EP Evaluator

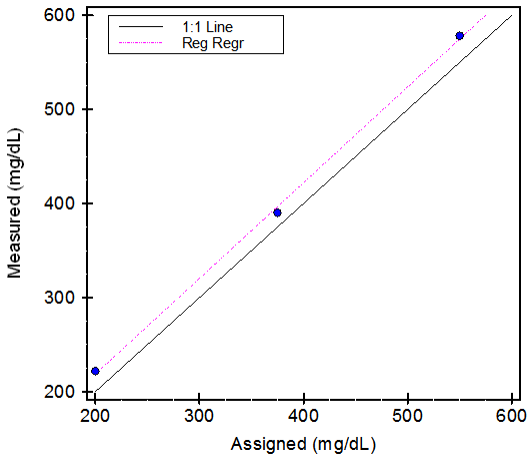
GLU CARD

Prepared for: Chemistry -- New Century Diagnostics

Instrument: Beckman LX-20

Linearity

Scatter Plot



Linearity Summary

	N	Slope	Intercept	Error
Reg. Regression	3	1.017 ± 0.033	15.2 ± 13.2	8.2

Statistical Analysis and Experimental Results

	Assigned	Est	Mean	Resid	% Rec.	Measured Concentrations
9501	50	--	--	--	--	--
9502	200	218.7	222.0	3.3	111.0	222
9503	375	396.7	390.0	-6.7	104.0	390
9504	550	574.7	578.0	3.3	105.1	578
9505	725	--	--	--	--	--

X: Excluded from calculations

User's Specifications

Allowable Total Error: --
Systematic Error Budget: --
Allowable Systematic Error: --

Supporting Data

Analyst: CC
Date: 15 Jun 2011
Value Mode: Preassigned
Units: mg/dL
Lot Number:
Comment:

Analytical Claim

The Linearity of GLU CARD was analyzed on Beckman LX-20 over a measured range of 222.0 to 578.0 mg/dL.

Accepted by: _____ _____

Signature Date

Linearity

Report Interpretation Guide

For EP Evaluator purposes, Linearity experiments are experiments that use specimens with defined concentrations. This includes Calibration Verification, Accuracy, and Reportable Range, as well as Linearity. The Linearity module can also verify Precision. This means you can verify three of the four CLIA '88 requirements with a single experiment.

User-selectable options determine which of these parameters 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 determine recovery using a single replicate, one gets a more reliable estimate when 2 to 4 replicates are assayed.

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

Reportable Range

Definition: As used in CLIA, this term 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 define how close the lowest and highest specimens must be to the Reportable Range limits.

Calibration Verification

verifies whether a method is properly calibrated. Calibration Verification is identical to verifying both Accuracy and Reportable Range. The only difference is that the report is titled to match the regulatory requirement.

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 it 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, 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, measures 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.

Precision

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

Verification Process: Measure the specimen many times. 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

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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 another 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. Recommended ranges of values are 25-50% for the Systematic Error Budget and 16-25% for the Random Error Budget.

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.
- 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.