D5421
(Rev. 140, Issued: 05-29-15, Effective: 05-29-15, Implementation: 05-29-15)

§493.1253 Standard: Establishment and verification of performance specifications

(b)(1) Verification of performance specifications. Each laboratory that introduces an unmodified, FDA-cleared or approved test system must do the following before reporting patient test results:

Interpretive Guidelines §493.1253(b)(1)

The laboratory is responsible for verifying the performance specifications of each nonwaived unmodified FDA-cleared or approved test system that it introduces, prior to reporting patient test results. The verification of method performance should provide evidence that the accuracy, precision, and reportable range of the procedure are adequate to meet the clients' needs, as determined by the laboratory director and clinical consultant. A laboratory may use the manufacturer's performance specifications as a guideline, but is responsible for verifying the manufacturer's analytical claims before initiating patient testing.

If a method was verified by someone other than the laboratory staff (e.g., manufacturer representative), the laboratory must demonstrate that this verification correlates with its in-house test performance. This may be accomplished by the laboratory testing "known" samples.

For some qualitative tests, the laboratory may verify the manufacturer's specifications by testing known positive and negative samples to ensure that the expected results are obtained. (Specimens of known quantitative value may be used to verify the accuracy of a qualitative test.)

Prior to introducing a test for routine patient testing, the laboratory must review and evaluate the verification data.

Each laboratory is responsible for determining that its performance specifications for each test system are not affected by the relocation of the laboratory or test system. (See manufacturer's package insert regarding critical requirements such as set-up, limitations, environmental conditions, etc.) When a temporary replacement (loaner) instrument is

received which is identical (i.e., same make and model, and method for the same analyte) to the instrument which is being replaced, the laboratory must verify performance specifications.

If calibration material is used to verify method performance specifications, the laboratory must demonstrate that there is a minimal matrix effect and the calibration material is appropriate for verifying test system performance specifications.

If the LIS performs any calculations to determine a laboratory result, the calculations must be verified immediately after the LIS is programmed and prior to initial calculation of patient results.

"Less than" is used for reporting test results that are below the laboratory's detection limits for an analyte. (Detection limits must be established through method verification.) "Equivalent designation" is used to report test results for those methods that yield results below a clinically significant level (e.g., for a quantitative immunology test, patient results may be clinically negative at a 1:8 titer and test results may be reported as "1:8 negative"). (The normal value is 1:8 or less.) "Greater than" is used for reporting test results that are above the laboratory's detection limits for an analyte. If patient test results exceed the laboratory's reportable range, the laboratory must report the result as greater than the highest detection limit, re-assay a diluted patient specimen and report the calculated result, or send the specimen to a reference laboratory.

Probes §493.1253(b)(1)

How does the laboratory determine if a new or revised LIS program (whether purchased or developed in-house) performs acceptably before it is integrated into routine operation?

(b)(1)(i) Demonstrate that it can obtain performance specifications comparable to those established by the manufacturer for the following performance characteristics:

Interpretive Guidelines §493.1253(b)(1)(i)

Laboratories may simultaneously verify multiple performance specifications by choosing appropriate samples; e.g., repeatedly test (precision) samples with known (accuracy) high and low values (reportable range). This testing should be performed among all operators on different days. In addition, for test systems of the same make and model, consider verifying performance specifications of these devices at the same time.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(1)(i)(A) Accuracy.

Interpretive Guidelines §493.1253(b)(1)(i)(A)

Accuracy- The laboratory is responsible for verifying that the method produces correct results. Verification of accuracy may be accomplished by:

- Testing reference materials;
- Comparing results of tests performed by the laboratory against the results of a reference method; or
- Comparing split sample results with results obtained from another method, which has already been shown to provide accurate results.

For qualitative methods, the laboratory must verify that a method will identify the presence/absence of the analyte.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(1)(i)(B) Precision.

Interpretive Guidelines §493.1253(b)(1)(i)(B)

Precision (Reproducibility) - The laboratory is responsible for verifying the precision of each test system by assessing day-to-day, run-to-run, and within-run variation, as well as operator variance. This may be accomplished by:

- Repeat testing of known patient samples over time;
- Testing QC material in duplicate and over time; or
- Repeat testing of calibration materials over time.

EXCEPTION: For fully automated systems that are not user dependent, operator variance does not need to be evaluated.

(b)(1)(i)(C) Reportable range of test results for the test system.

Interpretive Guidelines §493.1253(b)(1)(i)(C)

Reportable Range- The laboratory is responsible for verifying the reportable range of patient test results for each test system. Verification of reportable range may be accomplished by:

- Assaying low and high calibration materials or control materials; or
- Evaluating known samples of abnormal high and abnormal low values.

Hematology whole blood high range calibration materials are not generally available. Therefore, laboratories may use patient specimens with verified elevated cell counts to verify the upper limit of the reportable range.

Probes §493.1253(b)(1)(i)(C)

If a dilution procedure is used when patient results exceed the test system's reportable range, how does the laboratory ensure the appropriate diluent is used for each type of specimen?

How does the laboratory verify and document the accuracy of the results for diluted specimens?

§493.1253 Standard: Establishment and verification of performance specifications

(b)(1)(ii) Verify that the manufacturer's reference intervals (normal values) are appropriate for the laboratory's patient population.

Interpretive Guidelines §493.1253(b)(1)(ii)

Reference Range (Normal Values) - The laboratory may use the manufacturer's reference range provided it is appropriate for the laboratory's patient population (i.e., a normal range that reflects the type of specimen and demographic variables such as age and sex, as applicable). If the manufacturer has not provided reference ranges appropriate for the laboratory's patient population, the laboratory may use published reference range(s). The laboratory must evaluate an appropriate number of specimens to verify the manufacturer's claims for normal values or, as applicable, the published reference ranges.