

# Reportable Range, Linearity & Calibration Verification

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## Laboratory Technology

At the outset, validating a new instrument may seem like a daunting task. Lab accrediting agencies describe how these tasks should be accomplished, but their use of varying terminology adds confusion to the process. CLSI (Clinical and Laboratory Standards Institute) is an international, non-profit, educational organization that promotes the development and use of standards within the healthcare community. CLSI applies a consensus approach drawing from sources, including the College of American Pathologists (CAP), U.S. Clinical Laboratory Improvement Amendments (CLIA), the World Health Organization (WHO) and European Directives, in an attempt to standardize laboratory practices around the world. I rely on these CLSI guidelines, both for updates on best practices and for teaching.

## Guidelines, Clarification

Prior to implementing an FDA-cleared or approved test system and reporting patient results, U.S. laboratories subject to CLIA '88 must demonstrate that [their instrument] can obtain performance specifications comparable to those established by the manufacturer for the following performance characteristics:

- Accuracy
- Precision
- Reportable range of test results for the test system

- Reference intervals (normal ranges)

Specific to “reportable range,” a somewhat ambiguous term, CLSI provides clarification in document H26-A2, Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard-Second Edition. CLSI refers to the concept of reportable range as the Analytical Measuring Interval (AMI) while CAP uses the term Analytical Measurement Range (AMR). Both AMI and AMR refer to “the range of analyte values that a method can directly measure on the specimen without any dilution, concentration, or other pretreatment not part of the usual assay process,” and correspond to the CLIA reportable range.

CLSI and CAP recognize the Clinically Reportable Interval (CRI) or Clinically Reportable Range (CRR) as “the range of analyte values a method can measure, allowing for specimen dilution, concentration or other pretreatment used to extend the direct analytical measurement range.” To report a platelet (PLT) result that exceeds the upper limit of the AMI, the specimen is diluted and reanalyzed to bring the PLT concentration into that range, and the final result is calculated using the dilution factor. The CRI is established at the time of initial validation and is a decision made by the lab director to meet clinical needs.

## **Linearity**

Linearity is achieved when measured results are directly proportional to the concentration of the analyte in the test sample, within a given range. CLSI clarifies the term linearity in regards to the majority of hematology analyzers that function primarily as particle counters: “Linearity is a chemistry concept in relation to spectrophotometric absorbance/transmission and measurand [analyte]concentration. Technically, only the hemoglobin measurement on a hematology instrument is such a chemistry test.”

## **Calibration Verification**

Calibration verification is the assaying materials of known concentration in the same manner as patient samples to substantiate the instrument’s calibration throughout the reportable range for patient test results. If the calibration verification confirms that calibration settings are valid for a method, no further calibration actions are necessary. Calibration verification requires the use of materials with assayed values while verification of the reportable range does not.

The goal is to verify that the manufacturer’s claim for AMI performance is correct for the specific instrument or test method in the lab. Streck offers products to meet these AMI and calibration verification requirements, upon instrument install and during routine use.

Streck's Calibration Verification Assessment (CVA) and Retic-Chex® Linearity (reticulocyte assessment) provide assay values for the most common hematology systems in the U.S. By running these kits, the lab can simultaneously verify both the analytical measurement interval/range and calibration verification for RBC, Hgb, PLT and WBC. Instrument performance is also evaluated against a peer group. Many CLIA labs purchase CVA every six months. Labs without instrument-specific assay values receive a report to document verification of the AMI. Streck's A1c-Cellular® Linearity kits provide assay values for the most prevalent chemistry systems and the reports also include a peer comparison.

The lowest and highest acceptable means attained for each parameter (within the published ranges and given that the visual inspection of the graph is linear) are the system's proven upper and lower limits. CLSI H26-A2 explains that the AMI cannot extend lower than the background count or limit of blank (LoB). If the background counts are nonzero values, establishing a reportable range to zero would "lack scientific sense."