# EP Evaluator®

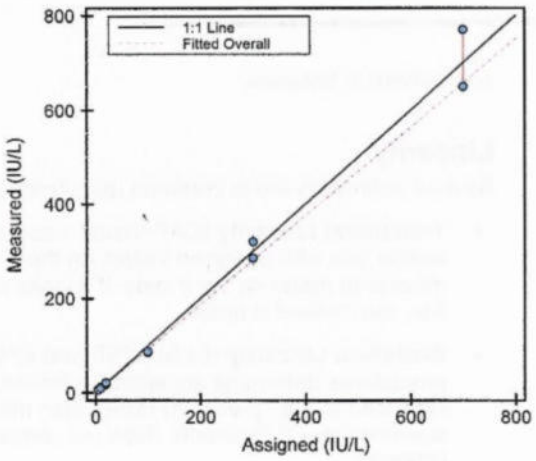
Core Laboratory

**ALT**

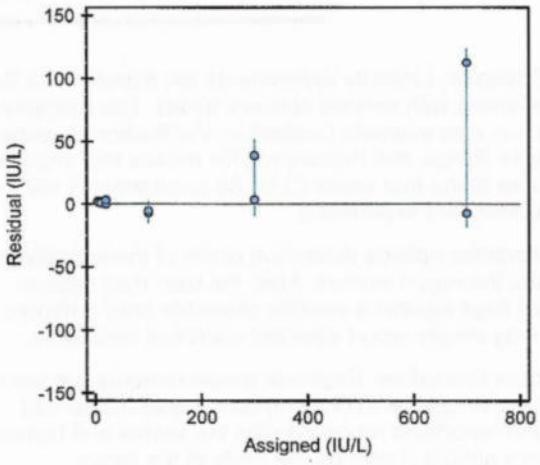
**Instrument Cobas Integra**

## Linearity

### Scatter Plot




### Residual Plot




### Linearity Summary

| | N | Slope | Intercept | Error | RSQ |
|---|---|---|---|---|---|
| Overall | 6 | 0.940 | -0.55 | 1.85 IU/L (concyWT/4% | |

LINEAR within SEa of 2.5 IU/L (cone) or 10.0%

S'

### Statistical Analysis and Experimental Results

| | Assigned | Est | Mean | Residual | Linear? | Measured Concentrations | |
|---|---|---|---|---|---|---|---|
| 1 | 5 | 4.15 | 6.00 | 1.85 | Pass | 6.5 | 5.5 |
| 2 | 10 | 8.85 | 10.25 | 1.40 | Pass | 11 | 9.5 |
| 3 | 20 | 18.25 | 19.75 | 1.50 | Pass | 18 | 21.5 |
| 4 | 100 | 93.44 | 87.00 | -6.44 | Pass | 86 | 88 |
| 5 | 300 | 281.43 | 302.50 | 21.07 | Pass | 285 | 320 |
| 6 | 700 | 657.41 | 710.00 | 52.59 | Pass | 650 | 770 |

See User's Specifications for Pass/Fail criteria

X: Excluded from calculations

### User's Specifications

| | |
|---|---|
| Allowable Total Error | 5 IU/L (cone) or 20.0% |
| Systematic Error Budget | 50% |
| Allowable Systematic Error | 2.5 IU/L (cone) or 10.0% |

### Supporting Data

| | |
|---|---|
| Analyst | XYZ Lab |
| Date | 03 Aug 2023 |
| Value Mode | Pre-Assigned |
| Units | IU/L |
| Controls | – |
| Reagent | – |
| Calibrators | – |
| Comment | |

## Evaluation of Results

The Linearity of ALT was analyzed on Cobas Integra over a measured range of 6.00 to 710.00 IU/L. Accuracy and Reportable Range were not evaluated in this experiment. Allowable systematic error (SEa) was 2.5 IU/L (cone) or 10.0%. The results are LINEAR.

Accepted by: _____ _____

Signature Date

# EP Evaluator®

Core Laboratory -- The Johns Hopkins Hospital

## Linearity

Report Interpretation Guide

In EP Evaluator, Linearity experiments are experiments that use specimens with defined concentrations. The Linearity module can also evaluate Calibration Verification, Accuracy, Reportable Range and Precision. This means that you can verify three of the four major CLIA '88 requirements with one properly designed experiment.

User-selectable options determine which of these analytical properties the report verifies. Also, the user may request Pass/Fail flags against a specific allowable error criterion, or he/she may simply report selected statistical measures.

Experiment Procedure: Replicate measurements are made on 3-11 specimens, with (known) concentrations spread across the reportable range. Ideally, the lowest and highest specimens should challenge the limits of the range.

### Accuracy (or Recovery)

**Definition:** The ability to recover the correct amount of analyte present in the specimen.

**Verification process:** Accuracy can be verified only when the "correct" amount of analyte **(the Assigned Value)** is known. While it is possible to evaluate recovery using a single replicate, assaying 2 to 4 replicates provides a more reliable estimate.

**Key statistic:** Recovery = 100 x Measured Mean / Assigned Value

### Reportable Range

**Definition:** As used in CLIA, Reportable Range refers to the Analytical Range or Assay Range -- the maximum range of values that can be assayed accurately without dilution. The CAP term "Analytical Measurement Range" (AMR) is a synonym for Reportable Range.

**Verification Procedure:** Reportable Range is verified if two conditions are met: 1) the assigned values of the lowest and highest specimens are within proximity limits of the Reportable Range limits, and 2) these two specimens are acceptably accurate.

**Proximity Limits:** Proximity Limits define how close the lowest and highest specimens must be to the Reportable Range limits.

### Calibration Verification

Calibration Verification verifies whether a method is properly calibrated by verifying both Accuracy and Reportable Range. The report is titled to match the CAP and CLIA regulatory requirements.

CLIA requires a minimum of three specimens, each assayed in duplicate. Two specimens challenge the lower and upper limits of the reportable range. The third specimen is somewhere in between.

### Linearity

Several definitions are in common use. Among them:

- **Traditional Linearity** (CAP Visual Inspection): Draw a scatter plot with assigned values on the X-axis and measured mean on the Y-axis. If it looks like a straight line, the method is linear.
- **Statistical Linearity** (CLSI EP6P and EP6-A): These procedures determine acceptability based on statistical significance (i.e., p-values) rather than medical significance. EP Evaluator does not compute Statistical Linearity.
- **Clinical Linearity:** The method is linear if it is possible to draw a straight line that passes within a user-defined allowable error of each specimen point.

Related concepts:

- **Best Fit Line:** If the user opts to verify Linearity, this line is obtained using the Clinical Linearity algorithm. Otherwise it is a regular linear regression line.
- **Outliers:** When verifying Linearity, the program first tries to determine an acceptable line using all specimens. If it fails, it then tries to find some subset of at least three specimens that are linear within allowable error. Specimens not in this acceptable subset are classified as outliers.
- **Slope and Intercept:** Coefficients of the Best Fit Line. The ideal slope is 1.00; the ideal intercept is zero.
- **Observed Error:** For Clinical Linearity, this is the minimum allowable error that could be defined for a data set and still have it be linear.
- **Standard Error of Estimate:** For regular regression, this measures the dispersion of the data points around the Best Fit Line.
- **Residual:** The difference between the best fit line and either an individual result or a mean measured value, depending on context.
- **RSQ:** The coefficient of determination r-squared (rsq) appears in the report's "Linearity Summary" or detail screen plot when enabled in the Preferences\Reports menu. It does not appear when "Clinical Linearity" is selected.

### Precision

**Definition:** Ability to obtain the same result upon repeated measurement of a specimen.

**Verification Process:** Measure the specimen many times.

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## Linearity

Report Interpretation Guide

Compute the SD and CV, and verify that they are acceptably small. While 2-4 replicates are adequate for assessing accuracy, a minimum of 10 (and preferably 20 or more) is required to verify Precision.

The **Precision Index** is the ratio of SD to Allowable Random Error (defined below). The ideal -- and probably unattainable -- Precision Index is zero. A value of 1.00 indicates borderline acceptability. Any further increase in SD would exceed allowable error.

The **95% Confidence Interval** (CI) for the Precision Index indicates how much sampling variation might be expected. The CI narrows as the number of replicates increases.

### Allowable Total Error (TEa), and the Error Budget

TEa states the laboratory's policy for how much error is medically (or administratively) acceptable. Regulatory requirements represent an upper limit. Example: the CLIA limit for Sodium is 4 mmol/L.

Total Error has two major components: **Systematic Error** (synonym Bias) and **Random Error** (synonym Imprecision). The **Error Budget** allocates a fraction of the Allowable Total Error for Systematic Error, and the remaining fraction for Random Error. Establishing an appropriate Error Budget allows the lab to control accuracy and precision separately, with reasonable confidence that Total Error will also remain in control. The recommended upper value for the Systematic Error Budget is 50%; for the Random Error Budget it is 25%.

### Pass or Fail?

The program reports Pass/Fail for Accuracy and Linearity based on Allowable Systematic Error (SEa). Pass/Fail for Precision is based on Allowable Random Error (REa).

- A specimen passes Accuracy if its mean measured value is within SEa of the Assigned Value. Note that if the lowest standard has an assigned value of zero, then the TEa conc must not be blank or "0". Otherwise the experiment will fail.
- The experiment passes Linearity if it is possible to draw a straight line (on the scatter plot of mean measured value vs. assigned value) that passes within +/- SEa of each specimen point.
- A specimen passes Precision if SD does not exceed REa.
- The experiment passes Reportable Range if 1) the assigned values of the lowest and highest specimens are within proximity limits of the Reportable Range Limits, and 2) these two specimens also pass accuracy.

### Preliminary Report

The word PRELIMINARY printed diagonally across the report indicates that the data is incomplete, and the report is not acceptable as a final report. Some or all of the statistics may be missing.

The Linearity report is preliminary if there are less than three specimens.