

Validation of Reportable Range of Hematology Instrumentation

One of the requirements to validate a new instrument

Regulatory agencies require that a laboratory validate an instrument before it is put into use for patient testing. The validation of the patient reportable range is one of those requirements. This requirement applies to all non-waived test systems introduced into the laboratory on or after April 24, 2003.

Laboratories are required to establish and verify the performance specifications of new instrumentation

Laboratories must have documentation that they have verified the performance of a new analyzer.

The Clinical Laboratory Improvement Amendment (CLIA) regulations state that the laboratory must demonstrate that it can obtain performance specifications comparable to those established by the manufacturer when it introduces a new hematology analyzer. Before reporting patient test results, the lab needs to demonstrate the accuracy and precision of the analyzer. They must also verify the reportable range of test results for the test system, as well as showing that the manufacturer's reference intervals (normal values) are appropriate for the laboratory's patient population.

Laboratories not only need to perform these validations, they must document them and have them available for inspection during a laboratory survey.

This document will explain the process used to validate the reportable range of a new hematology instrument. The document will not deal with the determination of the accuracy or precision of a new analyzer, nor will we discuss how to validate the laboratory's reference values.

Regulatory bodies require the establishment of performance specifications

Laboratories must establish the reportable range of new instrumentation.

The College of American Pathologists (CAP) and CLIA both require the establishment of an instrument's reportable range. CAP splits the reportable range requirement into two distinct groups: the analytical measurement range (AMR) and the clinically reportable range (CRR).

The CLIA regulations state the following:

Sec. 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:

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

- (A) Accuracy.
- (B) Precision.
- (C) Reportable range of test results for the test system.

The CLIA interpretive guidelines explain how to achieve the goal:

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.

Materials are available for assessment of a hematology instrument's reportable range.

The last statement, "*Hematology whole blood high range calibration materials are not generally available*" is outdated. Streck has calibration materials available for the assessment of the instrument reportable range. The products are CVA (Calibration Verification Assessment) and Retic-Chex Linearity. These products come with instrument-specific ranges for most hematology instruments on the market.

College of American Pathologists

CAP breaks the reportable range into the AMR and the CRR.

The College of American Pathologists utilizes the same criteria to establish the reportable range as CLIA. However, CAP splits these criteria into the two distinct groups: the analytical measurement range (AMR) and the clinically reportable range (CRR).

CAP Laboratory General Checklist states the following:

GEN.42085

Is the reportable range verified/established for each analytic procedure before implementation?

NOTE: The reportable range includes all results that may be reliably reported, and embraces two types of ranges:

1. The ANALYTICAL MEASUREMENT RANGE (AMR) is 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.

2. The CLINICALLY REPORTABLE RANGE (CRR) is the range of analyte values that a method can measure, allowing for specimen dilution, concentration, or other pretreatment used to extend the direct analytical measurement range.

Joint Commission on Accreditation of Healthcare Organizations

JCAHO requires linearity on hematology analyzers every six months.

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) not only requires verification of the reportable range when an instrument is put into initial service, but it also requires calibration verification every six months. Streck asked for guidance for the following situation:

Does JCAHO require linearity testing on hematology instruments every six months (the same as the standard for chemistry analyzers)? If so, how many levels would be required and are all of these parameters included: WBC, RBC, HGB, Platelet, and Reticulocyte Count?

Here is the answer provided by the JCAHO Standards Interpretation Group:

“Calibration verification requires a minimum of three levels that span the patient reportable range. It is required semiannually for all non-waived test systems that have a calibration process. Previously, it had only been required for high complexity testing.”

How your lab can fulfill these requirements

Streck offers two products to assist labs in determining the reportable range of a new instrument.

Streck offers two products to assist your lab in the validation of new hematology instruments. CVA (Calibration Verification Assessment) is a multi-level product designed to verify the reportable range for white blood cell count (WBC), red blood cell count (RBC), hemoglobin, and platelet count. Retic-Chex[®] Linearity verifies the reportable range of the reticulocyte portion of the red blood cell population. These products can also be used for periodic linearity assessments and calibration verification.

The laboratory runs the appropriate levels of these products and the results are graphed. Streck provides data analysis for both CVA and Retic-Chex Linearity through our *STATS*[®] department. If the values obtained are within the assay range for the specific instrument, the laboratory may report patient results between the lower and upper levels that have been verified. The upper or lower levels verified may not exceed the manufacturer's stated linearity limits.

For example:

The manufacturer states that the limits of the WBC on their instrument are 0-120.

The lowest level that could be verified is 0.5.

The upper level is 130.

The verified reportable range of the instrument is 0.5-120.

The reportable range can not exceed the manufacturer's limits.

The lower limit of the range is 0.5, because that is the lowest level that could be verified by the laboratory. The lab could not use the manufacturer's lower limit of 0 because they have not proven that the instrument values below 0.5 are valid.

The upper limit of the range is 120, because although the lab has shown that the instrument is linear to 130, the manufacturer does not make that claim. The laboratory may only go as far as the limit that the manufacturer has placed on their instrument.

A good rule of thumb to remember is to choose the value that gives the tightest range.

Summary

Regulatory agencies require that a laboratory validate an instrument before it is put into use for patient testing. The laboratory needs to demonstrate the accuracy and precision of the analyzer, as well the validation of the patient reportable range. Streck offers two products to assist in the validation of new hematology instruments. CVA, a multi-level product designed to verify the reportable range for WBC, RBC, hemoglobin, and platelet count; and Retic-Chex Linearity for reticulocytes. The laboratory can submit their data to Streck's *STATS* department for a complete linearity and reportable range analysis. There is no need for the laboratory to calculate its own data.

Establishing reportable range is easily accomplished with CVA and Retic-Chex Linearity.