LabGuide 15

Calibration Verification

This LabGuide pertains to QSE Equipment and the Analytic Phase of the Path of Workflow.

INTRODUCTION

On January 24, 2003, the Centers for Medicare and Medicaid Services (CMS) published updated laboratory regulations that became effective April 24, 2003. These updated CLIA requirements included revised standards for calibration verification of nonwaived (moderate and high complexity) test systems.

For analytes that require calibration, laboratories must continue to perform calibration as specified in the manufacturer's instructions. In addition, laboratories must also perform calibration verification at least every six months, using at least three levels of materials that are within the reportable range of the test. COLA accreditation criteria help ensure that COLA laboratories comply with the CLIA requirements for calibration verification.

This LabGuide begins by defining calibration and calibration verification, and explaining the difference between the two related processes. It continues by providing detailed information about calibration verification to help you understand the process and meet the CLIA and COLA requirements.

Calibration "sets" the instrument to give an accurate result for each analyte.

CALIBRATION

Calibration is the process of testing and adjusting the instrument or test system readout in order to establish a correlation between the instrument's measurement of the substance being tested (the analyte) and the actual concentration of that substance. In other words, calibration "sets" the instrument to give an accurate result for each analyte.

Calibration Frequency

The laboratory is responsible for performing calibration for each analyte at the frequency specified by the manufacturer of the test. Calibration may also be required when calibration verification does not give acceptable results. If calibration for your test system is less stable than the manufacturer's recommended frequency, then more frequent calibration and/or additional calibration materials may be required, as determined by your laboratory.

Calibration Exceptions

Calibration is not required for:

- Manual procedures that do not involve an instrument; and
- Microscopic procedures.

These tests use visual interpretations rather than instrument measurements, so there is nothing to calibrate.

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014

The following are examples of manual procedures:

- Microbiology cultures;
- Tilt-tube prothrombin times; and
- ABO group and D (Rho) typing.

The following are examples of microscopic procedures:

- Urine sediment examination;
- KOH and pinworm preparations; and
- Manual WBC differentials.

The following are examples of other tests that do not require calibration:

- Most prothrombin time devices;
- Point-of-care or unit-use devices that are factory calibrated and do not permit user calibration, or those where calibration is performed internally by the instrument.
  Note: Calibration VERIFICATION is required for nonwaived devices of these types.

Calibration Materials

The test system's instructions describe the process for performing calibration, as well as the number, type, and concentration of calibration materials to use for each analyte. Calibration materials (calibrators) are solutions that contain a known amount of the analyte being measured. Some calibrators contain, and can be used to calibrate, more than one analyte. Previously, the term "standards" was used when referring to calibration materials.

Calibration verification may be required even if calibration is not.

Calibration Summary

Calibration "sets" the instrument to give an accurate result for the analyte being tested. It is performed

- At the frequency specified by the manufacturer of the test, or more frequently if determined necessary by the laboratory;
- Using the number, type, and concentration of calibration materials specified by the manufacturer; and
- When calibration verification does not give acceptable results.

LINEARITY

Before the final CLIA regulations were published in 2003, laboratories were required to perform linearity studies every six months for quantitative high complexity tests. These studies involved:

- Replicate testing of five samples spanning the reportable range;
- Determining a mean for each sample; and
- Plotting the points to produce a linear curve.

Linearity studies, as such, are no longer required by CLIA, but they are considered good laboratory practice. Calibration verification has basically replaced the process of linearity studies.

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014

REPORTABLE RANGE

Reportable range is the range of results for an analyte, from minimum to maximum, that the test system can accurately measure. Determining reportable range and other requirements for verification of performance specifications is covered in detail in LabGuide 13.

CALIBRATION VERIFICATION

Calibration verification entails testing materials with known concentrations of the analyte in the same manner as patient specimens. At least three specimens that span the reportable range of the test are tested as unknowns. They must be tested in the normal patient test mode, not the calibration mode. Compare the result values to the known values of the materials. If the values obtained are acceptable, calibration of the analyte is verified. If not, a new calibration may be required.

In other words, calibration verification checks the instrument's calibration for the analyte to verify that calibration is still valid. A successful calibration verification confirms that the test system is providing accurate results for the analyte throughout the reportable range of the test.

Calibration verification checks the calibration to verify that it is still valid.

Calibration Verification Frequency

The laboratory is responsible for performing calibration verification, for each analyte measured by the test system, every six months. It is required more frequently if:

- Specified in the manufacturer's test system instructions; or if
- The lab has determined (when establishing or verifying performance specifications) that the calibration for this test system or analyte should be checked more frequently.

The laboratory must also perform calibration verification when:

- There is a change in the reagent lot number, reagent formulation, or reagent manufacturer used for the test;

  Note: A lab is not required to perform calibration verification after lot number changes if they have documented several instances where the calibration verification was acceptable after a lot number change.

- There is major preventive maintenance or replacement of critical parts; and
- Control materials do not perform as expected.

Calibration Verification Exceptions

The requirement for calibration verification is automatically met if the test system's calibration procedure for the analyte uses three or more levels of calibration material AND:

- Includes a low, mid-point, and high value; and
- Is performed at least once every six months.

If an acceptable calibration is performed at least every six months for an analyte, then calibration verification does not have to be performed for that analyte. Calibration at

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014

least every six months satisfies the requirement for calibration verification.

The calibration verification requirements for automated hematology cell counters (CBC instruments) that utilize the impedance method are met if the laboratory:

- Follows the manufacturer's instructions for instrument operation;
- Tests at least two levels of control materials each day of testing; and
- Obtains acceptable results for the daily controls.

Calibration Verification Materials

To perform calibration verification, materials of known concentration are tested in the same manner as patient specimens. There are several different materials of known concentration that can be used for calibration verification:

- Commercially available calibration materials or linearity sets;
  - Acceptability limits are established by the manufacturer.
- Proficiency testing samples with known results;
  - CLIA-defined acceptability limits are listed in the PT summary.
- Control materials with known results; (You must use a different lot number for calibration verification than you use for your routine quality control.)
  - Acceptability limits are established by the manufacturer.
- Patient specimens with known results;
  - Acceptability limits are established by your laboratory. Use limits that are reasonable for the analyte, i.e., ± 2SD, or ± a set amount or percentage. Proficiency Testing limits are a good guide.

Use "materials of known concentration" to perform calibration verification. These materials have several sources.

Since calibration verification is used to check if the test system is providing accurate results across the reportable range of the test, it is important to use calibration verification materials for each analyte that include at least:

- A low value at or near the lower limit of the instrument's reportable range;
- A mid-point value; and
- A high value at or near the upper limit of the instrument's reportable range.

Even though many commercially available calibration verification materials contain more than one analyte, you may still need to use more than one set of calibration verification materials in order to perform calibration verification for all of the analytes on all the test systems used in your laboratory.

Calibration Verification Performance

To perform calibration verification:

1. Document the date, the analyte, and the calibration verification materials used.
2. Run at least three levels of materials, in the same manner and test mode that patient specimens are tested, and record the results. One repetition for each level is adequate, but additional repetitions will supply more data that the laboratory may find useful.
3. Compare the results obtained to the acceptable limits.
4. Document the results and indicate if the results are acceptable.

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014

Calibration Verification Example

The following is an example calibration verification to help demonstrate how to evaluate the data.

Analyte: Total Cholesterol
Instrument: ChemXYZ
Calibration Verification Material Used: XYZ Brand Commercial Calibrators
Source of Acceptable limits: Manufacturer limits

Known Value of Material	Low – 20	Mid – 150	High – 300
Acceptable limits	18 – 22	135 – 165	270 – 330
Obtained result	20	152	269
Result acceptable?	Yes	Yes	No
Comments: Recalibration may be required. Will use troubleshooting checklist first.			

Since the results for the low sample and the midpoint sample fall within the range of acceptable limits, these points are acceptable. Since the high value sample result is below the acceptable limits, this point is unacceptable.

A successful calibration verification requires acceptable results for all materials tested. This data means the calibration verification for this analyte failed, which means that the instrument calibration for this analyte may no longer be valid and corrective action is needed.

Corrective action is needed whenever calibration verification fails.

When Calibration Verification Fails

If your calibration verification fails (results for one or more levels of materials are not acceptable) for any analyte, you may need to recalibrate the instrument for that analyte. A troubleshooting checklist is provided at the end of this LabGuide to help uncover potential problems that require corrective action. Proceed through the troubleshooting checklist and attach the completed form to your calibration verification worksheet.

If calibration verification fails on a test system that is factory-calibrated by the manufacturer and cannot be recalibrated by the laboratory, then contact the manufacturer for advice on what steps to take next.

Corrective Action

The troubleshooting checklist may uncover a problem that you can correct (e.g., replacing expired material). If so, calibration verification can simply be repeated once the correction has been made.

The checklist may also uncover a problem that indicates a new calibration (recalibration) is necessary. If so, recalibrate by following the manufacturer's instructions for calibration.

Corrective action is needed even if the troubleshooting checklist does not uncover the cause of the problem. Recalibrate the instrument for the analyte by following the manufacturer's instructions for calibration.

Document the calibration and indicate that it was performed in response to an

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014

unsuccessful calibration verification. Run all levels of controls after calibrating the instrument and document the results.

If the instrument still does not perform as expected, call the manufacturer for further troubleshooting advice.

Documentation

Document all actions taken when performing calibration verification, and those taken during an investigation of calibration verification failure. All corrective actions taken and those taken during follow-up of corrective actions should be documented also.

Retain this documentation for at least two years. The retention period may be longer depending on other Federal, State, local, and organizational regulations and requirements.

Calibration Verification Summary

The CLIA regulations published in 2003 specify requirements for calibration verification of nonwaived testing. The COLA criteria for calibration verification are derived from these requirements.

Calibration verification checks the test system's calibration at a point in time to determine if it is still providing accurate results for the analyte throughout the reportable range.

Perform calibration verification for each analyte at least once every six months, or whenever certain situations occur.

Perform calibration verification using materials of known concentrations.

Properly document all calibration verification actions and any corrective actions taken.

Retain records of all calibration verification activities for at least two years.

Document all actions taken and retain this documentation for at least two years.

REFERENCES

CLIA Regulations, Subpart K, 493.1255, *Standard: Calibration and calibration verification procedures*; http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1255

CMS Brochure #3 Calibration and Calibration Verification; http://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/6065bk.pdf

COLA Criteria for Quality Laboratory Performance, Evaluation Grouping: Calibration.

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014

CALIBRATION VERIFICATION
WORKSHEET AND DOCUMENTATION FORM

Date _____ Analyte _____

Instrument _____ Serial # _____

Reagent/strip/cassette Lot # _____ Expiration Date _____

Calibration Materials Used _____

Source of Acceptable Limits _____

	Low Level	Mid Level	High Level
Lot Number			
Expiration Date			
Expected Result			
Acceptable Limits			

Calibration Verification Results

	Low Level	Mid Level	High Level
Repetition #1			
Repetition #2			
Repetition #3			
Mean			
Results acceptable?			

Comments and/or Corrective Actions _____

_____

_____

Performed by _____

Reviewed by _____ Date _____

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014

CALIBRATION VERIFICATION TROUBLESHOOTING CHECKLIST

Date _____ Analyte _____

Instrument _____ Serial # _____

1. Check the analyte's Quality Control (QC) results.		
Are there any patterns seen in the control results?	☐ Yes	☐ No
Are all values below the mean?	☐ Yes	☐ No
Are all values above the mean?	☐ Yes	☐ No
Are there any noticeable shifts or trends over time?	☐ Yes	☐ No
Are accuracy and precision acceptable?	☐ Yes	☐ No
Comments _____		
2. Check the calibration verification materials.		
Are the materials appropriate and in-date?	☐ Yes	☐ No
Have the acceptable limits been properly determined?	☐ Yes	☐ No
Comments _____		
3. Check the reagents.		
Have the reagents changed in any way? (Include a check for discoloration, cloudiness, and contamination.)	☐ Yes	☐ No
Is there a new lot number in use?	☐ Yes	☐ No
Has the reagent manufacturer changed?	☐ Yes	☐ No
Has the reagent formulation changed? (Check the package insert.)	☐ Yes	☐ No
Are reagents in-date?	☐ Yes	☐ No
Comments _____		
4. Check instrument maintenance. *Review **all** maintenance logs (daily, weekly, monthly, quarterly, annually, etc.)*		
Are there any missing maintenance actions, any problems, or any changes?	☐ Yes	☐ No
Comments _____		
5. Check the environment.		
Has the instrument been moved recently?	☐ Yes	☐ No
Have there been any changes to the instrument's environment or surroundings?	☐ Yes	☐ No
Comments _____		
6. Check instrument service records.		
Has the instrument been serviced recently?	☐ Yes	☐ No
Have there been any software or hardware upgrades or changes?	☐ Yes	☐ No
Comments _____		
7. Check instrument operation.		
Are there new instrument operators?	☐ Yes	☐ No
Are all operators following established procedures for instrument operation?	☐ Yes	☐ No
Has the test procedure / technique been modified recently?	☐ Yes	☐ No
Comments _____		
8. Check a comparative method.		
Is there another laboratory that could test the calibration verification materials so results can be compared?	☐ Yes	☐ No
Comments _____		
9. Is recalibration indicated for the analyte?	☐ Yes	☐ No

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Original: 05/2007
Revised: 08/20/2012
Next Scheduled Review: 08/22/2014