by run number in each box (12 positions for each quarter), as shown in FIGURE 1. There is one designated vial for each week. 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	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
	B	Week 10	Week 11	Week 12						
Q2	C	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
	D	Week 10	Week 11	Week 12						
Q3	E	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
	F	Week 10	Week 11	Week 12						
Q4	G	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
	H	Week 10	Week 11	Week 12						
	I									

Figure 1: CDC AMP Sample Box Orientation

Procedure

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

Participants analyze **one CDC AMP sample (in duplicate) in one run** along with patient or study samples each week. Participants should refer to the list of samples provided by CDC to determine the appropriate sample for that week. Participants test the vial designated for the specific week and quarter.

IDs on the vials should be confirmed with the list of samples prior to analyses. Ensure that CDC AMP samples are completely thawed and homogenized. Do not vortex or shake vigorously. CDC AMP samples should be placed in random intervals with study samples or patient samples each week. Participants perform this step each week for a total of 12 weeks per quarter. If measurements are not performed weekly, contact standardization@cdc.gov for alternate procedures.

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

The deadline for data submission is the last day of each quarter. The data must be recorded and submitted using the data submission forms and procedures provided by CDC AMP. Individual measurements are to be reported in appropriate units (see Appendix A). In addition to measurement results, information regarding instrumentation, calibrators, and reagents must be provided.

Reference Values

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

Data Evaluation

Data is evaluated based on established protocols. All values will be rounded to 3 significant figures prior to data evaluation. Refer to Appendix A for performance criteria which the evaluation is based. Data Evaluation Reports and documents indicating Successful Participation or Recognition of Participation from each quarterly challenge is provided to the participants. The list of CDC AMP participants meeting criteria may be shared with the public.

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 in Male (TTM)	ng/dL	12.02
Total Testosterone in Female (TTF)	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].