

## TEST METHOD VERIFICATION



### Test Method Verification

As a result of the updated CLIA regulations, before reporting patient results laboratories will need to verify or establish the performance

specifications of all non-waived tests added to the laboratory menu on or after April 24, 2003. This process may also be called "new method validation." Before April 24, 2003, this requirement only applied to new high complexity tests. Now, for all nonwaived tests, you must perform this validation:

- Whenever you add a new instrument or method, including multiple versions of the same analyte or method
- When you add a new analyte to your menu that is performed on an existing instrument
- When switching methods or reagents for an analyte already on your menu
- Before using a "loaner" instrument
- After relocating an instrument

CMS did not set specific requirements or offer procedures for performing validation. It is up to the laboratory director and clinical consultant to establish appropriate procedures. The manufacturer can assist you by providing materials, procedures, and assistance, but they may not perform the validation for you.

### Verification of Performance Specifications

For unmodified FDA approved tests, you must verify that, in your laboratory environment and using your personnel, the test performance is similar to the manufacturer's claims for accuracy, precision, and reportable range. This verification will provide evidence that the performance specifications of the test method are adequate to meet

the needs of the clients served by the laboratory. You must also verify that the normal values given by the manufacturer are appropriate for your laboratory's patient population and you must verify **calibration and control procedures**.

### Establishment of Performance Specifications

Performance specifications must be **established** if the test method being introduced is a:

- Modified FDA-approved test
- Test not subject to FDA approval (includes "home-brew" tests)
- Test for which performance specifications are not provided by the manufacturer

The establishment of performance specifications should provide evidence that the **accuracy, precision, analytical sensitivity, analytical specificity, and reportable range** of the test method are adequate to meet the needs of the clients served by your laboratory. Your laboratory must also establish **normal values** for its patient population and determine **calibration and control procedures**.

### Accuracy

Accuracy is how close a test result is to the true value. Your laboratory is responsible for verifying/establishing that the test method gives correct results. Verification or establishment of **accuracy** can be accomplished by:

- Testing reference materials
- Comparing laboratory results with a reference method
- Comparing split sample results with a clinically valid method

For qualitative methods, your lab must verify/establish that the test correctly identifies the presence or absence of the analyte.

### Precision

Precision is the degree to which repeated test results (day-to-day, run-to-run, and within-run) on the same sample agree. You are responsible for verifying/establishing this variation, as well as considering operator variance. Verification or establishment of **precision** can be accomplished by:

- Repeat testing of known samples over time
- Testing controls in duplicate over time
- Repeat testing of calibrators over time

To check operator variance, make sure all individuals that perform the test are involved in testing the samples for the study. Operator variance does not need to be evaluated for fully automated systems that are not user dependent.

### Reportable Range

Reportable range is the range of test values (from low to high) which the instrument or method can accurately measure. Your laboratory is responsible for verifying/establishing the reportable range of patient results for the test method. Verification or establishment of **reportable range** can be accomplished by:

- Testing low and high level calibrators or controls
- Evaluating known samples that have abnormal low and abnormal high levels of the analyte

### Normal Values

You must establish a reference range that is appropriate for your laboratory's patient population. If available, you may use the normal values set by the manufacturer if they are appropriate for your laboratory's patient population. If they are not appropriate for the specific population served by your laboratory, then published ranges may be used. In either case, you must evaluate an appropriate number of specimens to establish a range or to verify the manufacturer's or published range that will be used.

### Analytical Sensitivity

Analytical sensitivity is the lowest concentration or amount of the analyte that can be measured or distinguished from zero. Results that are lower than the sensitivity limit should be reported as "less than" that number rather than "zero." You could establish sensitivity by testing progressively greater dilutions of known value samples until the analyte can no longer be detected.

### Analytical Specificity

Analytical specificity is the extent to which the test method measures the analyte being tested without interference from other substances you do not wish to measure. You could establish specificity by adding known amounts of various interfering substances to a sample with a known result and comparing the results obtained to the true value.

### Calibration and Control Procedures

The laboratory must determine the test method's calibration and control procedures based upon the performance specifications given above (that the laboratory has either verified or established). Through this process, the laboratory defines:

- The frequency of calibration and control performance
- The type, number, and concentration of calibrators and controls used

The frequency for calibration and control performance must not be less than the frequency specified by the manufacturer. To establish the frequency the laboratory must consider:

- Test system, instrument, and reagent stability
- Frequency the test is performed
- Technique dependence of the method
- Frequency of quality control failures
- Training, experience, and competency of the testing personnel

### Documentation

The laboratory must document all activities involved in verifying or establishing performance specifications. Retain this documentation for as long as the test method is in use, but no less than two years.

### Resources

- See CLIA Facts 16B for details on the regulations for establishment and verification of performance specifications and calibration.
- CMS has published a brochure called Verification of Performance Specifications that may be viewed on-line at [www.cms.hhs.gov/clia/downloads/6064bk.pdf](http://www.cms.hhs.gov/clia/downloads/6064bk.pdf).