

§ 493.1217 Standard; Calibration and calibration verification procedures.

Calibration and calibration verification procedures are required to substantiate the continued accuracy of the test method throughout the laboratory's reportable range for patient test results. Calibration is the process of testing and adjusting an instrument, kit, or test system to provide a known relationship between the measurement response and the value of the substance that is being measured by the test procedure. Calibration verification is the assaying of calibration materials in the same manner as patient samples to confirm that the calibration of the instrument, kit, or test system has remained stable throughout the laboratory's reportable range for patient test results. The reportable range of patient test results is the range of test result values over which the laboratory can establish or verify the accuracy of the instrument, kit or test system measurement response. Calibration and calibration verification must be performed and documented as required in this section unless otherwise specified in §§ 493.1223 through 493.1285.

(a) For laboratory test procedures that are performed using instruments, kits, or test systems that have been cleared by the FDA as meeting certain CLIA requirements for quality control, the laboratory must, at a minimum, follow the manufacturer's instructions for calibration and calibration verification procedures using calibration materials specified by the manufacturer.

(b) For each method or device, as specified in either § 493.1202 (a) or (b) or § 493.1203(a), the laboratory must—

(1) Perform calibration procedures—

(i) At a minimum, in accordance with manufacturer's instructions, if provided, using calibration materials provided or specified, as appropriate, and with at least the frequency recommended by the manufacturer; and

(ii) In accordance with criteria established by the laboratory, as required under § 493.1213(b)(2)(i)—

(A) Including the number, type and concentration of calibration materials, acceptable limits for calibration, and the frequency of calibration; and

(B) Using calibration materials appropriate for the methodology and, if possible, traceable to a reference method or reference material of known value; and

(iii) Whenever calibration verification fails to meet the laboratory's acceptable limits for calibration verification; and

(2) Perform calibration verification procedures—

(i) In accordance with the manufacturer's calibration verification instructions when they meet or exceed the requirements specified in paragraph (b)(2)(ii) of this section; or

(ii) In accordance with criteria established by the laboratory—

(A) Including the number, type, and concentration of calibration materials, acceptable limits for calibration verification and frequency of calibration verification;

(B) Using calibration materials appropriate for—

(1) The methodology and, if possible, traceable to a reference method or reference material of known value; and

(2) Verifying the laboratory's established reportable range of patient test results, which must include at least a minimal (or zero) value, a mid-point value, and a maximum value at the upper limit of that range; and

(C) At least once every six months and whenever any of the following occur:

(1) A complete change of reagents for a procedure is introduced, unless the laboratory can demonstrate that changing reagent lot numbers does not affect the range used to report patient test results, and control values are not adversely affected by reagent lot number changes;

NOTE: If reagents are obtained from a manufacturer and all of the reagents for a test are packaged together, the laboratory is not required to perform calibration verification for each package of reagents, provided the packages of reagents are received in the same shipment and contain the same lot number.

(2) There is major preventive maintenance or replacement of critical parts that may influence test performance;

(3) Controls reflect an unusual trend or shift or are outside of the laboratory's acceptable limits and other

means of assessing and correcting unacceptable control values have failed to identify and correct the problem; or

(4) The laboratory's established schedule for verifying the reportable range for patient test results requires more frequent calibration verification than specified in paragraphs (b)(2)(ii)(C) (1), (2), or (3) of this section; and

(3) Document all calibration and calibration verification procedures performed.

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§ 493.1218 Standard; Control procedures.

Control procedures are performed on a routine basis to monitor the stability of the method or test system; control and calibration materials provide a means to indirectly assess the accuracy and precision of patient test results. Control procedures must be performed as defined in this section unless otherwise specified in §§ 493.1223 through 493.1285 of this subpart.

(a) For each device cleared by the FDA as meeting certain CLIA requirements for quality control, the laboratory must, at a minimum, follow the manufacturer's instructions for control procedures. In addition, the laboratory must meet the requirements under paragraphs (c) through (e) of this section and, as applicable, paragraph (f) of this section.

(b) For each device, as specified in either § 493.1202 (a) or (b) or § 493.1203(a), the laboratory must evaluate instrument and reagent stability and operator variance in determining the number, type, and frequency of testing calibration or control materials and establish criteria for acceptability used to monitor test performance during a run of patient specimen(s). A run is an interval within which the accuracy and precision of a testing system is expected to be stable, but cannot be greater than 24 hours or less than the frequency recommended by the manufacturer. For each procedure, the laboratory must monitor test performance using calibration materials or control materials or a combination thereof.

(1) For qualitative tests, the laboratory must include a positive and nega-

tive control with each run of patient specimens.

(2) For quantitative tests, the laboratory must include at least two samples of different concentrations of either calibration materials, control materials, or a combination thereof with the frequency determined in § 493.1218(b), but not less frequently than once each run of patient specimens.

(3) For electrophoretic determinations—

(i) At least one control sample must be used in each electrophoretic cell; and

(ii) The control sample must contain fractions representative of those routinely reported in patient specimens.

(4) Each day of use, the laboratory must evaluate the detection phase of direct antigen systems using an appropriate positive and negative control material (organism or antigen extract). When direct antigen systems include an extraction phase, the system must be checked each day of use using a positive organism.

(5) If calibration materials and control materials are not available, the laboratory must have an alternative mechanism to assure the validity of patient test results.

(c) Control samples must be tested in the same manner as patient specimens.

(d) When calibration or control materials are used, statistical parameters (e.g., mean and standard deviation) for each lot number of calibration material and each lot of control material must be determined through repetitive testing.

(1) The stated values of an assayed control material may be used as the target values provided the stated values correspond to the methodology and instrumentation employed by the laboratory and are verified by the laboratory.

(2) Statistical parameters for unassayed materials must be established over time by the laboratory through concurrent testing with calibration materials or control materials having previously determined statistical parameters.

(e) Control results must meet the laboratory's criteria for acceptability prior to reporting patient test results.