

CLIA Proficiency Testing

Criteria for Acceptable Performance

CLIAC Meeting

September 1, 2010

Rex Astles, PhD, DABCC, FACB
Laboratory Practice Standards Branch
Division of Laboratory Science and Standards





Approval of Proficiency Testing Programs

CLIA Regulations Section 493.901

- ❑ PT programs are required to **assure that samples:**
 - **mimic actual patient specimens** when possible
 - are *homogeneous*, except for specific subspecialties such as cytology, and
 - will be *stable* within the time frame for analysis by proficiency testing participants
- ❑ **Must use *scientifically defensible process for determining the correct result* for each challenge offered**



Criteria for Acceptable Performance

- ❑ The correctness of a result is determined by the **criteria for acceptable performance** for each analyte or test
- ❑ For most analytes, the criteria include:
 - **Target Value**
 - defined for quantitative tests in Section 493.2
 - **Acceptance Limits**
 - not defined in the regulations
 - define the tolerance around the target value



Criteria for Acceptable Performance - Qualitative Tests

- **Examples of criteria for acceptable performance:**
 - Qualitative Syphilis Serology: reactive or nonreactive
 - General Immunology: reactive or nonreactive; positive or negative
 - Immunohematology: positive or negative
 - Hematology: cell identification, present or absent



Target Value for Quantitative Tests

Section 493.2 – Definition of Target Value

- ❑ Mean of all participant responses after removal of outliers (those responses greater than 3 standard deviations from the original mean), or
- ❑ Mean established by definitive or reference methods acceptable for use in the National Reference System for the Clinical Laboratory (NRSCCL) by the National Committee for the Clinical Laboratory Standards (NCCLS).



Target Value for Quantitative Tests

Section 493.2 – Definition of Target Value (cont.)

- In instances where definitive or reference methods are not available or a specific method's results demonstrate bias that is not observed with actual patient specimens, as determined by a defensible scientific protocol, a comparative method or a method group ("peer" group) may be used.**



Target Value for Quantitative tests

Section 493.2 – Definition of Target Value (cont.)

- If the method group is less than 10 participants, "target value" means the overall mean after outlier removal (as defined above) unless acceptable scientific reasons are available to indicate that such an evaluation is not appropriate.**

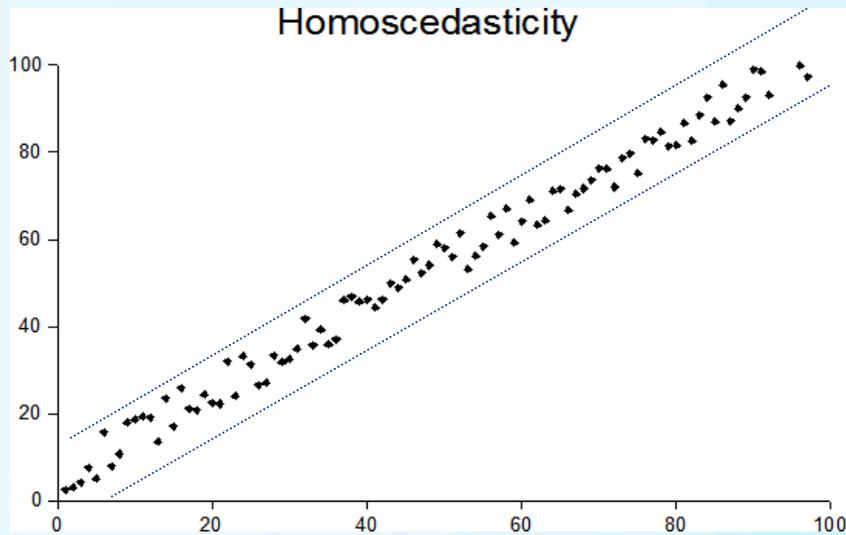


Acceptance Limits for Quantitative Tests

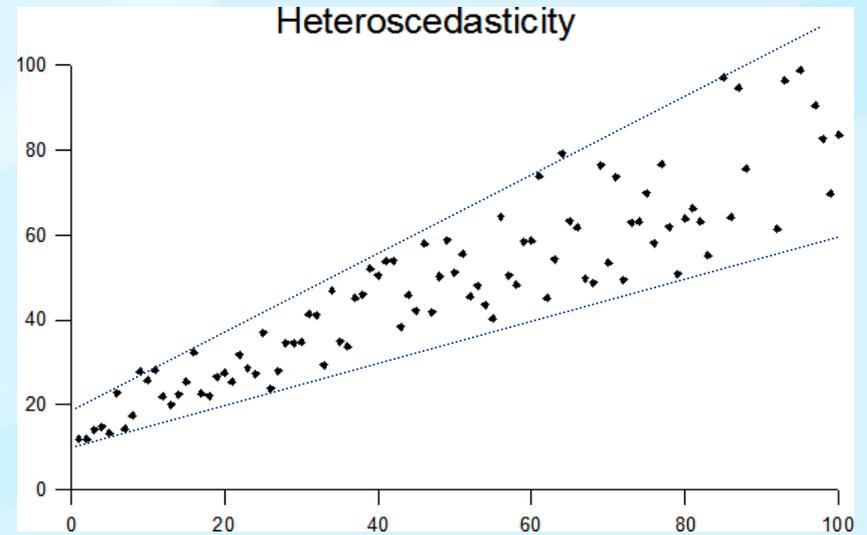
- ***Acceptance limits* are specified in terms of:**
 - fixed concentration limits (in concentration units)
 - fixed proportional limits (as a percentage), or
 - standard deviations



Acceptance Limits are Linked to the Analytic Variance



Constant Variance -
Fixed Limits Appropriate



Changing Variance -
Proportional Limits Appropriate



Acceptance Limits

Section 493.931 Routine Chemistry

- (1) To determine the accuracy of a laboratory's response for qualitative and quantitative chemistry tests or analytes, the program must compare the laboratory's response for each analyte with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories. = **Target Value**

- (2) For quantitative chemistry tests or analytes, the program must determine the correct response for each analyte by the distance of the response from the target value. After the target value has been established for each response, the appropriateness of the response must be determined by using **either fixed criteria based on the percentage difference from the target value or the number of standard deviations (SDs) the response differs from the target value.** = **Acceptance Limits**



Sec. 493.927

General Immunology

Analyte	Criteria for Acceptable Performance
Alpha-1 antitrypsin	Target value ± 3 SD
Alpha-fetoprotein (tumor marker)	Target value ± 3 SD
Antinuclear antibody	Target value ± 2 dilutions or positive or negative
Antistreptolysin O	Target value ± 2 dilution or positive or negative
Anti-Human Immunodeficiency virus	Reactive or nonreactive
Complement C3	Target value ± 3 SD
Complement C4	Target value ± 3 SD
Hepatitis (HBsAg, anti-HBc, HBeAg)	Reactive (positive) or nonreactive (negative)
IgA	Target value ± 3 SD
IgE	Target value ± 3 SD
IgG	Target value $\pm 25\%$
IgM	Target value ± 3 SD
Infectious Mononucleosis	Target value ± 2 dilution or positive or negative
Rheumatoid Factor	Target value ± 2 dilution or positive or negative
Rubella	Target value ± 2 dilutions or immune or nonimmune or positive or negative



Sec. 493.931

Routine Chemistry (partial)

Analyte	Criteria for Acceptable Performance
Alanine aminotransferase (ALT/SGPT)	Target value \pm 20%
Albumin	Target value \pm 10%
Alkaline phosphatase	Target value \pm 30%
Amylase	Target value \pm 30%
Aspartate aminotransferase (AST/SGOT)	Target value \pm 20%
Bilirubin, total	Target value \pm 0.4 mg/dL or \pm 20% (greater)
Blood gas pO ₂	Target value \pm 3 SD
pCO ₂	Target value \pm 5 mm Hg or \pm 8% (greater)
pH	Target value \pm .04
Calcium, total	Target value \pm 1.0 mg/dL
Chloride	Target value \pm 5%
Cholesterol, total	Target value \pm 10%
Cholesterol, high density lipoprotein	Target value \pm 30%
Creatine kinase	Target value \pm 30%
Creatine kinase isoenzymes	Creatine kinase isoenzymes
Creatinine	Target value \pm 0.3 mg/dL or \pm 15% (greater)



Summary of Current Regulations

- ***Target Values*** can be established by:
 - Definitive Method
 - Reference Method
 - All-methods Mean
 - Peer Grouping

- ***Acceptance limits*** are specified in terms of:
 - fixed concentration limits (in concentration units)
 - fixed proportional limits (as a percentage), or
 - standard deviations



Consensus Requirements for PT Scoring

- ❑ **Use either all participants or ≥ 10 referee laboratories**
- ❑ **Consensus must be $\geq 80\%$ for grading (of ten or more referee laboratories or all participants)**
- ❑ **Exception: Immunohematology**
 - 100% - referee laboratories, $\geq 95\%$ - all participants
 - Unexpected antibody detection/identification – $\geq 95\%$ - referee laboratories or all participants



Referee Laboratory

Section 493.2 – Definition of Referee Laboratory

- ❑ A laboratory currently in compliance with applicable CLIA requirements
- ❑ Record of satisfactory proficiency testing performance for all testing events for at least one year for a specific test, analyte, subspecialty, or specialty
- ❑ Designated by an HHS-approved proficiency testing program as a referee laboratory



Impact of Matrix Effects

- ❑ PT materials are typically artificial and therefore do not always behave like patient specimens.
- ❑ “Matrix effect,” refers to an analytical effect, inherent to the interaction between the PT material and the test system, which results in an analytical bias in PT results.
- ❑ Affected PT results tend to agree with PT results obtained using the same test system, but they will not agree with results from other, unaffected test systems.



Impact of Matrix Effects (cont.)

- ❑ Biases are not necessarily predictable or correctable, and the PT test results cannot be compared with results from a reference method or all-methods mean.
- ❑ PT results from the affected test methods must be peer-grouped and results compared against the peer-group mean.
- ❑ Ideally, a PT program scientifically demonstrates that their PT materials exhibit a matrix effect on a particular test system before peer-grouping.
 - A presumption of matrix effect might obscure real differences between test systems when patient testing, such as calibration differences.



CMS PT Reason Codes

Code	Reason
1	Failure to Participate. Did not send in PT results. (Score 0%)
2	Failure to Participate. Exclusion Requested (Score 100% for a valid reason.)
3	Untimely Return of Results (Score 0%) Did not send in results before cutoff date.
4	Ungradable. Sample could not be graded by PT Program. (Score 100%)
5	Would Refer. Test or any portion referred to another Laboratory. (Score 100%)
6	Result Variance
7	Method/Instrument Not Stated
8	Excused Participation - Natural Disaster (Score 100%)
9	Test Not Performed (Not Offered) or Blank (Score "OO")
10	Changed to Waived Method/Test (Score "OO")



Reasons for Ungraded Challenges

Program	Reason
1	Reason Code 4
2	Reason Code 4
3	Unspecified
4	No appropriate target Non-consensus Scientific committee decision Unsatisfactory specimen
5	Lack of participant consensus No comparison group found Unable to obtain result Lack of participant consensus Lack of referee lab consensus Possible matrix effect Result above analyzer range Questionable specimen integrity
6	Lack of Consensus # of labs less than minimum required