The Calibration Verification/Linearity Program: Meeting Regulatory Requirements and Improving Laboratory Quality

Anthony Killeen, MD, PhD
Patricia Styer, PhD
William Castellani, MD

May 6, 2011

www.cap.org

Speakers (in order of presentation)

- **Anthony Killeen, MD, PhD, FCAP**
  - **Chair, Instrumentation Resource Committee**
- **William Castellani, MD, FCAP**
  - **Inter-Regional Commissioner for the CAP Laboratory Accreditation Program and Chair of the CAP ISO15189 Committee**
- **Patricia Styer, PhD**
  - **Biostatistics Consultant, College of American Pathologists**

Outline

- **Introduction (Dr. Killeen)**
- **CLIA and LAP Regulations for Calibration Verification and AMR Validation (Dr. Castellani)**
- **Overview of the CAP Calibration Verification/Linearity Program (Dr. Styer)**
- **Examples and Troubleshooting (Dr. Killeen)**

CLIA Calibration Verification

- **Periodic verification that the calibration of the analytical system remains valid**
- **Required by Clinical Laboratory Improvement Amendment (CLIA) if the test system has not been recalibrated for 6 months**
- **Typically assessed by comparing test results from samples with those samples' expected target values**
- **If the calibration changes, then patient test result values will also change**

Linearity

- **From Clinical Laboratory Standards Institute (CLSI) document EP6-A (2003)**
  - **A quantitative analytical method is linear when there exists a mathematically verified straight-line relationship between the observed values and the true concentrations or activities of the analyte.**
  - **The linearity of a system is measured by testing levels of an analyte which are known by formulation or known *relative to each other* (not necessarily known absolutely).**

CLSI. *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.* CLSI document EP6-A (ISBN 1-56238-498-8). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2003.

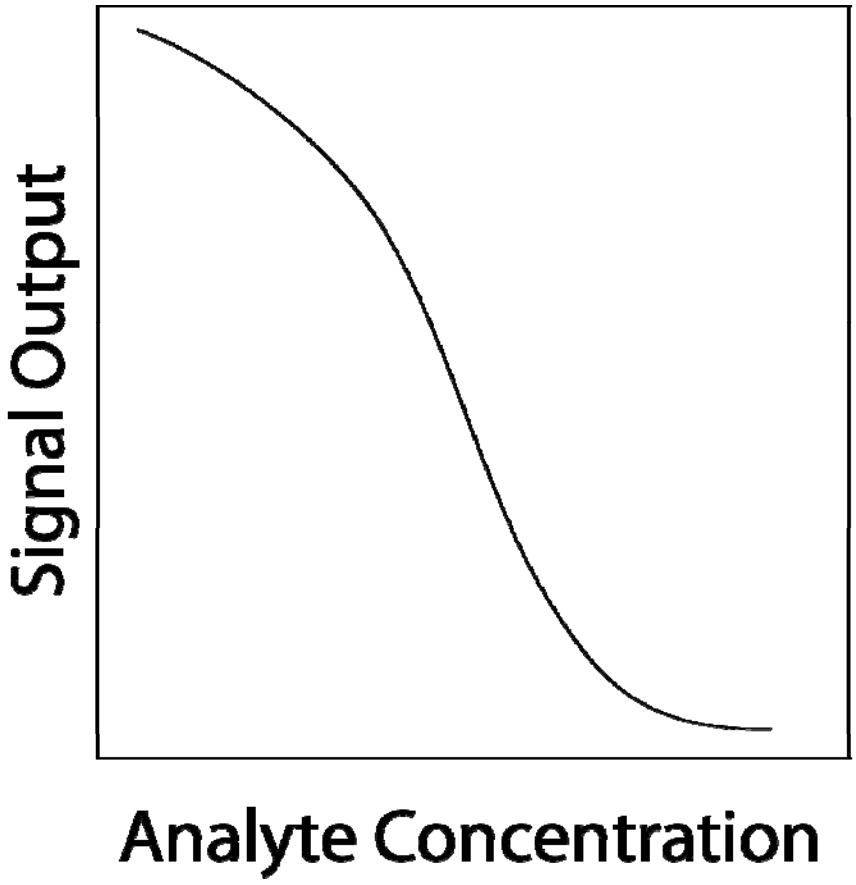
CLIA Calibration Verification vs. Linearity

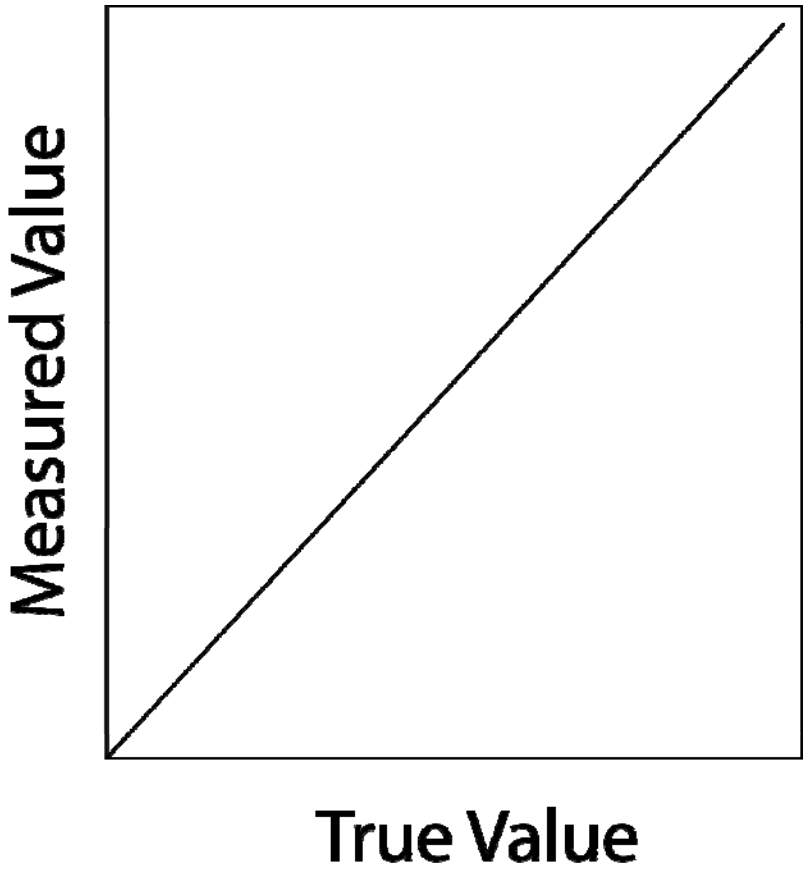
- **Calibration verification is the process of verifying agreement between calibrators (or other materials of known analyte concentrations) and measured values**
- **Calibrators should ideally be traceable to a reference method to ensure accuracy**
- **Linearity evaluation does not require knowledge of the "true" analyte concentration**
- **"Linearity" does not appear in CLIA**

Linearity vs. Instrument Response

- **Linearity typically refers to the final analytical result, *not the raw instrument output***
  - **A plot of analyte concentration vs. the raw instrument output may not be linear (e.g., competitive immunoassay)**
- **"Linearity" as used in this context means a straight-line relationship between "true" analyte concentrations and measured concentrations**

Linearity vs. Instrument Response

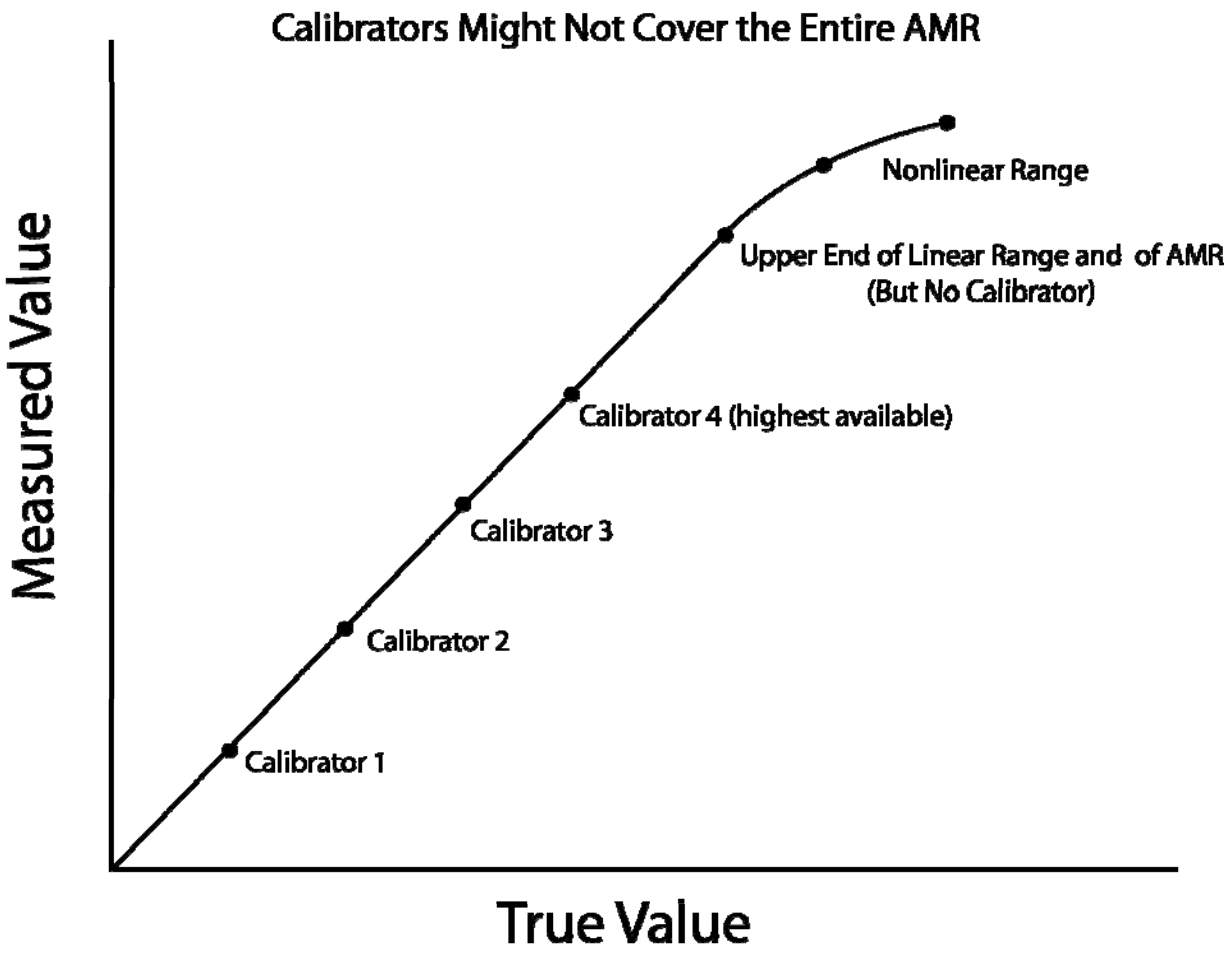




Linearity and the Analytical Measurement Range

- **The analytical measurement range is the range of concentrations that an instrument can measure without any pretreatment of the sample (e.g., concentration, dilution) that would change the concentration of an analyte**
- **An analytical system should show linearity over its analytical measurement range**

Linearity and the Analytical Measurement Range



Advantages to Participating in the CAP Calibration Verification/Linearity Program

- **CVL program provides test samples and data analysis to assist laboratories in meeting CLIA and LAP requirements**
- **Samples are prepared to challenge the full analytical measurement range**
- **Linearity testing often has smaller absolute limits for error, based on medically or analytically relevant criteria, than does PT**
- **Can detect problems earlier than QC or PT**

CLIA and LAP Requirements for Calibration Verification and AMR Validation

Presented by William Castellani, MD

Calibration and Calibration Verification

- **"Calibration" means a process of testing and adjusting an instrument or test system to establish a correlation between the measurement response and the concentration or amount of the substance that is being measured by the test procedure.**
- **"Calibration verification" means the assaying of materials of known concentration in the same manner as patient specimens to substantiate the instrument or test system's calibration throughout the reportable range for patient test results.**

- Centers for Medicare and Medicaid Services, State Operations Manual, Appendix C

Reportable Range

- ***Reportable range*** **means the span of test result values over which the laboratory can establish or verify the accuracy of the instrument or test system measurement response.**

- CLIA '88, Sec. 493.2, *Definitions*

Reportable Range Continued

- **Two components:**
  - **The primary range of measurement**
    - *Analytical measurement range*
    - *"Linear" range*
  - **Anything done to the system to expand this range**
    - *"Clinical reportable range"*
    - *Reportable range*

Requirements for Compliance

- **Validate or verify**
  - **Reportable range: as part of method validation**
  - **Analytical measurement range: as part of method validation and every six months thereafter (when necessary)**

Other Considerations

- Set criteria of acceptance
- Established protocol
- Medical relevance
  - All of this should be established by the laboratory director
  - All of this should be documented formally
  - The actual review may be delegated, though final authorization may be reserved for the director

General Principles

- **Establish a target value**
  - **May use a patient sample's result as the "target"**
  - **May use peer group mean of PT material**
  - **May be established by the provider of the material**
- **Establish an acceptable range around the target**
  - **May be a laboratory-assigned range [10%]**
  - **May use precision data for control material near the target**
  - **May be provided by the manufacturer**
- **Document your protocol (approved by director)**

CLIA Requirement for Calibration and Calibration Verification

- **493.1255: Calibration and calibration verification procedures are required to substantiate the continued accuracy of the test system throughout the laboratory's reportable range**

Calibration and Calibration Verification

- **Calibration: Establishes the relationship between analyte content and instrument measurement signal**
- **Calibration verification: Confirms that the current calibration settings remain valid**

CAP Interpretation of CLIA Calibration Verification

- **The Laboratory Accreditation Program considers CLIA calibration verification to be secondary to calibration**
  - **If calibration satisfies the CLIA requirements for calibration verification [i.e., calibrated at least every six months with appropriate calibrators], no further action is necessary**
- **The CAP also separates CLIA calibration verification (when required) into two parts:**
  - **Prove the calibration still is valid (CAP Calibration Verification)**
  - **Prove response over the entire analytical measurement range (CAP AMR validation)**

CLIA Calibration Verification Requirements

- **Sec. 493.1255(b)(2) [Perform and document calibration verification procedures] Using the criteria verified or established by the laboratory …**
  - **(i) Including the number, type, and concentration of the materials, as well as acceptable limits for calibration verification; and**
  - **(ii) Including at least a minimal (or zero) value, a mid-point value, and a maximum value near the upper limit of the range to verify the laboratory's reportable range of test results for the test system**

CAP Requirements for Calibration Verification

- ***Target values***
- ***Appropriate Matrix***
  - ***Calibrators used to calibrate the analytical measurement system (different lot)***
  - ***Materials provided by the analytical measurement system vendor for the purpose of calibration verification***
  - ***Previously tested unaltered patient/client specimens***
  - ***Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method***

CAP Requirements for Calibration Verification Continued

- ***Appropriate Matrix* (continued)**
  - ***Third party general purpose reference materials if commutable***
  - ***Proficiency testing material or proficiency testing validated material with matrix characteristics and target values appropriate for the method.***
  - ***QC Material if: appropriate matrix and a peer group interlaboratory mean value based on at least 10 different laboratories using comparable method.***
    - *In general, routine control materials are not suitable for calibration verification, except in situations where the material is specifically designated by the method manufacturer as suitable for verification of the method's calibration process.*

CAP Requirements for the Verification of the Analytical Measurement Range

- ***Target values***
- ***Sufficient samples (as discussed later)***
- ***Appropriate matrix***
  - ***Linearity material of appropriate matrix***
  - ***Proficiency testing survey material***
  - ***Previously tested patient specimens, unaltered***
  - ***Previously tested patient specimens, altered by admixture with other specimens, dilution, spiking or other technique***
  - ***Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method***
  - ***Calibrators used to calibrate the analytic measurement system***
  - ***Control materials, if they adequately span the AMR.***

Implementation of LAP Calibration Verification and AMR Validation

- **"Trueness" assumes that there is a value that the instrument should report for a specific sample**
  - **Calibration establishes this assignment; calibration verification shows that this is still true**
  - **Controls do not usually come with assigned values that are valid for the instrument *unless the manufacturer proves these values***
- **"Linearity" demonstrates a fixed relationship between two values**
  - **A doubling of a value indicates twice as much analyte**
    - *In this case, the actual "values" don't matter, only the relationship*
  - **The relationship between results must hold throughout the analytical measurement range, including when the range extends beyond the calibrator values**

Implementation of LAP Calibration Verification and AMR Validation Continued

- **If LAP calibration verification is needed:**
  - **Establish the "trueness" of the method**
    - *Most often easiest to perform at the calibration point(s)*
- **If AMR validation is required:**
  - **If you have established "trueness" (by calibration or calibration verification), verify that a linear relationship holds throughout the instrument AMR**
  - **Establish "trueness" throughout the AMR by comparing results to established target values**
  - **Use a combination of both comparison to target values and verification of linearity**

Number of Samples Required for AMR Validation

- **Three**
  - **CLIA minimal requirement (low, mid-point, high)**
- **Four**
  - **Various opinions**
- **Five**
  - **What I was taught as a resident**
- **More?**
  - **The more the points, the greater your confidence that any value actually reflects the concentration in the patient sample, but practical considerations (cost, time) constrain the laboratory**

Samples for Analytical Measurement Range Validation – How Low and How High?

- ***"Guidelines for analyte levels near the low and high range of the AMR should be determined by the laboratory director. Factors to consider are the expected analytic imprecision near the limits, the clinical impact of errors near the limits, and the availability of test specimens near the limits. It may be difficult to obtain specimens with values near the limits for some analytes (e.g., T-uptake, free thyroxine, free phenytoin, prolactin, FSH, troponin, pO_2). In such cases, reasonable procedures should be adopted based on available specimen materials."***
  - ***Chemistry and Toxicology checklist, 6/17/10***

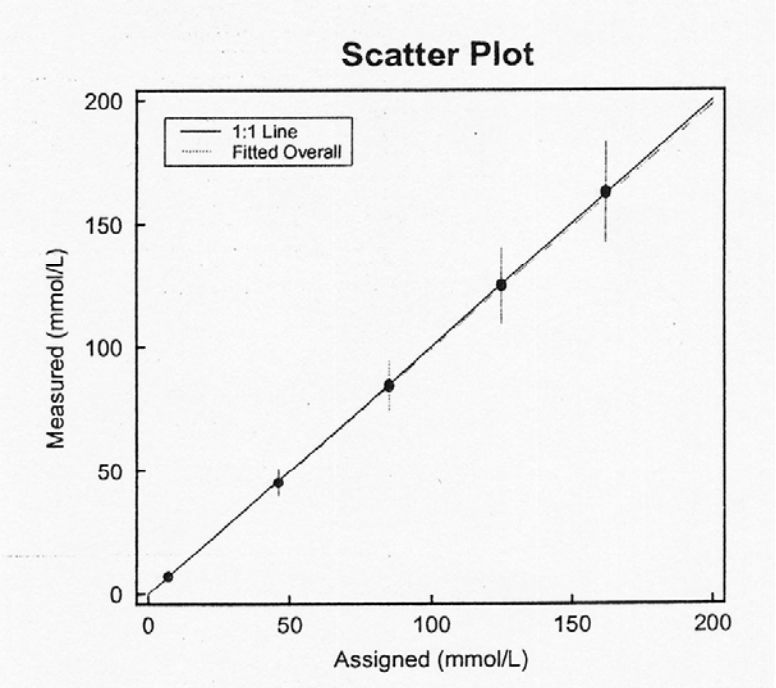
Samples for Analytical Measurement Range Validation – How low and how high?

- **Determined by available material:**
  - **Define the linear range as going from the low to the high target sample**
- **Fixed range:**
  - **Within 10% of the top end and 1% of the bottom end**
- **Clinical use and decision points**

The ability of commercial "available material" to span the entire range of an instrument is constrained by the cost of making samples with extremely high concentrations

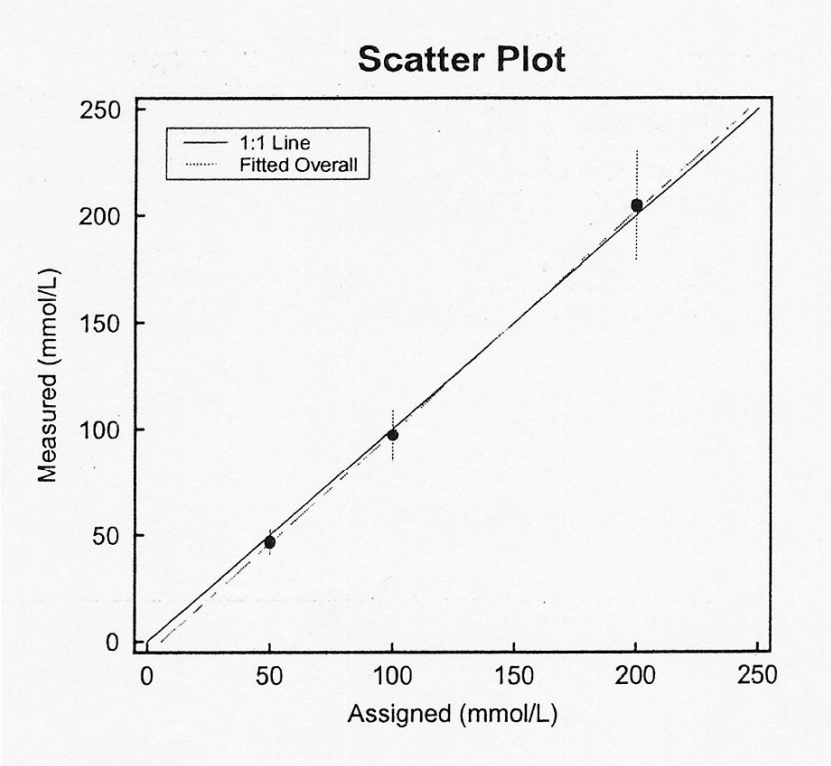
Extending the Verification Range

- **Available material with target values may not reach the upper limit of the analytical measurement range**
- **Example: urine sodium**
  - **manufacturer's range: 0 – 200 mmol/L**



Extending the Verification Range Continued

- **Prepare a stock sodium solution of 200 mmol/L**
- **Do two serial x 2 dilutions (100 and 50 mmol/L target)**
- **Assay each level and plot**



Measurement of Results Beyond the AMR

- **May decrease the lower limit of the analytical measurement range by:**
  - **Concentrating the sample**
    - *Amicon concentrator*
    - *Extraction and resuspension*
  - **Increasing the ratio of sample to reagent**
    - *Altering the programming of the instrument*

Measurement of Results Beyond the AMR Continued

- More commonly, may increase the upper limit of the analytical measurement range by:
  - Decreasing the ratio of sample to reagent
  - Diluting the sample before analysis
- Most often, the manufacturer provides the information or mechanism for this modification
  - Autodilution/autoconcentration
  - Dilution protocol
  - Concentration protocol
- Good laboratory practice would include verifying that these modifications work

Overview of the CAP Calibration Verification/Linearity Survey Evaluations

Presented by Patricia Styer, PhD

Purpose of the CAP Calibration Verification/Linearity Survey

- **Provide test samples and analysis for AMR validation**
  - **Exceed the minimal requirements for the number of specimens and possible analyses**
  - **Review and modify material specifications for optimal AMR coverage**
- **Provide information for ongoing quality monitoring**
  - **Performance criteria are usually more stringent than proficiency testing**
  - **Detect possible problems before they impact PT or patient testing**

Another Use of the Term "Calibration Verification"

- **Previous slides have defined CLIA calibration verification and LAP calibration verification**
- **We also have the calibration verification evaluation in the CAP CVL Program**
- **In the CVL Program, the calibration verification evaluation compares participant results to target values**

Components of a CAP Calibration Verification/Linearity Survey

- Participants receive a set of vials with varying concentrations of analyte(s)
- Participants submit results for two assays from each vial, within the same run if possible
- The CAP provides two individual evaluations and several peer group summaries
  - Calibration verification evaluation
  - Linearity evaluation
  - Peer group summary statistics
  - Peer group performance summaries

Participant Data Input

- **Participants receive a set of numbered vials and a result form.**
- **Participants specify an instrument, method, and/or reagent for each analyte.**

Serum Ethanol Survey

Results - Ethanol mg/dL

Method

010 ○ 1164 Alcohol Dehydrogenase/Radiative Energy (eg, Abbott AxSYM, TDx)

○ 1165 Alcohol Dehydrogenase/UV or Visible Spectrophotometry (eg, Beckman, Roche, Siemens ADVIA, Siemens Dimension)

○ 1740 Enzyme Oxidation - dry film (Vitros)

○ 1064 Gas Chromatography (GC)

○ 0010 Other, specify in final section

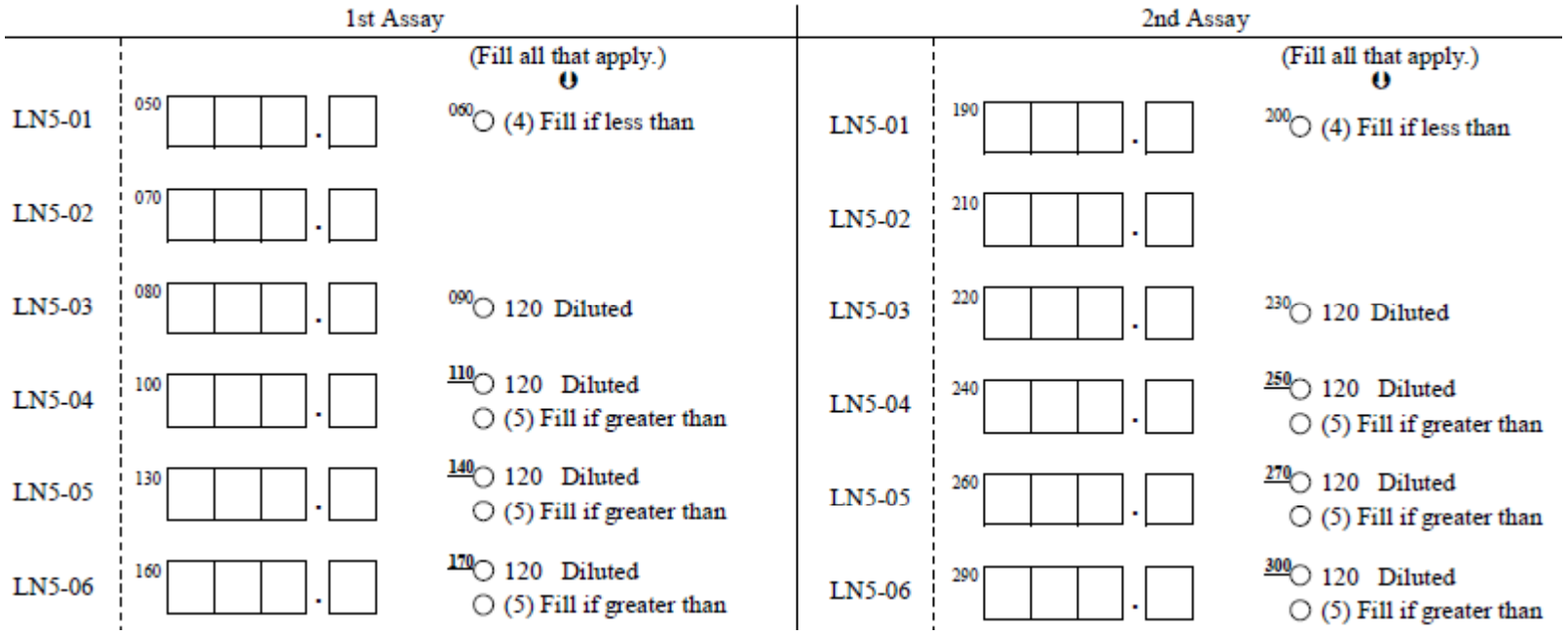
Automated Hematology

White Blood Cells - 10^9/L

330 Instrument Code

Participant Data Input Continued

- **Participants perform two assays from each vial within the same run.**



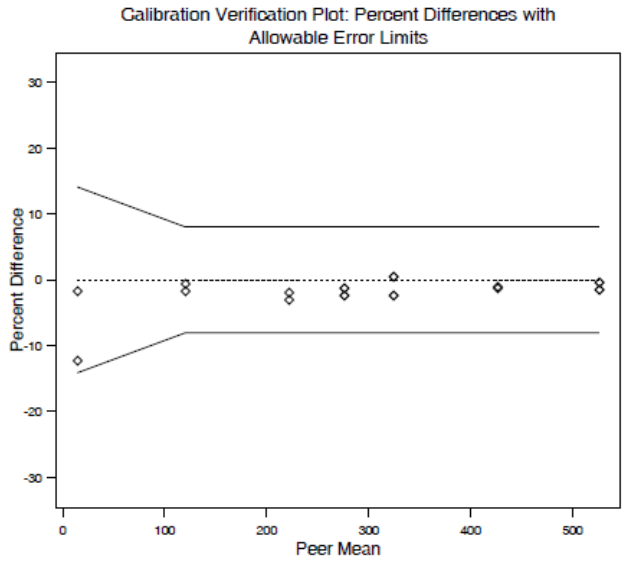
Calibration Verification Example for Serum Ethanol mg/dL

- **Assay means compared to target values**
- **Differences evaluated using allowable error limits by specimen level**
- **Allowable errors can be larger on percentage scale for lower concentrations**
- **Result is Verified over full range**

Evaluation Result: Verified from 13.25 to 521.40
Peer Method: ALCOHOL DEHYDROGEN UV

Goal for Total Error: 16%
Minimum Detectable Difference: 2 mg/dL

Specimen	Assay 1	Assay 2	Your Mean	Peer Mean	Peer N	Difference	Allowable Error
LN11-01	12.5	14.0	13.25	14.26	693	-7.1%	± 14.0%
LN11-02	119.3	118.0	118.65	119.98	695	-1.1%	± 8.0%
LN11-03	217.2	214.6	215.90	221.51	695	-2.5%	± 8.0%
LN11-04	269.6	272.7	271.15	275.90	695	-1.7%	± 8.0%
LN11-05	325.9	316.7	321.30	324.30	695	-0.9%	± 8.0%
LN11-06	421.9	420.5	421.20	426.15	695	-1.2%	± 8.0%
LN11-07	524.4	518.4	521.40	526.23	673	-0.9%	± 8.0%



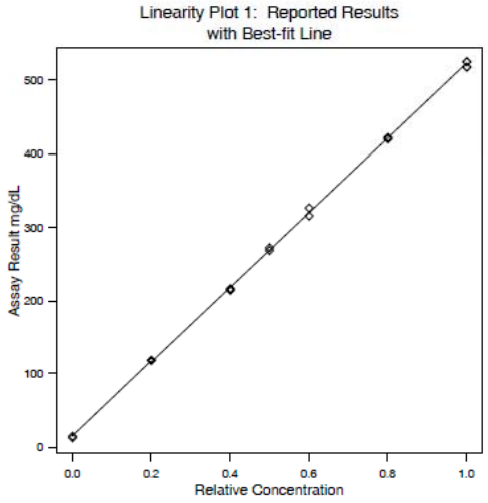
Linearity Example for Serum Ethanol mg/dL

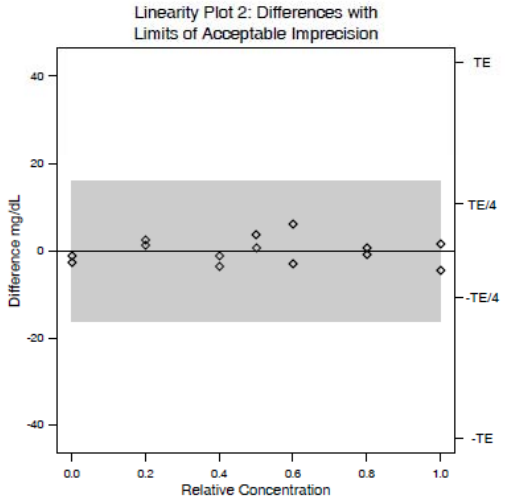
- **Results compared to fitted straight line**
- **X-axis shows relative concentrations (from material production)**
- **Evaluation based on average deviations from fitted straight line**
- **Evaluation can be**
  - **Linear**
  - **Nonlinear**
  - **Imprecise (Poor Repeatability and/or Fit)**

Evaluation Result: Linear from 13.25 to 521.40
Method: ALGOHOL DEHYDROGEN UV

Evaluation Type: Standard
Goal for Total Error (TE): 16%
Mean of Included Results: 268.98 mg/dL

Specimen	Assay 1	Assay 2	Your Mean	Best-fit Target	Relative Concentration
LN11-01	12.5	14.0	13.25	15.14	0.000
LN11-02	119.3	118.0	118.65	116.67	0.200
LN11-03	217.2	214.6	215.90	218.21	0.400
LN11-04	269.6	272.7	271.15	268.98	0.500
LN11-05	325.9	316.7	321.30	319.75	0.600
LN11-06	421.9	420.5	421.20	421.28	0.800
LN11-07	524.4	518.4	521.40	522.82	1.000





Serum Ethanol Example – Interpretation of Results

- **Evaluation results**
  - **Verified from 13.25 to 521.40 (good agreement with peer-based target values)**
  - **Linear from 13.25 to 521.40 (expected linear relationship is confirmed)**
- **Sometimes evaluation results will not agree**
  - **Review peer group data and summaries**
  - **Matrix effects can cause linearity problems**
  - **Mixed reagent lots can cause calibration verification problems**

Calibration Verification Example for Hemoglobin A_{1c} %

- **Participant means compared to accuracy based target values**
- **Peer groups for performance summaries**
- **All other components of evaluation are the same**

Evaluation Result: Verified from 5.15 to 12.10

Your Method: VITROS 5,1 FS & 5600

Specimen	Assay 1	Assay 2	Your Mean	Target Values	Difference	Allowable Error
LN15-01	5.2	5.1	5.15	5.21	-1.2%	± 7.0%
LN15-02	6.6	6.6	6.60	6.58	0.3%	± 7.0%
LN15-03	8.1	8.1	8.10	7.94	2.0%	± 7.0%
LN15-04	9.5	9.4	9.45	9.31	1.5%	± 7.0%
LN15-05	10.7	10.8	10.75	10.67	0.7%	± 7.0%
LN15-06	12.1	12.1	12.10	12.04	0.5%	± 7.0%

Peer Results Summary Table

Your Peer Group: VITROS 5,1 FS & 5600

Peer Group Size: 56

Range	Calibration Verification		Linearity Evaluation		
	% Verified	% Different	% Linear	% Nonlinear	% Imprecise
LN15-01 - 06	55.6	16.7	81.5	0.0	1.9
LN15-01 - 05	13.0	0.0	7.4	0.0	0.0
LN15-02 - 06	11.1	0.0	7.4	0.0	0.0
LN15-02 - 05	1.9	0.0	0.0	0.0	0.0
LN15-03 - 06	1.9	0.0	1.9	0.0	0.0

Extended/diluted Linearity Example for White Blood Cells 10^9/L

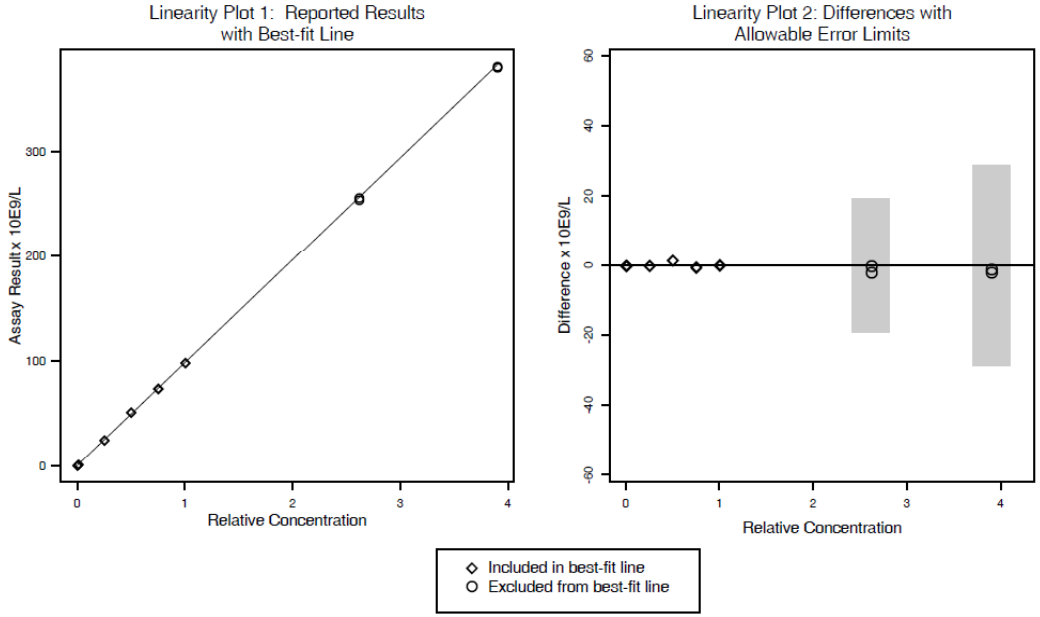
- **Extended range specimens are indicated in the linearity evaluation summary table.**
- **We fit a line to the non-extended range specimens.**
- **The non-extended range specimens must be linear for the evaluation to continue.**
- **Means of the extended range specimens are compared to the extrapolated line (Extended Range Specimen Analysis – next slide).**

Specimen	Assay 1	Assay 2	Your Mean	Best-fit Target	Relative Concentration
LN9-01W	0.4	0.4	0.40	0.54	0.000
LN9-02W	1.2	1.2	1.20	1.32	0.008
LN9-03W	24.8	24.6	24.70	24.99	0.250
LN9-04W	50.6	50.8	50.70	49.45	0.500
LN9-05W	73.1	73.5	73.30	73.90	0.750
LN9-06W	98.2	98.3	98.25	98.35	1.000
§ LN9-07W	254.3	256.2	255.25	256.52	2.617
§ LN9-08W	379.6	380.6	380.10	382.02	3.900

§ Extended range specimen

Extended/diluted Linearity Example for White Blood Cells 10^9/L Continued

- The plot on the left is the same; the difference plot shows allowable error bars for the extended range specimen results.
- We complete the same analysis for diluted specimens when we have at least five undiluted specimens to fit the initial line.



Your Extended Range Specimen(s) Analysis

Specimen	Your Mean	Best-Fit Target	Difference	Allowable Error
LN9-07W	255.25	256.52	-1.27	± 19.24
LN9-08W	380.10	382.02	-1.92	± 28.65

Interpreting CVL Evaluations With Problematic Results

- **Participants have many pieces of information for troubleshooting problems.**
- **In the next section, Dr. Killeen will show additional examples, with troubleshooting suggestions, from problematic calibration verification or linearity results.**

Examples and Troubleshooting

Presented by Anthony Killeen, MD, PhD

Example 1. Linearity Standard Evaluation: Specimens Excluded from the Linear Range

EVALUATION
ORIGINAL

LN2-A 2007 Chemistry/Lipid/Enzymes Calibration Verification/Linearity
Urea mg N/dL Linearity Evaluation

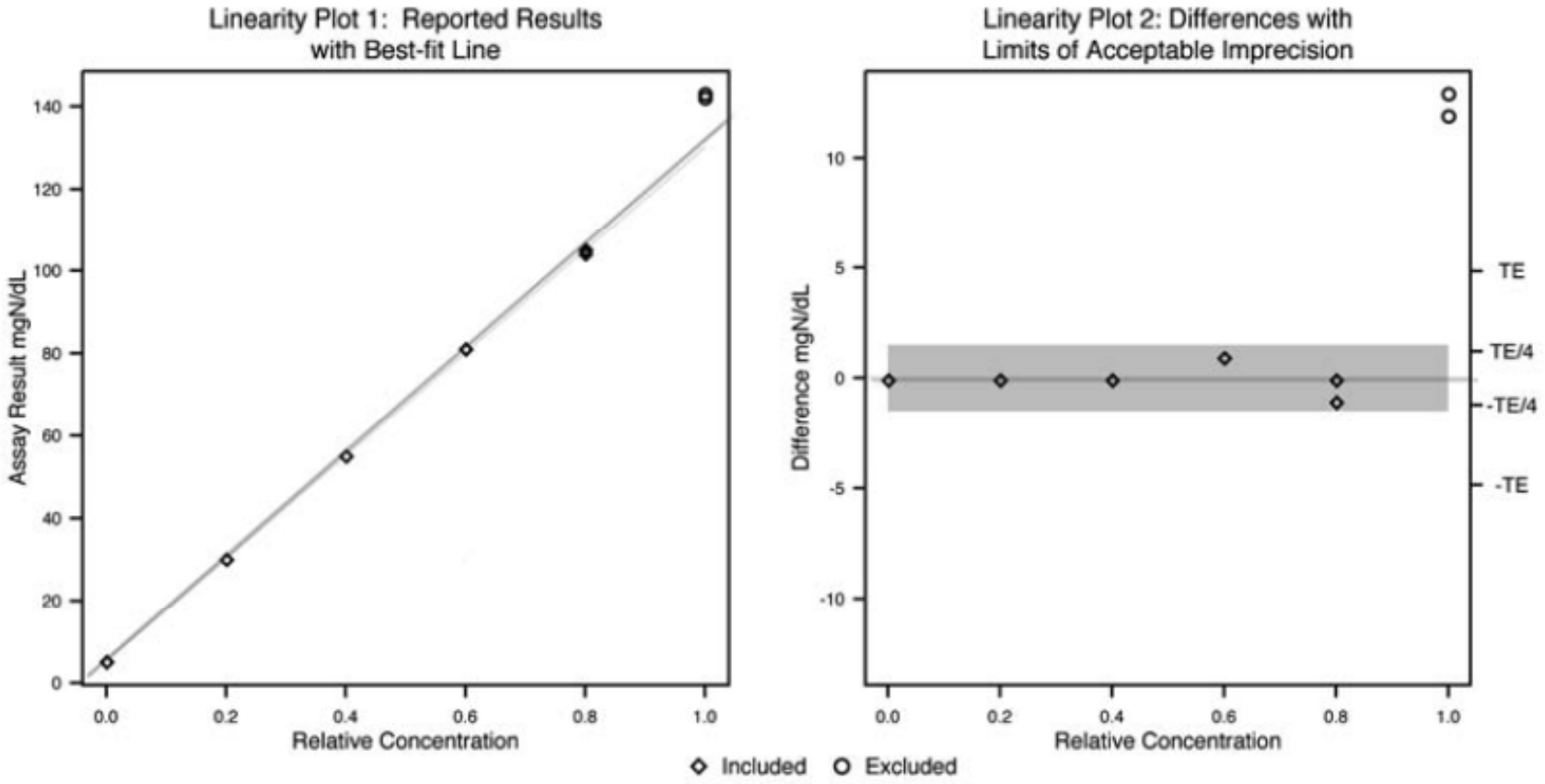
Evaluation Result: Linear from 5.0 to 104.5
Evaluation Type: Standard

Goal for Total Error: 8.8%
Mean of Included Results: 55.1 mgN/dL

Specimen	Assay 1	Assay 2	Your Mean	Best-fit Target	Relative Concentration
LN-01	5	5	5.0	5.1	0.000
LN-02	30	30	30.0	30.1	0.200
LN-03	55	55	55.0	55.1	0.400
LN-04	81	81	81.0	80.1	0.600
LN-05	105	104	104.5	105.1	0.800
LN-06	142	143	142.5	130.1	1.000

Linearity demonstrated for LN-01 to LN-05 only

Example 1. Linearity Standard Evaluation: Specimens Excluded from the Linear Range



Example 1. Troubleshooting

- **Does the linear range cover the AMR? If the high specimen is above the AMR, did you dilute? Was the dilution protocol followed?**
- **If the linear range does not cover the AMR, then there may be problems with reagents, specimen handling, or the test system**
- **Check QC, PT, calibration data**
- **Address identified problems and re-run linearity**
- **Consider adjusting AMR to cover the linear range**

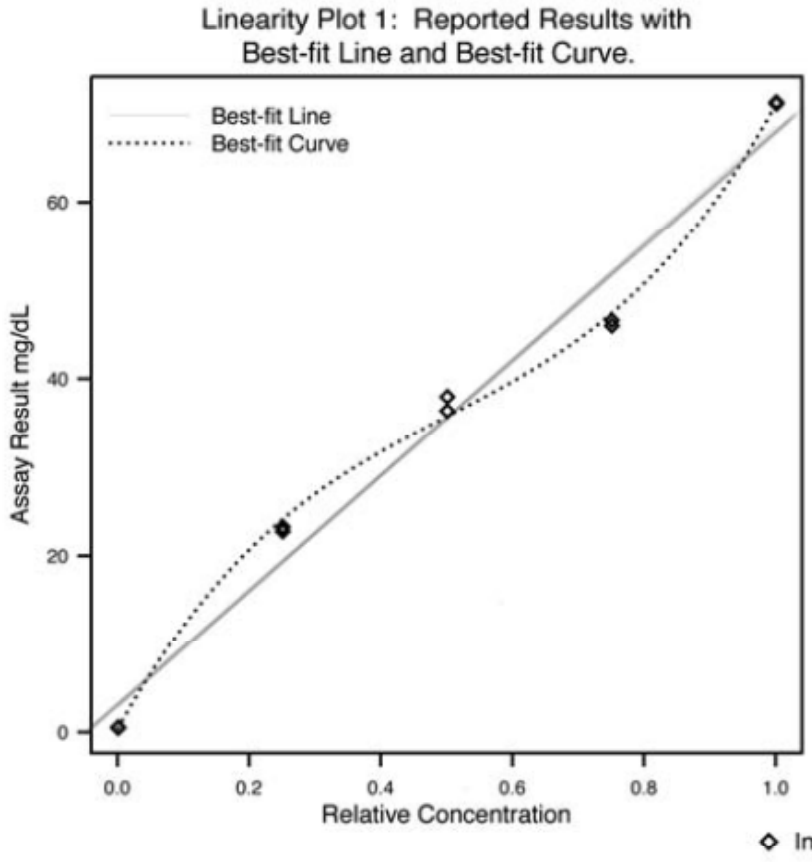
Example 2. Linearity Standard Evaluation: Nonlinear Data

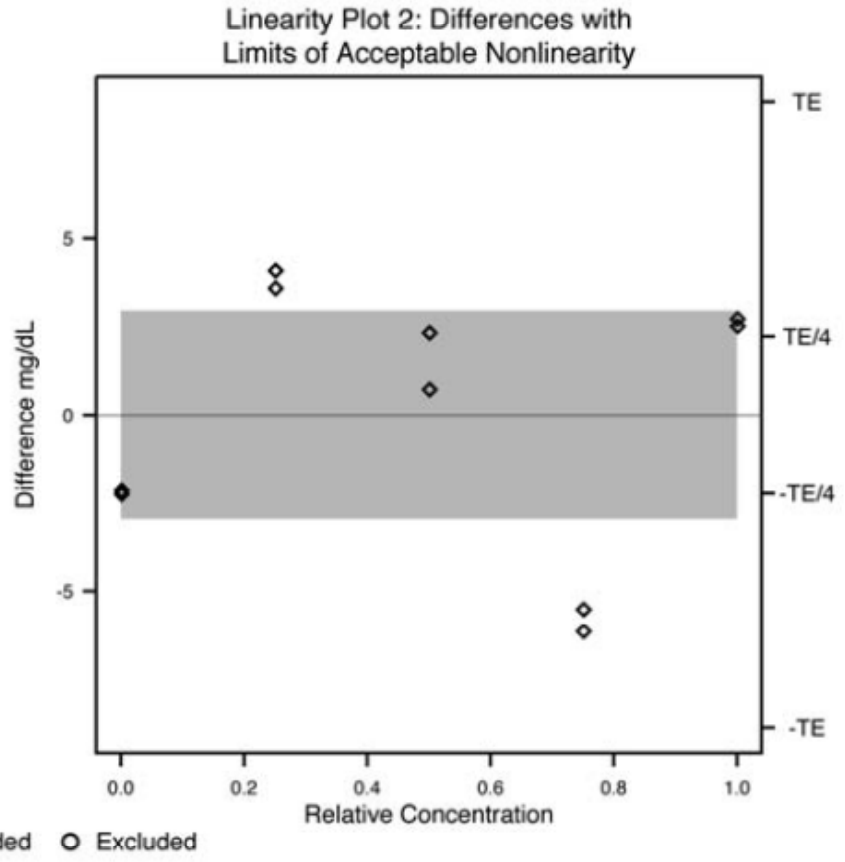
Evaluation Result: Nonlinear
Evaluation Type: Standard

Goal for Total Error: 25%
Mean of Included Results: 35.66 mg/dL

Specimen	Assay 1	Assay 2	Your Mean	Best-fit Target	Relative Concentration
LN6-26	0.5	0.6	0.55	2.75	0.000
LN6-27	22.8	23.3	23.05	19.21	0.250
LN6-28	36.4	38.0	37.20	35.66	0.500
LN6-29	46.6	46.0	46.30	52.11	0.750
LN6-30	71.1	71.3	71.20	68.57	1.000

Example 2. Nonlinear Data





◇ Included ○ Excluded

Example 2. Troubleshooting Approach

- Is the peer group generally linear?
- If the peer group is generally linear then there may be problems with specimen handling or the test system
- Review QC, calibration, PT data
- Eliminate specimen or reagent handling errors
- Diagnose fix any identified test system failures
- Re-run linearity study

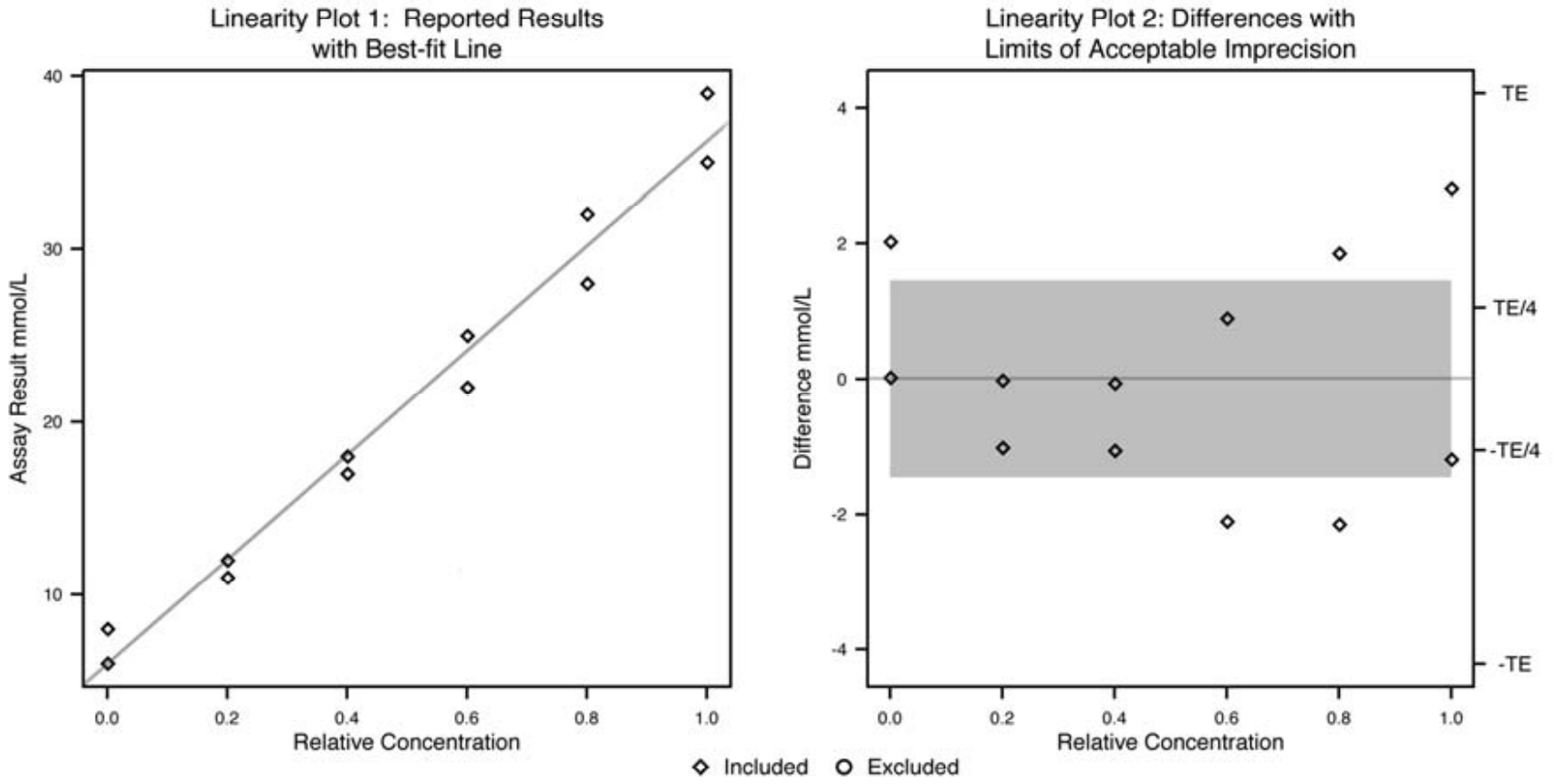
Example 3. Linearity Standard Evaluation: Large Replicate Imprecision

Evaluation Result: Imprecise
Evaluation Type: Standard

Goal for Total Error: 20%
Mean of Included Results: 21.08 mmol/L

Specimen	Assay 1	Assay 2	Your Mean	Best-fit Target	Relative Concentration
LN-01	6.0	8.0	7.00	5.98	0.000
LN-02	12.0	11.0	11.50	12.02	0.200
LN-03	18.0	17.0	17.50	18.06	0.400
LN-04	25.0	22.0	23.50	24.10	0.600
LN-05	32.0	28.0	30.00	30.15	0.800
LN-06	39.0	35.0	37.00	36.19	1.000

Example 3. Linearity Standard Evaluation: Large Replicate Imprecision



Linearity Example 3. Troubleshooting

- **Pattern suggests pipetting problems which should be carefully investigated**
- **Fix any identified test system failures**
- **Re-run linearity study**

Example 4: Linearity Extended Range Evaluation: Imprecise in Non-Extended Range, Extended Range Sample(s) not Evaluated

EVALUATION
ORIGINAL

LN13-B 2008 Blood Gas Calibration Verification/Linearity
PO2 mm Hg Linearity Evaluation

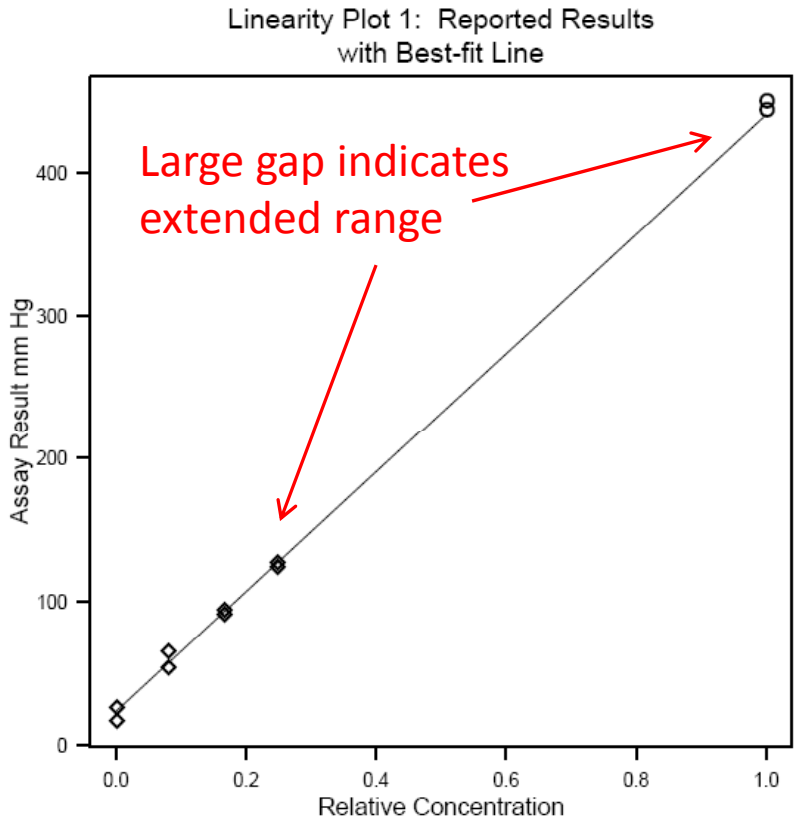
Evaluation Result: Imprecise
Evaluation Type: Extended Range

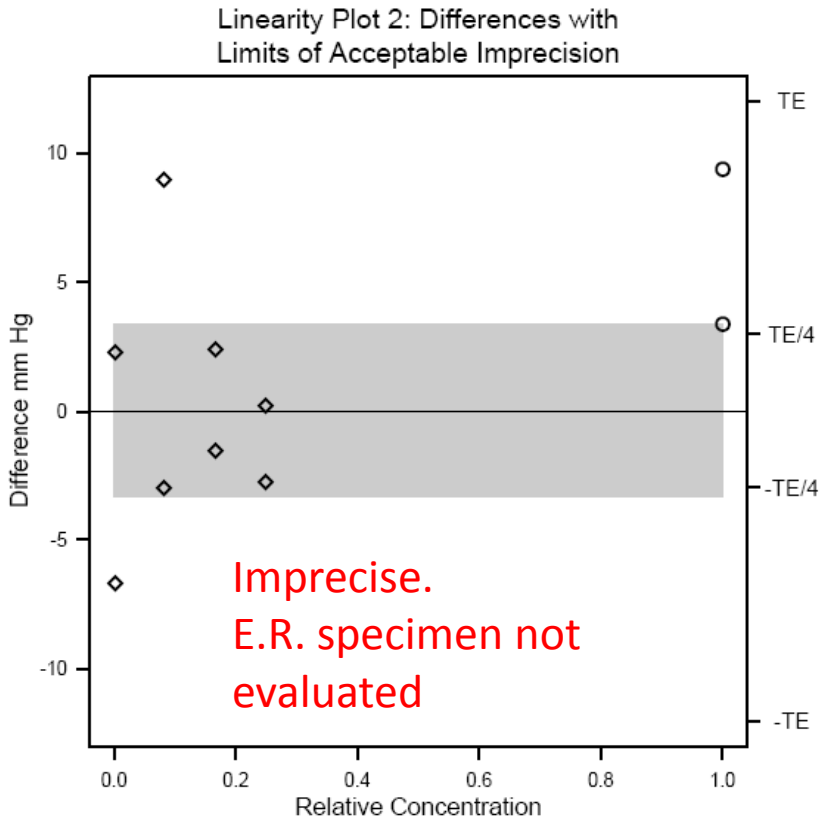
Goal for Total Error: 16%
Mean of Included Results: 75.0 mm Hg

Specimen	Assay 1	Assay 2	Your Mean	Best-fit Target	Relative Concentration
LN13-06	26	17	21.5	23.7	0.000
LN13-07	54	66	60.0	57.0	0.080
LN13-08	95	91	93.0	92.6	0.165
LN13-09	127	124	125.5	126.8	0.247
* LN13-10	450	444	447.0	440.6	1.000

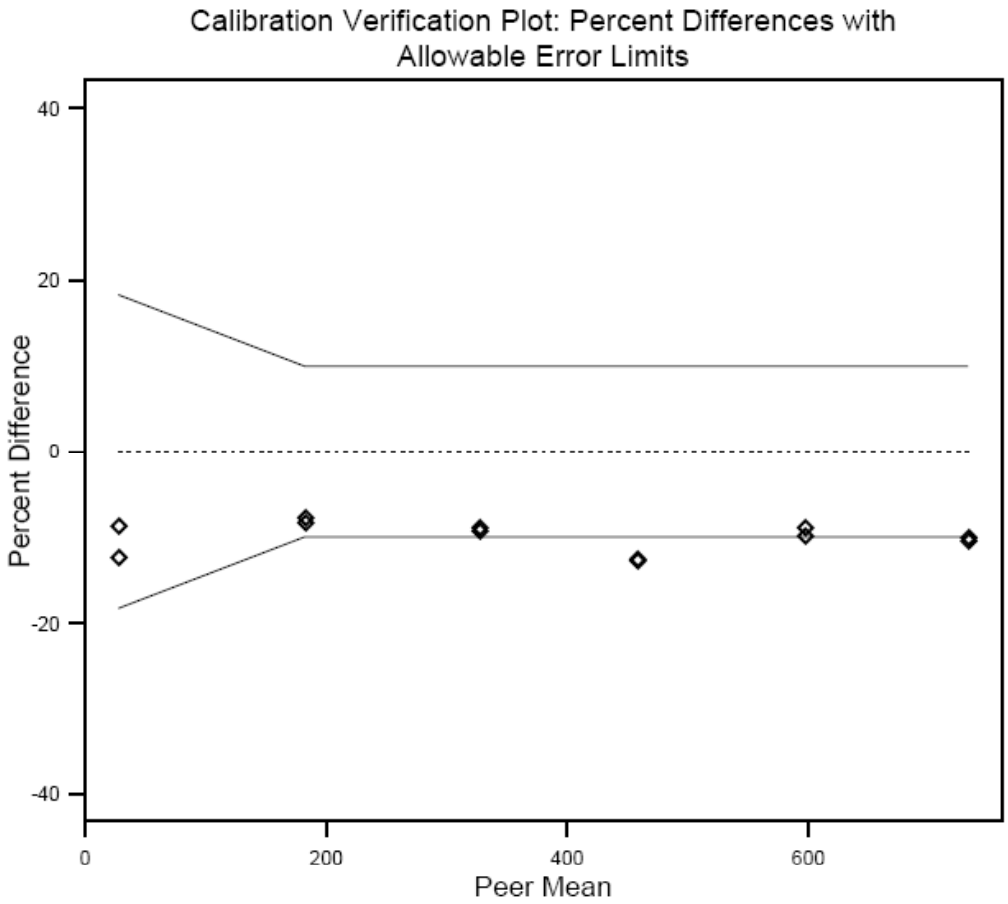
* Extended range specimen

Example 4: Linearity Extended Range Evaluation: Imprecise in Non-Extended Range, Extended Range Sample(s) not Evaluated





Example 5. Calibration Verification “Different”



Example 5. Calibration Verification "Different"

Evaluation Result: Different

Peer Instrument: ROCHE MODULAR
Peer Reagent: ROCHE/37 C

Goal for Total Error: 20%
Minimum Detectable Difference: 5 U/L

Specimen	Assay 1	Assay 2	Your Mean	Peer Mean	Peer N	Difference	Allowable Error
LN-17	25	24	24.5	27.4	137	-10.5%	± 18.3%
LN-18	168	167	167.5	181.8	137	-7.9%	± 10.0%
LN-19	298	297	297.5	327.0	137	-9.0%	± 10.0%
LN-20	401	400	400.5	457.8	137	-12.5%	± 10.0%
LN-21	544	538	541.0	596.5	137	-9.3%	± 10.0%
LN-22	657	660	658.5	732.5	137	-10.1%	± 10.0%

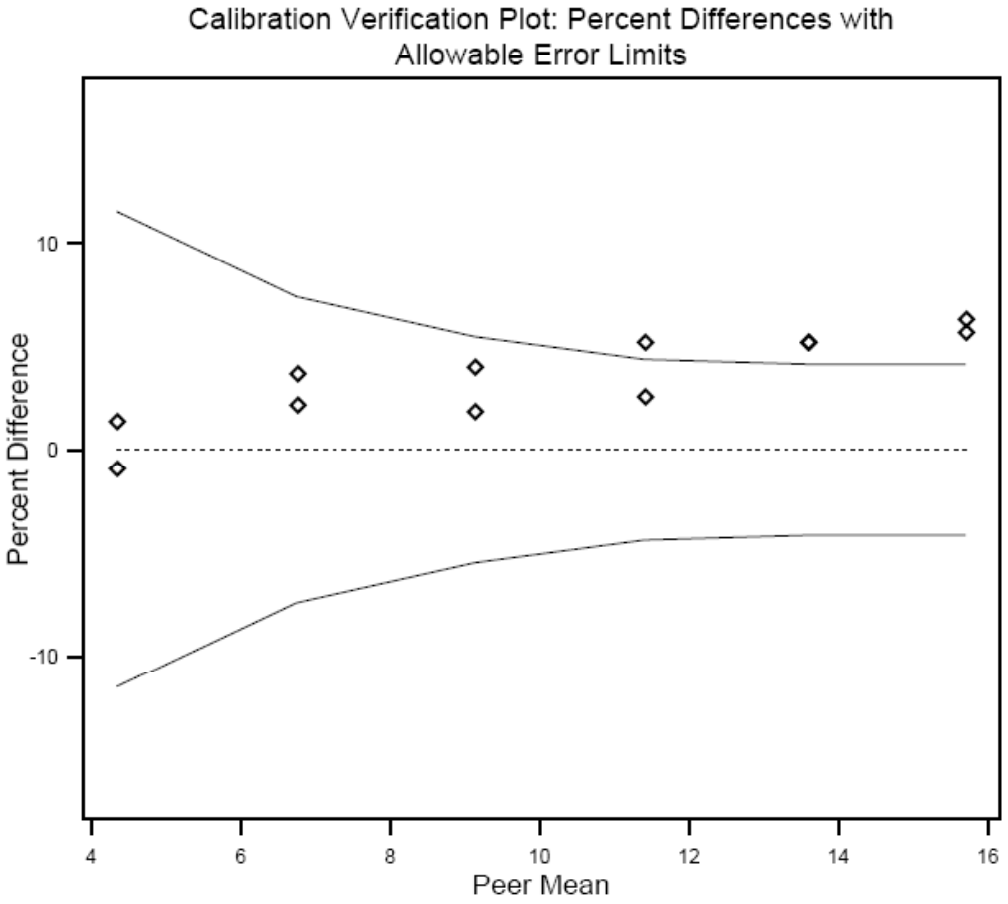
Peer Results Summary Table

Peer Group Size: 137

Range	Calibration Verification		Linearity Evaluation		
	Verified	Different	Linear	Nonlinear	Imprecise
LN-17 - 22	80.3	14.6	97.1	0.0	0.0
LN-17 - 21	2.2	0.0	1.5	0.0	0.0
LN-18 - 22	0.0	0.0	1.5	0.0	0.0
LN-17 - 20	2.9	0.0	0.0	0.0	0.0

Linearity study show the data were linear

Example 6. Calibration Verification Verified, Partial Range



(Calcium)

Example 6. Calibration Verification Verified, Partial Range

EVALUATION
ORIGINAL

LN2-B 2008 Chemistry/Lipid/Enzymes Calibration Verification/Linearity
Calcium mg/dL Calibration Verification Evaluation

Evaluation Result: Verified from 4.35 to 11.85

Peer Instrument: ROCHE MODULAR
Peer Method: CRESOLPHTHALEIN COMPL

Goal for Total Error: 8.3%
Minimum Detectable Difference: 0.5 mg/dL

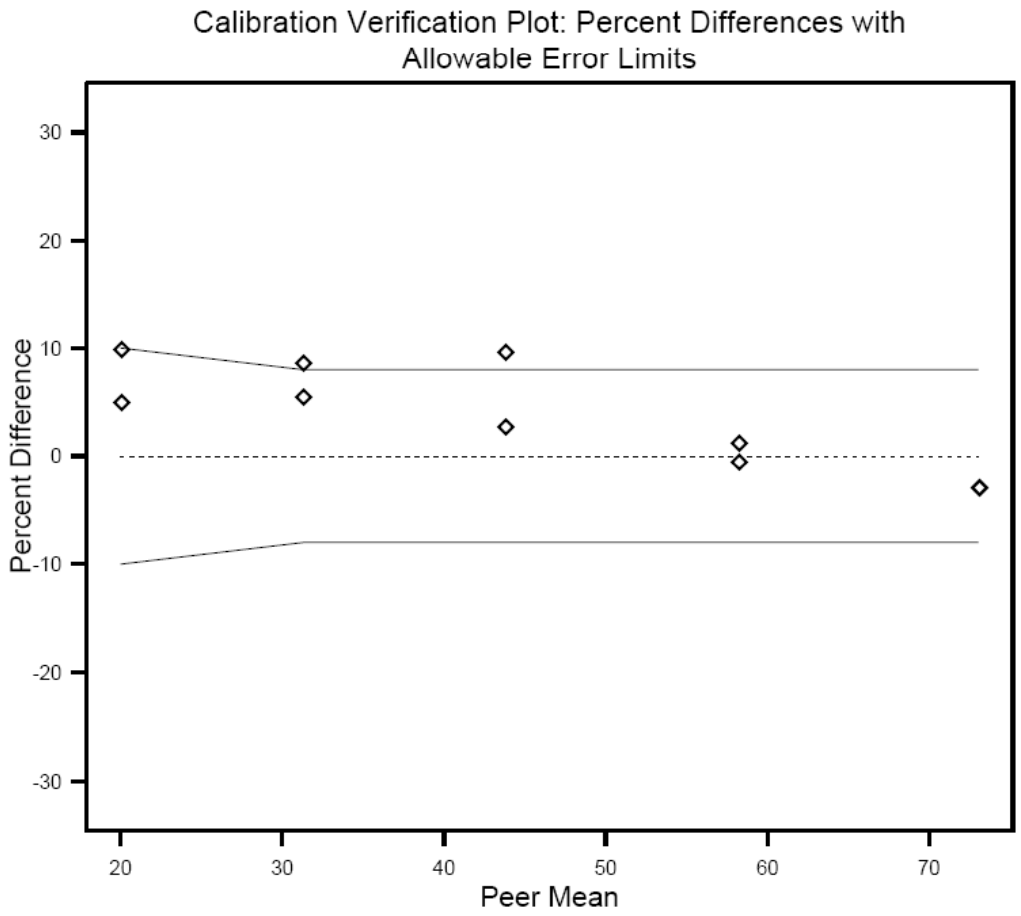
Specimen	Assay 1	Assay 2	Your Mean	Peer Mean	Peer N	Difference	Allowable Error
LN-17	4.4	4.3	4.35	4.34	149	0.3%	± 11.5%
LN-18	6.9	7.0	6.95	6.75	151	3.0%	± 7.4%
LN-19	9.3	9.5	9.40	9.13	151	3.0%	± 5.5%
LN-20	11.7	12.0	11.85	11.40	151	3.9%	± 4.4%
LN-21	14.3	14.3	14.30	13.59	151	5.2%	± 4.2%
LN-22	16.7	16.6	16.65	15.70	151	6.1%	± 4.2%

Peer Results Summary Table

Peer Group Size: 151

	Calibration Verification		Linearity Evaluation		
Range	Verified	Different	Linear	Nonlinear	Imprecise
LN-17 - 22	90.7	2.6	97.4	0.0	0.7
LN-17 - 21	3.3	0.0	0.7	0.0	0.0
LN-18 - 22	1.3	0.0	1.3	0.0	0.0
LN-17 - 20	2.0	0.0	0.0	0.0	0.0

Example 7. Calibration Verification Verified in the Full Range



Example 7. Calibration Verification Verified in the Full Range

EVALUATION
ORIGINAL

LN20-A 2009 Urine Microalbumin Calibration Verification/Linearity
Urine Creatinine mg/dL Calibration Verification Evaluation

Evaluation Result: Verified from 21.50 to 71.00
Peer Instrument: VITROS 5,1 FS CHEM SYST

Goal for Total Error: 16%
Minimum Detectable Difference: 2 mg/dL

Specimen	Assay 1	Assay 2	Your Mean	Peer Mean	Peer N	Difference	Allowable Error
LN20-05	21.0	22.0	21.50	20.00	44	7.5%	± 10.0%
LN20-04	34.0	33.0	33.50	31.27	44	7.1%	± 8.0%
LN20-03	48.0	45.0	46.50	43.76	44	6.3%	± 8.0%
LN20-02	58.0	59.0	58.50	58.24	44	0.4%	± 8.0%
LN20-01	71.0	71.0	71.00	73.05	44	-2.8%	± 8.0%

Peer Results Summary Table

Peer Group Size: 44

Range	Calibration Verification		Linearity Evaluation		
	% Verified	% Different	% Linear	% Nonlinear	% Imprecise
LN20-05 - 01	43.2	45.5	70.5	2.3	9.1
LN20-05 - 02	6.8	0.0	18.2	0.0	0.0
LN20-04 - 01	4.5	0.0	0.0	0.0	0.0

Executive Summary Page from CVL Survey

College of American Pathologists
325 Waukegan Road, Northfield, Illinois 60093-2750
800-323-4040 - http://www.cap.org

Advancing Excellence

CAP Number: [redacted]
Institution:
Attention:
City/State:

Kit ID: 21645561
Kit Mailed: 04/13/2009
Original Evaluation: 05/13/2009
Next Mailing Date: 10/12/2009

EVALUATION
ORIGINAL

LN7-A 2009 Immunology Calibration Verification/Linearity

Executive Summary

Analyte	Calibration Verification	Linearity Evaluation	Page #
Alpha-1 Antitrypsin mg/dL	Verified from 23.00 to 542.50	* Linear from 23.00 to 373.00	2 - 3
Complement C3 mg/dL	Verified from 14.80 to 326.50	Linear from 14.80 to 326.50	4 - 5
Complement C4 mg/dL	Verified from 3.55 to 87.40	Linear from 3.55 to 87.40	6 - 7
Immunoglobulin A mg/dL	Verified from 27.25 to 613.50	Linear from 27.25 to 613.50	8 - 9
Immunoglobulin G mg/dL	Verified from 134.0 to 3045.0	* Linear from 134.0 to 2030.0	10 - 11
Immunoglobulin M mg/dL	Verified from 23.80 to 496.00	Linear from 23.80 to 496.00	12 - 13
Transferrin mg/dL	Verified from 43.30 to 877.00	Linear from 43.30 to 877.00	14 - 15

* This range does not include all reported specimens. Review your results to determine if excluded specimens reveal possible analytical problems.

Accuracy Based Surveys

- **Creatinine: LN24**
- **Testosterone & Estradiol: ABS**
- **Lipids: ABL (PT)**
- **Hemoglobin A_{1c}: GH2 (PT), LN15 (2011)**
- **Neonatal Bilirubin (NB) (PT); NB2**

Summary of Topics Covered

- **Calibration Verification**
- **Linearity**
- **Analytical Measurement Range**
- **The CAP CVL Surveys**
- **Examples and Troubleshooting**