
Quality Control
The Analytical Examination Process
LOGO

CONTENTS

INTRODUCTION

- **The purpose of a clinical laboratory test is:**
  - **to provide information on the pathophysiologic condition of an individual patient**
  - **to assist with diagnosis**
  - **to guide or monitor therapy**
  - **to assess risk for developing a disease or for progression of a disease.**

INTRODUCTION

- **Quality Management System**

Integrates good laboratory practices to ensure that results are suitable for use in patient care decisions.

- **Internal QC is in the process management category of the quality management system because its primary function is to ensure that measurement procedures meet specifications at the time patient testing occurs.**

Quality Management System

1. Organization; management responsibility
2. Documents and records
3. Service agreements; purchasing
4. Customer advisory services
5. Nonconformities management
6. Continual improvement
7. Evaluation and audits
   - EQA/PT
   - Quality indicators
8. Personnel
9. Environment; facilities
10. Equipment and reagents
11. Process management
    - o Preexamination
    - o Examination (analytical)
      - Internal quality control
    - o Postexamination
12. Information management

INTRODUCTION

- **Quality Management System**

Integrates good laboratory practices to ensure that results are suitable for use in patient care decisions.

- **EQA/PT is in the evaluation and audits category because its primary function is external assessment that measurement procedures conform to specifications for agreement of results among laboratories.**

Quality Management System

1. Organization; management responsibility
2. Documents and records
3. Service agreements; purchasing
4. Customer advisory services
5. Nonconformities management
6. Continual improvement
7. Evaluation and audits
   - EQA/PT
   - Quality indicators
8. Personnel
9. Environment; facilities
10. Equipment and reagents
11. Process management
    - o Preexamination
    - o Examination (analytical)
      - Internal quality control
    - o Postexamination
12. Information management

INTRODUCTION

- **Quality Management System**

Integrates good laboratory practices to ensure that results are suitable for use in patient care decisions.

- **Quality indicators are also part of the evaluation and audits category and are used to assess the performance of the QC plan and to identify opportunities for continuous quality improvement.**

Quality Management System

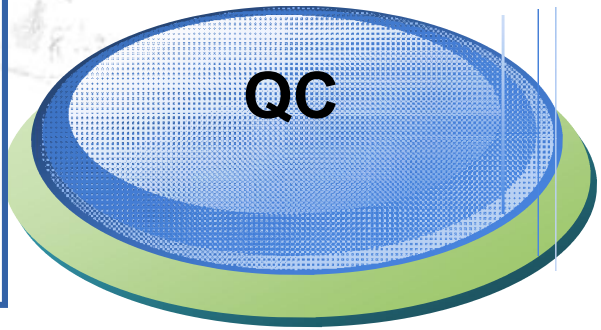
1. Organization; management responsibility
2. Documents and records
3. Service agreements; purchasing
4. Customer advisory services
5. Nonconformities management
6. Continual improvement
7. Evaluation and audits
   - EQA/PT
   - Quality indicators
8. Personnel
9. Environment; facilities
10. Equipment and reagents
11. Process management
    - o Preexamination
    - o Examination (analytical)
      - Internal quality control
    - o Postexamination
12. Information management

INTRODUCTION

- **Quality control (QC) of the analytical examination process monitors a measurement procedure to verify that it meets performance specifications appropriate for patient care or that an error condition exists that must be corrected.**

INTRODUCTION

Recovery of the expected target values for the QC samples allows the laboratory to verify that a measurement procedure is working correctly and the results for patient samples are reliable enough to be released.



The results for the EQA/PT samples are compared with results from other laboratories to verify that a laboratory's measurement procedures conform to expected performance.

Internal includes control procedures performed **within a laboratory** using surrogate samples that are intended to simulate clinical samples from patients.

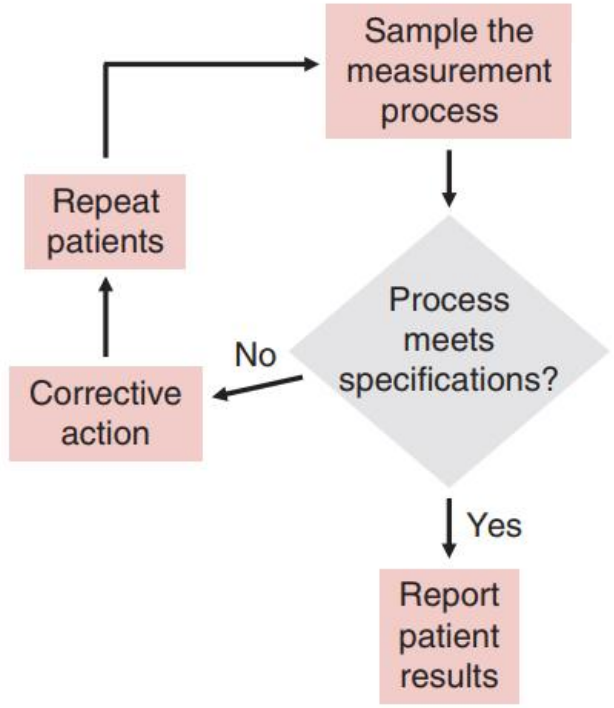
The QC samples are measured at intervals along with patient samples.

Uses the results from patient samples as part of the QC monitoring process

External is a monitoring process in which surrogate samples are received **from an independent external organization** and the expected values are not known by the laboratory

INTRODUCTION

Internal QC evaluates a measurement procedure by periodically measuring a QC sample for which the expected result is known in advance



Note that QC acceptance criteria may be designed to provide a warning of gradual changes.

INTRODUCTION

Measurement procedures fall into one of two general categories from a QC plan perspective.

Batch

- **The results for patient samples and QC samples are completed before the results are reported.**
- **Results are not reported if an error condition is identified.**

Continuous

- **Patient sample results are reported during the interval between QC sample measurements.**
- **There is a possibility that erroneous results have already been reported if an error condition is identified by the next QC sample measurement(s)**

INTRODUCTION

- In either category, a measurement error that affects only one or a few patient results: called a nonpersistent (random) error (May not be identified by the results for the QC samples).
- QC procedures only identify persistent error conditions at the point in time when a QC sample is actually measured.
- Consequently, the choice of criteria to evaluate QC results and the frequency that QC results are measured become important QC plan design considerations.

INTRODUCTION

The design of a QC plan:

- **Analytical performance capability of a measurement procedure.**
- **The risk of harm to a patient that might occur if an erroneous laboratory test result is used for a clinical care decision.**

- **An erroneous laboratory test result is a hazardous condition that may or may not cause harm to a patient depending on what action or inaction is taken by a clinical care provider based on the erroneous result.**

MEASUREMENT PROCEDURE PERFORMANCE

A prerequisite for a quality control plan

1. **Calibration Traceability to a Reference System and Commutability Considerations**
2. **Calibration of a Measurement Procedure and Verification of Calibration Stability**
3. **Analytical Bias and Imprecision**
4. **Performance of a Measurement Procedure for Its Intended Medical Use**

CALIBRATION TRACEABILITY

Calibration Traceability to a Reference System:

- **Calibration of clinical laboratory measurement procedures should be traceable to a higher order reference measurement procedure or certified reference material.**

- **Ensuring that calibrations of clinical laboratory measurement procedures are traceable to the highest order reference system components available ensures that results for patient samples are equivalent within medically acceptable limits irrespective of the measurement procedure or laboratory making the measurements.**

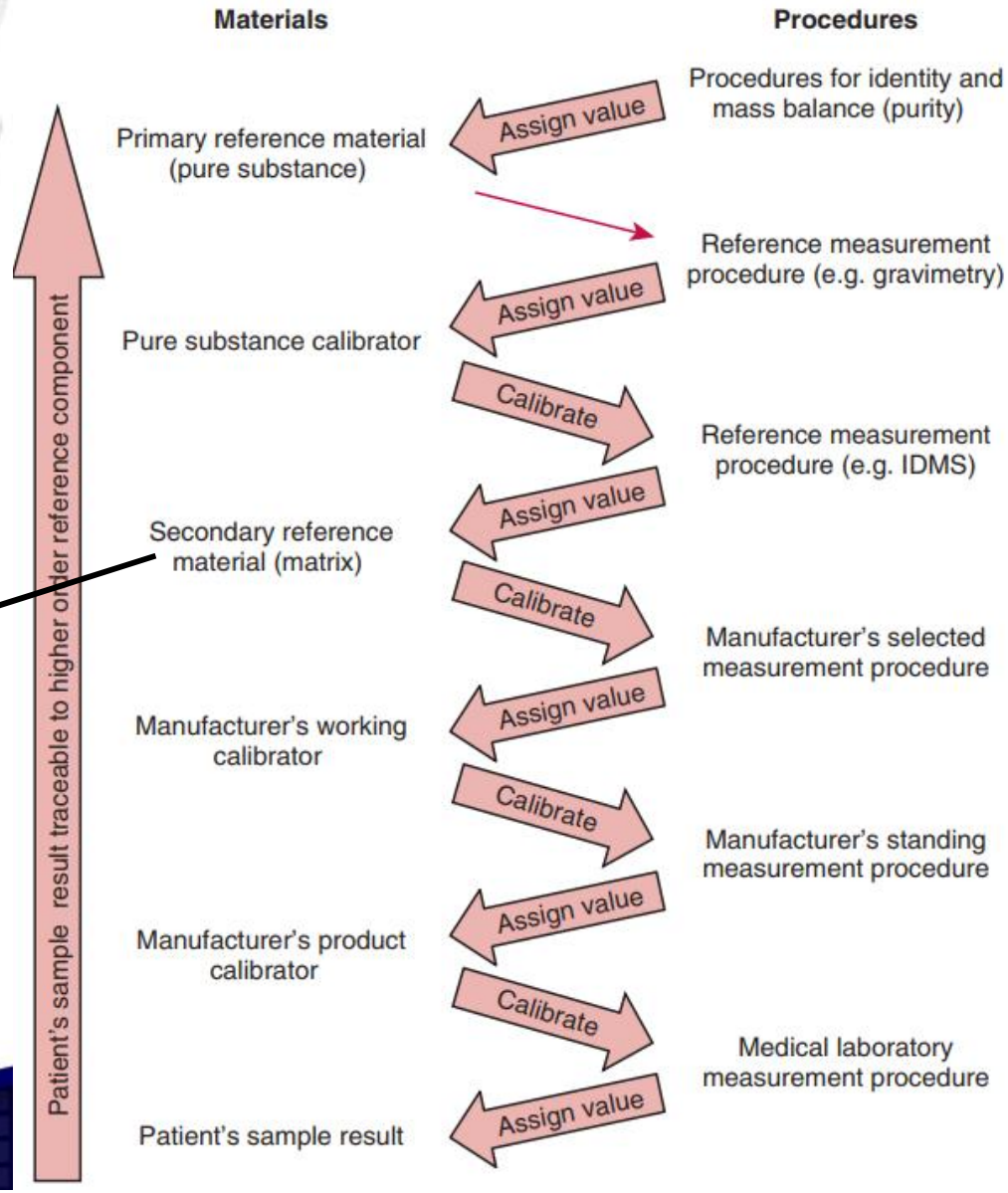
CALIBRATION TRACEABILITY

Calibration Traceability to a Reference System:

- **A complete reference system provides traceability of the results from a routine clinical laboratory measurement procedure to the Système Internationale (SI) unit based on a series of calibrations that link the routine measurement procedure calibrator to a higher order reference material or reference measurement procedure.**

- **The highest order primary calibrator in the traceability chain is prepared from a well-characterized pure substance primary reference material.**

CALIBRATION TRACEABILITY



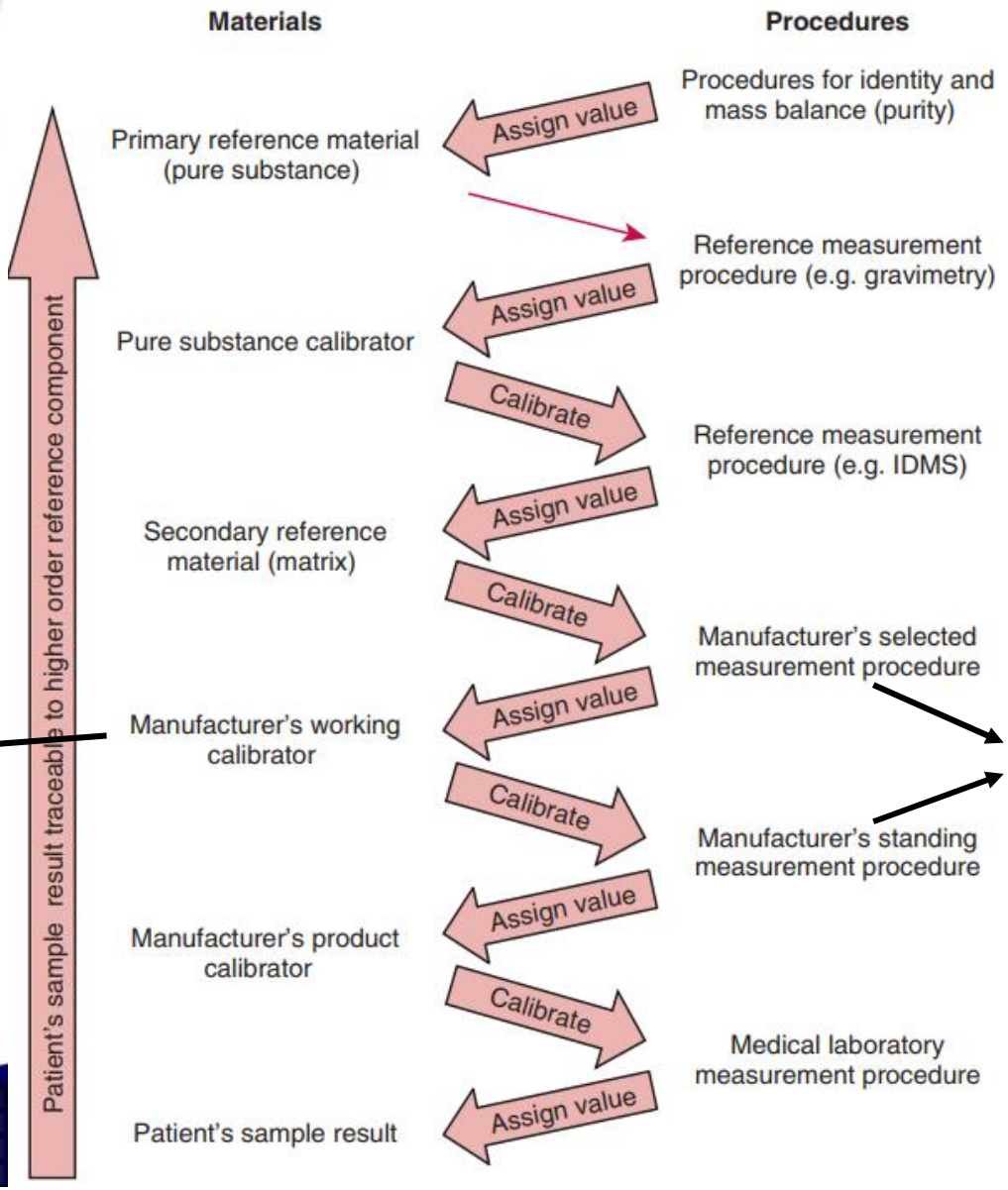
May be a panel of clinical patient specimens.

Typically provided by a national metrology institute

Isotope dilution mass spectrometry:

1. **high selectivity for the measurand**
2. **Very small imprecision**
3. **minimal influence by sample matrix components.**

CALIBRATION TRACEABILITY



Master lot of calibrator:

Used for many years to transfer traceable calibration to many lots of product calibrator.

May be the same but used to fulfill two purposes in the calibration traceability scheme.

CALIBRATION TRACEABILITY

Calibration Traceability to a Reference System:

- The Joint Committee for Traceability in Laboratory Medicine (JCTLM) lists certified reference materials, reference measurement procedures, and reference laboratories that conform to the ISO standards for such reference system components.

- In laboratory medicine, there are a large number of measurands for which there are no higher order reference materials.
- In these situations, the calibration traceability ends with the manufacturer's or laboratory's internal working calibrator.
- In this situation, results for patient samples frequently differ depending on the routine measurement procedure used or the laboratory performing the measurements.

MEASUREMENT PROCEDURE PERFORMANCE

standardized and harmonized measurement procedures:

- **Are frequently used interchangeably to refer to clinical laboratory measurement procedures that are calibrated such that results for patient samples are equivalent among different measurement procedures.**

- **Standardized is more appropriately used when calibration is traceable to any category of traceability described in ISO standard 17511 that is of higher order than to a manufacturer's or laboratory's internal working calibrator.**

MEASUREMENT PROCEDURE PERFORMANCE

standardized and harmonized measurement procedures:

- **Are frequently used interchangeably to refer to clinical laboratory measurement procedures that are calibrated such that results for patient samples are equivalent among different measurement procedures.**

- **Harmonized remains a term that can be used whenever results measured by any clinical laboratory procedure are equivalent irrespective of the process used to achieve that condition.**

COMMUTABILITY

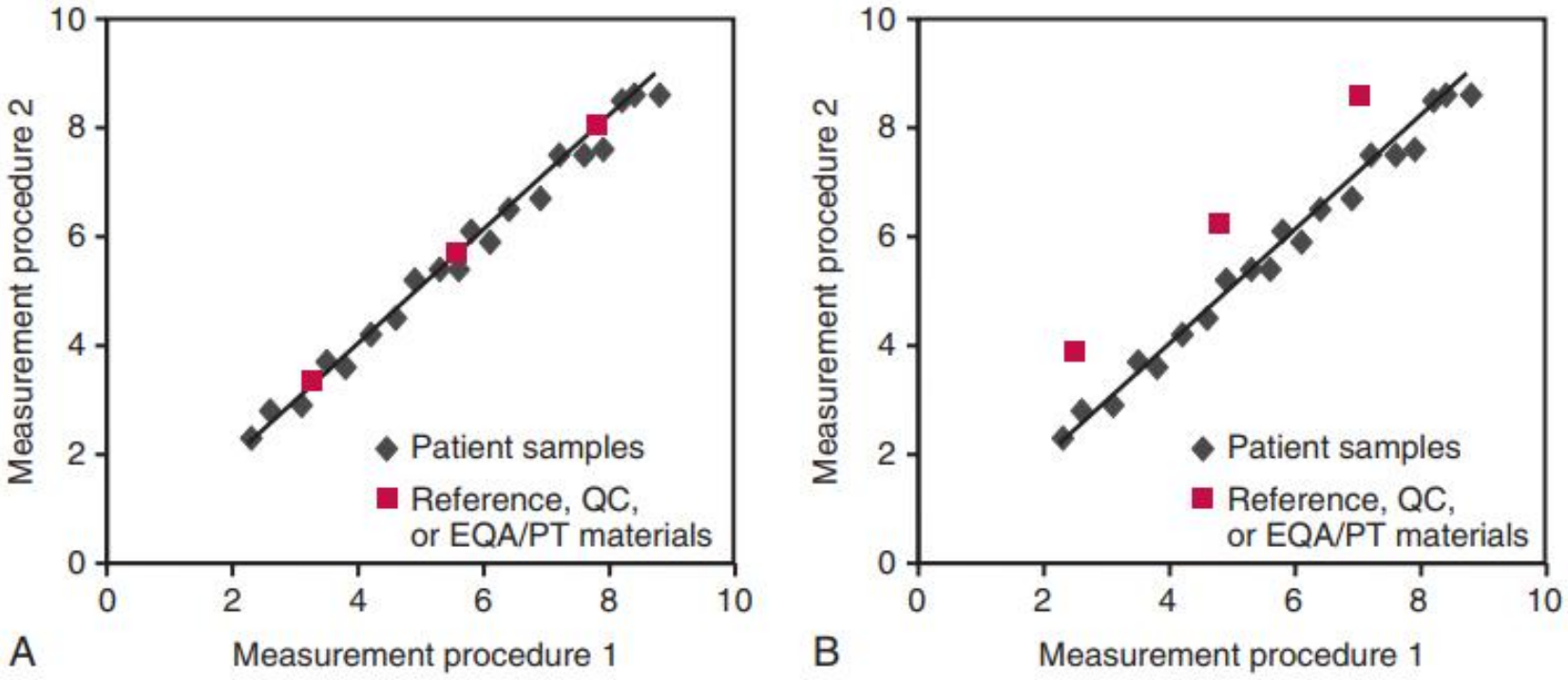
Commutability:

- **A commutable reference material has a numeric relationship between (or among) two (or more) measurement procedures that closely agrees with the relationship observed for a panel of clinical patient samples.**

- **Consequently, a commutable reference material (that may be used as a calibrator) reacts in a measurement procedure to give a numeric result that would be in close agreement to that observed for a patient sample with the same amount of analyte.**

COMMUTABILITY

Commutability:



COMMUTABILITY

Commutability:

- **Commutability is a challenge for secondary reference materials because their matrix may be modified from that of a clinical patient specimen during preparation.**
- **Commutability is also a desirable property of QC materials.**
- **Most QC materials are noncommutable.**
- **If such a measurement procedure–specific calibrator is used with a different measurement procedure, it will cause miscalibration.**
- **As for measurement procedure–specific calibrators, such measurement procedure–specific QC materials typically have matrix characteristics and target values that are intended only for use with the specific measurement procedures AND/OR specific reagent lots.**

CALIBRATION TRACEABILITY AND COMMUTABILITY

Calibration traceability and Commutability:

- **A clinical laboratory has limited resources to verify the calibration traceability of a measurement procedure.**

1. **National and international certified reference materials are available for some measurands.**
2. **Not all reference materials listed by JCTLM have been validated for commutability.**

- **A reference material's certificate of analysis should be reviewed for commutability documentation.**
- **If a reference material is commutable with patient samples for a given measurement procedure, it can be used for calibration or to verify the traceability of calibration to the reference system**

CALIBRATION TRACEABILITY AND COMMUTABILITY

Calibration traceability and Commutability:

- **Using a noncommutable reference material as a calibrator will cause the routine measurement procedure to be miscalibrated and produce erroneous patient results.**
- **Use of a noncommutable reference material to verify calibration traceability will give incorrect information regarding the traceability of a measurement procedure.**
- **If a reference material's commutability status is unknown, it must be assumed not to be commutable with patient samples.**
-

CALIBRATION TRACEABILITY AND COMMUTABILITY

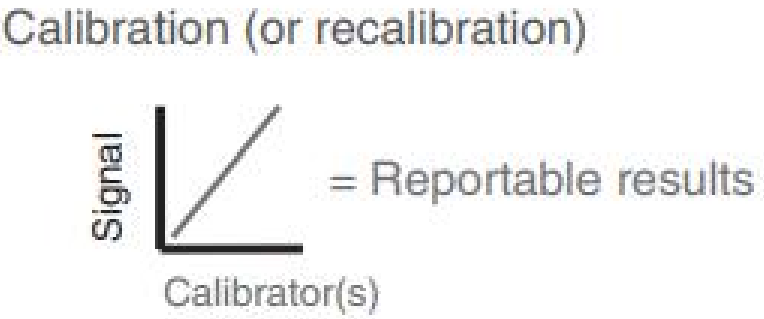
Calibration traceability and Commutability:

- **Not validated for commutability with clinical samples for different routine measurement procedures.**
- **They do not have target values that are traceable to higher-order reference measurement procedures.**
- **When third-party QC materials are used in an interlaboratory comparison program with measurement procedure-specific peer group mean values, these values can be used to confirm that a laboratory is using a specific measurement procedure in conformance with other users of the same measurement procedure.**

CALIBRATION OF A MEASUREMENT PROCEDURE

Calibration of a Measurement Procedure:

- **Calibration of an analytical measurement procedure is an essential step for achieving quality results.**



- **This relationship is used to convert the measurement signal from a patient sample into a reportable concentration for the measurand.**

CALIBRATION OF A MEASUREMENT PROCEDURE

Calibration of a Measurement Procedure:

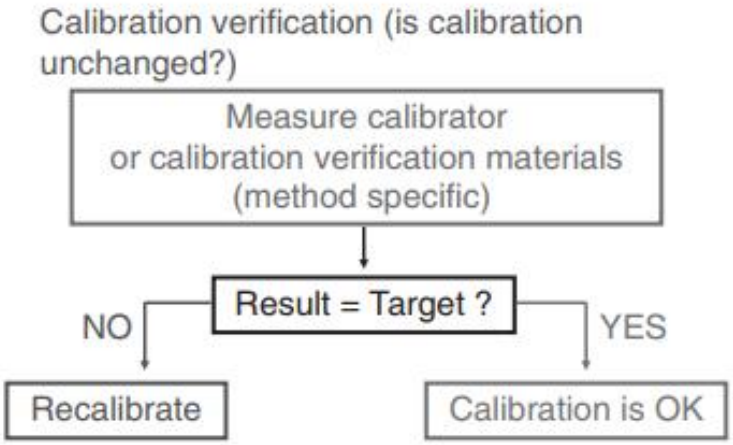
Some general principles for implementing calibration procedures:

1. A measurement procedure should be calibrated only when evidence indicates that the current calibration is no longer valid.
2. Evidence that a recalibration is needed could come from QC sample results that demonstrate a shift or trend in bias over a time period.
3. QC results have random variability that may make it difficult to identify when recalibration is needed.
4. It is common practice to recalibrate measurement procedures on a time schedule that is established based on experience with stable QC results.

VERIFICATION OF CALIBRATION STABILITY

Verification of Calibration Stability:

- **Calibration verification rather than perform a recalibration.**



- **Not performing a recalibration can avoid introducing small changes in the calibration relationship.**

VERIFICATION OF CALIBRATION STABILITY

Verification of Calibration Stability:

- **The laboratory must establish criteria for agreement with the calibrator target value for calibration verification.**
- **Conservative criteria for agreement, such as ±1 SD from the target value, should be considered to avoid misinterpretation of calibration status.**

ANALYTICAL BIAS AND IMPRECISION

Analytical Bias and Imprecision:

Some terms:

- **Trueness**
  - **Bias**
- **Precision**
  - **Imprecision**
- **Accuracy**
  - **Uncertainty**

ANALYTICAL TRUENESS AND BIAS

Analytical Trueness and Bias:

Some terms:

- **Trueness (of measurements): Closeness of agreement between the average value obtained from a large series of results of measurements and the true value [A qualitative term: low, medium, or high].**
  - **Bias: The difference between the average value and the true value.**
  1. **A measure of the systematic error**
  2. **Is expressed numerically [A quantitative term]**
  3. **Is inversely related to the trueness.**

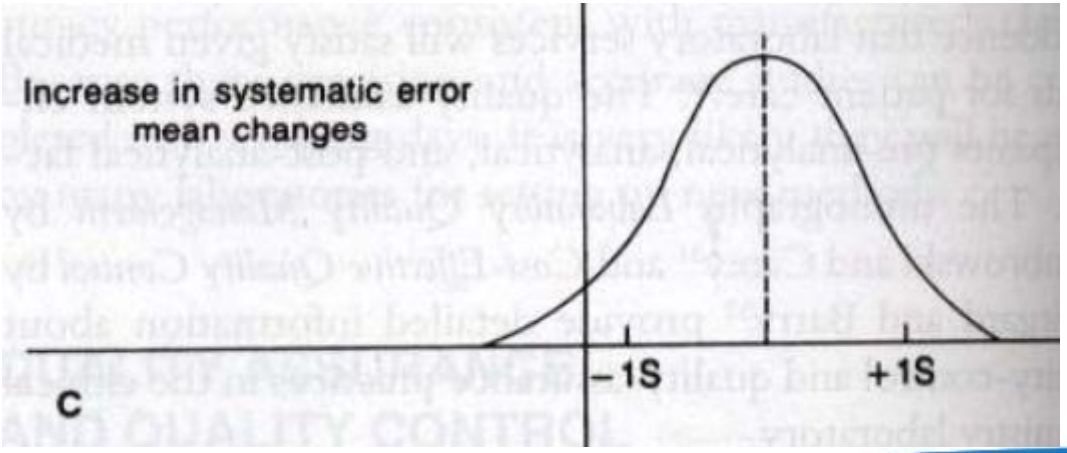
- **Trueness can be evaluated by comparison of measurements by the new test and by some preselected reference measurement procedure.**

ANALYTICAL TRUENESS AND BIAS

Analytical Trueness and Bias:

Some terms:

- **Trueness (of measurements): Closeness of agreement between the average value obtained from a large series of results of measurements and the true value [A qualitative term: low, medium, or high].**



ANALYTICAL PRECISION AND IMPRECISION

Analytical Precision and Imprecision:

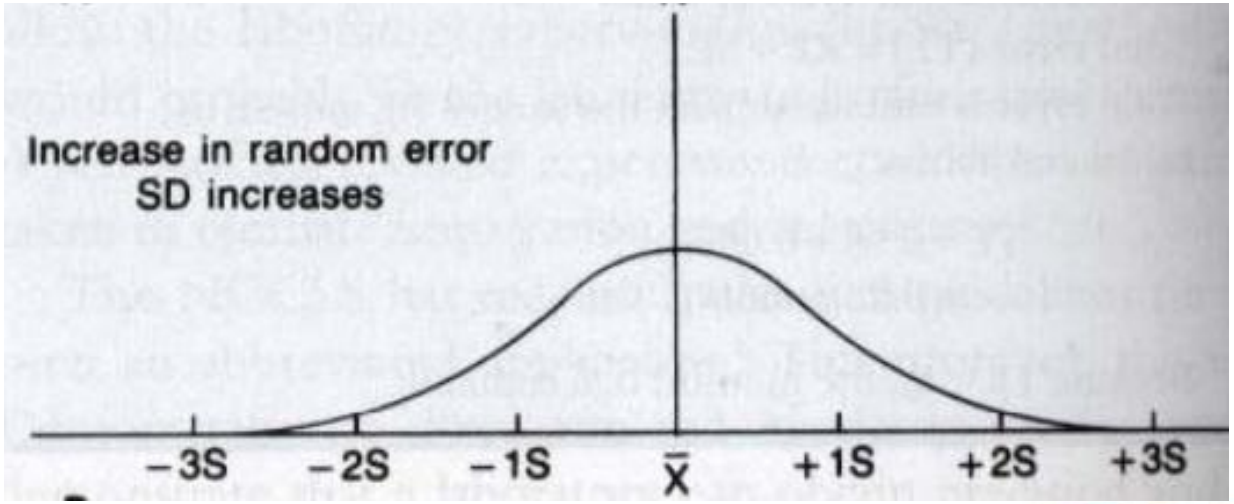
- **Precision: the closeness of agreement between independent results of measurements obtained under stipulated conditions**
  - **Imprecision: the degree of precision is usually expressed on the basis of statistical measures of imprecision, such as SD or CV.**

1. **Is solely related to the random error of measurements**
2. **Has no relation to the trueness of measurements.**

ANALYTICAL PRECISION AND IMPRECISION

Analytical Precision and Imprecision:

- **Precision: the closeness of agreement between independent results of measurements obtained under stipulated conditions**



PRECISION AND IMPRECISION

Precision and Imprecision:

Repeatability vs. Reproducibility

- **Repeatability:** closeness of agreement between results of successive measurements carried out under the same conditions (ie, corresponding to within-run precision).

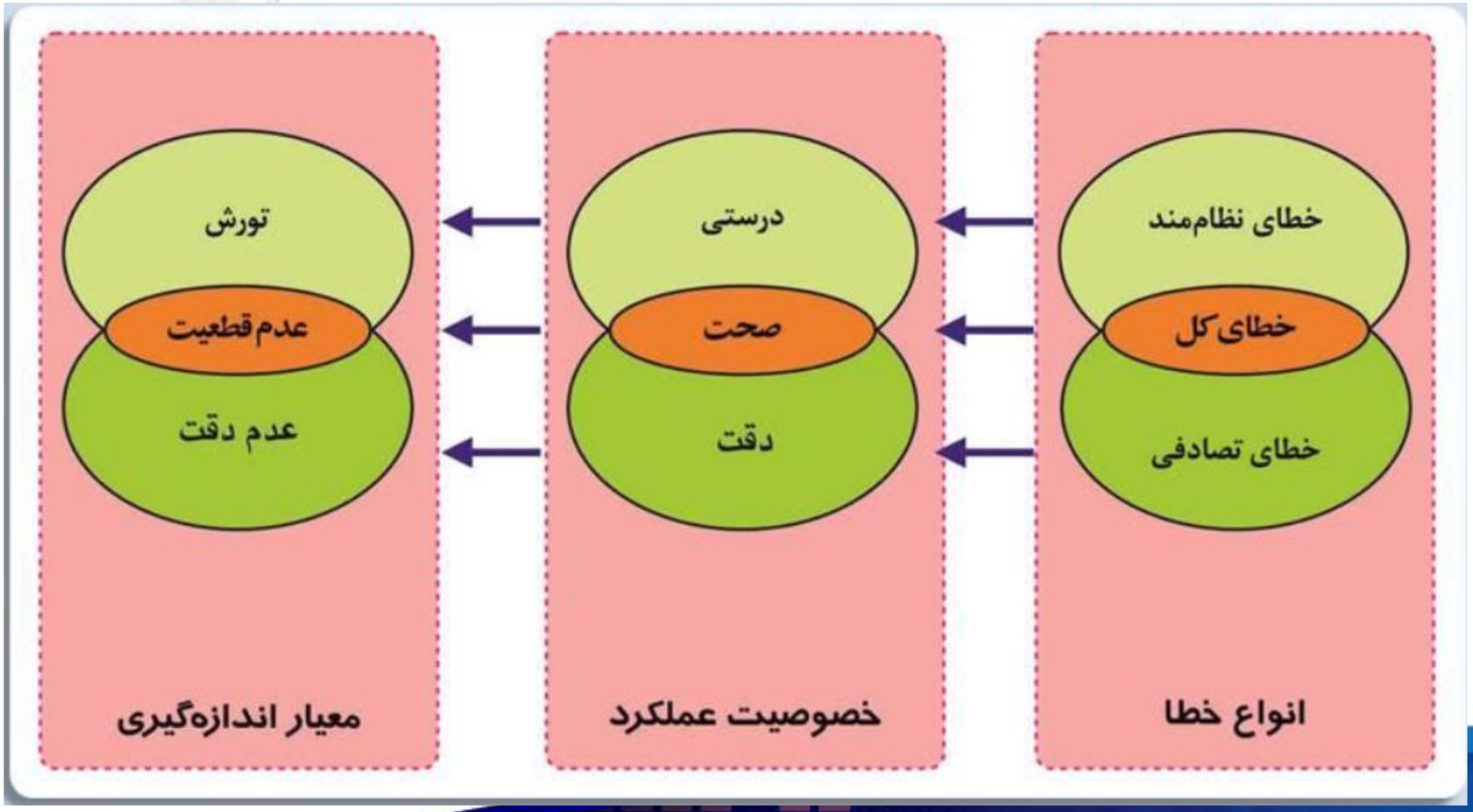
- **Reproducibility:** closeness of agreement between results of measurements performed under changed conditions of measurements (eg, time, operators, calibrators, reagent lots).

ANALYTICAL ACCURACY AND UNCERTAINTY

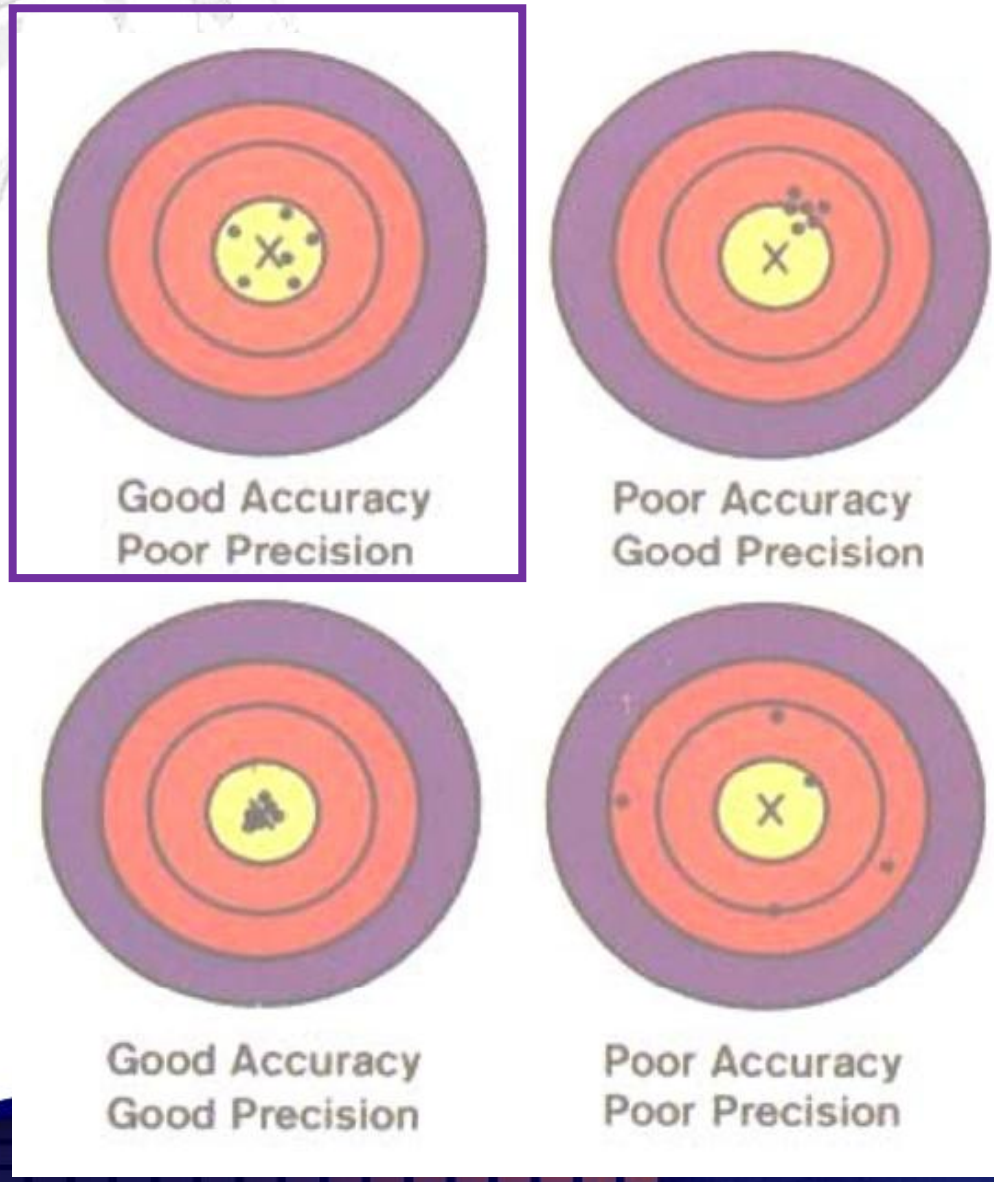
Analytical Accuracy and Uncertainty:

- **Accuracy: closeness of agreement between the result of a measurement and a true concentration of the analyte [a qualitative term].**
  - **Uncertainty: is inversely related to the accuracy.**
  1. **Is influenced by both bias and imprecision**
  2. **Reflects the total error (random and systematic errors).**

MEASUREMENT PROCEDURE PERFORMANCE



MEASUREMENT PROCEDURE PERFORMANCE




Thank You !
LOGO