Clinical Chemistry
Trainee Council

PEARLS OF LABORATORY MEDICINE

"QC Design: Things You Need to Know" Series

Allowable Total Error (TE_a)

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Lakshmi Kuchipudi-Yerneni
Bio-Rad Laboratories

www.traineecouncil.org

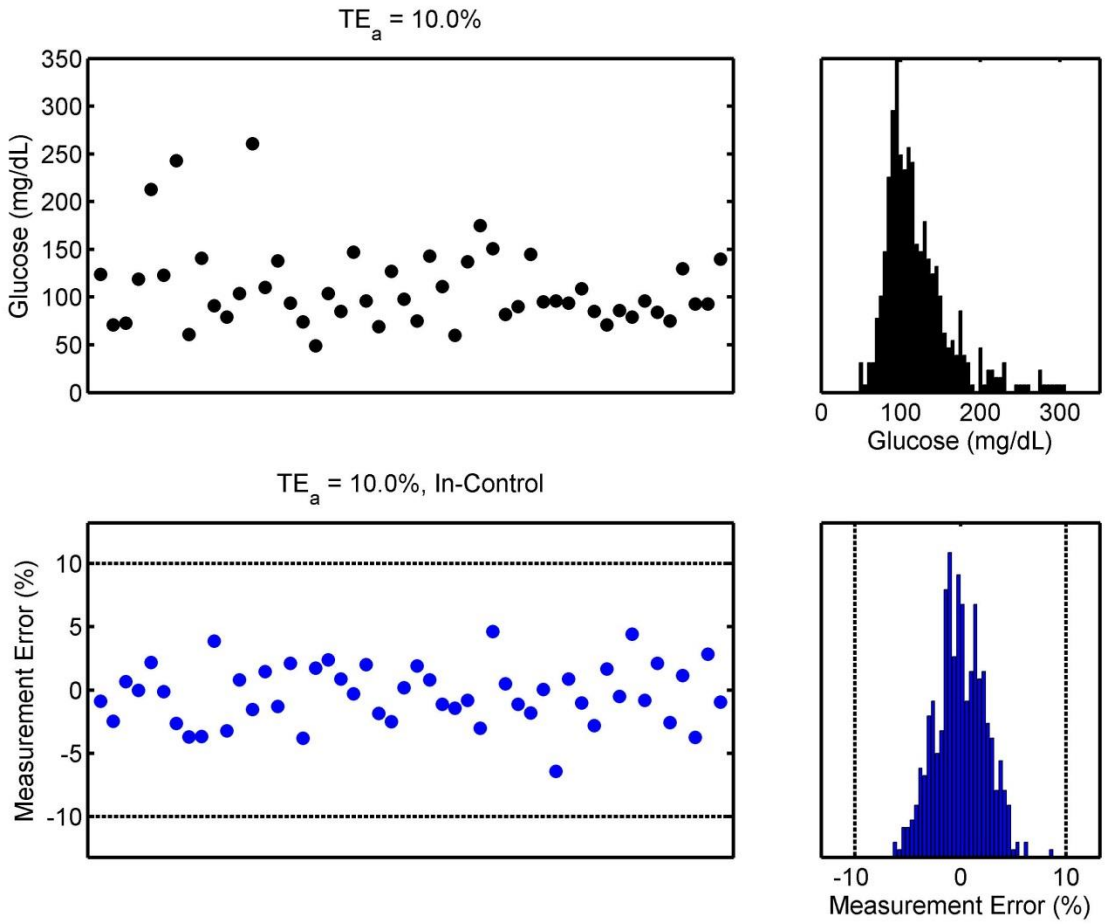
The need for quality specifications

- Specifying the quality required in a patient result dictates the performance characteristics that must be realized in our test systems for them to satisfy their purpose.
- In the absence of patient results quality specifications, there is no way to determine whether the control procedures being utilized are appropriate or if patient result quality is acceptable.

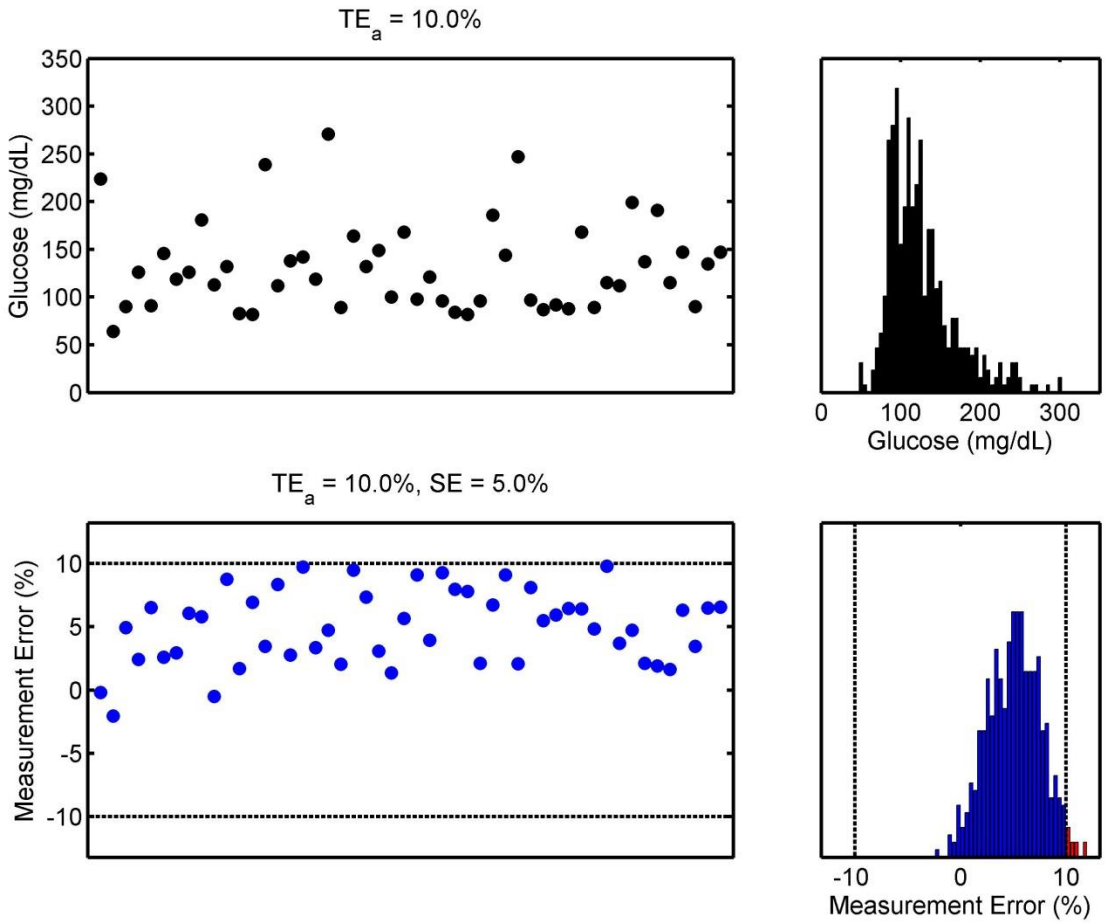
Allowable Total Error (TE_a)

- Quality specifications are generally defined in terms of allowable total error (TE_a) limits
  - TE_a limits specify the measurement error requirements that must be met for test systems to satisfy their purpose
  - If the absolute difference between the reported value and the actual value exceeds TE_a, then the patient result is unreliable.

Process In-Control



Process Out-of-Control



How are Quality Specifications Obtained?

- A hierarchy for defining quality specifications was developed at a conference in Stockholm, Sweden in April 1999 by the IFCC, WHO, and the International Union of Pure and Applied Chemistry (IUPAC).
- Participants with published papers on various quality specification models attended from 23 countries.

The Quality Specification Hierarchy

1. Quality specifications in specific clinical situations
2. Quality specifications based on general clinical use of test results
3. Quality specifications from professional recommendations
4. Quality specifications based on regulation and external quality assessment
5. Quality specifications based on State of the Art

1. Specific Clinical Situations

- The ideal error specification is based on assessing how analytical performance affects specific clinical decisions.
- The problem is very little analysis has been done in a manner that lends itself to universal use.

2. General Clinical Situations

- Quality specifications based on the general clinical use of the results fall into two groups:
  - Specifications based on biological variation
  - Specifications based on the analysis of clinician's opinions

Biological Variation

- Biological variation based quality specifications are derived
  - by evaluating the inherent biological variation of an analyte
  - by determining how large imprecision and bias can be before they mask significant biological changes in the analyte
  - TE_a = Allowable Bias + 1.65*(Allowable Imprecision)
    - Allowable Imprecision is based on within person BV
    - Allowable Bias is based on within person and between person BV
- http://www.qcnet.com/Portals/0/PDFs/BVValues1Final.pdf

Minimum, Desirable and Optimum Performance Specifications

- Three sets of performance specifications have been derived for biological variation values:
  1. Minimum performance
  2. Desirable performance
  3. Optimum performance

Biological Variation Specifications

- Quality specifications based on biological variation have the following benefits:
  - Firmly based on medical requirements
  - Usable in all laboratories
  - Generated using simple models
  - Widely accepted

3. Professional Recommendations

- Various groups of experts have published quality specifications for specific sets of analytes.
- The National Cholesterol Education Panel in the US has published recommendations for the precision, accuracy and total allowable error for lipids.
- The American Diabetes Association has documented quality specifications for self-monitoring blood glucose, etc.

4. Regulatory Agencies

- Mandated performance goals set by regulation – like CLIA'88
- CLIA TE_a specifications
  - Glucose - Target value ± 6 mg/dL or ± 10%, whichever is greater
  - Chloride - Target value ± 5%
- Outside the US, proficiency programs have a variety of mechanisms for grading performance. They can all be translated into analytical goal specifications.
- http://www.qcnet.com/Portals/0/PDFs/CLIALimits(3-3-04).pdf

5. State of the Art

- State of the Art refers to deriving quality specifications by what is currently possible.
- Example - “State of the Art” precision specification might be the median CV from a group of laboratories.
- “State of the Art” specifications can be derived from proficiency testing programs or inter-laboratory consensus programs.

Conclusion

- Consideration should be given to what quality specifications are used.
- Biological variation based quality specifications are very defensible and should be the logical selection.
- CLIA'88 Proficiency specifications should always be the minimum.

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Disclosures/Potential Conflicts of Interest

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